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Inspection of Medical Devices

For Regulatory Purposes

Second Edition

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Contents

Introduction

Almir Badnjević

Significant progress has been made in healthcare with regards to medical devices, which have a crucial function in the diagnosis, monitoring, and treatment of health conditions. These devices incorporate advanced sensors and measurement technologies, allowing for the assessment of physiological or anatomical parameters, as well as the measurement of energy or volume of substances administered to or extracted from the body. The precise and accurate measurement capabilities of medical devices are vital in ensuring the overall quality and dependability of the healthcare system [1].

To uphold the utmost standards of quality and safety, medical devices undergo comprehensive evaluation and regulatory procedures throughout their lifespan, encompassing both pre-market and post-market phases. Pre-market activities encompass assessing a device's design, performance, and safety prior to its availability to healthcare professionals and patients. This entails obtaining the required approvals and clearances from regulatory entities, conducting clinical trials, and adhering to specific regulatory guidelines. Once a medical device enters the market, post-market surveillance becomes a critical aspect of ensuring ongoing safety and effectiveness [2]. The surveillance activities involve monitoring the device's performance, identifying any adverse events or issues, and taking appropriate actions to mitigate risks. This comprehensive approach to medical device management and maintenance aims to safeguard patient well-being and optimize the overall healthcare system.

Legal metrology, a scientific discipline that focuses on accurate and reliable measurements, plays a crucial role in the field of healthcare. Metrology principles guide the design, production, and maintenance of medical devices, ensuring that they provide accurate, precise, and stable measurements within the limits specified by manufacturers. The understanding and application of metrological concepts are

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essential for interpreting measurement results in healthcare, be it for medical diagnosis, treatment, or the management of medical devices. To enhance traceability, cooperation, and transparency in the medical device domain, various databases have been established to store and manage surveillance data. These databases, such as the Food and Drug Administration (FDA) [3] Manufacturer and User Facility Device Experience and Recall databases (MAUDE), Medical Product Safety Network (MedSun) [5], and the European database on medical devices (EUDAMED) [4], aim to collect information on adverse events, device problems, and recalls. However, the existing databases face limitations in terms of data quality, completeness, and timeliness. The need for standardized methodology and data formats to ensure accurate and comprehensive surveillance data becomes evident. ***The ongoing digital transformation presents a significant opportunity to harness standardized conformity assessment approaches for testing the safety and performance of medical devices.*** These methods produce reliable, accurate, comprehensive, verified, impartial, and standardized data, thereby addressing the limitations of current surveillance databases. Embracing standardized conformity assessment practices, conducted by independent third-party organizations or manufacturers and distributors, would promote transparency, bolster safety, and enhance quality within the medical device industry [6]. The integration of standardized data into existing databases would enable advanced analysis techniques and facilitate more efficient data mining, leading to enhanced decision-making and proactive maintenance strategies [7–9]. In line with the United Nations Sustainable Development Goal 3, it is imperative to ensure access to safe, effective, quality, and affordable medical devices. The integration of digital technologies, adherence to standardized methodologies, and the application of artificial intelligence hold tremendous potential in transforming the medical device landscape. Predictive management of maintenance, driven by data analysis and artificial intelligence algorithms, can revolutionize clinical engineering practices, optimize device performance, and enhance personalized healthcare.

This new edition of the book delves into the intricacies of the medical device lifecycle, the importance of legal metrology in healthcare, and the significance of standardized conformity assessment methodologies. It explores the challenges and opportunities associated with medical device surveillance databases, while highlighting the potential for digitalization, data standardization, and predictive maintenance strategies. By combining the expertise of various stakeholders and embracing technological advancements, we can strive towards ensuring access to safe, effective, quality, and affordable medical devices, ultimately contributing to the well-being of individuals and the advancement of healthcare as a whole.

Chapter 2: Regulations and Directives—Past, Present, Future This chapter examines the historical evolution of regulations and directives governing medical devices. We explore the significant milestones and changes in regulatory frameworks, from past to present, and discuss the anticipated future developments in this dynamic field. Understanding the regulatory landscape is essential for ensuring compliance and enhancing patient safety.

Chapter 3: Legal Metrology System—Past, Present, Future Here, we dive into the world of legal metrology and its relevance in healthcare. We explore the historical

developments and current practices in legal metrology, emphasizing its vital role in ensuring accurate and reliable measurements in medical devices. Furthermore, we discuss the future trends and potential advancements that may shape the legal metrology system in the coming years.

Chapter 4: Medical Device Maintenance Regimes in Healthcare Institutions This chapter focuses on the management and maintenance of medical devices within healthcare institutions. We explore the various maintenance regimes employed to ensure the optimal performance and longevity of these devices. Topics such as preventive maintenance, calibration, and adherence to manufacturer's guidelines will be covered, highlighting the importance of robust maintenance practices.

Chapter 5: Post-market Surveillance of Medical Devices Post-market surveillance is a critical aspect of monitoring the safety and performance of medical devices after they have been introduced to the market. In this chapter, we delve into the existing databases and systems for post-market surveillance, such as the FDA MAUDE, MedSun, and EUDAMED. We discuss the challenges and limitations of current databases and propose solutions to enhance traceability, cooperation, and transparency in medical device surveillance.

Chapter 6: Application of AI for Management Maintenance and Prediction of Performances Artificial intelligence (AI) has the potential to revolutionize medical device management and maintenance. In this chapter, we explore the applications of AI in predicting device performance, optimizing maintenance schedules, and identifying potential issues before they occur. We examine the integration of AI algorithms and data analytics to improve the efficiency and effectiveness of device management [10–12].

Chapters 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16: Inspection and Testing of Specific Diagnostic and Therapeutic Devices These chapters provide comprehensive insights into the inspection and testing of specific medical devices used for diagnostic and therapeutic purposes. We cover a range of devices, including ECG devices, noninvasive blood pressure measuring devices, diagnostic ultrasound devices, EEG, EMG, and ER equipment, defibrillators, mechanical ventilators, anesthesia machines, dialysis machines, pediatric and neonate incubators, and infusion pumps. Each chapter focuses on the inspection and testing protocols, standards, and best practices for ensuring the accuracy, reliability, and safety of these devices.

Chapter 17: Cost Effectiveness Analysis of Medical Devices in Legal Metrology System In this final chapter, we explore the cost-effectiveness analysis of medical devices within the legal metrology system. We discuss the methodologies for evaluating the economic impact of device management and maintenance practices, considering factors such as device lifespan, maintenance costs, and patient outcomes. Understanding the cost-effectiveness of medical devices can guide decision-making and resource allocation in healthcare institutions.

With this comprehensive exploration of medical device management, maintenance, and related topics, our book aims to provide a valuable resource for healthcare professionals, clinical engineers, regulators, and researchers. By staying up-to-date with the latest advancements and best practices, we can ensure the safe and effective use of medical devices, ultimately improving patient care and outcomes. **Finally,**

the book highlights the importance of data in our lives and emphasizes the role it plays in shaping our future. By relying on trustworthy and accurate data, we can make informed decisions and pave the way for a better tomorrow. It underscores the value of data-driven insights, innovation, and responsible use of information as we navigate towards a brighter future.

In data, we trust, for the future we shape!

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Regulations and Directives—Past, Present, Future

Haris Memić, Alen Bošnjaković, Zijad Džemić, and Almir Badnjević

Abstract Throughout the past few decades, there has been a considerable evolution in the regulation of medical devices, with modifications made to maintain patient safety and enhance device functionality. Medical device regulation used to be less strict, and many devices were certified without going through rigorous testing. This raised various safety issues, and a series of high-profile incidents demonstrated the necessity for more stringent regulation. In order to address this problem, regulators from all over the world established guidelines and laws requiring manufacturers to give proof of the safety and effectiveness of their devices. The Medical Devices Directive (MDD), enacted in Europe in 1993, established the legal foundation for medical device regulation within the European Union. The Medical Device Amendments of 1976 were introduced in the United States of America. Currently, medical device regulation is more comprehensive, with more rigorous testing and evaluation procedures in place. In the US, the Food and Drug Administration (FDA) oversees the regulation of medical devices, and requires manufacturers to provide evidence of safety and efficacy before a device can be approved for use. In Europe, the MDD has been replaced by the Medical Device Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR), which impose stricter requirements on medical device manufacturers, distributors, and importers. In other parts of the world, medical device regulation is also becoming more stringent. Medical device legislation is probably going to keep changing in the future. The use of real-world evidence (RWE) to guide regulatory choices is receiving more attention, and this trend is likely to continue. With the provision of a more thorough understanding of how devices function in the actual world, the usage of RWE can aid in enhancing the accuracy of regulatory decisions. The usage of digital health technology, such as wearables and smartphone apps, is also gaining popularity. Healthcare could be transformed by these technologies, but they also present new regulatory difficulties. As a result, regulatory organisations all

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around the world are investigating fresh ideas for regulating digital health technologies. Globally, the past, present and future of medical device regulation show how critical it is to protect patient safety and improve device functionality. Although the regulations have tightened over time, they still need to adapt and change to meet the demands of the ever-changing healthcare environment, which presents challenges not only for the manufacturers themselves but also for the competent bodies that carry out the conformity assessment of the products in question.

1 Introduction

Health has always been, is and will always be the most important thing that for sure should be taken care of. Even with all technological development of modern society, there are still a lot of challenges in maintaining the health of the population worldwide. Development of medical devices have dramatically changed the way medical care is provided to patients.

The previous edition of the book Inspection of Medical Devices provided valuable insights into how the development of medical devices has revolutionised healthcare delivery, highlighting the importance of maintaining health and addressing the challenges that come with it [1]. Various regulatory bodies provide definitions of the term medical device, such as US Food and Drug Administration (FDA), World Health Organisation (WHO), and European Commission, which gives the most comprehensive one. According to the European Commission, a medical device is defined as "*any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes*". Since medical devices include a variety of types and models and given the fact that they have direct impact on health, these devices are under strict control worldwide. Their safety and performance characteristics are subject to strict conformity assessments also to ensure the quality and reliability of diagnosis and treatment.

To define appropriate regulations and quality assessment for medical devices, firstly the classification system needs to be defined. Medical devices are usually divided into different groups or classes. The differentiation into classes can vary from country to country. Some countries have a medical device classification system consisting of the following categories: general medical devices, active implantable medical devices (AIMD) and in vitro diagnostic devices (IVD). This system is adopted in Europe and many other countries in the world, while in very few countries these products are categorised into the same group. More specifically, all medical devices are classified based on the risk. In the European Union (EU) general medical devices are classified as class I, class I sterile, class I measuring, class IIa, class IIb or class III where class III devices represent the highest risk. Active implantable medical devices are not classified and in vitro diagnostic devices have their own classification system. The previous edition also provided information on the classification of medical devices in the United States as Class I (general controls), II (special

controls), or III (premarket approval), where Class III devices pose the greatest risk and require greater control. In Europe medical devices are divided into three different groups; active implantable medical devices (AIMD), general medical devices and in vitro diagnostic devices (IVD).

Observed worldwide, the classification doesn't differ very much between countries. The main difference is the way medical devices are regulated. Some countries issue regulations covering all groups of medical devices, and others define regulations for each class separately. Also, in some countries they are regulated as drugs, while in other countries they are regulated by special regulations. The variety and differences in medical device regulations present in countries are creating obstacles for the medical device market. In order for a manufacturer to introduce a new medical device to the market it must comply with a variety of regulations depending on the country in which this device will be sold. In the end, this affects the quality of care provided to patients because in this way some new medical devices become unavailable in certain countries due to specific regulations.

The directives and regulations outline every step of medical device development, including ideation, design, and development phases, as well as testing, approval, and certification prior to manufacturing, the actual production process, and post-market surveillance. In the European Union, Medical Device Directives were replaced by Medical Device Regulation in 2020. In the United States of America, the FDA is regulating all aspects of medical device regulation. In other regions and countries of the world, the area of medical devices is under strict control and supervision. A large number of countries outside the Europe base their legislation in the area of medical devices on EU legislation. Other countries in the world have adopted a similar regulatory framework for medical devices, as it has been mentioned above for the EU and USA. In all regions, the manufacturer governs the overall process from ideation to market, whereas independent third parties give approval and certification before placing the device on the market.

2 EU Legislation

EU legislation is divided into two levels with primary legislation embodied by the treaties, and secondary legislation given in the form of regulations, directives and decisions which are used to implement the policies set out within the treaties [2]. Secondary legislation is made by the EU institutions. It is the third major source of Community law after the treaties (primary legislation) and international agreements. It comprises:

- binding legal instruments (regulations, directives and decisions)
- non-binding instruments (resolutions, opinions).

In order to increase safety in the production of industrial products, manufacturers have to follow the relevant legislation. This legislation in the EU is given through the directives and regulations followed by appropriate harmonised standards set out in

the directives and regulation. In addition to the stated documentation, there are also other acts of European Union Law. Legislation serves us primarily to protect citizens. It means the end consumers from low-quality products that do not comply with the minimum requirements related to the safety of products intended to be released on the market of a country. These requirements are precisely stated through directives and regulations if it is EU regulations or some other type of regulations in other countries of the world with regulated markets.

The description and meaning of legal acts in accordance with EU law is given bellow [3, 4]:

- A "**regulation**" is a binding legislative act. It must be applied in its entirety across the EU.
- A "**directive**" is a legislative act that sets out a goal that all EU countries must achieve. However, it is up to the individual countries to devise their own laws on how to reach these goals.
- A "**decision**" is binding on those to whom it is addressed (e.g. an EU country or an individual company) and is directly applicable.
- A "**recommendation**" is not binding. When the Commission issued a recommendation that EU countries' law authorities improve their use of videoconferencing to help judicial services work better across borders, this did not have any legal consequences. A recommendation allows the institutions to make their views known and to suggest a line of action without imposing any legal obligation on those to whom it is addressed.
- An "**opinion**" is an instrument that allows the institutions to make a statement in a non-binding fashion, in other words without imposing any legal obligation on those to whom it is addressed. An opinion is not binding. It can be issued by the main EU institutions (Commission, Council, Parliament), the Committee of the Regions and the European Economic and Social Committee. While laws are being made, the committees give opinions from their specific regional or economic and social viewpoint.

Review of EU legislation can be made via the official website of the EU which is especially dedicated to this issue. An integral part of the directives are harmonised standards. A **harmonised standard** [5] is a European standard developed by one of the recognised European Standards Organisation: CEN [6], CENELEC [7], or ETSI [8]. It was created following a request from the European Commission to one of these organisations. Manufacturers, other economic operators, or conformity assessment bodies can use harmonised standards to demonstrate that products, services, or processes comply with relevant EU legislation. The references of harmonised standards must be published in the Official Journal of the European Union. The purpose of this website is to provide access to the latest lists of references of harmonised standards and other European standards published in the Official Journal of the European Union (OJEU).

EUR-Lex provides free access to EU law and other documents considered to be public. The content on the official website is available in 24 official languages of the European Union. This chapter has the purpose to describe the legislation used

in the EU in the field of industrial products, and the approaches to be followed by producers (manufacturer) of those products in order to be approved and placed in the EU market.

3 Placing of Products in the Market of EU in Accordance with EU Legislation

Only products that meet all applicable requirements can be released on the EU market. The conformity assessment procedure is carried out before the actual release of the product on the market, i.e. before the product in question can be put on sale. Before placing a product in the market, implying that it is ready for use, the product has to be approved by a competing body providing conformity assessment of a tested subject with appropriate reference. There are different recognized approaches in the process of approval.

Industrial products must comply with the rules established by EU legislation, either by Directive or Regulation related to specific products prior to being put in the market and/or put into service in the EU, the European Economic Area, or Switzerland. All industrial products intended for the EU market must bear CE mark, which represents the conformity assessment with relevant legislation. In addition to this mark, certain industrial products must be marked with some other marks, such as the requirement in the field of measuring instruments and non-automatic weighing instruments, which refers to a supplementary metrology marking. The CE marking and the supplementary metrology marking shall be affixed before the measuring instrument is placed on the market. The supplementary metrology marking shall consist of the capital letter 'M' and the last two digits of the year of its affixing, surrounded by a rectangle. CE marking and the supplementary metrology marking are accompanied by the EU declaration of conformity which gives us brief insight in legislation and harmonised standards used in production of the subject product and its conformity with these documents [9]. Since the United Kingdom left the European Union, they have also introduced a new conformity mark. The UKCA (UK Conformity Assessment) mark is the new UK product marking that will be required for certain products being placed on the market in Great Britain (England, Wales and Scotland). It covers most products that previously required the CE mark (measuring instruments, medical devices, etc.).

It will not be recognized in the EU market. Products that require CE marking will still need a CE marking to be sold in the EU [10]. In the field of medical devices, whether they are produced for the EU or American market, the manufacturer is obliged to place a Unique Device Identification (UDI) on the product itself or the packaging. The unique device identification is a unique numeric or alphanumeric code related to a medical device. It allows for a clear and unambiguous identification of specific devices on the market and facilitates their traceability [11].

4 EU Legislation in the Field of Medical Devices

One of the legislation aligned with the New Legislative framework is Regulation 2017/745/EU on medical devices. Medical devices require special attention because they are directly related to health, which represents one of the categories of legal metrology, as described in paragraph 7. (Medicine in the field of Legal Metrology). First of all, it is necessary to clarify what a medical device represents. In accordance with regulation 2017/745/EU, medical device has the following meaning: *Medical device means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:*

- *diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- *investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- *providing information by means of* in vitro *examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.*

Legislation in the field of medicine in the European Union, i.e. legislation relating to medical devices, is based on Regulation (EU) 2017/745 of 5 April 2017 [12]. This regulation further relies on the following directives:

- Directive **93/68/EEC** (CE Marking);
- Directive Regulation (EU) 2017/746 on in vitro diagnostic medical devices.;
- Regulation (EU) 2020/561 of the European Parliament and of the Council of 23 April 2020 amending Regulation (EU) 2017/745 on medical devices

In the past, one more directives were in force, but they have been repealed with legal acts mentioned above. As mentioned in the introduction, beside legislation on medical devices, there are a great number of written standards used in manufacturing of medical devices. Changes in legislation are not very frequent and if, they are mostly related to technological changes in the specific products which they apply to. Directives are replaced by amending or adding new requirements and are assigned with a new codification. For example, in the field of measuring instruments, the currently valid directive from 2014 bears the codification 2014/32/EU, and the earlier directive on measuring instruments from 2009 bore the designation 2009/34/EC. From the codification itself, it is possible to state that the period that passed between the last two editions of the directive on measuring instruments was 5 years.

This is not the same in a case of medical devices. This is a very important area from the point of view of risk for user and treatment of patients, and currently in this

area in force is regulation (EU) 2017/745 (from 2017), which replaced directive 93/442/EEC from 1992. When it comes to medical devices it is possible to conclude, the earlier act, which was a directive, was replaced by a regulation in 2017, which rarely happens, and this further indicates how important this area is and how this harmonised act has become a binding legislative act in all EU countries. Although a long period has passed since the publication of the directive from 1993 until its replacement by the regulation in 2017, this does not mean that there have been no changes since 1993. The directive from 1993 was revised several times, but it contained the same codification during the 29 years it was in force (it ceased to be valid on 05/25/2021 due to the transition period to (EU) 2017/745). In order to improve the internal market for goods and strengthen the conditions for placing a wide range of products on the EU market, in 2008 the New Legislative Framework (NLF) was adopted. The NLF represents the set of measures that aim to improve market surveillance and boost the quality of conformity assessments. In the past it was recognised by New Approach, which was a regulatory technique used for removing technical barriers to trade in Europe. The NLF which is closely related to New Approach, consist of following legislation:

- Regulation (EC) 765/2008 Search for available translations of the preceding setting out the requirements for accreditation and the market surveillance of products
- Decision 768/2008 Search for available translations of the preceding on a common framework for the marketing of products, which includes reference provisions to incorporate in product legislation revisions. In effect, it is a template for future product harmonisation legislation
- Regulation (EU) 2019/1020 Search for available translations of the preceding on market surveillance and compliance of products.

The NLF improves market surveillance, sets clear and transparent rules for accreditation of conformity assessment bodies, boosts the quality of and confidence in the conformity assessment of products clarifies the meaning of CE marking and establishes a common legal framework for industrial products in the form of a toolbox of measures for use in future legislation. Number of legislation which is currently covered by NLF is 24 different directives, regulations and delegated acts, covering the fields like measuring instruments, electromagnetic compatibility, medical devices, Radio equipment and industry fields where product safety is very important, etc. In relation to the conformity assessment the manufacturer has certain responsibilities, reflected depending on the applied procedures. The manufacturer must take all necessary measures to ensure that the production process satisfy conformity of the product in order to set the CE mark on the product, which includes drawing technical documentation and creating EC[1] declaration of conformity. It is very important that the

[1] As part of conformity assessment, the manufacturer or the authorised representative must draw up a Declaration of conformity (DoC). The declaration should contain all information to identify:
- the product.
- the legislation according to which it is issued.

product is accompanied by a product declaration of conformity that provides information about the product in question, which is the obligation of the manufacturer or his authorised representative if the manufacturer is not from the EU. The declaration itself must contain information indicating the essential elements of the product in question and compliance with the relevant regulations, directives and harmonised standards.

Depending on the legislation, it is possible to claim from the manufacturer to submit products for testing and certification by a third party (usually a notified body) or to certify quality systems by a notified body.

5 Notified Bodies for Conformity Assessment

A notified body is an organisation designated by an EU country to assess the conformity of certain products before being placed on the market. These bodies carry out tasks related to conformity assessment procedures set out in the applicable legislation, when a third party is required. The European Commission publishes a list of such notified bodies [13].

Notified bodies must fulfil requirements prescribed by certain legislation. This mainly refers to the confirmation of the competences by a third party, an accredited body in accordance with some of the required standards for conformity assessment or through peer review by peers (e.g. the area of measuring instruments). Bodies performing conformity assessment shall be accredited by the national accreditation body for specified standards. Accreditation implies confirmation of competences of the third party to an authority that may perform conformity assessment, respectively conformity with the requirements of applicable standards and additional requirements for the subject matter. For example, for the area of measuring instruments, notified bodies must be accredited or peer reviewed in accordance with the standards of the ISO 17000 family, depending on the module of conformity assessment (described in paragraph 5. Conformity assessment of industrial products), such as, for example:

- EN ISO/IEC 17020- Conformity assessment — Requirements for the operation of various types of bodies performing inspection
- EN ISO/IEC 17021- Conformity assessment — Requirements for bodies providing audit and certification of management systems
- EN ISO/IEC 17025—General requirements for the competence of testing and calibration laboratories
- EN ISO/IEC 17065- Conformity assessment — Requirements for bodies certifying products, processes and services.

• the manufacturer or the authorised representative.
• the notified body if applicable.
• a reference to harmonised standards or other normative documents, where appropriate.

Setting out the requirements for accreditation and market surveillance relating to the marketing of products is done by Regulation 765/2008/EC [14], which should be seen as a complementary to Decision 768/2008/EC (on a common framework for the marketing of products). Accreditation provides authoritative statements about technical competence of bodies whose task is to ensure conformity with the applicable requirements.

The situation is different in the field of medical devices, where notified bodies do not have to be accredited, but are subject to even stricter requirements as prescribed by Regulation 2017/745(EU) also known by its abbreviation MDR. The MDR expands the powers of notified bodies with regard to post-market clinical surveillance (e.g. unannounced audits, spot checks and product reviews). In accordance with the MDR any EU Member State that intends to designate a conformity assessment body as a notified body, or has designated a notified body, to carry out conformity assessment activities under the MDR shall appoint an authority for notified bodies, which may consist of separate constituent entities under national law and shall be responsible for setting up and carrying out the necessary procedures for the assessment, designation and notification of conformity assessment bodies and for the monitoring of notified bodies, including subcontractors and subsidiaries of those bodies. Where the authority responsible for notified bodies is a different authority from the national competent authority for medical devices, it shall ensure that the national authority responsible for medical devices is consulted on relevant matters.

In the phase of the production, Medical devices are subject to compliance with certain legislation and harmonised standards. Currently, in Europe, the applied EU Legislation for the production of measuring devices are Directive 93/42/EEC (notified bodies designated under Directive 93/42/EEC as listed here are no longer able to issue new certificates under that Directive, but only allowed to carry out surveillance activities for certificates validly issued under that Directive in the transitional period) and Regulation 2017/745/EU. The greatest responsibility in the production of medical devices holds the manufacturer himself, who has to ensure that the product meets the applicable legal requirements and, on the other hand, there is a notified body for conducting conformity assessment appointed by EU governments and with the obligation to validate and ensure that the product fulfil all the relevant requirements prescribed by the relevant directives.

At the moment, NANDO [15] database comprises 36 registered bodies competent to perform conformity assessment of medical devices in accordance with Regulation 2017/745/EU which indicates a significantly lower number in relation to the number of notified bodies in accordance with the Directive 93/42/EEC when there were 58 registered bodies. This significantly lower number of notified bodies in accordance with the Regulation 2017/745/EU compared to the number of notified bodies which have been nominated in accordance with the Directive 93/42/EU is related to the stricter requirements specified in the regulation. Experts assume that the number of notified bodies under the MDR does not cover the needs of manufacturers, especially in relation to the existence of clinical competence. In addition, not all notified bodies cover the entire technical spectrum. As the requirements for notified bodies through

the MDR became stricter, it is logical that they also became stricter for the manufacturer themselves. Smaller companies in particular will find it difficult to practically implement the documentation effort and to refinance it on the market. As a result, there is a risk that a number of medical products and medical technology companies will have to leave the market [16].

Notified bodies perform tasks related to conformity assessment procedures, according to the applicable harmonised technical legislation when it requires the participation of a third party. Notified bodies may offer their services in the EU, but also to third countries.

6 Conformity Assessment of Industrial Products

Conformity assessment is a process that is performed by the manufacturer in order to demonstrate if all specific requirements related to the product have been met. The product itself is subject to conformity assessment in the stages of design and production. EU legislation requires the conduction of the process composed of one or two modules of conformity assessment.

The modules for the conformity assessment procedures to be used in the EU harmonised legislation were initially set out in Council Decision 93/465/EEC of 22 July 1993 concerning the modules for the various phases of the conformity assessment procedures and the rules for the affixing and use of the CE conformity marking, which are intended to be used in the technical harmonisation directives. Decision 768/2008/EC, one of three acts of New Legislative Framework, replaced earlier Decision 93/465/EEC. This Decision provides for a menu of modules, enabling the legislator to choose a procedure from the least to the most stringent, in proportion to the level of risk involved and the level of safety required.

In order to ensure equal treatment of economic operators, consistency in the technical application of the modules must be ensured. That can best be achieved through appropriate coordination and cooperation between notified bodies. Manufacturers should be able to choose the procedure of conformity assessment/module in accordance with applicable harmonised EU legislation, in respect of a particular product. The following criteria should give the manufacturer an insight into selection of the appropriate conformity procedure/module:

(a) whether the module concerned is appropriate to the type of product;
(b) the nature of the risks entailed by the product and the extent to which conformity assessment corresponds to the type and degree of risk;
(c) where third party involvement is mandatory, the need for the manufacturer to have a choice between quality assurance and product certification modules;
(d) the need to avoid imposing modules which would be too burdensome in relation to the risks covered by the legislation concerned.

Conformity assessment and conformity assessment modules, although already present in EU countries for a long time, still not have a satisfactory application in

countries that are on the path of integration into the EU. In order to adequately implement the requirements of the corresponding directives/regulations/harmonised standards or other recognized normative documents, there are numerous requirements to be fulfilled, but mainly very competent-trained staff and adequate testing laboratory infrastructure and of course manufacturers who want to place their products on the market.

Despite the presence of government institutions in developed countries whose responsibility is to monitor the market, it is essential that every user or citizen is aware when purchasing a medical product with a measuring function to compare and ensure compliance with the regulations presented in this chapter [17]. Conformity assessment procedures that are applied, for example, to non-automatic weighing instruments in accordance with Directive 2014/31/EU, perhaps the most common used measuring instruments around the world, refer to different accuracy classes, but according to the information in the NANDO database, conformity assessment (different modules) are applied (beside accuracy classes) to the following categories of non-automatic weighing instruments:

- determination of mass for commercial transactions
- determination of mass for the application of laws or regulations or for an expert opinion given in court proceedings
- determination of mass for the calculation of a toll, tariff, tax, bonus, penalty, remuneration, indemnity or similar type of payment
- determination of mass in the practice of medicine for weighing patients for the purposes of monitoring, diagnosis and medical treatment
- determination of mass for making up medicines on prescription in a pharmacy and determination of mass in analyzes carried out in medical and pharmaceutical laboratories
- determination of price on the basis of mass for the purposes of direct sales to the public and the making-up of pre packages

Comparing this scope of non-automatic weighing instruments, the scope of medical devices is much more extensive and demanding, in addition to being divided by risk class levels (with 22 classification rules) they are also divided by its type. Medicinal products for the purpose of conformity assessment procedures, and for the given level of risk for the user, are divided into:

- Class I—medical devices with a low level of risk for the user,
- Class IIa—medical devices with a higher degree of risk for the user,
- Class IIb—medical devices with a high degree of risk for the user,
- Class III—medical devices with the highest degree of risk for the user [18].

As found in NANDO database, under MDR conformity assessment can be performed on the following products:

Active implantable devices:

- stimulation/inhibition/monitoring,
- delivering drugs or other substances

- supporting or replacing organ functions
- utilising radiation and other active implantable devices.

Active non-implantable devices for imaging, monitoring and/or diagnosis:

- imaging devices utilising ionizing radiation
- imaging devices utilising non-ionizing radiation
- devices for monitoring of vital physiological parameters.

Active non-implantable therapeutic devices and general active non-implantable devices:

- utilising ionising radiation
- utilising non-ionizing radiation
- utilising hyperthermia/hypothermia
- shock-wave therapy (lithotripsy)
- stimulation or inhibition
- extracorporeal circulation, administration or removal of substances and hemapheresis
- respiratory devices
- wound and skin care
- ophthalmologic device
- ear, nose and throat
- surgical devices
- prostheses, devices for rehabilitation and devices for patient positioning and transport
- processing and preservation of human cells, tissues or organs including in vitro fertilisation (IVF) and assisted reproductive technologies (ART)
- Software
- Medical gas supply systems and parts thereof cleaning, disinfection and sterilisation
- Other active non-implantable devices (not listed above).

Non-active implants and long term surgically invasive devices:

- cardiovascular, vascular and neurovascular implants
- osteo- and orthopaedic implants
- dental implants and dental materials
- soft tissue and other implants.

Non-active non-implantable devices:

- anaesthesia, emergency and intensive care
- administration, channelling and removal of substances, including devices for dialysis
- guide catheters, balloon catheters, guidewires, introducers, filters, and related tools
- wound and skin care
- orthopaedic and rehabilitation devices

- ophthalmologic devices
- diagnostic devices
- instruments
- dental materials
- used for contraception or prevention of the transmission of sexually transmitted diseases
- for disinfecting, cleaning and rinsing
- for processing and preservation of human cells, tissue or organs including in vitro fertilisation (IVF) and assisted reproductive technologies (ART)
- composed of substances to be introduced into the human body via a body orifice or the dermal route
- used in healthcare and other non-active non-implantable devices.

A very important role in the preparation of guidelines related to the work of notified bodies has Medical Device Coordination Group (MDCG). MDCG deals with key issues from the medical devices sector, from Notified Body oversight or standardisation to market surveillance, passing by international matters, new technologies and clinical investigation [19].

Its expertise originates from its division in 13 subgroups, which respectively provide advice and draft guidance on their expertise field. One of those 13 subgroups is Notified bodies oversight (NBO). This subgroup shares experiences and exchanges views on issues relating to notified bodies and the application of conformity assessment procedures with the aim of a consistent application of requirements and procedures. It drafts technical recommendations on matters relating to notified bodies and conformity assessment [20]. In the "Blue Guide" [21] on the implementation of EU rules on the products, the modules that are used to carry out conformity assessment are listed. In total, there are eight modules labelled with letters A through H, while some of them have variants. Modules specify responsibilities of the manufacturer and level of participation of in-house accredited bodies or notified bodies for conformity assessment (Table 1.). It is important to notice that an in-house body cannot act as a notified body, but they must demonstrate the same technical competence and impartiality to external bodies through accreditation as notify bodies. The following tables show modules in accordance with the "Blue guide", their description and related standards which have to be applied (or combination) in order to fulfil requirements of conformity assessment.

For the field of medical devices, conformity assessment modules are not labelled by letters, but compared to the modules in table above they can be recognised as modules D, B and F.

The modules of conformity assessment in accordance with MDR [22] are recognised as:

Annex IX: conformity assessment based on a quality management system and on an assessment of technical documentation.

Annex X: conformity assessment based on type-examination.

Annex XIA: conformity assessment based on production quality assurance.

Annex XIB: conformity assessment based on product verification.

Table 1 Overview of modules

Module	Description of the module
A Internal production control	Covers both design and production The manufacturer himself ensures the conformity of the products to the legislative requirements (no EU-type examination)
A1 Internal production control plus supervised product testing	Covers both design and production. A + tests on specific aspects of the product carried out by an in-house accredited body or under the responsibility of a notified body chosen by the manufacturer
A2 Internal production control plus supervised product checks at random intervals	Covers both design and production. A + product checks at random intervals carried out by a notified body or an in-house accredited body
B EU-type examination	Covers design. It is always followed by other modules by which the conformity of the products to the approved EU-type is demonstrated. A notified body examines the technical design and/or the specimen of a type and verifies and attests that it meets the requirements of the legislative instrument that apply to it by issuing an EU-type examination certificate. There are 3 ways to carry out an EU-type examination: (1) production type, (2) combination of production type and design type and (3) design type
C Conformity to EU-type based on internal production control	Covers production and follows module B Manufacturer must internally control its production in order to ensure product conformity against the EU-type approved under module B
C1 Conformity to EU-type based on internal production control plus supervised product testing	Covers production and follows module B. Manufacturer must internally control its production in order to ensure product conformity against the EU-type approved under module B. C+ tests on specific aspects of the product carried out by in-house accredited body or under the responsibility of a notified body chosen by the manufacturer (*)
C2 Conformity to EU-type based on internal production control plus supervised product checks at random intervals	Covers production and follows module B. Manufacturer must internally control its production in order to ensure product conformity against the EU-type approved under module B. C+ product checks at random intervals tests on specific aspects of the product carried out by a notified body or in-house accredited body
D Conformity to EU-type based on quality assurance of the production process	Covers production and follows module B. The manufacturer operates a production (manufacturing part and inspection of final product) quality assurance system in order to ensure conformity to EU type. The notified body assesses the quality system

(continued)

Table 1 (continued)

Module	Description of the module
D1 Quality assurance of the production process	Covers both design and production. The manufacturer operates a production (manufacturing part and inspection of final product) quality assurance system in order to ensure conformity to legislative requirements (no EU-type, used as in module D without module B). The notified body assesses the production (manufacturing part and inspection of final product) quality system
E Conformity to EU-type based on product quality assurance	Covers production and follows module B. The manufacturer operates a product quality (=production quality without the manufacturing part) assurance system for final product inspection and testing in order to ensure conformity to EU-type. A notified body assesses the quality system. The idea behind module E is similar to the one under module D: both are based on a quality system and follow module B. Their difference is that the quality system under module E aims to ensure the quality of the final product, while the quality system under module D (and D1 too) aims to ensure the quality of the whole production process (that includes the manufacturing part and the test of final product). E is thus similar to module D without the provisions relating to the manufacturing process
E1 Quality assurance of final product inspection and testing	Covers both design and production. The manufacturer operates a product quality (= production quality without the manufacturing part) assurance system for final product inspection and testing in order to ensure conformity to the legislative requirements (no module B (EU-type), used like E without module B). The notified body assesses the quality system. The idea behind module E1 is similar to the one under module D1: both are based on a quality system. Their difference is that the quality system under module E1 aims to ensure the quality of the final product, while the quality system under module D1 aims to ensure the quality of the whole production process (that includes the manufacturing part and the test of final product). E1 is thus similar to module D1 without the provisions relating to the manufacturing process
F Conformity to EU-type based on product verification	Covers production and follows module B. The manufacturer ensures compliance of the manufactured products to approved EU-type. The notified body carries out product examinations (testing of every product or statistical checks) in order to control product conformity to EU-type. Module F is like C2 but the notified body carries out more systematic product checks
F1 Conformity based on product verification	Covers both design and production. The manufacturer ensures compliance of the manufactured products to the legislative requirements. The notified body carries out product examinations (testing of every product or statistical checks) in order to control product conformity to the legislative requirements (no EU-type, used like F without module B) Module F1 is like A2 but the notified body carries out more detailed product checks

(continued)

Table 1 (continued)

Module	Description of the module
G Conformity based on unit verification	Covers both design and production. The manufacturer ensures compliance of the manufactured products to the legislative requirements. The notified body verifies every individual product in order to ensure conformity to legislative requirements (no EU-type)
H Conformity based on full quality assurance	Covers both design and production. The manufacturer operates a full quality assurance system in order to ensure conformity to legislative requirements (no EU-type). The notified body assesses the quality system
H1 Conformity based on full quality assurance plus design examination	Covers both design and production. The manufacturer operates a full quality assurance system in order to ensure conformity to legislative requirements (no EU-type). The notified body assesses the quality system and the product design and issues an EU design examination certificate. Module H1 in comparison to module H provides in addition that the notified body carries out a more detailed examination of the product design. The EU-design examination certificate must not be confused with the EU-type examination certificate of module B that attests the conformity of a specimen 'representative of the production envisaged', so that the conformity of the products may be checked against this specimen. Under EU design examination certificate of module H1, there is no such specimen. EU design examination certificate attests that the conformity of the design of the product has been checked and certified by a notified body

Probably the most demanding of the conformity assessment procedures is the conformity assessment in accordance with the type examination module, which requires well developed laboratories and competent staff. In the field of medical products 14 out of a total of 36 notified bodies, can provide type examination services, but not all of the providing this kind of service for all types of medical products.

There are 4 (actually 3) possible involvements by Notified Bodies:

No Notified Body involvement at all: module A;

Involvement, but only in the production phase: modules A1, A2;

Involvement in the design phase: module B followed by production phase: modules C1, C2, D, E, F;

Involvement in design and production phases: modules D1, E1, F1, G1, H, H1 [23].

Some of the conformity assessment modules are only possible in combination with others, i.e. in order to carry out a certain conformity assessment module, an earlier one had to be carried out first.

For example, Non-automatic weighing instruments 2014/31/EU, which requires combination of the following modules B + D or B + F, Modules D1 or F1 or Module G.

7 Standards Used in Manufacturing Process

Standards aren't the same as regulations and following a standard doesn't guarantee that you are within the relevant laws. In fact standards rarely cite the law as legislation could change within the lifetime of the standard.

To successfully carry out the harmonization process within the legal metrology framework, it is necessary to take appropriate steps by harmonizing requirements for benchmarks, test methods, test reports, and certificates, which the government often relies on standards for when creating legislation or guidance documents to establish technical details, enabling the legislation to focus on long-term policy objectives such as product safety or environmental protection [24].

In a case like this, compliance with the standard will often mean you're compliant with the relevant legislation, although there are usually ways of being compliant with legislation without using a standard.

Standards are voluntary which means that there is no automatic legal obligation to apply them. However, laws and regulations may refer to standards and even make compliance with them compulsory.

A technical regulation is a Government document that lays down product characteristics or their related processes and production methods, including the applicable administrative provisions, with which compliance is mandatory. It may also include or deal exclusively with terminology, symbols, and packaging, marking or labelling requirements as they apply to a product, process or production method. No consensus is necessary for establishment of the regulation.

The difference between a standard and a technical regulation lies in compliance. While conformity with standards is voluntary, technical regulations are by nature mandatory.

International standards should be used as a basis for preparing technical regulations except when they are not appropriate to fulfil legitimate interests, for instance, because of fundamental climatic or geographic factors or fundamental technological problems.

For a government, avoiding unnecessary obstacles to trade means that when it is preparing a technical regulation to achieve a certain policy objective—whether protection of human health, safety, the environment, etc.—the regulation shall not be more trade-restrictive than necessary to fulfil the legitimate objective.

Technical regulations adopted in pursuance of legitimate interests and in accordance with relevant international standards are presumed not to create unnecessary obstacles to international trade.

European harmonised standards are those that are considered to satisfy the relevant essential safety requirements specified in European product directives or regulation.

For example in the field of metrology there are 23 harmonized standards related to the MID (2014/32/EU) and 17 normative documents which are also used in conformity assessment procedures. Comparing to the field of medical devices, we can find 17 harmonised standards linked to the 2017/745/EU regulation [25]. This may lead to conclusion that MID has stricter requirements.

The difference is reflected in the fact that harmonized standards and normative acts in the field of metrology are directly related to individual measuring instruments covered by the MID, while harmonized standards in the field of medical products are related to the general requirements of medical products, and the number of standards that are directly related to individual medical products is significantly larger.

In the field of medical devices, used in manufacturing process, there are ca. 200 standards among those which are harmonized, which have been issued under the European Committee for Standardization CEN (without revision), and close to 100 standards issued under the European Committee for Electrotechnical Standardization CENELEC (without revision). Taking into account such a large number of standards regulating the requirements for a particular product group, it is easy to conclude that this area of manufacturing presents an area where most attention is paid in relation to the safety of the product itself and its users.

One of the most widely used standards in the area of manufacturing of the medical devices is the standard IEC 60601-1 Medical electrical equipment—Part 1: General requirements for basic safety and essential performance.

Standard IEC 60601-1 is a basic document comprised of two parts that relate to the safety of medical devices (collateral standards) and to various types of medical equipment (particular standards). The basic version of the standard was published for the first time in 1977 and was related to the issues of electrical and mechanical safety.

Standards marked with IEC 60601-1-X are collateral standards (where X represents sub-standards, altogether 11).

Standards marked with IEC 60601-2-X are specific standards (where X represents sub-standards, altogether 58).

The basic standard IEC 60601-1 is applied for the purpose of basic safety and essential performance of Medical Electronical Equipment and Medical Electrical Systems. The content of the standard describes protection against electrical Hazards from Medical Electrical Equipment, protection against mechanical Hazards of Medical Electrical Equipment and Medical Electrical Systems, protection against unwanted and excessive radiation Hazards, and protection against excessive temperatures and other Hazards.

In this part of the chapter the main activities on protection against electrical Hazards from Medical Electrical Equipment will be described, since the patients and operators are exposed to this hazard the most when operating or using the equipment which did not fulfil the requirements stated in the corresponding standard. Requirements set in the standard IEC 60601-1 give the manufacturer a possibility to better understand how to reduce risks of harm or to bring them to the acceptable limits.

Protection against electrical Hazards from Medical Electrical Equipment in accordance with standard IEC 60601 covers requirements related to maximum permissible voltage, current, energy, power sources, needed insulation, testing of leakages, etc. In order to satisfy prescribed limitation of voltage, current or energy, means for reducing the risk due to electric shock in accordance with the requirements of standard IEC 60601-1 which can be divided in two categories:

- Means of patient protection (MOPP)—Means of protection for reducing the risk of electric shock to the patient.
- Means of operator protection (MOOP)—Means of protection for reducing the risk of electric shock to persons other than the patient.

Standard also covers specific measurement tests of current leakage, insulation requirements, creepage distances and air clearances.

Another very important harmonized standard for the manufacturers, among the 17 connected to the regulation 2017/745/EU, from the point of a high quality of medical products, is standard ISO 13485 [26].

ISO 13485 is an internationally recognized standard for quality management systems in the medical products industry. It specifies the requirements for a quality system in which an organization must demonstrate its ability to deliver medical products, and that the services associated with this can consistently meet customer requirements and relevant laws and regulations. It is designed and intended for use by organizations to carry out the design, development, production, installation, maintenance and sale of medical products.

The primary objective of ISO 13485 is to establish a system that is fully capable of meeting legal and quality system requirements. ISO 13485 is an independent standard. It is largely based on the structure of ISO 9001 [27], but includes certain specific requirements for medical products such as: risk analysis, sterile production and traceability.

It is designed to be used by organizations throughout the life cycle of a medical device, from initial conception to production and post-production, including final decommission and disposal. It also covers aspects such as storage, distribution, installation and servicing, and the provision of associated services. In addition, the standard can be used by other internal and external parties, such as certification bodies, to help them with their certification processes, or by supply chain organizations that are required by contract to conform. ISO 13485 helps an organization design a quality management system that establishes and maintains the effectiveness of its processes. It reflects a strong commitment to continual improvement and gives customers confidence in its ability to bring safe and effective products to market [28].

8 Medicine in the Field of Legal Metrology

Medical measurements are an essential component of everyday life and serve as a fundamental process for the prevention, diagnosis, and treatment of diseases. In Europe, there is a growing focus on metrology and conformity assessment decisions, which are crucial for carrying out accurate measurements that safeguard public health, particularly in light of the digital transformation's impact on medical device management, where data gathering and evidence-based informed decision-making have become imperative.

Products with a measuring function must be designed and manufactured in such a way to provide sufficient accuracy and stability within appropriate limits of accuracy, taking into account the intention of the use of the product. The accuracy limits (permissible errors) are specified by the manufacturer himself. The measurements done by the device with a measuring function must be expressed in legal units of measurement in accordance with the provisions of Directive 80/181/EEC [29].

Metrology with its measurements is an integral part of our daily life. All measurements which are carried out with the purpose of any economic transactions, or measurements with which it's possible to take certain legal measures against or in someone's benefit, protection in the field of health and the environment, are to be classified as measurements of legal metrology. Individual governments proscribe regulations under legal metrology to meet its needs, except for the harmonized area which is equal and obligatory in all member states (11 measuring instruments, MID 2014/32/EU and NAWI [30] 2014/31/EU). One issue is common for all state economies and that is a fact that legal metrology is founded for the purpose of protection of the consumers (end users). OIML—International Organization of Legal Metrology has divided this category of metrology into four parts.

Those parts are:

- Legal Metrology and Trade
- Legal Metrology and Safety
- Legal Metrology and Health
- Legal Metrology and the Environment.

The accurate and precise measurements in the field of medicine allow easier diagnosis and identification of diseases on the basis of which it is possible to precisely determine the appropriate treatment of the patient, in order to help the patient in the best and safest way to receive effective treatment, but all through the usage of adequate medical instruments/ devices which fulfil the requirements described in the relevant legislation and standards.

In accordance with OIML D1 [31] document, governmental regulatory responsibilities include **health**, safety and environmental law. While these functions are disparate in nature, a common feature is that compliance with the law depends on measurement results. The scope of legal metrology may be different from country to country.

Therefore, the process of measurement is of direct concern to the government. Providing the laws and regulations, controlling measurement through market supervision and developing and maintaining the infrastructure that can support the accuracy of these measurements (e.g. through traceability) is essential in fulfilling the role of government.

The scope of the legal metrology regulations (e.g. which types of measurements and measuring instruments or systems are subject to legal requirements) will depend on those markets that are important to the economy, on the categories of users that the government considers necessary to protect, and on the ability of the users to protecting themselves against abuse.

Since there are only 11 harmonized instruments, it is easy to conclude that the non-harmonized sector comprises of much higher number of instruments.

Non-harmonised sectors [32] are not subject to common EU rules and may come under the national rules. These sectors should still benefit from Treaty provisions governing free movement of goods according to Arts. 34–36 TFEU (Treaty on the Functioning of the European Union). National rules on these products are subject to a notification procedure that ensures they do not create undue barriers to trade.

In order to ensure the free movement of goods in non-harmonised sectors, the principles of mutual recognition, the 98/34 notification procedure and the application of Arts 34–36 TFEU are essential.

In some regions, due to the treaties or agreements, regional legislation may have precedence over national laws and regulations or may be recommended to national authorities. This is the case for example in the European Union, where European Regulations and European Directives are accorded higher status than national legislation.

Referring again to OIML Document D1 „Considerations for a Law on Metrology “, the recommendation for government bodies building their metrology systems are encouraged to keep the following:

The priority is to set up the legal provisions related to the status of the bodies to which tasks will be allocated, and the financial provisions that will ensure their sustainability (national institutes, accreditation bodies), the general framework for legal metrological control and the first list of priorities for categories to be subjected to legal control, and the infringements, penalties and the powers of agents in charge of metrological supervision.

The scope of legal metrology, that is the list of categories of measuring instruments, must start with the most important categories for which the available resources allow the regulation to be correctly enforced. The scope can then be progressively extended as additional resources become available.

The obligations resulting from the OIML Treaty and from the WTO TBT Agreement (obligation to use OIML Recommendations as far as possible, and encouragement by the TBT Agreement to participate in OIML recognition and acceptance arrangements) should also be taken into account, as well as other obligations deriving from regional treaties or agreements.

Measuring instruments under legal metrology have to be regularly verified. Verification [33] of a measuring instrument represents conformity assessment procedure (other than type evaluation) which results in the affixing of a verification mark and/or issuing of a verification certificate.

As described in OIML Document D1 “Fields of use of measuring instruments subject to verification” Instruments, substances, and devices used in the diagnosis and treatment of humans and animals, in the manufacture of medicines, and in the monitoring of the medical environment (patient and hospital) should be considered for verification.

OIML has published a certain number of recommendations which indicate on verification procedures of medical devices. This will be described more in detail in

the chapter dedicated to legal metrology. Medical devices covered by International Organization of Legal Metrology [34] are as follows:

- Medical syringes, covered by OIML recommendation R 26 (1978)
- Standard graduated pipettes for verification officers, covered by OIML recommendation R 40 (1981)
- Electroencephalographs—Metrological characteristics—Methods and equipment for verification, covered by OIML recommendation R 89 (1990)
- Electrocardiographs—Metrological characteristics—Methods and equipment for verification, covered by OIML recommendation R 90 (1990)
- Measuring instrumentation for human response to vibration, covered by OIML recommendation R 103 (1992)
- Pure-tone audiometers (including Annexes A to E), covered by OIML recommendation R 104 (1993)
- Clinical electrical thermometers for continuous measurement, covered by OIML recommendation R 114 (1995)
- Clinical electrical thermometers with maximum device, covered by OIML recommendation R 115 (1995)
- Equipment for speech audiometry, covered by OIML recommendation R 122 (1996)
- Non-invasive non-automated sphygmomanometers, covered by OIML recommendation R 148 (from 2020)
- Non-invasive automated sphygmomanometers, covered by OIML recommendation R 149 (from 2020).

OIML has covered only a part of medical devices with measuring function; however the number of medical devices in use is much higher. For medical devices that are applied in the EU but which are not covered by legal metrology in some countries calibration process has to be ensured with an adequate traceability chain. Requirements for harmonizing a large number of medical devices in legal metrology are constantly increasing. There is growing interest in the role of metrological decisions and conformity assessment, notably where measurements are made to safeguard health [35].

Measurements are essential in medical diagnosis and the prevention and treatment of diseases, risk assessment and monitoring of patients. Such measurements are performed every day; moreover, as the measurement results become more important in medicine so they must be more accurate and also comparable in different locations over time. Only then is it possible to optimize patient care and to efficiently manage healthcare funds.

Some countries of South-east Europe, namely Bosnia and Herzegovina and Serbia, (which are not members of the EU), are members of WELMEC (European Cooperation in Legal Metrology) and OIML, who are regularly taking part in activities of those organisations. The national metrology institutes of those countries have introduced certain medical devices in the field of legal metrology in accordance with their national regulation, as part of regular subject of legal control, namely verification.

Medical instruments with measuring function, which are part of the Legal metrology system in B&H and Serbia, are as follows:

- Defibrillator,
- Infusomats and perfusors,
- Patient monitors,
- Neonatal and paediatric incubators,
- Respirators,
- Anaesthesiology machines,
- Therapeutic ultrasound devices,
- Dialysis machines,
- Electrocardiographs ECG/EKG.

Beside those medical devices, Serbia has also measuring devices that are an integral part of high-frequency surgical knives and high-frequency surgical accessories as subject of national control [36].

This action proved to be very successful, according to the feedback from the legal entities responsible for performing verification in this subjected field. The majority of devices tested have shown certain non-conformities related to the requirements prescribed in legal documents and/or by the manufacturer [37–41].

Unlike other measuring instruments covered by legal metrology, many of the medical devices need to be traceable to one measuring standard which is not fully developed yet. The future of development in this field of metrology lies in facilitating the process of calibration, i.e. establishment of a traceability chain via a single measuring standard for a certain type of medical device.

Turkey has also already recognised the importance of metrology in medicine and has initiated via Turkish Institute of Metrology (UME) [42] a study on appropriate traceability of medical devices. The aim of the study is to develop a five year roadmap and a plan for providing reliability and metrological traceability in medical measurements. To get closer to its intended aim, UME has established a Medical metrology research laboratory.

Comparing the current situation of those countries dealing with medical instruments in a controlled area it is obvious that the main issue in general refers to how to ensure or improve adequate metrological traceability. Looking at the history in the field of medical devices and the connection with metrology, it can easily be concluded that OIML recognized this connection a long time ago. More and more authorised state institutions recognize this connection and introduce a certain number of medical devices as subject of legal control. Medical devices which are currently under legal control are those which are most often used in practice and where a reliable result based on the measured results is key in the treatment of patients.

9 Regulation of Artificial Intelligence Usage in Medical Devices

Since the era of digitization begun in the late twentieth century, continuous advancements have been made in the field [43]. Even though most people remained unaware of it, the 4th industrial revolution [44, 45] has already impacted life as we know it and most of our daily activities rely on the advancements provided for humans by means of industry 4.0. Industry 4.0, also known as the fourth industrial revolution, refers to the integration of advanced technologies and systems to automate and optimize various industrial processes. In the healthcare sector, Industry 4.0 has the potential to revolutionize the way healthcare is delivered, managed, and monitored.

The healthcare sector is an inexhaustible source of data gathered every day through measurements of patient-related parameters or device-related parameters. Although modern technology has accelerated the development of new diagnostic procedures and interventions, it remains tightly controlled by human operations. Medical devices, which assist medical practitioners in diagnosing and treating diseases, have evolved significantly over time and have been modernized alongside other devices used in practice. The fourth industrial revolution has largely influenced the improvement of these devices, paving the way for process digitalization and the utilization of data generated by IoT networked devices. To advance healthcare, data generated by medical devices must be understood, stored long-term in cloud-based servers, and selectively used to develop "smart solutions." Big data structures are at the center of all "smart" solutions, with one way to make devices smart being to supply them with AI-based algorithms. AI-based methods are evaluated based on their accuracy when compared to that of medical professionals. To be considered a potential candidate for further development, the AI model must be "trained" with a large dataset that covers as much variation in input parameters as possible and "validated" by comparing their outputs with that of an experienced consortium of medical professionals. Medical professionals who work with medical devices daily are beginning to appreciate the potential that technology advancements have for patient diagnosis, treatment, and prognosis.

The European Commission has taken a proactive approach towards AI regulation in healthcare. In April 2021, the European Commission proposed new rules for AI that would apply to all AI systems used in the European Union (EU), including those used in healthcare. The proposal is a part of a broader strategy to establish Europe as a global leader in AI development and deployment. The proposed rules aim to ensure that AI systems are safe, transparent, and accountable. Regardless of their use or purpose, the proposed regulations will require compliance with strict requirements and standards for AI systems. Specifically, the proposed rules would classify AI systems into four categories based on their risk level: unacceptable risk, high risk, limited risk, and minimal risk. Healthcare AI systems are likely to be classified as high-risk or limited-risk systems, depending on their intended use. High-risk systems may include AI systems which are used for clinical decision-making, while limited-risk systems may include AI systems used for administrative purposes.

Also, high-risk systems would require mandatory third-party conformity assessments before they can be placed on the market, and would also be subject to ongoing surveillance and monitoring. The goal of these assessments is to ensure that high-risk AI systems are safe, reliable, and comply with relevant regulations. Ongoing surveillance and monitoring would help identify any potential issues or risks with AI systems that have already been placed on the market. Limited-risk systems would require less stringent requirements, but would still need to comply with transparency and data protection requirements, so that users can understand how the AI system is making decisions. Data protection requirements would also ensure that personal data is processed in a lawful and transparent way. The proposed rules also address ethical concerns related to AI in healthcare, such as ensuring that AI systems are designed to respect fundamental rights, and that their outputs are explainable and auditable. This means that AI systems should not be used to discriminate against individuals based on factors such as race, gender, or age. Users should be able to understand how the system arrived at its decision. The European Commission has emphasized the need for human oversight and intervention in AI decision-making, particularly in cases where AI systems are used to make decisions that could have significant impacts on individuals' health or well-being, meaning that AI systems should not be used as a replacement for human decision-making, but rather as a tool to support it [46, 47].

For medical devices—the European Union (EU) has introduced regulations to govern the usage of artificial intelligence (AI)s. These regulations require that AI-based medical devices comply with the EU's existing regulatory framework for medical devices, which includes the Medical Device Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR). AI-based medical devices must meet the same safety and performance standard as other medical devices. In addition to complying with these regulations, AI-based medical devices must also adhere to specific requirements related to their AI components. These requirements include ensuring that the algorithms used in the device are transparent, explainable, and verifiable, and that the device is designed in a way that minimises the risk of error or bias. The EU regulations also require that AI-based medical devices undergo a thorough assessment of their safety and performance before being placed on the market. This assessment includes a review of the device's technical documentation, clinical data, and risk management plan, and must be carried out by a notified body. This ensures that AI-based medical devices are safe and effective, and provide accurate and reliable diagnostic results.

The future of AI regulation is a topic of ongoing debate and discussion. As AI technology continues to advance and become more widespread in various industries, including healthcare, there is increasing recognition of the need for effective regulation to ensure that these technologies are developed and used responsibly. Overall, the regulations aim to ensure that AI-based medical devices meet the same safety and performance standards as traditional medical devices, while also addressing the unique challenges and risks associated with the use of AI in healthcare.

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Legal Metrology System—Past, Present, Future

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Abstract Through the chapter Legal Metrology System—Past, Present, Future, a significant legal metrology role is presented in human civilization development, which has led to measurement consistencies in everyday life. In addition to this, the current state of legal metrology at the international level is described, focusing on the European level. Furthermore, the European Union legislation is presented, including the New Approach Directives. Through this chapter, the need for launching measuring devices into the legal metrology framework is presented. Also, a legal metrology role and its key future impact indicators are described.

1 Introduction

Consciously or unconsciously, we often tend to quantify an object of study to obtain a meaningful perspective. "Measure twice, cut once." is something usually heard. It is used when people want to emphasize the importance of decision making, thinking, planning and preparation before certain action to prevent serious failures, and to ensure that the purpose will be fulfilled. If you want to make food you follow a recipe and measure the weight of ingredients, you measure the amount of oil in a car engine to ensure it runs smoothly, you measure blood pressure, heart rate, weight, and height to stay healthy, and many more. So, measurements have deep effect on our lives, but they also add elements of science in areas that seem completely "science free."

Metrology, as defined by the International Bureau of Weights and Measures (BIPM) is "*the science of measurement, embracing both experimental and theoretical determinations at any level of uncertainty in any field of science and technology.*" Metrology (derived from the Greek word *metron* meaning measure, and

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logos meaning science, studying) represents a basis for developing all scientific disciplines. Metrology development is related to human civilization development, which required measurement consistencies in everyday life. This scientific discipline arose from political motivation to standardize units of measurements that were the basis of trade at a time. Historically, the development of metrology as a field has roots in the French revolution, when first steps were undertaken to establish a base unit system [1]. Today, it defines metrological characteristics in all aspects of human activity, from science, industry, home environment and healthcare. These requirements shaped the uniform measuring system that eventually grew into the international system of units—the SI system.

Metrology primarily deals with measuring units, development, realization, maintenance, and improvement of standards (SI), dissemination of the values reproduced to achieve traceability, measuring instruments, measuring, uncertainty, and reliability. Generally, metrology is divided into three main fields covering different levels:

- **Scientific metrology**—establishing measurement units and system, developing new measurement methods, measuring standards realization, transferring traceability from these standards (measurement results) to users in society, and responsibility for international representation in matters related to scientific metrology.
- **Industrial metrology**—dealing with measurement science applications to manufacturing including other processes and applying these principles in society and ensuring the suitable of measuring instruments including calibration and testing, and responsibility for international representation in matters related to industrial metrology.
- **Legal metrology**—concerning with regulatory measurement requirements of measuring instruments that impact transaction transparency, security, environmental, and health protection, and responsibility for international representation in matters related to legal metrology.

Fundamental metrology has no internationally accepted definition, but it can be described as a part of scientific metrology.

Measurements are one of the first technical activities where international cooperation is established. Internationalization and harmonization are essential measurement features. The basis for dealing with measurement issues at an international level are the Metre Convention and International Organization of Legal Metrology (OIML). Metre Convention is an international agreement which is established by the International Bureau of Weights and Measures (Bureau International des Poids et Mesures—BIPM). This diplomatic contraction was signed by representatives of 17 countries in Paris in 1875. In addition to this, the structure was established, which helped governments of Member States to deal with metrology issues [2].

As for the legal control of measuring instruments, which are used in the legal metrology field, it includes the following activities [3]:

1. Type evaluation and approval • testing laboratories • certification bodies (issuing authorities)	**2. Initial verification** • field officials • manufacturer declaration
3. Subsequent verification • field officials • readjustment • maintenance and repair	**4. Market surveillance** • identifies, records, and notifies individual instrument failures • recalls the instrument types that are displaying failure records • requires from the manufacturers to implement adjustments in place or in production

The purpose of legal metrology regulations (e.g., which types of measurements and measuring instruments or systems are subject to legal requirements) depends on those markets that are important to some economies. In addition to this, it depends on categories of society that some government considers necessary to protect, and on society ability to protect them against abuse. Another key legal metrology feature is to provide confidence in measurement results by applying the legal metrology provisions. The needs and requirements on measuring results should be considered prior to addressing needs and requirements on measuring instruments.

Primary terms and definitions that are used in the legal metrology field are given in the text below [4, 5]:

Legal metrology: Practice and process of applying statutory and regulatory structure and enforcement to metrology.

Note 1 The scope of legal metrology may be different from country to country.

Note 2 Legal metrology includes:

- setting up legal requirements
- control/conformity assessment of regulated products and regulated activities
- supervision of regulated products and of regulated activities
- provision of necessary infrastructure for the traceability of regulated measurements and measuring instruments to SI units or national standards.

Note 3 There are also regulations outside the field of legal metrology pertaining to the accuracy and correctness of measurement methods.

Type (pattern) evaluation: A conformity assessment procedure must be done on one or more specimens of an identified type (pattern) of measuring instruments, which results in an evaluation report and/or an evaluation certificate.

Type approval: Decision of legal relevance, based on the review of the type of evaluation report that the type of a measuring instrument complies with the relevant statutory requirements and results in the issuance of the type of approval certificate.

Initial verification: Verification of a measuring instrument which has not been verified previously.

Subsequent verification: Verification of a measuring instrument after a previous verification.

Note 1 Subsequent verification includes:

- mandatory periodic verification
- verification after repair
- voluntary verification.

Note 2 Subsequent verification of a measuring instrument may be carried out before expiry of the period of validity of the previous verification either at the request of the user (owner) or when its verification is declared as no longer valid.

Metrological supervision: Activity of legal metrological control performed to check the observance of metrology laws and regulations.

Note 1 Metrological supervision also includes checking the correctness of quantities indicated on and contained in pre-packages.

Note 2 The means and methods such as market surveillance and quality management may be utilized to achieve stated application.

The previous edition of the book Inspection of Medical Devices offered valuable insights into medical device inspection and legal metrology framework [6].

2 Legal Metrology Organizations

Legal metrology deals with responsibility for regulation policy, responsibility for legislation, responsibility for international presentation in matter related to legal metrology, advice on metrology legislation and on relevant standards, and development and international harmonization of metrological checks. In addition to this, it deals with pre-market and post-market to ensure essential fair trade, security, environmental, and health protection. This is achieved by an adequate legal metrology system and measuring instrument controls. In addition to this, the legal metrology's primary goal is to protect consumers from fraudulent practices in trade and commerce. This includes ensuring that products sold by weight or volume are measured correctly and that measuring instruments used in these commercial transactions are verified to ensure consumers' protection. Furthermore, the legal metrology helps to prevent environmental damage by ensuring that measuring instruments related to pollutants, noise levels, and other environmental factors are tested and verified. Legal metrology is governed by national and international standards and laws and regulations set by governmental organizations. These laws, instructions and regulations help to ensure that measurements are consistent and reliable across different regions and industries. The authorized bodies for legal metrology control the legal metrology system according to the needs and opportunities for a particular country. The COVID-19 pandemic has emphasized the crucial importance of conducting regular inspections on medical devices with measuring functionality to guarantee their proper functioning [7]. By enforcing standards, instructions and regulations on measuring instruments, government can help to protect consumers, promote fair competition, and support the growth and development of industries that rely on the legal metrology framework.

2.1 International Organization of Legal Metrology—OIML

The International Organization of Legal Metrology OIML [8] was established in 1955 as the contractual intergovernmental organization. Its purpose is to empower economies creating effective legal metrology infrastructures that are mutually equal and internationally recognized, for all fields where governments have their responsibility, such as motivation by trade, establishing mutual confidence and harmonizing the level of costumers' protection worldwide [9]. According to that, the organization is given a definition of legal metrology on its official website and as it follows [2]:

> Legal metrology is the application of legal requirements to measurements and measuring instruments

The legal metrology is used extensively in trade, health, safety, and environmental protection. These mentioned fields or legal metrology activities extensively protect individuals within society and society with its legal metrology regulations. Furthermore, the legal metrology regulations are focused to measurement results and legal control performed on the government's behalf. In addition to this, OIML aims to promote the procedures and recommendations within the legal metrology field and their global harmonization and application within the metrology community and wider. OIML developed a structure that allows its members to participate in the OIML Technical Committee work and propose topics that are relevant to them or other issues (national, regional, etc.). The OIML documents and recommendations are related to measuring instrument legal provisions, and they are available to all stakeholders via the official OIML webpage, thus avoiding unnecessary guides and documents that each county needs in this process. Furthermore, participating in the OIML work, its members have access to all information from other members such as new technologies, conformity assessment procedures, good practices in the legal metrology, etc. Also, the OIML members can affect the OIML policy and propose recommendations for the OIML strategy. In this way, the members secure that their needs are considered and addressed in the organization work. The strategy deals with general organization policy and it supports developing national authorized bodies for legal metrology with special focus to developing countries. More about these benefits regarding the OIML membership can be found on the official website. According to the research, published by World Bank in 2007, the OIML members cover 86% of the world population and 96% of the global economy [2]. From this information, it can be concluded that the impact of legal metrology is crucial to our daily life, and it creates a huge profit from the invested money.

OIML has 63 Member States and 64 Correspondence Member States (Observers) with headquarters in Paris until 2016 [2]. OIML had 57 Member States and 56 Correspondence Member States (Observers) until 2010 [10]. Based on this information, it can be concluded that there is continuous interest for becoming a part of the OIML community with the aim to strengthen the individual legal metrology system and society protection within Member States.

Member States are those who have ratified the OIML Agreement Convention and requested access to the OIML membership to the French government. All member

states are morally committed that they will apply legal metrology system as soon as possible in their countries.

Correspondent Members (Observers) are countries or economies that cannot become or have not yet become the full member, but they are interested in the OIML work and want to participate in it. These countries may be represented by an authorized government body, authorized legal metrology body, authorized trade chamber, state institutes, and institutes responsible for legal metrology issues in that country.

International Organization of Legal Metrology OIML has the following tasks:

- Developing regulations, standards and similar documents used by authorized metrology bodies and industry
- Providing mutual recognition system which reduces trade barriers as well as costs on the global market
- Representing interests of the legal metrology community in the frame of international organizations and forums dealing with metrology, standardization, certification, testing and accreditation
- Promoting and facilitating transfer of knowledge and competencies of legal metrology community worldwide
- Cooperating with other authorities to raise awareness about importance the uniform legal metrology infrastructure contribution, and development of a modern economy.

International Organization of Legal Metrology OIML has the following authorities [10]:

- International Conference of Legal Metrology
- International Committee of Legal Metrology
- Technical Committees (TC)
- International Bureau of Legal Metrology.

International Conference of Legal Metrology is the supreme body of the Organization. It consists of representatives of the Member States always coming from an authorized body of legal metrology. Also, Correspondence Members (Observers) have the possibility to access the Conference as Observers and organizations which OIML cooperates with may be invited to attend the meeting as Observers. The conference meets every four years. The conference's role and its action field are the following [2].

- Studying issues related to the OIML goals and making decisions
- Providing Administrative bodies structure
- Confirming Technical Committee members
- Examining and approving reports submitted by the OIML bodies
- Making adoption and approval of the budget and determination of the registration fee amount for the OIML members.

International Committee of Legal Metrology (CIML) [2] is the OIML working body. CIML members (one per country) are designated by the government of country

of origin. Designated members are usually officers in departments that deal with measuring instruments or play an official active role in the legal metrology field. CIML members are the permanent OIML partners, and they have a double role: firstly, to represent their country at the Conference and secondly OIML in their country. Correspondence members (Observers) have the possibility to access CIML as Observers, and organizations which CIML cooperates with, may be invited to attend the meeting as Observers. The Committee meets once a year, and in its working scope brings the following resolutions [2]:

- Approving the OIML strategy and BIML annual working plan [4]
- Approving the BIML director financial report
- Designating the BIML Director and Assistant Director
- Adopting different international regulations, procedures, etc.
- Approving amendments related to the OIML technical program
- Adopting the OIML recommendations, documents, and other publications, etc.

Technical Committees (TC) consist of the Member States and Correspondence Members (Observers) representatives and organizations cooperating with OIML. Committees are responsible for making the OIML documents and recommendations based on the activities assigned by CIML. These documents provide the legal basis for the adoption of legislation for different types of measuring instruments in the legal metrology scope of Member States. Only Member States representatives have the right to vote in the committees. There are 18 Technical Committees and 50 Subcommittees, whose tasks include:

- The scope and application of metrology,
- Metrological requirements,
- Methods and equipment for testing and verification of compliance with the metrological requirements, etc.

Technical Committees (TC) which work and operate under the CIML supervision are [11]:

- TC 1 Terminology
- TC 2 Units of measurement
- TC 3 Metrological control
- TC 4 Measurement standards and calibration and verification devices
- TC 5 General requirements for measuring instruments
- TC 6 Pre-packaged products
- TC 7 Measuring instruments for length and associated quantities
- TC 8 Measurement of quantities of fluids
- TC 9 Instruments for measuring mass and density
- TC 10 Instruments for measuring pressure, force, and associated quantities
- TC 11 Instruments for measuring temperature and associated quantities
- TC 12 Instruments for measuring electrical quantities
- TC 13 Measuring instruments for acoustics and vibration
- TC 14 Measuring instruments used for optics

- TC 15 Measuring instruments for ionizing radiations
- TC 16 Instruments for measuring pollutants
- TC 17 Instruments for physic-chemical measurements
- TC 18 Medical measuring instruments.

International Bureau of Legal Metrology (BIML) is the OIML executive body. It cares about all activities, including long-term planned activities, to be processed timely. BIML's responsibilities are as follows [2]:

- Organizing the Conference and Committee meetings
- Taking Implementing decisions that are made in the Conferences and Committees
- Preparing the Conference Technical Committees meetings
- Supervising and coordinating the OIML Technical Committees work, publishing and distributing the OIML publications
- Publishing the OIML newsletters, and maintaining the OIML official website
- Maintaining contacts with organizations and performing activities on behalf of the organization
- Preparing and implementing the OIML budget.

The primary activity of different technical committees (TC) is to prepare documents and recommendations. The recommendations provided by Member States and Contracted Members (Observers) are base for establishing the unified national legislation that reduces trade barriers. In addition to this, it protects manufacturers and users from frauded measurements. [2]. OIML is an Observer in WTO (TBT) [12]. In line with that, the OIML recommendations represent the international standards based on the Agreement on Technical Recommendations in Trade [13]. Considering the OIML recommendations applicability in the legal metrology framework, increased manufacturers implement these recommendations in their system to fulfill the prescribed requirements for measuring instruments given by the OIML recommendations. The recommendations are mostly related to the type of approval and contain the following instructions regarding the type of approval [13]:

1. Metrological requirements:
   - Accuracy class
   - Maximum permissible error:

     rated operating conditions, reference conditions
     rated operating conditions with influential factors.

   - Influential factors:

     ambient conditions (temperature, humidity, etc.)
     mechanical factors
     electromagnetic factor.

   - Repeatability and reproducibility
   - Discrimination and sensitivity
   - Reliability over time

- Mutual recognition and acceptances arrangements.

2. Technical requirements:

- Indication of the results
- Software
- Markings
- Operating instruction
- Suitability for use.

3. Test program and procedures
4. Format and report tests
5. Conformity declaration or certification.

In addition to this, the OIML recommendations are related to verification because initial and subsequent verification is the legal metrology activities according to national or regional regulations.

OIML system [2] was established in 1991 with the purpose to simplify administrative procedures and reduce costs related to international trade of measuring instruments in the legal metrology field. In the beginning, the system was called the OIML Certificate System, and now it is called the OIML Basic Certificate of Conformity. The purpose is clearly to make the difference between the OIML Basic Certificate of Conformity and OIML MAA Certificate System. This system allows manufacturers to get an OIML Basic Certificate and an OIML Basic Report (Test report) based on which is confirmed that a particular instrument complies with the legal requirements that are prescribed by a relevant OIML recommendation. All information related to the OIML system, such as steps, rules, conditions, and uses, are given in the OIML document OIML B3 [14]. These certificates are issued by the OIML Member States. In addition to this, these Member States can have more than one body for testing measuring instruments. There is no limitation regarding this issue. This type of certificate can be accepted by other countries without any additional examinations. This helps manufacturers launch their products (measuring instruments) on the global market.

OIML MAA refers to type testing, and its purpose is to increase the mutual confidence level that is given by the OIML Basic Certificate. The OIML MAA is voluntary, but it provides a lot of benefits. It enhances the level of trust in conducted assessment for laboratory testing, which is included in type testing. It brings benefits to the OIML Member States and Correspondent Members (Observers), which do not have established laboratories for testing. It gives an opportunity to have considered (Declaration of Mutual Confidence—DoMC) the additional state requirements or regional requirements (which can only apply relevant OIML recommendations). The OIML MAA purpose for the participants is to accept and use MAA test reports that are verified by the OIML MAA Certificate of Conformity. Participants in the MAA either publish (Issuing Participants) or use (Utilizing Participants) test reports. The benefit for manufacturers is to avoid duplication of testing in different countries. The participants confirm their participation in the system by signing the Declaration of Mutual recognition. The OIML MAA implementation was started in 2005 [15]. All

information related to the MAA system, such as steps, rules, conditions, and uses, are given in the OIML document OIML B10 [16].

As for the authorized bodies that issue the OIML certificates, they should demonstrate compliance with the requirements according to ISO/IEC 17065 [17] by using the results from laboratories for testing which have implemented the requirements according to ISO/IEC 17025 [18]. The OIML MAA confidence in test reports is followed by an official and mandatory peer review process. This process proves the compliance of authorized bodies for certification (OIML Member States) with testing laboratories applying required standards and laboratories for testing to perform tests. In order to prove their competencies, authorized bodies for certification and laboratories for testing should be accredited or pass through the peer review process [15], respectively.

The OIML Certification System (OIML-CS) aims to facilitate, accelerate, and harmonize the work of national and regional bodies that are responsible for type evaluation and approval of measuring instruments subject to the legal metrological control.

The main OIML-CS objectives are [14]:

- Promoting the global harmonization
- Interpreting and implementing the legal metrological requirements for measuring instruments and/or modules on a uniform way
- Avoiding unnecessary re-testing when obtaining national type evaluations and approvals
- Supporting the measuring instrument recognition and modules under legal metrological control
- Achieving and maintaining confidence in the results in support for facilitating the global trade instruments
- Establishing rules and procedures for fostering mutual confidence among the OIML members.

There are three OIML-CS participants categories, as follows [14]:

- OIML Issuing Authorities are conformity assessment bodies from the OIML Member States that issue the OIML certificates and associated OIML type evaluation reports in following Scheme A or B.
- Utilizers are national issuing authorities or responsible national bodies from OIML Member States that utilize and accept OIML Certificates and/or OIML type evaluation reports issued under Scheme A or B as the basis for giving a national or regional type approval.
- Associates are national issuing authorities or national responsible bodies from the OIML Corresponding Members that utilize and accept the OIML Certificates and/or the OIML type evaluation reports issued under Scheme A or B as the basis for issuing a national or regional type approval. Associates do not have voting rights in the Management Committee.

The requirements for participating in the OIML Issuing Authorities and their associated Test Laboratories in Scheme A or B are the same, but the method for

demonstrating compliance is different. OIML Issuing Authorities are required to demonstrate their compliance with ISO/IEC 17065 or ISO/IEC 17020 including additional requirements and Test Laboratories are required to demonstrate compliance with ISO/IEC 17025. Participating in Scheme B is sufficient to demonstrate compliance based on self-declaration with some additional supporting evidence. However, compliance shall be confirmed by peer evaluation based on accreditation or peer assessment for participating in Scheme A.

The OIML and OIML MAA systems represent the old approach for mutual confidence among the OIML members in the measurement results under legal metrology control. The OIML Certification System represents the new approach for mutual trust among the OIML members in the measurement results under legal metrology control. The old approach is not applicable anymore to the OIML members.

The global legal metrology perspective is located within this Organization, and it reflects through the harmonization legal metrology process, as well as trade and administrative barriers removal with the uniform approach in this field. Considering that OIML provides infrastructural support for developing countries, countries that still need to achieve the OIML membership are motivated to be involved in the most significant legal metrology organization in the world to improve their legal metrology systems. As for developed countries, their motive is a constant improvement of their metrology systems through exchange of experience with other countries.

The following OIML recommendations are used for testing medical devices with metrological characteristics, as follows:

- R 149—Non-invasive automated sphygmomanometers
- R 148—Non-invasive non-automated sphygmomanometers
- R 135—Spectrophotometers for medical laboratories,
- R 115—Clinical electrical thermometers with maximum device
- R 114—Clinical electrical thermometers for continuous measurement
- R 26—Medical syringes, R 89—Electroencephalographs—Metrological characteristics—Methods and equipment for verification
- R 103—Measuring instrumentation for human response to vibration
- R 104—Pure-tone audiometers
- R 122—Equipment for speech audiometry.

All these recommendations are composed of metrological and technical requirements. Based on these requirements, it is possible to perform type approval and verification procedure. All these recommendations are well known to the metrology community, and they could be used for testing medical devices with metrological characteristics. In addition, these recommendations are accepted worldwide what represents a massive benefit for all included parties in the legal metrology framework.

2.2 Regional Legal Metrology Organizations

In addition to the International Organization of Legal Metrology—OIML there are also other regional legal metrology organizations. The regional legal metrology organizations aim to accomplish exchanging information among countries and their economies. They also have the aim to achieve a harmonized and consistent approach for fulfilling the legal metrology requirements in their region. The regional organizations for the legal metrology are [2]:

- European Regional Organization of Legal Metrology—WELMEC [19]
- Inter-American Metrology System—Legal Metrology Working Group (SIM - LMWG) [20]
- Asia–Pacific Legal Metrology Forum (APLMF) [21]
- Euro-Asian Cooperation of National Metrological Institutions (COOMET) [22]
- Euro-Mediterranean Legal Metrology Forum (EMLMF).

2.2.1 Western European Cooperation in Legal Metrology—WELMEC

The legal metrology system is composed of the technical and administrative procedures established by the laws and authorized bodies with the purpose to guarantee the quality of measurement results performed during the commercial transaction, official controls, etc.

WELMEC (Western European Cooperation in Legal Metrology) was established in 1990 by signing the Memorandum of Understanding among 18 [19] Member States that represented the authorized legal metrology bodies in the European Union and three EFTA [23] Member States. WELMEC Committee is composed of three separate categories, and they are: Members, Associate Members, and Observers. At the beginning of the organization establishment, there were altogether 18 Members and 10 Associated Members. The Associated Members come from the Central and Eastern Europe countries. WELMEC Members are national bodies for legal metrology in the Member States of the European Union and EFTA, i.e., altogether it contains 31 Members and 6 Associate Members. WELMEC primary purpose is to establish a harmonized structure in application of European Legal Metrology System as well as [19]:

- Developing the legal metrology confidence among national bodies
- Harmonizing the legal metrology activities
- Identifying the legal metrology specific needs such as certification, and testing
- Exchanging information among the Member States
- Promoting the legal metrology system for the purpose to remove trade barriers
- Promoting consistency in interpretation and application of regulatory documents including suggestions for facilitating their implementation
- Identifying technical problems that could be subject for cooperation
- Maintaining relationship with other relevant bodies with interest in the legal metrology system

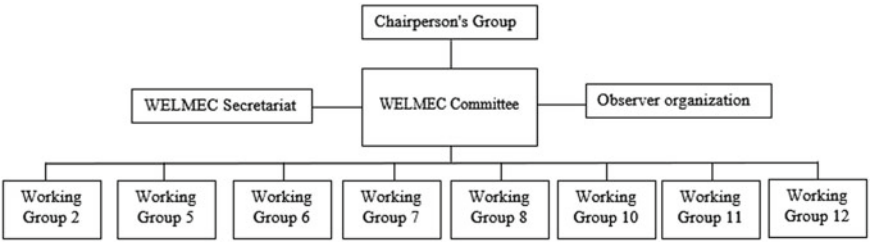

Fig. 1 WELMEC organization scheme

- Supporting trends and establishing criteria for the legal metrology system and maintaining channels for continued transfer of knowledge.

WELMEC, the European Commission, and the European Union Council are responsible for implementing and developing the legal metrology system in the European Union. The WELMEC Committee is composed of the Members and Observers delegates and other regional bodies interested in the legal metrology system in the European Union. The Committee meets once a year, and its work is supported by the WELMEC working groups. In addition to this, the organization working groups draft guidelines for harmonizing the legal metrology system implementation in the European Union. This approach protects European citizens from fraud measurements that could influence their health or commercial transactions.

WELMEC gives access to countries that are not a part of the European Union, but they are located in Europe. In this way, these countries promote their legal metrology systems and harmonize them with the European Union legislation. Furthermore, a unique economic field is created, and there are no trade barriers that give potential for developing their economies and societies.

To strengthen and develop a WELMEC role in cooperation, in November 2019, WELMEC members founded a formal legal entity. All association activities are continued by WELMEC e.V., established in Braunschweig (Germany) by September 2020 (Fig. 1).

WORKING GROUP 2 (Non-automatic and Automatic Weighing Instruments) implements Directive for Non-automatic Weighing instruments—NAWI (2014/31/EU) [24] and Measuring Instruments Directive MID (2014/32/EC) [25] regarding Automatic weighing instruments (AWIs). These directives are considered from the legal metrology perspective and their implementation into them. In addition to this, the working group considers the following OIML recommendations such as OIML R 47—Standard weights for testing of high capacity weighing machines, OIML R52—Hexagonal weights—Metrological and technical requirements, OIML R111—(all parts) "Weights of classes E_1, E_2, F_1, F_2, M_1, M_{1-2}, M_2, M_{2-3} and M_3", and OIML 134—(all parts) "Automatic instruments for weighing road vehicles in motion and measuring axle loads" for harmonizing the European legal metrology system with the international one.

WORKING GROUP 5 (Measurement Surveillance): establishes the legal metrology confidence by cooperating with the WELMEC Member States. In addition to this, this working group promotes equally valuable metrological control levels in the European Union. Also, it drafts the guidelines for the market surveillance and inspection among the WELMEC members.

WORKING GROUP 6 (Pre-packed products) implements directives and regulations that are related to these products (pre-packed products, nominal quantity, packaging, and sampling). Also, the working group has a platform for exchanging information. This platform deals with each question that refers to pre-packed products sold in a particular quantity given in the European or National legislation. Furthermore, the group provides the European Commission advice about aspects that need to be considered in the new regulations and existing ones. Also, the working group develops guides for pre-packed products.

WORKING GROUP 7 (Software) is responsible for harmonizing the software conformity assessment procedure for measuring instruments. These activities are carried out through the working group guidelines. In addition to this, the working group uses the OIML recommendations in its work. Furthermore, this working group has a subgroup which deals with digital transformation from the legal metrology perspective.

WORKING GROUP 8 (Measuring Instrument Directive) implements Measuring Instruments Directive (MID) and exchanges information among the WELMEC members. Furthermore, this working group considers the WELMEC and OIML definitions and explains where differences are noticed.

WORKING GROUP 10 (Measuring equipment for liquids other than water) is responsible for harmonizing procedures for type approval and first verification for non-water fluids by developing guidelines. The working group uses Measuring Instruments Directive (MID) and the OIML recommendations in its work, such as OIML R 117—Dynamic measuring systems for liquids other than water, OIML R80—Road and rail tankers with level gauging, OIML R81—Dynamic measuring devices and systems for cryogenic liquids, etc.

WORKING GROUP 11 (Utility Meters) is responsible for harmonizing the legal metrology system related to utility meters by implementing Measuring Instruments Directive (MID). It provides a support to new measurement techniques for measuring instruments covered by the directive scope and its application.

WORKING GROUP 12 (Taximeters) considers Measuring Instruments Directive (MID) and other regulatory documents or harmonized standards related to taxi meters, and it examines other aspects that impact taxi meters in vehicles (signal, additional devices, etc.), not only in inspection, application, and subsequent verification.

More about the WELMEC working groups and their work can be found on their official website.

2.2.2 Inter-American Metrology System—Legal Metrology Working Group (SIM -LMWG)

SIM has 34 Member States from the Organization of American States (OAS). SIM aims to promote international cooperation and interoperability among their members and establish regional cooperation with other regional legal metrology organizations. In addition to this, SIM promotes and supports an integrated measurement system in Americas.

2.2.3 Asia–Pacific Legal Metrology Forum (APLMF)

APLMF consists of the authorized bodies that come from the legal metrology field. In addition to this, APLMF aims to develop the legal metrology and promote free and open trade in the region, through harmonization as well as removal of technical or administrative barriers when it comes to the trade field of legal metrology.

2.2.4 Euro-Asian Cooperation of National Metrological Institutions (COOMET)

COOMET is composed of the national metrology institutes that are in the Central and Eastern Europe. It was established in 1991, and it was renamed to "Euro-Asian Cooperation of National Metrological Institutions" in 2000 and by now it has had 19 Member States.

2.2.5 Euro-Mediterranean Legal Metrology Forum (EMLMF)

The Euro-Mediterranean Legal Metrology Forum (EMLMF) is an international organization that aims to promote the harmonization of legal metrology practices and regulations in the Euro-Mediterranean region. The EMLMF, based in Marrakech, Morocco, brings together representatives from national metrology institutions, industry, and other stakeholders to discuss and collaborate on legal metrology issues. The mission is to promote the use of metrology as a tool for trade facilitation, consumer protection, and environmental sustainability.

3 Legal Metrology System—Past, Present

The legal metrology origin and current overview status at the international and European levels are given in this section. In addition to this, the other regional legal metrology organizations are presented previously.

In the past, the legal metrology evolved parallel to the civilization that required measurement consistencies in everyday life. The country and legal metrology relationship is mutual and very close. Each country needs information from the legal metrology system to protect its citizens. In addition to this, the legal metrology needs a country authority to ensure the measurement uniformity [8]. The first step for organizing the legal metrology system, as mentioned above, was signing the International Convention. By signing this contract, the International Organization of Legal Metrology (OIML) was established. However, the contract did not cover the legal metrology definitions, so the first document which included these definitions was OIML (OIML D1) document [9].

The OIML consists of Project Groups (PG) within the OIML's Technical Committees (TC) and Subcommittees (SC). These structures develop the Organization's technical publications. OIML works closely with other international organizations such as the International Bureau of Weights and Measures (BIPM) and International Organization for Standardization (ISO) to ensure compatibility between each organization's work. The organization has no legal authority to impose solutions on its members, but its Recommendations are often used by Member States as part of their own domestic law. Just like, European NMI's gathered in the European Association of National Metrology Institutes (EURAMET) to ensure internationally competitive measurement infrastructure for Europe, a body at European level was developed that promotes European cooperation in the field of legal metrology. That body is named WELMEC, European Cooperation in Legal Metrology (originally Western European Legal Metrology Cooperation). The members of WELMEC are drawn from the national authorities responsible for legal metrology in European Union (EU) and European Free Trade Association (EFTA) member states. The International Organization of Legal Metrology (OIML) and European Organization of Legal Metrology (WELMEC) are presented in the previous sections by including their activities, roles, and tasks. Furthermore, the other regional organizations and main ideas for the future developing in the legal metrology field are presented.

Throughout history, the country role in the legal metrology is reflected through the adoption of regulations for governing the legal metrology system to protect its citizens. Monitoring the legal metrology field helps in creating confidence in conducted activities. On the other hand, the legal metrology requires complete independence in the measuring process, making it one of the main reasons for linking the legal metrology with a country, i.e., the country economy. More developed countries imply existing active legal metrology systems and higher confidence in measurement results. Less developed countries usually have less developed legal metrology systems, but not necessarily lower confidence in measurement results. Each country was developing its legal metrology system throughout history. These different approaches and requirements for implementing the legal metrology system are contributed to the legal market fragmentation. It is certain that such a fragmented system inevitably generated trade barriers by imposing different country requirements for the measuring instruments, methods, and measuring units.

In the present, legal metrology has expanded to include a wider range of measurements and measuring instruments. Governments have established regulations and

standards for a variety of measuring instruments, including scales, meters, gauges, and other devices including medical devices, used to measure weight, volume, length, temperature, and other physical quantities. Advances in technology have also led to the development of more sophisticated measuring instruments. As a result, legal metrology has become increasingly important in ensuring that these instruments are accurate, reliable, and consistent across different locations and industries. Today, legal metrology systems typically involve government agencies responsible for enforcing regulations and standards related to measuring instruments. These agencies may also be responsible for inspecting and testing measuring instruments to ensure that they meet these standards. In many countries, legal metrology also involves the use of seals or other marks to indicate that an instrument has been tested and verified to meet certain standards. These seals and marks can help to ensure that consumers can trust the measurements provided by the instrument. Overall, the legal metrology system has become an essential component of modern society, helping to ensure that measurements used in trade, commerce, health and safety, and the environment are accurate, reliable, and consistent. As technology continues to advance, it is likely that legal metrology will continue to evolve to meet the changing needs of society and industry.

3.1 European Union Legislation Framework

European countries had individual national legislations for measuring instruments until the 1990s, the so-called Old Approach. The old approach directives provide very detailed technical requirements for all products. All provisions given by these directives are binding. The old approach directives implement harmonization which lays down technical specifications for certain products. By the old approach directives, there is no common harmonization model, but each field is regulated separately. Entry into force Directive for Non-automatic Weighing Instruments 90/384/EEC (NAWI) since 1993 and Directive for Measuring Instruments 2004/22/EU (MID) since 2006, the legal metrology harmonization process in the European Union has started, so-called New Approach. The European Union Legislation is based on a dual approach i.e., Scheme approach, it is based on New and Global Approach, and Sectoral Approach. New Approach has a significant role in supporting free movement regarding the European Union market. In addition to this, New Approach limits countries intervention for some important issues and allows companies to choose a module on how to fulfill their obligation towards society.

The new approach directives require fulfilling all requirements prescribed by mentioned directives before measuring instruments are launched on the market. A manufacturer is obliged to fulfill these requirements or Notified Body. A product (measuring instrument) after conformity assessment procedure is marked with "CE" mark [26] and it is accepted by all European Union Member Countries. In addition, not fulfilling these requirements for the product that is launched on the market brings sanctions for the manufacturer according to Member Countries provisions. The CE

mark symbolizes that the product is harmonized with all requirements from the new approach directives. Technical barriers in the legal metrology field are removed by entering into force of these directives, and conditions for a unique economic space in the European Union are formed.

Furthermore, Directive (NAWI) prescribes provisions for the weighing measuring instruments, from the manufacture to the application, which are used in commercial, legal, medical, and industrial purposes. Thus, Directive (MID) prescribes provisions for the following measuring instruments such as water meters, gas meters, electricity meters, heat meters, fuel meters, automatic weighing instruments, taximeters, materialized measures, dimensional measuring instruments, and exhaust gas analysers (in total ten instruments).

Although these directives prescribe provisions for the measuring instruments that are used in the legal metrology scope, all European Union Member Countries do not have the same legal metrology scope. The member countries can decide which measuring instruments are subject to legal control in their country. The information about individual European Union Member Country legal metrology scope [27], i.e., Member Country and Associate Members can be found on the official WELMEC website.

In line with the new approach, the authorized national bodies designated competent bodies for testing the legal measuring instruments for the European Union market. The measuring instruments that have EC Type Approval and EC Initial Verification are presented on the European Union market without any additional re-examination and re-approval by third parties. By this approach, a unique economic field is formed. According to the new approach directives (NAWI and MID), all manufacturers are obliged to mark measuring instrument with the CE mark, additional metrological information, and notified body number. All notified bodies have their number that allows their identification. In addition to this, a manufacturer can perform verification if its quality management system is assessed positively by Notified Body. In this case, the manufacturer uses the Notified Body number for launching its products on the market [28]. The Notified Bodies prove their competencies through an accreditation process [29] or self-declaration (National Metrology Institutes) fulfilling criteria for acquiring the notified body status. The notified bodies status in the European Union can be checked in the NANDO [30] database.

There are 91 notified bodies for Directive (MID), 71 bodies for Directive (NAWI), and 34 bodies for Medical Device Regulation—MDR (2017/745). Medical Devices Regulation (MDR) deals with medical products. In addition to this, it deals with medical products which have metrological characteristics. These medical products are not covered by the legal metrology system in the European Union. These devices are important for society health protection. Based on this fact, these medical products, in some countries, are covered by the legal metrology system. The most notified bodies are nominated for Directive (MID). This consequence results from approved and launched devices on the market covered by MID and NAWI directives.

The conformity assessment procedure implies that testing instruments, single instrument, or instrument series, are harmonized with the legal provisions applicable

to this instrument type [31]. This procedure, together with Directive (MID) requirements, is done by selecting an appropriate Directive (MID) conformity assessment module. The conformity assessment procedures are described in Directive (MID) annexes. The type of approval document represents a decision with legal relevance that a particular type complies with the relevant requirements. In addition to this, it confirms that this type of instrument can be used in the legal metrology system and provides reliable measurement results in a prescribed time interval. The measurement instruments verification procedure is the conformity assessment procedure other than type approval that results in adding a verification mark and/or issuing a verification certificate. The certificate proves and confirms that an instrument compiles the legal requirements. The medical devices with metrological characteristics from the legal metrology perspective represent a challenge for the legal metrology, i.e., placing them into the legal metrology framework to protect society health by providing accurate and precise measurement results.

The European Parliament Decision (768/2008/EC) [32] from 2008 established the procedure for launching measuring instruments i.e., it has set up the conformity assessment procedure. Also, the decision contains the European Commission obligation to allow exchanging information among authorities responsible for the national designation policies to ensure coordination and cooperation between the bodies according to the existing laws or other legislation, and to act as a group of the bodies [32]. According to this decision, NMi [33] (the Netherlands) took the initiative to establish the European platform for coordinating the bodies that work in the legal metrology field. The following bodies, CMI [34] (Czech Republic), LNE [35] (France), NMO [36] (UK), METAS [37] (Switzerland), and NMI (the Netherlands), contacted the other bodies to establish the European Platform. In this way, the platform for cooperation among the Notified Bodies in the European Union was formed in 2010, so-called NoBoMet. This is the European platform for collaboration with the Notified Bodies that act in the legal metrology system [38]. The platform purpose is to optimize conditions under the Notified Bodies work and make the conformity assessment procedures more transparent for all measuring instrument manufacturers. Thus, the platform promotes performance equality among Notified Bodies.

3.2 Legislation Framework in United States of America

The legislative framework in the United States of America is complex, structured around a federal system of government. The legislative division of the federal government is responsible for creating laws, which are subsequently enforced by the executive division and interpreted by the judicial division [39].

The oversight of medical devices in the United States falls under the responsibility of the Food and Drug Administration (FDA), which is responsible for ensuring that the medical devices sold or distributed in the United States are safe and effective. The FDA's regulation of medical devices is governed by numerous laws and regulations.

In accordance with the FDA's regulatory framework for medical devices, these devices are classified into one of three categories, depending on the risk level they pose to patients. Devices classified as Class I are considered low-risk devices, examples of which are tongue depressors and bandages. These devices are subject to the least amount of regulatory oversight. Class II devices are considered moderate risk, for example, powered wheelchairs and pregnancy test kits, and necessitate a more thorough premarket review process. Class III devices are deemed high-risk, including implantable pacemakers and artificial heart valves, and demand the most rigorous premarket review process.

Apart from the three primary classes of devices, there are also specific types of devices subjected to unique controls. Examples of such devices are those employed to diagnose or treat life-threatening or rare diseases, or those that use novel or unconventional technology.

In order for a medical device to be introduced to the US market, it must first undergo clearance or approval by the FDA, a process that may necessitate clinical trials, laboratory examinations, and other types of data to demonstrate the device's safety and effectiveness. Upon receiving FDA clearance or approval, the device becomes subject to continuous post-market surveillance by the FDA to ensure that it remains safe and effective, and to recognize any potential safety issues that may develop over time [40].

To ensure the safety of medical devices in the market, the FDA has mandated Medical Device Reporting (MDR) that necessitates medical device manufacturers, importers, and user facilities to inform the agency about specific adverse events or issues related to their products. The primary purpose of MDR is to enable the FDA to identify and track any potential safety issues with medical devices available on the market. The intention behind the reporting requirements is to offer timely and accurate data to the FDA about possible safety problems related to medical devices. Based on this information, the agency tracks the safety of medical devices available on the market and takes necessary actions, such as issuing safety alerts or recalls, if required [41].

Along with the obligation to report certain adverse events or product issues, the MDR regulation mandates medical device manufacturers to create and maintain protocols for detecting and disclosing adverse events and record all adverse event reports and manufacturer follow-up actions. Not complying with the MDR requirements may lead to the FDA taking regulatory actions like issuing warnings, imposing fines, and confiscating products. The FDA may also conduct inspections to ensure that medical device manufacturers comply with the MDR regulations as well as other regulatory requirements.

3.3 Middle East and North Africa Legislation Framework

The regulatory frameworks for medical devices in the Middle East and North Africa (MENA) region vary widely among the diverse range of countries within it. Despite

this, there are some common features and characteristics that can be identified [42]. In numerous MENA countries, the regulatory framework for medical devices is still evolving and may be comparably weaker than those in developed countries. Often, there is inadequate capacity, expertise, and infrastructure to regulate medical devices effectively [43].

There are regulatory bodies in the MENA region, such as the Saudi Food and Drug Authority, the Emirates Authority for Standardization and Metrology, and the Jordan Food and Drug Administration, which have been established to register medical devices, carry out pre-market evaluations, and implement post-market surveillance [44]. Medical devices in MENA countries are classified based on their risk level, and the classification criteria may vary from country to country. According to GHTF/IMDRF guidelines, manufacturers are responsible for determining the classification of their devices, while Regulatory Authorities (RA) establish procedures for conformity assessment. Classification of a Medical Devices has to be done accurately as the risk class determines the appropriate conformity requirements. An inaccurate classification may result in an unsuitable conformity assessment procedure for the specific device. The GHTF/IMDRF has developed a classification system for medical devices consisting of four classes, with Class A indicating the least hazardous and Class D the most. The classification should be based on guidelines derived from the medical device's potential to cause harm to the user or patient, its intended use, and the technologies it employs [45].

In MENA countries, medical device manufacturers usually have to apply to the appropriate regulatory body in order to gain regulatory approval. This application includes various documents, such as clinical data, technical specifications, and evidence of conformity with applicable standards. The regulatory bodies may conduct a review of the application and, in certain circumstances, ask for additional information or data before granting approval [44].

Foreign medical device manufacturers may face challenges in entering the market in some MENA countries due to the preference for locally manufactured medical devices. Moreover, in certain countries, regulatory approval may only be granted after local certification or testing has been completed [46]. To succeed in entering the MENA market, medical device manufacturers need to remain informed of the regulatory requirements, since the regulatory landscape keeps evolving. Also, it is imperative to work with local partners who possess the necessary experience and knowledge of the regulatory environment in the region [47].

3.4 Legislation Framework in Asia—Pacific Region

While the legislation framework for medical devices in the Asia–Pacific region differs significantly from country to country, there are some shared features and patterns that can be identified.

The regulation of medical devices in the Asia–Pacific region is carried out by national regulatory bodies that create and implement the applicable laws, regulations, and guidelines. Notable regulatory bodies in the region include the Japanese Pharmaceuticals and Medical Devices Agency (PMDA), the Australian Therapeutic Goods Administration (TGA), the Chinese National Medical Products Administration (NMPA), and the South Korean Ministry of Food and Drug Safety (MFDS) [48].

A trend commonly observed in the Asia–Pacific region is the adoption of regulatory frameworks that resemble those employed by the European Union. This includes the use of the European Medical Devices Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR) as models for medical device regulations in countries such as Australia and Japan. The implementation of these frameworks has led to an increased focus on ensuring the safety and effectiveness of medical devices and harmonizing regulations across borders [49].

Another trend is the emphasis on post-market surveillance and vigilance, with regulatory bodies increasingly focusing on monitoring the safety and effectiveness of medical devices once they are on the market. This includes the use of adverse event reporting systems and the establishment of post-market surveillance programs. Additionally, the importance of traceability and labelling requirements has become more emphasized [50].

In addition, some countries in the region have established specific requirements for certain types of medical devices. For example, in Japan, there are specific regulations for software as a medical device, while in Australia, there are regulations for in vitro diagnostic medical devices. China has also implemented specific requirements for clinical trials for medical devices [51].

The regulatory landscape for medical devices in the Asia–Pacific region is complex and rapidly evolving. Medical device manufacturers must stay up to date with the latest regulations and guidelines in each country they wish to market their products in and work closely with local partners to navigate the regulatory process. In addition, the region is seeing an increased emphasis on harmonizing regulations across borders to promote greater consistency and standardization in the regulatory landscape [52].

4 Legal Metrology System—Future

The future of the legal metrology system is likely to be shaped by several factors, including advances in technology, changes in consumer behaviour and expectations, and the continued growth of international trade and commerce. Taking into account networking at the globalization level, the needs and demands for the legal metrology system are increasing. As international trade and commerce continue to grow, there will be a greater need for global harmonization of legal metrology practices. This may involve the development of new international standards and regulations, as well

as greater cooperation and information sharing between national metrology institutes and other organizations. In line with this, all countries should recognize the legal metrology system as an important part of their society and future developing. Identifying the legal metrology as a key driver for society developing means adopting regulations for harmonizing the legal metrology system with the international one. The harmonized legal metrology system is achieved by taking part in the work of international, regional, and local legal metrology organizations. The legal regional metrology organizations and international ones have an important role in shaping the future legal metrology system throughout developing methods, exchanging information, drafting documents and recommendations, and mutual test recognition reports and certificates issued by the authorized bodies. Accomplishing the harmonization process in the legal metrology framework successfully, the following steps should be done through harmonizing measuring instruments requirements, testing methods, testing reports, and certificates [4, 53].

The legal metrology development is encouraged by expanding new research fields such as digitalization in metrology and vice versa. These new fields drive society developing and bringing better society protection, what the ultimate goal of legal metrology in the community is. Furthermore, these new fields will have an impact on developing new products and new tools for the legal metrology purposes. By appearing in the new products and tools, the new uniform legal metrology requirements have to be developed which ensure trustworthiness in measurement results. In addition to this, new technologies are present such as smart mobile phones with built-in sensors for monitoring the legal metrology requirements, DNA chips or micro-chips for analytical systems, etc. [54]. The ongoing global digital transformation is impacting the field of medical device management, as more measuring instruments become digitized, which requires the legal metrology system to adapt to ensure accurate, reliable, and secure digital measurements. This adaptation may involve the development of new testing and calibration procedures, as well as the establishment of new regulations and standards related to digital measuring instruments, to collect data and use it for informed, evidence-based decision making in medical device management.

The number of applications of Data Science in scientific and legal metrology is increasing. Statistical concepts are combined by data science with algorithms to extract knowledge from measurement data. Data science approaches help reduce extensive data and remove the information of interest, especially where large amounts of data are collected. The application of Data Science for processing data and transferring results is needed for challenges such as energy transition and climate change. Some National Metrology Institutes (NMIs) have established new groups dedicated to applying data science techniques in scientific and legal metrology to create the best practices for measurement data processing and dissemination [55]. The problem is that current regulations need to regulate these new techniques. Therefore, additional rules are needed, especially from the legal metrology perspective. In addition, measurement uncertainty quantification is an essential part of legal metrology. The measurement results are mainly used for assessing compliance with some regulatory tolerance limits. In line with that, the measured value and associated expanded

uncertainty are often taken as inputs for applying decision rules. The OIML G 1–100 document gives inputs for calculating measurement uncertainty from the legal metrology perspective.

The legal metrology users expect to be protected in modern digital ways. This implies that communication should be digital with digital certificates, i.e., paperless. These digital reports should be machine-readable (computer vision), i.e., read and processed by software. Furthermore, applying digital technologies should be accepted by the legal metrology service providers to meet society and regulator expectations. For international institutes and bodies to communicate with each other, some international bodies for scientific and quality infrastructure have signed a "Joint Statement of Intent" that formulates the readiness for coordination and cooperation in broader digital transformation [56]. The digital transformation consequences and outcomes can be found in almost all areas, such as the health sector, industry where the sustainable use of resources is enabled by using digital technologies such as blockchain and cloud.

As for the legal metrology system from the medical devices perspective, the most significant challenges are imposed by digital transformation. For example, the first wearable devices were certified as medical devices. These devices are not used only for home care. Furthermore, healthcare facilities have been starting using these devices. These devices (sensors) are used, e.g., for measuring blood pressure, heart rate, sugar levels, oxygen saturation, etc. From the legal metrology perspective, it should be developed entirely new traceability routes and a legal metrology framework. Machine learning methods have a high potential for supporting future clinical decision-making. Currently, there are no universally accepted approaches for validating these methods objectively. Partially because of the lack of resources and the complexity of building up such advanced capabilities, only a few national metrology institutes are currently taking their first steps to standardising machine learning quality assessment methods in the medical field. To sum up, these new wearable medical devices promise faster diagnosis and earlier access to the necessary treatment for the benefit of patients [57]. On the other hand, this new challenge should be accompanied by the legal metrology requirements.

The legal metrology role system will remain the same by ensuring accurate and precise measurements to protect society interest.

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Medical Device Maintenance Regimes in Healthcare Institutions

Clark Daniel

Abstract Maintenance of medical devices is a key aspect of ensuring the safety and reliability of healthcare systems. Healthcare facilities are required to adhere to strict maintenance regimens to prevent device failures and maintain optimal device performance. This paper describes the current state of medical device maintenance in healthcare facilities, focusing on the challenges and opportunities presented by new technologies. The various maintenance regimes used by healthcare facilities are commented on, including preventive, corrective and predictive maintenance. It also discusses the impact of regulatory requirements on maintenance practices and the importance of staff training and education in ensuring the effectiveness of maintenance programs. Ultimately, the need for healthcare facilities to develop comprehensive maintenance regimens tailored to their specific needs and to continually evaluate and improve their maintenance practices to ensure the safety and effectiveness of medical devices is emphasized.

1 Introduction

1.1 Health Technology Management

Modern healthcare is hugely dependent on medical equipment. Responsible healthcare providers will maximise the potential of this equipment for the benefit of patients and careers whilst minimising the risks. As the World Health Organisation (WHO) states: *Medical devices are assets that directly affect human lives. They are considerable investments and in many cases have high maintenance costs. It is important, therefore, to have a well-planned and managed maintenance programme that is able to keep the medical equipment in a health-care institution reliable, safe and available for use when it is needed for diagnostic procedures, therapy, treatments and*

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monitoring of patients. In addition, such a programme prolongs the useful life of the equipment and minimizes the cost of equipment ownership [1].

Whilst considering medical equipment maintenance it is important to recognise that it is only one part of a wider range of activities required to ensure safe and effective utilisation of technology in healthcare, a range of activities generally referred to as Healthcare Technology Management (HTM). Although this chapter deals primarily with maintenance regimes, we touch here on those wider activities as they have considerable impact on medical equipment maintenance.

The previous version of the book Inspection of Medical Devices offered significant knowledge about the impact of medical device development on healthcare delivery, emphasizing the importance of managing health and confronting the difficulties that arise along the way [2].

It is important to recognise that HTM activities start before equipment is even delivered to the healthcare facility and continue throughout its lifetime until after it has been decommissioned. It is convenient to describe the tasks required in a comprehensive HTM programme by reference to the medical equipment lifecycle.

1.2 Medical Equipment Lifecycle

The phrase cradle to grave if often used when describing the support needed for medical equipment. However, it might better be referenced as 'conception to afterlife' since consideration of how to manage medical equipment should start before any thought of acquisition and should continue beyond the point of decommissioning [3]. Various depiction of this 'lifecycle' have appeared in the literature and we present out representation here in Fig. 1. By the nature of a 'cycle' you can start at any point and continue round but for convenience, we start here at the top with Integrated Planning.

1.2.1 Integrated Planning

Healthcare Technology Management should be patient-centric: everything starting with the patient needs. In the Planning phase of the equipment lifecycle all aspects of the provision of healthcare for our patients should be considered. This will include current and future patient needs, current and future healthcare system needs and limitations, physical resources (available buildings and facilities) and financial resources. The outcome of the planning phase will be a requirement specification centred on patient needs.

1.2.2 Evaluation and Selection

There might be a number of technical solutions that can meet this requirement specification and the Evaluation and Selection phase of the lifecycle seeks to identify the

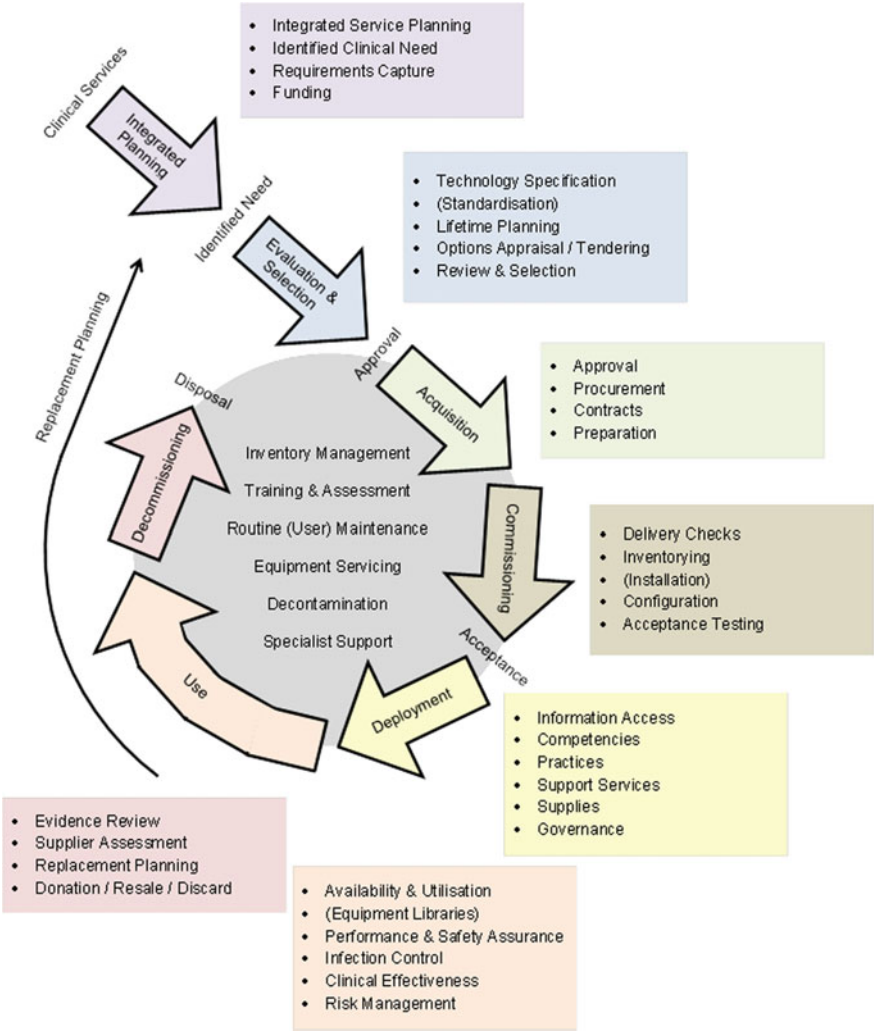


Fig. 1 Medical equipment lifecycle

solution that best meets the need within the constraints of the healthcare organisation. Usually this means finding a compromise between technical functionality and quality on the one hand with facilities and finances on the other.

A key part of the evaluation and selection phase is to consider the whole life management of the equipment. Some equipment might meet the need now but require significant resources and planning to keep it in a condition required to continue to meet the need into the future. Assessing the anticipated equipment maintenance regime is therefore a key aspect of this phase of the lifecycle and must be appropriately waited in any selection criteria.

1.2.3 Acquisition

Generally, the Acquisition phase is processed by procurement teams and based on contracts and finances. However, it is important to consider the anticipated equipment maintenance regimes during this phase. Who will be responsible for the maintenance (in-house teams, the original equipment manufacturer (OEM) or third party agents)? Are resources available (through contracts or within the in-house teams)? Are the requirements of the maintenance programmes understood and are the responsibilities for carrying them out clearly defined? Are the technical teams who will be undertaking this work suitable qualified, do they have enough staff to take on the work, do they have suitable facilities (workshops) and tools (test equipment) to carry out the work?

These questions should be asked and appropriately answered before committing to purchase any new equipment to avoid difficulties and short-falls afterwards.

1.2.4 Commissioning

The Commissioning Phase of the lifecycle takes the equipment from first delivery on site to the point at which it can be safely deployed into clinical use. It is clearly a key phase and one at which all the details of the future management of that equipment must be confirmed. This will include delivery checks, inventorying, installation (connecting to hospital facilitates as appropriate), configuring (setting up to meet the hospital's needs) and safety and functionally testing (to make sure the equipment is working safely and as intended by the manufacturer). Commissioning will also include a range of ancillary (that is, non-clinical engineering) tasks such as establishing the required IT connectivity (if required), special safety measures for example radiation protections (if required) and decontamination (including first time sterilisation if required and processes for future re-processing).

A key task during commissioning is to ensure that the future maintenance regimes are understood and planned (see Sect. 3.1). Processes should be in place to prevent the equipment from being deployed until these maintenance regimes are confirmed to be in place.

1.2.5 Deployment

This phase of the lifecycle is where the equipment is handed over to clinical teams for use. During this phase it is important to confirm that clinical teams are competent to use the equipment. Requirements for training and competency assessment will have been confirmed during the earlier phases but need to be completed before deployment. Similarly, processes need to be in place to ensure clinical teams have access to accessories and consumables, that any user maintenance is understood and can be performed locally and that clinical staff know how to contact support services (in the event of breakdown and, importantly, for future planned maintenance).

1.2.6 Clinical Use

It is to be anticipated that once deployed into clinical use, the medical equipment will continue to deliver safe and effective healthcare for many years. However, planned maintenance is often essential to keep the equipment in the right condition to perform safely and effectively. Additionally, in the event of a fault occurring or of the equipment being damaged, it is important to ensure timely and appropriate corrective maintenance (repairs) to keep clinical staff and patients safe.

1.2.7 Decommissioning and Replacement Planning

There will come a point when the equipment is no longer appropriate for use in the healthcare organisation. Perhaps because it can no longer be effectively maintained (parts and labour to keep maintaining it are either unavailable or too expensive), or it becomes obsolete (the manufacturer no-longer supplies spares and accessories or recommends its removal from service), or because better technology exists that can replace it or perhaps because the hospital no longer needs that technology because it no longer performs that clinical service. Whatever the reason, when the equipment is no longer required or appropriate for continued clinical use it needs to be decommissioned and, usually, replaced. Replacement planning should ideally start long enough before required decommissioning to ensure the replacement devices are ready for deployment before the old device needs to be removed.

1.3 Medical Equipment Maintenance

If a healthcare organisation requires medical equipment to provide services to its patients, then it needs to have a maintenance programme for that equipment. The size and complexity of that programme will be determined by the size and complexity of the healthcare organisation but principles will remain the same. Medical Equipment Maintenance is most usually associated with the *Clinical Use* phase of the equipment lifecycle but as we can see from Sect. 1, it is also important to consider it during the evaluation and selection phase, the acquisition phase, the commissioning phase and the deployment phase. It is important to recognise that medical equipment maintenance applies equally howsoever the equipment was acquired: purchase, loan, consumables deal, research project or donation. The timescales and individuals involved might change depending on the acquisition circumstances but the principles outlined here will still apply.

We can divide medical equipment maintenance into three broad categories (Fig. 2).

The protocol outlined in this chapter pertains to the inspection of medical devices that possess a measuring function.

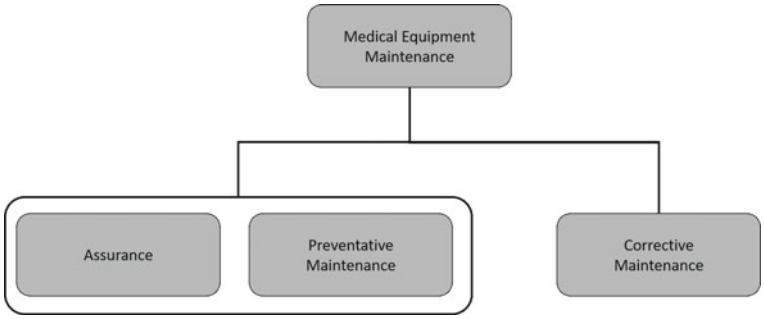


Fig. 2 Medical equipment maintenance—categories

1.3.1 Assurance

Assurance: a series of tasks or activities designed to provide assurance that the equipment is working safely and correctly (as the manufacturer intended) to within determined tolerances. Given the importance of medical equipment to modern healthcare, perhaps the single most important responsibility of any Clinical Engineering Department is to provide this assurance to clinical teams and ultimately to the patient, that the equipment required for their care is safe and working correctly. Manufacturers' technical manuals should instruct servicing teams what tests to undertake and what tolerances to accept. If medical equipment is found to be performing outside of these stated tolerances, service departments will need to correct this and consider if remedial action is required. See Sect. 3.7.

1.3.2 Preventative Maintenance

Preventative Maintenance: a series tasks or activities designed to extend the life of medical equipment and to prevent deterioration of performance to levels outside the manufacturers' expectations. Failure to undertake certain preventative maintenance tasks is likely to increase the risk of in service breakdown, with potentially serious patient safety issues and impact on clinical service delivery. Manufacturers should state a time period by which these required tasks and activities should be undertaken. Batteries might need replacing every two years, for instance, or filters replaced annually. These time periods are based on the probability of failure and are clearly, therefore, not exact, but responsible organisations should aim to service equipment within these time periods or as close as reasonably practical unless there is strong evidence to defer (see Sect. 3.1.4).

1.3.3 Corrective Maintenance

Often referred to as repairs, corrective maintenance is a series of tasks required when medical equipment is damaged or develops a fault. Medical equipment can develop faults or be damaged at any time so by their nature, repairs will be reactive and responsive. Some equipment will be urgently needed by a clinical service and therefore the servicing teams will need to respond quickly to affect the corrective maintenance and return the equipment to service. In other cases there might be less urgency and therefore it might be possible to plan to undertake the corrective maintenance at some point in the future. Servicing teams will need to consider if assurance testing and preventative maintenance is should be undertaken immediately post a repair. If the repair was minor in nature, perhaps just a fitting a new light bulb, there might be no need to undertake assurance and preventative maintenance tasks. More significant repairs, however, will merit assurance testing to make sure the equipment is still safe and performing correctly after the repair. See Sect. 4.5.

1.3.4 Modifications (Manufacturer-Instructed Device Upgrades and Safety Actions)

It is not uncommon for medical equipment manufacturers to implement upgrades to their devices during their lifetime. This is most common in the case of software revisions but can sometime also include hardware and firmware. Healthcare providers and clinical engineering services in particular should have systems in place to ensure they receive and act upon any manufacture instructed upgrades.

It is also not uncommon that manufacturers or local and regional competent authorities or regulators to issue safety alerts relating to medical equipment. Such alerts usually originate from incidents at healthcare providers or as part of the manufacturers' vigilance programmes. Healthcare providers and particularly clinical engineering services must have systems in place to ensure they receive these and act upon them.

Generally, upgrades improve the performance of a device and as such might be considered optional. Safety actions, on the other hand, will affect patient safety and should be considered essential.

1.4 Assurance and Preventative Maintenance (APM) Programmes

Whilst corrective maintenance can be required at any time, assurance and preventative maintenance are generally programmed at defined time intervals. Usually, both assurance and corrective maintenance are required at the same time so it is customary

to programme both these activities together and to establish assurance and preventative maintenance (APM) programmes. These APM programmes will be described more fully in Sects. 2, 3 and 4.

2 Assurance and Preventative Maintenance—Purpose

2.1 Safety Features and Essential Performance

Medical equipment can be intrinsically hazardous to patients or can provide features or functions which, if they were to malfunction or fail, would then lead to hazardous conditions for the patient. It is therefore important to consider both the safety features of the equipment and the essential performance features when considering APM.

Safety feature might include, for example: alarms to indicate when a device has encountered a hazardous setting, automatic 'failsafe' stops when dangerous conditions are approached, internal software limits to prevent unsafe settings being reached or cut-outs that prevent tampering.

Features or functionality that, if it were to fail or malfunction, would result in a hazard, are often referred to as the 'essential performance'. This might include, for example: blood warmers that need to keep the infused blood product at the correctly set temperature; mechanical ventilators that keep patients breathing; infusion devices that provide controlled drugs at a set rate.

It is clearly important that assurance be provided to the clinical staff (and through them to the patients) that these safety features and essential performance levels are being met at all times. The manufacturers' technical service manuals will describe these features and outline how a servicing team can check they continue to operate within expected tolerance.

If medical equipment malfunctions or fails while in clinical service, it might present a hazardous or adversely affect patient care. Sometime, that malfunction or failure will be obvious before any harm is done [4–6]. For example, the equipment doesn't turn on at all and the clinical staff have time to realise this and seek an alternative piece of equipment. But sometime that malfunction is not obvious to then clinical user. For example, a thermometer might go out of calibration, under-reading the temperature by a degree or two. In this case the patient's increased temperature, that could be a sign of serious untoward condition, is missed and the patient continues to deteriorate. Or perhaps an infusion device set to deliver 10 ml/h is actually delivering 15 ml/h. The staff would not notice the increased dose rate that, with some medications, could result in serious harm. In these cases, a programme to check the equipment is functioning as expected will provide the assurance needed that equipment continues to perform as expected.

If medical equipment malfunctions or fails while in clinical service it might affect the operational service capability. For example, if a theatre only has one operating microscope and it breaks down on the morning of the theatre list, then the whole

day's operations might have to be cancelled with the obvious inconvenience to staff and patients. A programme of preventative maintenance will reduce the chances of breakdowns and increase clinical service uptime.

If medical equipment malfunctions or fails while in clinical service it might lead to more expensive repairs later or even the need to replace the equipment. A programme of preventative maintenance will keep medical equipment in good condition longer and reduce costly repairs.

Some items of equipment will require assurance checks to confirm they are still performing within the manufacturers' tolerance but require little, if any, preventative maintenance. A pulse oximeter, for example needs to be checked to ensure it is continues to meet its essential performance and safety functions (alarms), but there is almost no servicing actions that will increase its longevity or reduce the risk of future breakdown.

Some items of equipment will require servicing tasks; components replaced or re-lubricated, filters changed, for example. Failure to do these servicing tasks at the right time will increase the risk of device malfunction or failure.

Many items of equipment require both the assurance checks and the preventative servicing and an APM programme will need to reflect these differing needs across the full fleet of medical equipment.

2.2 Purpose

A medical equipment maintenance programme forms the bed rock of most clinical engineering department services often representing the majority of the work undertaken. But why do we need to have a maintenance programme, what is the purpose?

2.2.1 Patient Safety

During the COVID-19 pandemic, regular inspections of medical devices with measurement functionality have been identified as critically significant in ensuring their effective operation while maintaining a secure patient environment is the foremost priority in managing medical equipment [7]. APM is an essential requirement of that. Many items of medical equipment are clearly intrinsically hazardous: electrosurgical units deliver large amounts of electrical energy into patients; ventilators need to work reliable to keep patients breathing; x-ray machines deliver potential harmful ionising radiation. But even apparently 'low risk' items might cause harm to patients if not working correctly: a simple thermometer, if under-reading a patient's temperature might result in a misdiagnosis of sepsis with significant consequences; a cot side on a bed might cause entrapment hazard if not properly maintained and an syringe driver might give harmful levels of medication if the over-infusion alarm is

not working correctly. Even the simplest devices can lead to problems for patients if not appropriately maintained.

2.2.2 Regulatory Compliance

It is a requirement under most regulatory systems (for example: UK MDR 2002 [8]) for a manufacturer of medical equipment to provide all the information needed to verify whether the device can operate correctly and safely, plus details of the nature and frequency of the maintenance and calibration needed to ensure that the device operates properly and safely at all times.

Healthcare organisations are not generally under the same obligation to undertake these actions but must be able to justify any decision not to. In most cases, a healthcare organisation will be under associated obligations to provide safe healthcare (for example: UK CQC [9]). These obligations will generally expect the organisation to provide risk-based approach to providing safe care for their patients. The easiest way to demonstrate this, in respect to medical equipment, will be by adherence to the regulatory requirements on manufacturer and then, where necessary, justifying any deviations from this. Most commonly, this deviation will be due to resource limitations, i.e. the healthcare organisation simply cannot afford to comply with every aspect of the manufacturer's requirements for maintenance for every single item of medical equipment. However, other factors might also apply—see Sect. 6 Risk-based management.

2.2.3 Asset Management

A well-managed equipment maintenance regime will not only help ensure that the equipment is safe and working correctly, it will also keep it in good condition longer, extending its life of the equipment, delaying the time at which it will need replacing and reducing the overall cost of equipment a health care organisation. A well-managed maintenance regime should therefore been seen as key part of the financial management of the organisation's assets.

Medical equipment ranges from simple and relatively inexpensive devices such as thermometers and sphygmomanometers to complex analysers and imaging equipment with large price tags—often referred to as 'big ticket items'. Whilst these big ticket items trend to catch the eye senior hospital staff, in fact, the cumulative value of the many smaller items and their impact on the medical care of the patients, is usually much greater. A well-planned equipment maintenance regime, will therefore take account of the needs of the service, regardless of the individual value of the equipment [10].

3 Assurance and Preventative Maintenance—Process and Implementation

The following steps outline the broad steps required to implement an APM programme.

3.1 Assessment

Responsible healthcare organisation should assess the APM requirements of every item of medical equipment ideally before it is acquired and certainly before it is brought to site and deployed into clinical use. The APM requirements could be an influential criteria in the Evaluation and Selection phase: different equipment options might be similar in terms of functionality, quality and cost to purchase but one might be require expensive tools, test equipment and even off-site servicing whereas the other might be easy for the in-house service teams to maintain so it is always best to assess these needs at the evaluation stage.

However, responsible healthcare organisation should always assess the APM requirements prior to committing to purchase, contract or accept medical equipment onto their clinical settings. Maintenance programmes are important to ensure patient safety, regulatory compliance and financial management; committing to acquire equipment without fully understanding how these APM requirements will be delivered could leave the organisation open to difficulties once the equipment is in clinical use.

Assessment of the APM requirements needs to be undertaken by a suitably competent clinical engineering practitioner and can only be done with reference to the manufacturers' technical manuals. For some equipment expert opinion from other stakeholders will also be required, for example Sterile Services staff on reprocessing requirements.

During the assessment, it is reasonable to ask the following questions.

3.1.1 Does the Equipment Need an APM?

In general, all medical equipment will require an APM scheduling however, there might be some exceptions. If equipment is coming into the organisation for a short period only—perhaps on a short-term loan to cover the temporary loss of other equipment, perhaps as part of a time-limited clinical trial—then the item might be returned before the APM is due. In these cases, completing and scheduling and APM will not be necessary. However, caution is needed to make sure the equipment is indeed removed from clinical use prior to the expected APM date.

3.1.2 Does the Equipment Need Assurance Checks?

Many, indeed most, medical equipment will have safety features and essential performance that needs to be checked to confirm it is still working within manufacturer tolerances. If device malfunction or failure could be hazardous and/or adversely affect patient care then the answer will almost certainly be yes.

3.1.3 Does the Equipment Need Preventative Maintenance?

If device malfunction or failure could be hazardous and/or adversely affect patient care, or if it could compromise the delivery of patient services, or if it could be costly to the organisation then preventative should be considered if that preventative maintenance would reduce the likelihood of the failure of malfunction.

3.1.4 What APM is Required?

The default position for any APM programme will be the manufacturers' instructions. The manufacturer will have specified the tests needed to confirm the safety features are working correctly and that the device is meeting its essential performance. They will also specify the frequency of these checks. The manufacturer will additionally describe actions that should be undertaken to keep the equipment in good working order and again the frequency of such tasks.

Given the manufacturer's design knowledge of the equipment and there experience of post-market vigilance and support, their recommendations can be assumed to be 'best practice' until and unless additional reliable information becomes available. It is possible, for example, that after a time servicing a particular device, local technical teams build an understanding that enables them to make suggested changes to the manufacturers' recommendation. For example, in the local conditions some components wear out more quickly and need to be replaced more frequently; or that failure rates are so low as to suggest extending the service period. However, caution should be exercised with any such suggestion. The risks and benefits will need to be assessed within the local organisations governance framework and a robust decision framework implemented and any decision recorded.

3.1.5 What Resource (Effort) is Required to Undertake the Servicing Tasks?

It is helpful for future planning if an assessment of the effort—the time required—to perform the required APM actions is made at this stage. When the future jobs for APM are generated, team leaders will need to manage the generated workload and an estimate of the APM effort will facilitate this. Moreover, estimating the APM effort

at this stage supports teams in understanding if they have the capacity to support equipment and helps managers make business case for increased resources.

3.1.6 What Servicing Priority Needs to Be Assigned?

Ideally, every item of medical equipment will be serviced to the agreed standards and at the recommended interval. However, in reality there are often operational pressures, financial and capacity pressures which mean decisions need to be taken on which equipment can be serviced and which need to be postponed. When making that decision, often at a time of operational pressure, it is helpful if an assessment of priority has already been undertaken.

Therefore, a servicing priority level should be considered for each item based on the impact on the patients and the organisation should the APM schedule not be met. A simple three level priority system—High, Medium or Low—is usually sufficient. Local risk tolerances and culture will vary but criteria used to categorise might include:

- Application and Criticality—what type of clinical service uses the equipment and how important is the equipment to that service.
- Safety Assessment—what intrinsic hazards are present (one criteria for this would be to use the Medical Devices Regulations Hazard Classifications: I, IIa, IIb, III)
- Service Impact—if the equipment was withdrawn or failed, what level of disruption would the clinical service suffer
- Any particular requirements—standards, regulations or specific recommendation for service actions
- Nature of use—is the equipment used all day every day or just occasionally
- Local experience—are there local findings that need to be considered.

Establishing the servicing priority not only allows individual capacity decision to be made but will help management decide on APM targets.

Local teams will develop their own systems for assessing and recording the APM requirements, but the form in Appendix A is offered as one practical solution [11].

3.2 Inventory Management

Effective implementation of an APM programme will require a relatively sophisticated Computerised Equipment Inventory System. Many propriety systems are available on the market and some organisations still make effective use of in-house developed and maintained inventory systems. A minimum requirement is that the inventory can store details from the APM assessment (as above) against each individual item of equipment, and has the facility to schedule future jobs for those individual items at their due date.

Most equipment needs a maintenance activity to be scheduled per fixed period of time, typically every year. However, some equipment needs more than one level of servicing, for example some tasks to be done every 3 months, others every 6 months and some every 12 months. More sophisticated inventory might be required to meet these requirements.

However these future 'planned' jobs are to be scheduled, it is important to programme these into the inventory. Clearly, the future APM jobs will be scheduled based on their commissioning date or last APM job plus the time interval set at the assessment stage. As a result, the future total workload of APM jobs might fluctuate throughout the year. If, for example, a large number of devices were all commissioned in January, they might all become due for APM the following January. Managers might need to take account of this and move the schedules slightly to smooth out the workload demand thought the year.

Most computer inventory systems have a facility to set the next due date automatically, scheduling the next due date form the date of the last APM job plus the agreed interval.

3.3 APM Recall Lists

Having programme the APM interval into the computerised inventory the system will ordinarily produce monthly reports of the equipment that is due its APM. This is sometimes referred to as the APM Recall list. Local technical managers will then need to review the list and create work plans for the technical workforce. Mangers will need to take account of any servicing priority (if set) resources available (there might be staff absences due to sickness, leave of study etc.) or other work commitments (there might be significant commissioning that month or a project that will take technical staff away from the workshop). Local managers might also need to take account of clinical preferences—if there are clinical pressures in one clinical department they might not be able to release the equipment for service. They will need to exercise a level of judgment about which equipment must be serviced on its due date and which might, if needs be, can be delayed a month or two. Items which have been deferred for operational reasons will appear on the next month's recall list. There is no substitute here for an experienced technical manager—someone who knows the equipment, their staff and the hospital operational activities and can balance all these pressures. They can review this list and refine it and then generate a final list of items of equipment that will be retrieved from clinical use and serviced.

3.4 Retrieval

Local systems for retrieval will vary dependent of circumstances. However, one way or another the equipment identified on the APM recall list needs to be retrieved from

clinical use to be serviced. There might need to be an arrangement made with the clinical team first—some will simply be able to manage without the equipment for the time needed to get it serviced, some will need to arrange a specific day when they will not require it, others will need a replacement while theirs is being serviced. Local, hospital-based staff generally work collaborative with their clinical colleagues to achieve this. Third party agents brought in from outside the hospital might find this aspect more challenging and rely on hospital-based staff to undertake this task.

3.5 Servicing Activities

If the assessment and inventory have been done correctly, and if the local manager has managed the recall list appropriately, then the technical team responsible for servicing need simply need to retrieve the equipment and undertake the tasks as described by the manufacturer (or agreed variations). APM protocols, either directly from the manufacturers' serving manual or derived from them, should be available to the servicing team. Local team leaders will allocate work only to technical staff who are trained and competent in servicing that specific item.

3.6 Record Keeping

All aspects of servicing activity need to be appropriately recorded. Local system will vary but it is an essential step to record the APM work as having been completed; confirm the required testing has been undertaken and satisfactorily passed; note any corrections needed or settings changed and finally confirm the APM job has been completed.

Findings during the APM activities provide important information and can lead to changes in the APM schedules (see Sect. 3.8). For example, if a significant number of component failures are found, or equipment performance has reduced then the period between future scheduled APM jobs might need to be reduced. Conversely, if no components need changing and assurance checks remain good, there might be an argument to extend the APM period [12].

If assurance checks show that the equipment is performing outside of expected tolerances, then this need to be draw to the attention of senior staff who will need to assess the likely clinical impact and consider remedial action. Local clinical engineering managers, in conjunction with appropriate clinical leaders, should assess if the out of tolerance medical equipment might have had a negative impact on individual patients. For example, if a diagnostic test needed a reading from the medical device, but that device was now found to be always reading too low, would some patients have been missed on diagnosis? Clinical leaders will need to be responsible for recalling patients in such circumstances.

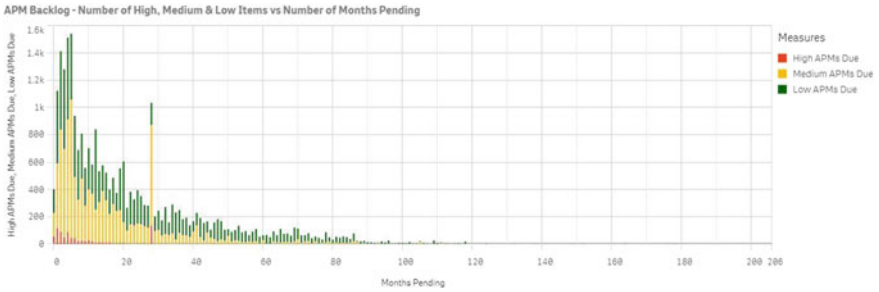


Fig. 3 APM backlog

Additionally, local managers and senior hospital managers will need to see activity reports and completion rates to help manage and improve performance—see Sect. 5.4. Good record keeping is essential if these reports are to be valid and meaningful.

Usually, the next APM job is only scheduled when the current one is recorded as complete. Failure to do this last step will result in equipment remaining in clinical use and not being picked up on the APM Recall list.

3.7 Reporting

It is helpful to generate reports on APM activity both to manage the operational performance of the maintenance programmes and also to demonstrate performance to management teams and help drive improvements. For example, Fig. 3 shows a typical APM backlog report, stratified by servicing priority. In this example, the hospital has over 70,000 items in total; of which 37,000 have been assigned as medium priority (yellow in the chart); of which 11,000 are currently overdue their APM servicing. The chart also shows how many months overdue these items are. See Sect. 5 for more details of operational and performance management.

3.8 Review

Responsible healthcare organisations will review their APM programme and individual assessments as things change:

- Manufacturers might send out updates on safety and performance or technical support requirements of their devices based on their experience from the field. These updates might lead to a hospital revising the period of APM required or the tasks.

- Local service team experience will also influence the technical service requirements. A team might learn that a certain component always needs changing before its APM due date, or there might be a higher than expected number of failures on a given device. Such local experience can be used to modify the APM schedules. However, any derivation from the manufacturer's instructions should be supported by documented risk assessment.
- Safety notices from national authorities or experience of other healthcare users might also influence the requirements of the APM schedule.

Systems should be in place to be able to respond to new information and review if APM schedules need to be modified [13].

4 Corrective Maintenance

From time to time medical equipment will fail or be damaged in service. A responsible healthcare organisation will have systems in place to assess the reported fault or damage and affect a timely repair so as to return the medical equipment back clinical use as soon as possible. Corrective maintenance presents many challenges to the technical servicing teams:

- they can occur at any time so the servicing team won't necessarily have the right staff available;
- they are often urgent (the clinical team needs the equipment back in order to continue its work);
- they are by their nature unplanned so the servicing team might not have the right spares or accessories available in stock;
- the nature of the fault is unknown at the outset and could be anything from a simple component failure (a battery change for example) to a complex multi-factor error requiring skilled technical staff to investigate and fault find.

Servicing teams therefore need good systems to be able to respond quickly and appropriately to these varied demands. Local systems will, of course, vary considerably but the following aspects will be common to all.

4.1 Capturing Initial Information

Clinical staff or patients will become aware that the equipment is not performing as they expect. Sometimes this is obvious: the equipment was dropped, the case cracked and now it doesn't even turn on. Sometimes it is less obvious: the clinical team just feel it is not being as effective as usual. The circumstances of the reported failure can be helpful in finding a solution and being to affect a timely and thorough repair so it worth putting effort into gaining this information from the end-user. When the

fault is reported a checklist or booking-in form will help ensure, as far as possible, that the right information is captured:

- Basic details—where, when and how was the fault notice.
- Contact details—it is really important to have the contact details of a member of the clinical team who can be contacted in the event that the servicing team need further information later.
- Fault description—as much details as possible about the nature of the fault. A significant amount of time can be saved if the technical team know what the fault is—if it only occurs in certain operating modes, for example.
- Clinical incident—was the fault the cause of a clinical incident, or might it have been. It is important to know as early as possible if there has been a clinical incident so that the relevant team can start to investigate and examine the equipment before any repair is undertaken.
- Urgency—do the clinical team need the equipment back quickly, has clinical activity been suspended because the equipment is out of use, is there a planned date for the next clinical episode (theatre list for example)
- Alternative equipment—can the clinical team access alternative equipment while the repair is underway.

4.2 Exchange Equipment (Equipment Library/Pools or Supplier Loans)

Technical service teams are often aware of the urgency with which the clinical teams need their equipment back, but corrective maintenance can be time consuming and rushing the work can lead to incomplete resolution, further faults once back in service or even cause unsafe equipment to be allowed back into clinical use. It is important, therefore, to try to create an environment where the technical team have the time and space needed to undertake a thorough repair. The best way to achieve this is to supply the clinical team with an alternative item of equipment so their clinical service is not interrupted by the repair. Holding spare medical equipment just in case of a breakdown is unlikely to a cost-effective solution but manufacturers or suppliers can often lend devices to the hospital to cover the repair time. For common medical equipment where there are many items in the hospitals, equipment libraries or pools will also allow the clinical team to be issued with a replacement device while theirs is repaired.

4.3 Skill Mix Requirements

Corrective maintenance tends to require more experienced technical staff owing to the unpredictable nature of the work. APM work is scheduled and planned and generally

the servicing team can follow a well-rehearsed protocol. Corrective maintenance requires higher skill levels and more experience. Having a wide range of skills in the technical service team helps facilitate this mix of APM and repairs.

External servicing agents and particularly the original equipment manufacturer often play an important part. If the local servicing team cannot cover the necessary skill mix required, then sending equipment away for repairs or calling in OEM servicing engineers is often the prudent alternative. Whilst using OEMs to undertake repairs can seem an expensive option, because they have the skills, experience and importantly parts needed, the repairs can be quicker justifying the additional cost.

4.4 Stock Levels and Supply Lines

The unpredictable nature of corrective maintenance means you can't buy in spares in advance. Where possible, some commonly anticipated spares might be held in stock but often the required items will need to be ordered as and when needed. It is thereof important to have good supply line management wherever possible.

4.5 Post Repair APM

Assurance testing: It is advisable to undertake assurance testing post repair. If the repair is very minor, for example just replacing the power-on LED, then the full range of assurance checks might not be needed but in most cases it makes sense to perform them anyway so that the clinical team can be assured the equipment is safe and working correctly when it is returned to them.

Preventative maintenance: Part of the challenge with an APM programme is getting access to medical equipment, getting it released from clinical use and getting it back into the workshop. Therefore, whenever an item is in the workshop for a repair, servicing teams should consider the merits of also undertaking the APM servicing. Preventative maintenance can be time consuming and expensive in terms of fitting parts so the consideration should balance these factors against the effort of retrieving the equipment when its APM is due. Generally, if the APM is due relatively soon, then it will be worth undertaking those task now. If the APM is further away, it might make sense to leave it until nearer the due date. This decision can only be taken in the light of local experience and operating pressures.

4.6 Escalation—Repair or Replace

Fault finding and repairing medical equipment can be both time consuming and expensive. Consideration needs to be made as to the value of completing a repair when compared with the cost of replacing the equipment with a new one. Sometimes, the repair simply can't be done, perhaps the parts are no longer available or the damage is simple too great—in which case the decision is made for you. In other cases, the repair is possible but will take time, effort and money. The cost of repairing needs to be considered in comparison with the cost of replacement, bearing in mind that the new replacement should be more reliable. Clinical teams often want the cheapest option in absolute terms and technical teams might need to escalate to senior managers to make a decision.

4.7 Record Keeping

All aspects of servicing activity need to be appropriately recorded. Local system will vary but it is an essential step to record work done during the corrective maintenance. Time taken to complete the repair and success rates are important performance measures (see also Sect. 5.4) and the activities undertaken can also influence the APM schedules and be a factor in equipment replacement decisions [15].

5 Management of Medical Equipment Maintenance

5.1 Resource Management

Supporting medical equipment maintenance in healthcare institutions is a complex and challenging task and needs to be managed robustly to deliver an effective service. Clinical Engineering departments face many pressures in addition to equipment maintenance. These will vary depending on local service but might include: planning for equipment replacement; evaluation and selection of new equipment; acquisition of new equipment; installation and deployment of equipment; training of clinical staff; running equipment libraries; supporting device incident investigations; managing safety alerts; providing technical support to service development projects; supporting clinical research and delivering engineering research. Balancing these various pressures is all part of the challenge of providing clinical engineering services and requires adequate and appropriate resources [14].

5.1.1 Financial

Several business models are employed to manage medical equipment maintenance in hospitals.

- Some centres employ in-house technical teams with the range of skills required to maintain most of the hospital's medical equipment. However, even the largest in-house teams usually find they cannot maintain the skills necessary to service all the equipment; therefore they also tend to place a small number of contracts, usually with the OEM, to cover the more specialist or unusual equipment.
- Some centres tender for and contract out to third party organisations to provide the bulk of their servicing needs. Retaining a smaller on-site team to oversee the operations and manage the contract performance.
- Some centres use a combination of in-house teams and outsourced contracts and indeed, most centres will use a mix of all of the above as best meets their local needs.

Clearly, a factor in deciding which business model to use is the costs. For an in-house service, this cost is the total cost of the staff time utilised on corrective maintenance and APM activities, plus the cost of all parts, accessories and consumables used and any additional costs when referring work to OEMs. In-house service models have the advantage of flexibility—staff can be used across other activities and across all equipment types. However, supporting an in-house team has overhead costs to consider, including providing cover for sick leave, holidays, and internal staff training. Notwithstanding these costs, the in-house service is almost always the most cost-effective solution to medical equipment maintenance provision. Additionally, on-site teams tend to be more responsive, have better local knowledge and working relationships with clinical colleagues and are more flexible.

Some organisation chose to outsource most or all of their medical equipment maintenance to third party service suppliers. This has the advantage of simplicity for hospital management as all the responsibility is delivered through a single contract with no overheads or management costs on supporting local staff. Generally this service model is more expensive than in-house teams as the third party organisation itself needs to make a profit. However, a third party service organisation can deliver some cost savings for smaller hospitals if they can amalgamate contracts and drive down costs with OEMs. In general, larger hospitals should be able to manage in house teams to provide higher quality maintenance services at lower costs than third party providers. Smaller hospitals can manage in-house teams effectively but the advantages of outsourcing can be relevant to their needs.

In both cases, recourse to the OEM will sometimes be required. This might be because the OEM has specialist skills and facilities that local teams cannot acquire or it might be that maintaining the local skills and competencies to support a small number of specialist items is not cost-effective for the in-house teams. Use of OEMs should provide high quality reliable maintenance albeit usually at a premium cost.

Whichever business model is employed to provide medical equipment maintenance it is important to manage the budget carefully. In practice this is the same as

for managing any operational budget: establish a budget required and measure actual costs (in-house team, parts, external team, OEM contracts) against that budget. Any differences—over or under—should be reviewed and explained. Where there are clear over-budget trends resulting from genuine activity pressures, local clinical engineering management team will need to make business cases to the organisation for an increased budget. Information from reports (see Sects. 3.7, 4.6 and 5.4) will form the basis of any business case. Corrective maintenance can sometime cause unexpected and substantial budget variations due to the unpredictable nature of repairs. A single repair to a critical and expensive item can cause a one-off cost pressure. However, although unpredictable, such events are not unexpected and the budget should, as far as possible, be set so as to allow for these unpredictable events throughout the year. It can be helpful to have separate budgets for Corrective Maintenance and APM to avoid the latter being detrimentally affected by a spate of high cost repairs.

The budget required to maintain medical equipment will change over time. If the total number of items of equipment increases, it stands to reason that the cost of maintaining it will similarly increase. Whilst obvious to clinical engineers, this is not always seen by hospital finance managers so might need to be drawn to their attention during annual planning reviews. Other factors can also influence the budget requirements: older equipment is generally more expensive to maintain, requiring more repairs for instance, whereas new equipment is often covered by warranties during the first year or two.

5.1.2 Physical Resources

Physical resources are required to be able to provide an equipment maintenance service. Most obviously there is a need to have appropriate workshops that need to be adequate in terms of size, location and facilities. Various standards will apply at national level for the types of workshop required. Attention must be given particular to electrical supply and safety standards, but also to medical gases, temperature and other special hazards (laser protection, microwave or radiation, for example). Expert engineer assessment and consultation is required when specifying medical equipment workshops.

Space and location are also important. Space on a hospital site is always a premium and patient facing services tend to be given the priority. It is important that clinical engineering managers make the case for suitable space for equipment support. Providing effective APM and timely and effective corrective maintenance is heavily dependent on having the right workshop environment in the right location.

Even if corrective and preventative maintenance is undertaken off site—perhaps back at the OEMs serving centre—assurance testing must always be done on site and as close to the clinical environment as practicable. Transporting medical equipment, even under ideal conditions, presents the risk of unseen damage to the equipment. It is therefore essential to undertaken assurance testing on-site. As an absolute minimum, a responsible healthcare provider will ensure there is sufficient workshop space on site to undertake assurance testing.

Test equipment is an essential part of providing a maintenance service [15]. This will include certain generic test equipment (for example infusion device testers and electrical safety testers) as well as test equipment specific to certain items of medical equipment. A key aspect of the acquisition process (see Sect. 1.2.3) is to ensure the clinical engineering department has or can get the right test equipment. Clearly, the test equipment needs to be fit for purpose. Selection of appropriate test equipment therefore requires an assessment of the measurement uncertainty in relation to the expected task. There is no point, for example, using test equipment with an uncertainty of ± 1.0 J if the output of the medical equipment is specified to be within ± 0.5 J. There is also a distinction to be made between generic test equipment (for example an electrical safety tester that can be used on a wide variety of medical equipment) and specific test equipment that is dedicated to a single item (or suite of items) of medical equipment. Test equipment itself requires to be maintained. Usually this will require using the OEM or a specialist third party company who can confirm the performance of the test equipment and issue calibration certificates to support this.

5.1.3 Human Resources

The most important element of any maintenance programme are the technical staff employed to deliver it. Corrective maintenance and APM tasks must only be allocated to staff who can demonstrate they are trained and competent to perform those activities. Regardless of the business model utilised to deliver equipment maintenance (in-house, OEM, third party organisation or hybrid) the servicing personnel must be component in their roles.

The Clinical Engineering department is responsible for ensuring that the in-house team receive appropriate competency-based training. Technical competencies can be considered to be either generic or equipment-specific. A productive clinical engineering practitioner needs a wide range of generic competencies, including but of course not limited to: basic engineering workshop practice; electrical, mechanical and information technology skills; healthcare awareness (depending on the institution); clinical understanding (the needs of the patient); health and safety; decontamination of medical equipment and local procedures and practices. Clinical Engineering departments should have systems in place to support their staff in acquiring and maintaining these generic competencies.

In additional to these generic competencies, specific equipment training and competency is needed for most medical equipment. This should only be delivered by the OEM or their authorised agents. OEMs will charge to deliver this training so it is important that clinical engineering departments budget for this. One way to pay for this training is to include the cost of it in the cost of the equipment purchase. This is not always possible, however, so budget must be available to cover the cost of training. Not all staff will need to work on all equipment so local managers will identify which staff will be trained in what type of equipment and assess the number of staff needed to be trained on each type (model) of equipment. This will depend on the number of items of that type, their distribution, the criticality of the equipment to

the clinical service and how heavily they use the equipment. Enough technical staff need to be competent to service the equipment to cover expected staff absences due to leave and sickness. However, it must also be remember that technical staff will need to see the equipment quite often in order to maintain their competencies—so more trained staff is not always better.

Sending staff on the OEM approved training should be the default position but on occasions the use of cascade training might be considered. This is where one or two staff are sent on the OEM course and they then come back and train some more of their colleagues. This should only be considered where there is a robust training support system in place locally to assess the cascade training to avoid the potential to pass on learned mistakes or poor habits. Moreover, an increasing number of medical equipment now consist of computer-based multi-component systems. Some aspects of the APM is auto-performed by the on-board software. Obtaining access to these systems and their codes usually only comes following approved OEM training.

Third-party suppliers and even OEM employed service staff should also be able to demonstrate their training and competence to service medical equipment. When placing contracts with external service suppliers, it is therefore essential to build into that contract the requirement that all staff used must have appropriate competency-based training. Moreover, hospital-based staff, usually in clinical engineering department, should audit external service providers to ensure compliance with this requirements [16].

5.2 Risk Management and Prioritising

Having established APM schedules (see Sect. 3.1) and programmed them into the computerised maintenance management system (CMMS) local service managers will be able to identify the total number of APM jobs required annually and, if the effort per job has also been programmed, able to estimate the total effort (technical time) needed to complete those jobs. In all likelihood, the total effort required to perform all the scheduled APMs and meet all the other obligation on the clinical engineering service will exceed the available resources. As such, some form or prioritisation will be required: amongst all that expected work (of which APM will be a large fraction) how much is essential, how much is a really should do and how much would be good to do but could probably be deferring or perhaps even just not done at all.

These are difficult decisions to make and will be dependent on local factors, of course, but key considerations will include.

5.2.1 Patient Safety and Clinical Need

Our first priority as a clinical engineering service is to the clinical teams we support and the patients. It is therefore only right that our first consideration when considering

workload and setting priorities is the impact of our activities, or the lack of activities, will have on patient care.

- Corrective maintenance work tends to be given a high priority. Often, when an item of equipment is damaged or develops a fault and has to be removed from clinical service, that clinical service stops or is reduced.
- Commissioning new equipment is also usually given a high priority. Often, new equipment is needed to replace old items which might have been removed from service. Again, without the new equipment the clinical service might be suspended or reduced.
- APM is often given a lower priority to corrective maintenance or commissioning because generally, equipment due its APM is still in service and apparently working well. Not performing the APM doesn't immediately put the clinical service at risk. However, APM is a critical part of providing high quality healthcare and so well planned equipment maintenance services will nonetheless allocate appropriate time and resources to this element of activity

5.2.2 Regulatory Requirement

Sometime medical equipment is subject to specific regulations requiring particular servicing (for example some ionising radiation devices might need to have their outputs calibrated according to a nature standard) or are part of a national programme (for example a screening programme) that has mandatory servicing requirements. Clearly, any such requirements will need to be accounted for in the operational management priority settings.

5.2.3 OEM Recommendation

The manufacturer is obliged to describe both the activities required and period of servicing. These time periods will for part of the scheduled APM. Ordinarily, a degree of flexibility can be applied to these periods; if the manufacture states service every 12 months, the medical equipment does not suddenly become unsafe 1 day after the 12 months. However, in some circumstances, there might be specific instructions within the manufacturer technical manual that makes the time period more critical. This is usually around the degradation of some components that are time-limited.

5.2.4 Clinical Operational Arrangements

A clinical operational procedure might have a planned downtime—perhaps theatres always close for one month every summer to allow for other work to be done. This one month might be the only time that the medical equipment can be released for servicing so it is more important to keep to that APM due date.

5.2.5 Backlog APMs

Either for legitimate operational reasons or because the specific equipment could not be found or released from clinical use, some items of equipment scheduled for their APM in any given month will be missed. These items will still be due APM the following month but should now be given a higher priority. Clearly, if they get missed a second month then their priority for the next month increases again.

5.2.6 Evidence-Based Maintenance

Given the impact of the ongoing global digital transformation in the medical device management field, the collection of data for informed, evidence-based decision-making is crucial, and Clinical Engineers should manage prioritization based on the available evidence [17–19]. Many publications exist in the literature of evidence-based maintenance systems [15] which describe the use of evidence acquired locally, nationally or indeed internationally, to support risk-managed approaches to maintenance priorities. Increasingly, research suggests a role for AI in supporting these decisions but this in not (at time of publication) in widespread use.

5.2.7 Risk Management

Ultimately, our role as clinical engineers is to maximise the potential of medical devices and minimise the risks. Successful management of medical equipment maintenance programmes is about trying to minimise those risks. If we had unlimited resources then we would be able to complete all the scheduled APMs to the manufacturers' recommendation whilst also being able respond appropriate to all corrective maintenance requests and discharge all our other responsibilities. Unfortunately, none of us have unlimited resources so successful management of medical equipment maintenance is about setting priorities and managing risks. Acknowledging that it is likely to be impractical to do everything requested of a clinical engineering department, responsible organisations should have systems in place to ensure that what does not get done has been actively selected to be the lowest risk to the organisation and most importantly to the patient [20].

5.3 Communications

Good communications are key to successful equipment maintenance programmes. It will be important that the APM programme is understood by clinical teams, that they appreciate its importance and support its delivery. Clinical engineering teams cannot make the equipment available but rely on clinical colleagues to locate and

retrieve equipment. Close working relationships with clinical colleagues is clearly critical.

5.3.1 Recall Lists

Each month the recall list of equipment expected for APMs is generated and needs to be communicated to the relevant clinical teams. This is likely to be a long list and therefore targeted distribution is helpful. The method of communications will be governed by local arrangements and structures—some centres will send the list to senior clinical managers and expect them to distribute to relevant local leaders in their area. Other centres will send to local staff directly. Others still will 'publish' lists in central areas and local clinical staff will know to look for items relevant to their own areas. Whatever the mechanism of communications, it is important that local clinical teams know what is expected of them, know how to retrieve the equipment and return to the servicing department and how to collect it again after the APM.

5.3.2 Labels

All inventoried medical equipment should have a label with a reference number uniquely identifying items within the inventory. This number should be included on a label attached to the equipment so that anyone can identify the equipment from its label. Additionally, it is good practice to include a label on the equipment that indicates when the APM is next due. This is a quick easy check to tell if the item is within date or overdue for its APM. (Some centres chose to use the last completed date instead. This has some advantages but has the disadvantage that staff cannot tell from the label alone if the equipment is overdue or not, without knowing the period, which might not be apparent in the clinical locations, for example). Having a next due date provide assurance to clinical staff (and patients) that the equipment is within date [21].

5.4 Performance Management

Effective management of medical equipment maintenance requires good metrics of performance. There are no generally agreed standards for performance measures and managers need to agree local measures and targets. In some nations and regions, benchmarking is used to compare performance between organisations but this can be problematic—most hospitals have different structures, different range of medical equipment, different business models for clinical engineering services and different resources available. As such, performance per se can be difficult to compare—it is often a case of comparing apples with oranges. Within a given organisation, however,

it is helpful to agree expected performance, establish systems to measure against that expectation and set targets for local teams to work towards [22].

5.4.1 Key Performance Indicators (KPIs)

Corrective Maintenance. Generally, the most commonly used metric for corrective maintenance is the response time, usually measured from the point of first notification to the point of making clinically available again. Local practices vary but it is common to set priorities against corrective maintenance, for example:

CM priority	Performance target
Low	50% within 15 days
Medium	60% within 10 days
High	80% within 3 days
Critical	90% within 3 days

Each month, the actual achievement can then be recorded against these targets (see typical example below) (Fig. 4).

In this example, it is clear there was an operational issue with critical responses in August. Reports such as this can be sued by local team leaders to identify and rectify operational issues.

Assurance and Preventative Maintenance. The most common APM report is the completion rate report usually simply a measure of the percentage of items receiving their APM within the due date. Again, local practice can vary but it is common to set targets either against each servicing priority (if set) or the whole equipment asset base, for example:

Servicing priority	Performance target
Low	Not set
Medium	75%

(continued)

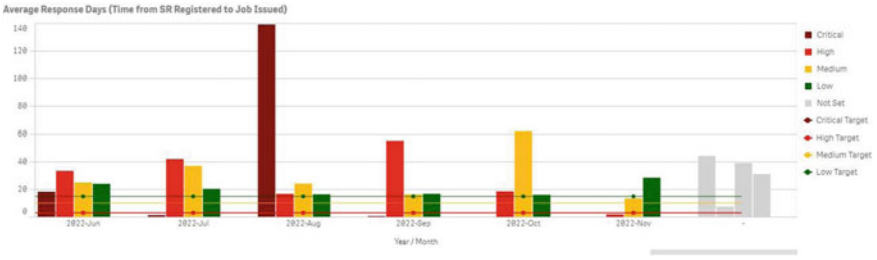


Fig. 4 Example corrective maintenance response report

(continued)

Servicing priority	Performance target
High	95%
All	Not set

In this example, no target is set for low servicing priority items. This is because effort should first be used on High or Medium servicing priority items. Each month, the completion rate for can be measured and presented against target as in Fig. 5.

Performance reports can be used by local managers to identify issues or trends and seek solutions and improvements. These reports can also be used to provide assurance to senior hospital managers or external inspection agencies of the local servicing teams' performance.

Other metrics are, of course, possible but will depend on local arrangements and systems.

5.4.2 Performance Improvement

Performance reports are used to provide assurance to senior managers but more importantly can be used as a tool to improve service delivery. By setting realistic targets, agreed with service leaders and senior managers, and measuring against these, local managers can identify any issue of underperformance and hence seek opportunities to improve. If APM achievement is decreasing over time it might be an indication of staff shortages or of increased equipment to manage leading to business cases to increase available resources, for example. Local managers will be able to drill down and investigate if performance drops below expectation as there might be a variety of reasons why; anything from supply chain issues to clinical areas being under increased operational pressures, to technical teams being short staff, to accommodation issues. Performance reporting is often the first step to identify and therefore being able to resolve these issues [23].

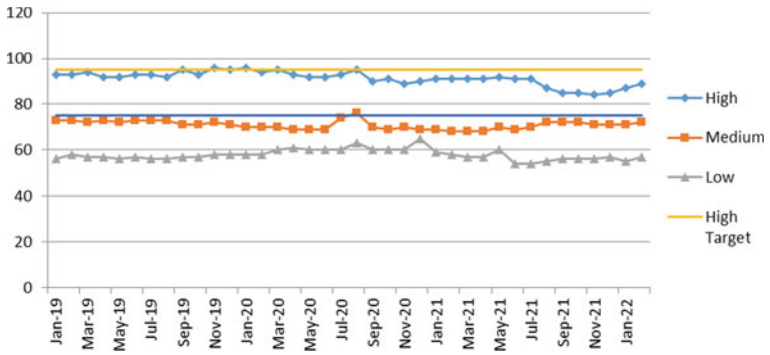


Fig. 5 Illustrative APM performance against time

Additionally, the appropriate use of performance report and dashboards can act as an incentive to local servicing teams.

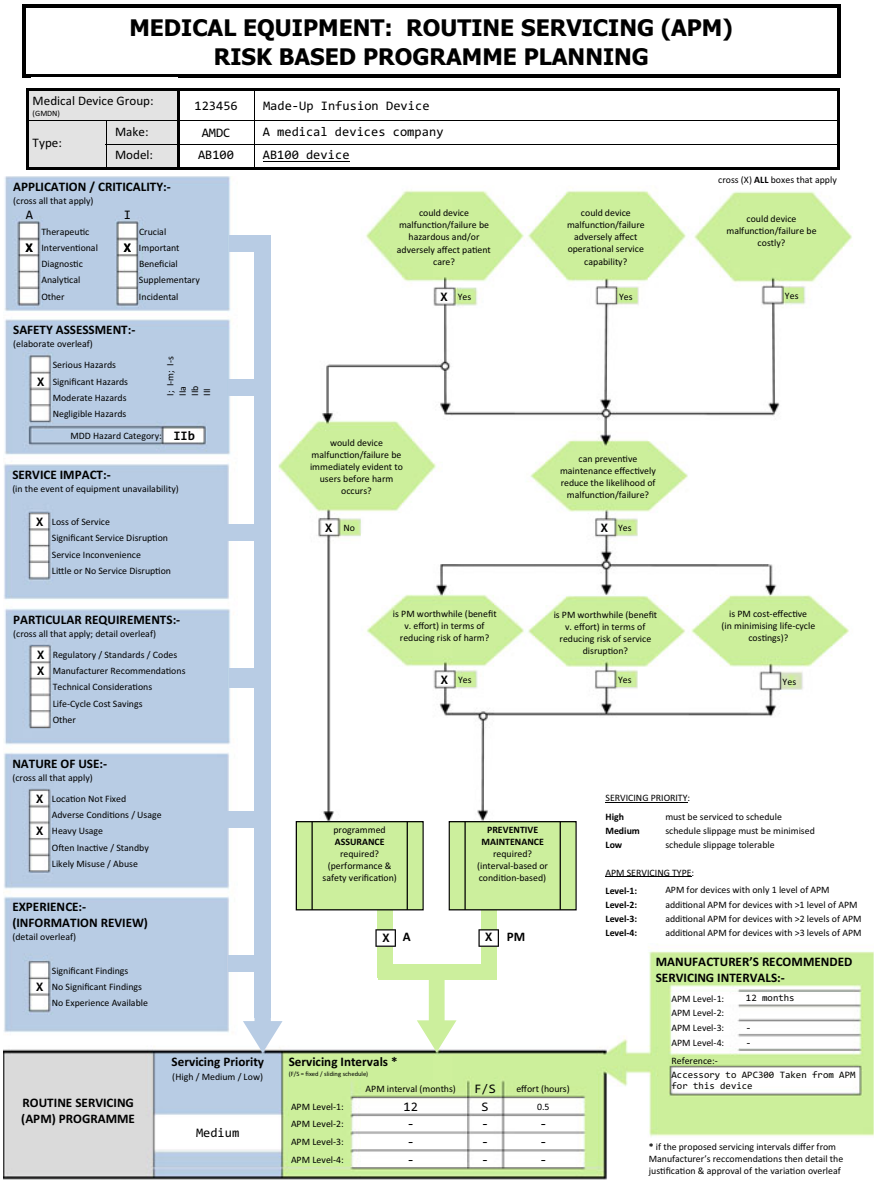
5.4.3 External Reporting

Whilst the primary reason for generating and reporting is to support improvement of local performance, there are occasions where external reporting is required or desirable. For instance, at a national or regional (Health authority or health ministry) level it can be helpful to have oversight of all healthcare organisations, partly to manage resources and support between them and partly to help develop national or regional strategies. Additionally, information on the performance of medical devices from maintenance programmes is a valuable tool for post market surveillance (PMS). Generally, local healthcare organisations are not responsible for supporting PMS, which is a manufacturer obligation, but research has shown [16] how valuable such data can be in improving the design and manufacture of devices [24].

6 Conclusion

Medical equipment is essential in providing modern healthcare. Clinical engineering's mission is to maximise the potential of this equipment whilst minimising the risks. Well-planned medical equipment maintenance will help both maximise the potential, by helping to ensure the equipment continues to work as expected, and minimise the risk, by helping to ensure it continues to be safe and effective.

Appendix A—APM Schedule Templates



SUPPORTING INFORMATION -

SAFETY ASSESSMENT: identify hazards presented by device malfunction / failure consider performance of both functional and protective features (including latent hazards arising from failure of the latter)	**PARTICULAR REQUIREMENTS:** summarise any particular requirements relating to the device assessed
EXPERIENCE (INFORMATION REVIEW): summarise any device-related experience relevant to the assessment	**SUPPLEMENTARY INFORMATION:** provide explanatory notes as necessary to clarify decisions made overleaf

Assessed by: (Chief Technician)		**Date:**	

does the proposed APM Servicing Programme differ from Manufacturer's recommendations?

☐ Yes → Detail the justification for variation from Manufacturer's recommendations:-

☒ No

Approved by:
(Authorising Engineer)

Date:

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Post-market Surveillance (PMS) of Medical Devices: From a Clinical Engineering Perspective

Thomas Judd

Abstract Postmarketing surveillance (PMS) is a critical process for ensuring the safety and efficacy of medical devices once they have been approved for use. The purpose of PMS is to monitor the performance of medical devices in real-world environments and identify any adverse events or safety issues that may occur. This paper provides an overview of the PMS process for medical devices, highlighting key challenges and opportunities for improvement. It also discusses regulatory requirements for PMS, including the need for robust reporting systems and the importance of timely and accurate data collection. The role of stakeholders, such as healthcare professionals and patients, in reporting adverse events and providing feedback on device performance is also described. Overall, this paper highlights the critical importance of PMS in ensuring the safety and efficacy of medical devices and emphasizes the need for continuous evaluation and improvement of PMS programs to meet the evolving needs of patients and healthcare systems.

1 Introduction

Medical devices represent the backbone of the modern healthcare system. Considering their importance in daily medical practice, the process of manufacturing, marketing, and usage is often regulated at all levels. Post-market surveillance (PMS) refers to the requirement that manufacturers monitor their medical devices after being approved for sale and observe their in-market use. PMS is a regulatory requirement in significant markets, including the European Union (EU) and the United States (USA).

PMS refers to monitoring a medical device post-market for safety and is part of pharmacovigilance, or drug and device safety. The COVID-19 pandemic has emphasized the essential significance of carrying out frequent inspections of medical devices that possess measuring function to ensure their appropriate operation [1]. PMS is a critical part of a device's lifecycle: monitoring the device in use by a larger population

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provides much more data and information than that collected in the pre-marketing clinical trial phase. ***Clinical engineers***—those trained and experienced biomedical engineers who manage technology at the point of care—have an important place in this process. Their real-world evidence offers an ongoing and more complete picture of the safety and effectiveness of a device.

In developing a robust PMS process, manufacturers should consider whether or not the product or technology is new to the manufacturer and/or the marketplace. Where a manufacturer has a long history of development and marketing of similar device types, they are likely to have a clear understanding of the patient population and the reasonably foreseeable risk associated with the device. Available data regarding state-of-the-art market experience for similar products and technology may be adequate for low-risk devices with a long history of clinical use. For those manufacturers pursuing the literature route to support clinical evaluation requirements [2, 3] these data types often give the manufacturer knowledge of the patient population, co-morbidities and the effect of different patient demographics for the use of the device. Literature of high quality (e.g., randomized control trials, meta-analysis) will give manufacturers quantified clinical data regarding the safety profile of these device types.

In the case of new technology, manufacturers often have a limited understanding of the patient population and the complexities of the disease state, which may affect the performance of the device. This limited knowledge may result in under or over representation of risks in the pre-market assessment of the device design and its interaction with the patient and user. Manufacturers introducing technology new to an organization should respond accordingly with an increased monitoring program to ensure early detection of problems not foreseen in development; ***clinical engineers*** typically should be engaged to augment this monitoring. Another concern is the extent of available scientific knowledge for new devices. In the case of novel or new treatments, knowledge of long-term effects may be limited. Post-market clinical follow-up (PMCF) may be warranted to ensure adequate characterization of the real-world clinical use of the device [4].

The preceding edition of the book Inspection of Medical Devices provided notable understanding of the influence of medical device advancement on healthcare delivery, highlighting the significance of handling health concerns and facing the challenges that arise during the process [5].

2 Data Collection and Reporting

Traditionally, PMS relies on **reactive data** gathering. Manufacturers collect and report adverse events (AE) from a device post-market, often using manual methods, called medical device report (MDR). Medical equipment purchasers and users also report; ***clinical engineers*** have both a responsibility and opportunity in this reporting. These adverse events are either directly reported to the manufacturer or they could be reported to regulatory bodies like Food and Drug Administration (FDA) in the USA (MAUDE database), Medicines and Healthcare products Regulatory Agency

(MHRA) in the United Kingdom (UK), Health Canada in Canada, etc. Starting in January 2021, trading of certain goods such as medical devices and in vitro diagnostic (IVD) devices in the UK market required UK Conformity Assessment certification or the UKCA mark. To allow manufacturers time to adjust to the new requirements, "CE" (*Conformité Européenne*) marking was accepted in the UK until January 1, 2022, for some products [6].

Manufacturers are obligated to investigate each medical device regulation and deliver the MDR to the regulatory authorities within a given time period. This approach continues to reassess medical device's benefit/risk ratio as well as its safety and effectiveness in the post-market phase.

However, technological advances and increased regulatory requirements—particularly the more stringent ones included in the new European Union Medical Device Regulation (EU "MDR")—are pushing for a more proactive process. The enhanced regulatory requirements dictate that the post-market surveillance process has a feedback loop with *Design Quality, Clinical Evaluation and Technical* Documentation to utilize real-time performance data of the device, allowing for anticipation and curtailing of events before they occur. Again, ***clinical engineers (CEs)*** can assist as they frequently encounter device-related near misses as well as failures and AEs that they are required to report. The impact of the current global digital transformation is being felt in the field of medical device management, necessitating the accumulation of data and its application for informed evidence-based decision making [7–9]. Additionally, CEs are attuned to the changes and challenges in devices due to the emergence of their integration with Digital Health (Health IT tools). Table 1 shows examples of proactive and reactive PMS data that can be produced.

Collecting quality, performance, and safety data throughout the lifetime of a device helps manufacturers build a complete risk/benefit profile for their device and rapidly

Table 1 Examples of PMS data and their respective action types

Proactive	Reactive
• Customer surveys	• Customer complaints, adverse events, and failures
• Post "CE mark" clinical trials, including PMCF	• Unsolicited user feedback (other than complaints)
• Manufacturer-sponsored device tracking and implant registries	• ***Clinical Engineering*** or Manufacturer Maintenance/service reports
• Expert user groups (focus groups)	• ***Clinical Engineering*** In-house testing (routine)
• ***Clinical Engineers*** tracking and analyzing near misses	• ***Clinical Engineering*** or Manufacturer Failure analysis
• ***Clinical Engineers*** monitoring device challenges due to their integration with Digital Health (Health IT) tools & resources	• Social media
	• Literature reviews
	• Regional or national device registries

Modified by author from Ref. [2]

course-correct should any issues arise. As part of PMS, manufacturers also collect data on related devices from competitors. To ensure safety for their medical device assets, users, e.g., health delivery organizations (HDOs) and ***clinical engineers***, can also track safety performance, typically via near misses, adverse events, MDRs, device recalls, and Health IT-device deployment challenges.

These data can be collected as part of vigilance analysis:

- internal vigilance by manufacturer-established internal databases that collect post-market customer complaints, failure analysis, near misses, or adverse event reports, or
- external vigilance by country specific regulatory authorities' medical device reports databases.

The internal vigilance data is typically compared to the sales figure of the devices to continue to assess its risk/benefit ratio. EU-MDR is one of the first regulations to document expectations for reassessment of calculated risk ratios during the development of a device with real world vigilance and sales data in the post-market phase.

Systematic and periodic literature search as well as continuous monitoring through publication alerts for manufacturers and competitor's devices can alert for off label use in populations and indications for which the device is not intended. In summary, medical device manufacturers use real-world evidence from PMS to:

- Detect adverse events as part of pharmacovigilance;
- Compare a new device's performance against current standards of care;
- Comply with regulatory requirements;
- Continue to monitor the safety and effectiveness of the device in the intended patient population.

PMS is implemented differently from country to country, or region to region, but there are major similarities. In some countries, a legal metrology system is in place [10], in others, PMS is part of quality management system in the healthcare institutions, or performed by distributors and manufacturers in correlation with regulators [11–13]. This chapter describes a protocol specifically designed to inspect medical devices that are equipped with a measurement function.

3 Manufacturers Obligation in Post-Market Surveillance

At a high level, manufacturers must take these steps to conduct PMS [14]:

1. Develop a PMS plan, which includes an assessment of whether Post-Market Clinical Follow-up is required
2. Implement the plan
3. Generate PMS reports based on the findings.

A PMS plan details a manufacturer's strategy for continuously monitoring and collecting data and safety information. The PMS plan is part of the device's technical documentation and outlines the criteria for the risk/benefit assessment of the device and processes for:

A. Collecting and analyzing data
B. Following up on collected complaints
C. Communicating information to regulators and users
D. Taking corrective actions on devices
E. Producing a PMCF plan, or a rationale for why PMCF is not required.

PMS Reporting requirements vary by region. Most reports typically include data analysis and a description of the corrective and preventative actions taken.

- In the USA, FDA requires that manufacturers submit a Periodic Adverse Drug Experience Report (PADER/PAER).
- In the EU, manufacturers of low-risk Class I devices must create a post-market surveillance report (PMSR). Manufacturers of Class IIa, Class IIb, and Class III devices must submit a periodic safety update report (PSUR).

PMS Regulations: These reports are part of a device's technical documentation, and manufacturers must update them regularly according to the relevant regulatory bodies' timelines. For the USA and EU, manufacturers must comply with PMS regulations for the region where they sell their devices.

USA PMS Requirements [14]

You can access the USA requirements via links to the pertinent sections of the Code of Federal Regulations (CFR) and the USA FDA, see ***Appendix***:

- 21 CFR Part 822 details the requirements for PMS in the USA.
- The FDA uses MedWatch for health care professionals and consumers to submit adverse event reports.
- FDA also utilizes the MAUDE database to house medical device reports submitted to the FDA by mandatory reporters—manufacturers, importers and device HDO facilities and voluntary reporters such as health care professionals including ***clinical engineers,*** patients and consumers.
- The FDA also conducts PMS activities; see a full list of PMS requirements for medical devices in the Appendix.

PMS & Device Class: In short, a device's class determines requirements, with higher-risk devices more likely to require PMS. Class I medical devices typically do not need PMS, as they are lower risk.

European Union (EU) PMS Requirements [15]

In the USA, PMS is required only for higher-risk devices. However, in the EU, EU MDR not only mandates PMS for all devices but introduces new and expanded requirements that increase compliance efforts. Annex III of the MDR 2017/745 details the EU requirements for PMS. [The Council of the European Commission

has concluded their December 9, 2022, meeting meant to address member states' concerns over the challenges and issues in meeting current MDR deadlines. MDD certificates for medical devices will continue to be accepted for an additional three to four years beyond current MDR deadlines, with limited exceptions. https://www.rimsys.io/blog/eu-mdr-transitional-period-to-be-extended].

PMS & PMCF: Also, note that any manufacturer with a device planned for sale in the EU must prove that it has performed Post-Market PMCF plan for their medical devices or justify its omission. PMCF is one component of PMS activities, and the two main criteria for mandatory PMCF are the device's risk and novelty. Specifically, devices with high-risk designations and those that are the first of their kind require PMCF. The EU MDR took effect on May 26, 2021. Manufacturers had to ensure that their PMS processes were fully compliant by this date.

4 Post-market Surveillance and Quality Management Systems

Medical Device Quality Management Systems (QMS) are a structured system of procedures and processes covering all aspects of design, manufacturing, supplier management, risk management, complaint handling, clinical data, storage, distribution, product labeling, and more. Although the QMS focus is getting a safe device to market, it also has a strong component of ensuring ongoing safe performance, as shown through post-marketing surveillance. See Fig. 1.

QMS Complexity: Most medical devices will require some form of a QMS; the complexity of the QMS will vary based on the classification of the device. For example, in the USA, companies making medium-risk (Class II) or high-risk devices (Class III) devices will require a different QMS implementation than companies making low-risk, non-sterile, non-measuring, non-reusable surgical instrument devices (Class I).

From an EU perspective [15]:

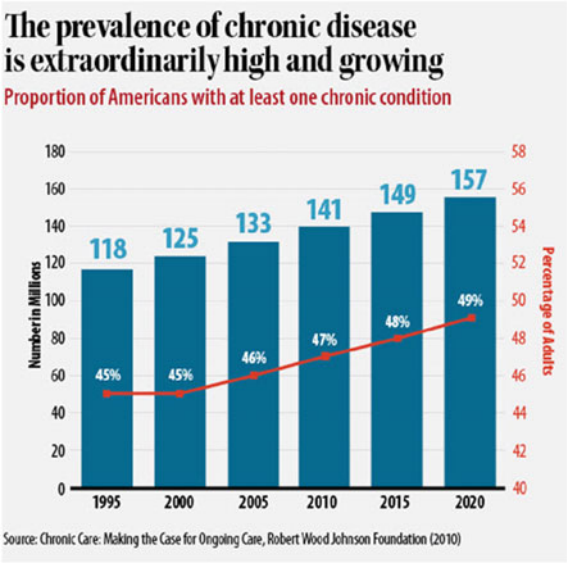
- The "market surveillance" (performed by the Competent Authority) is the set of activities carried out and the measures taken to verify and guarantee that the devices are compliant with MDR (Art. 93) and IVDR (Art. 88). The ultimate goal is to ensure that devices placed on the market do not endanger health and safety.
- **"**Post-market surveillance" (PMS, performed by the Manufacturer) is a proactive and systematic process, designed to monitor the performance of a medical device by collecting and analyzing information regarding its use in the field (Ref. Art. 83 of MDR and Art. 78 of IVDR). An integral part of the Quality Management System (QMS) process, the PMS is based on a PMS plan and is carried out in collaboration with other economic operators.

- Finally, "vigilance" (performed by the Manufacturer, the Authorized Representative EU representative and the competent Authority) is a reactive process and consists in reporting serious incidents and field safety corrective actions (FSCA) to the Competent Authorities involved. Both MDR (Art. 87), and IVDR (Art. 82) describe the requirements for this process, as well as the established deadlines for reporting based on the seriousness of the serious incident. Manufacturers must also report side effects trends, as well as trends of expected unwanted accidents that are not classified as serious.

A. **Situation**: Quality is an ever-increasing topic of importance, both for health technology, ***clinical engineering***, and healthcare in general. The key question: How do we get the best clinical outcomes for our patients? PMS involvement is one way that ***clinical engineers*** can contribute to ongoing safety and quality for medical devices.
B. **Background**: Medical devices are needed for Chronic Disease Management (CDM). The USA Centers for Disease Control have noted that historically 75% of healthcare expenses are devoted to CDM. There is an ongoing need for government initiatives to align incentives between providers, payers, patients [17]. See Fig. 2.
C. **Assessment—*Device*** [18]: In context of ongoing device growth, Adverse Events (AE) and recalls have matched growth and are barriers to improved quality, see Fig. 3.

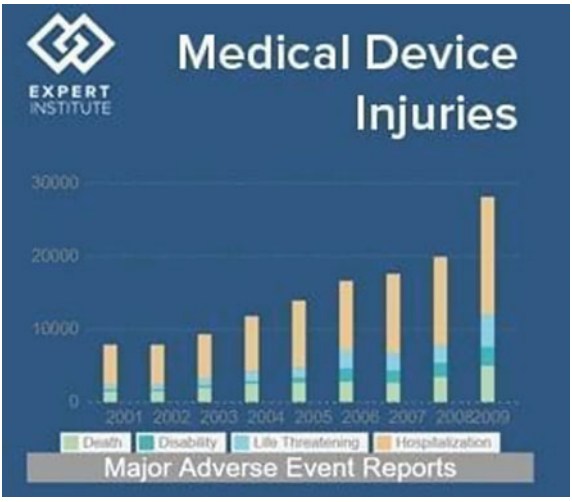
Fig. 1 QMS [16]

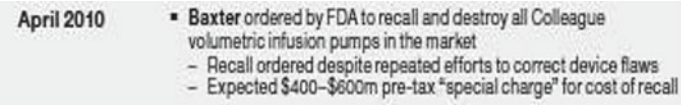
Fig. 2 USA CDM [17]



- *Serious AE*: By product code, Cardiovascular and Diabetes care lead in this segment.
- *Recalls*: Infusion, Imaging, Ventilator, Surgery, Lab devices lead in this segment.
- Many of these AE and recalls can be linked to Chronic Disease Management care.

Fig. 3 USA AE [18]





Example [19]

D. **Assessment—*Manufacturers*** [20]:

- A device that consumers consider to be of high quality is a key consideration in purchasing; quality typically means *efficacy, durability,* and *ease of use.* Device QMS needs to catch up with industry demands, through its value chain, including manufacturers and regulators as well as payors, doctors, and patients for risk areas.
- Factors in rising complexity of device/user environment include: (1) Interoperability; (2) Wireless; (3) mHealth; (4) Device Security; (5) Human Factors, predominantly as a result of Health IT innovations or what is now called Digital Health. All of these factors significantly contribute to quality and QMS issues and are particularly addressed by ***clinical engineers***.

E. **Recommendations** [20]

A 2013 study by the McKinsey Center for Government titled *The Business Case for Medical Device Quality* noted the following:

1. *Design and reliability engineering* can be improved through validation of use and software (SW) robustness.
2. *Post-production monitoring & feedback* into design & manufacturing.
3. *Supplier management processes*, including both material and process change controls.
4. *Quality metrics and measurement systems beyond regulatory compliance.*
5. *Quality organization* that integrates cross-functionally throughout organization.
6. *Performance management* where key roles and quality outcomes are incentivized.
7. *Quality culture* that can be identified and improved for companies experiencing severe quality issues.

The study concluded that:

- *FDA needs to*: address quality gaps, improve processes, and increase collaboration with Industry.
- *Industry needs to*: increase visibility of comparative quality, increase quality versus time to market; balance investment versus cost, address increasing complexity of medical devices and usage environments, and help FDA address that regulatory framework is misaligned with assurance of quality where regulation compliance does not improve quality.

4.1 Case Studies

Each case study illustrates how industry, HDOs and **clinical engineers** *need to work together for safer devices.*

4.1.1 USA: Baxter Infusion Pumps Recall & FDA 2010 [19]—an Unhealthy Example

Problem: ***Numerous design flaws were identified over 5 years***, e.g., wrong shut-down, restart, battery failure, false alarms, failure to alarm, and software (SW) "glitches". These were attributed to the rising complexity of the device user environment noted earlier.

Response:

1. This led to ***FDA's April 2010 Infusion Device Initiative/Guidance*** for added requirements for SW defects, user interfaces, and mechanical/electrical failures, addressed with ***increased pre-market Hazard & Risk analysis***.
2. ***FDA also issued the Total Product Life Cycle-TPLC in 2010*** [21]: As a result of Baxter, etc., the approach utilizes post-market information (TPLC forms, Facility inspections, Recalls, and MDRs) to drive pre-market Reviews.
3. ***In 2014, the Pew Charitable Trust*** [22] gathered stakeholders from FDA, the Centers for Medicare & Medicaid (CMS), the medical device industry, and the physician, patient and consumer communities to discuss key issues around facilitating device innovations that would enhance medical device safety and foster innovation to benefit patients.
   (a) This group requested a new approach to device development. Firstly, for devices to treat patients with serious, unmet medical needs, while ensuring that needed data on device safety and effectiveness is ultimately collected. Secondly, accepting more uncertainty about potential risks of these products at the time they are marketed and then leveraging post-market tools to collect additional data.
   (b) FDA was requested to ensure the following: (1) pre-market studies are completed on time; (2) robust post-market surveillance infrastructure is executed; (3) unique device identifier (UDI) are captured in electronic health records (EHRs); and (4) use of clinical registries are implemented to expedite access to live-saving medical devices technologies.
4. Similarly in 2014, FDA addressed ***Health IT (HIT) challenges*** [23] through FDA Safety and Innovation Act (FDASIA).
   (a) Noting that ***HIT*** incorporates a wide range of products, technologies, and services (e.g., EMR/EHRs) designed for use by health care entities, health care providers, and consumers, to electronically maintain, access, and Health Information Exchanges (HIEs).

(b) ***A nationwide HIT infrastructure*** offers tremendous benefits to the American public: for the prevention of medical errors, a reduction in unnecessary tests, increased patient engagement, advancing patient-centered medical care delivery, improvements in efficiency and coordination of care and HIE among healthcare providers and organizations, facilitating the identification of and rapid response to public health threats and emergencies, and fostering health-related research.

(c) ***Risk-based framework for HIT*.** Four key priority areas and next steps to realize the benefits of HIT:

1. Promote the Use of Quality Management Principles
2. Identify, Develop, and Adopt Standards and Best Practices
3. Leverage Conformity Assessment Tools and
4. Create an Environment of Learning and Continual Improvement.

5 ***How medical devices are typically used in EHR Workflows*** [24]: device association; specifying how device used; device data acquisition; algorithms to improve device data quality; automated device data into flow sheets with user validation; display of data in remote locations; messaging is audio, text, waveforms; documenting procedures; event review, storage, retrieval; and Infusion Drug Error Reduction Systems, just to name a few. These uses are typically overseen in HDOs, by a team of providers, ***clinical engineers***, and IT.

6. ***Technology evolution to HIT in Medical Devices*** [25]: ***A CE expert*** notes that this started with *Discrete* devices (20+ years ago) to *Multi-purpose computers* (15+ years ago) then devices/systems migrating to *Proprietary* (10+ years ago), then *Enterprise* networks (10 years ago); and today—*Hardware + Application SW*, 50% networked on *Enterprise network* and rising. This evolution resulted in challenges, such as: increased complexity, numerous Single Points of Failure (SPoF) to address and multiple vulnerabilities including security. See Fig. 4 from HIMSS (the global Health IT leader organization—https://www.himss.org/) in 2014.

4.1.2 *EU: Industry Business Case Industry, 2013* [20]: A Healthy Example Using All of the Recommendations Noted Earlier

***Problem*: A "European supplier of high-tech medical devices faced several major challenges, e.g.,** quality costs above competitor levels, a focus on problem resolution after delivery rather than problem prevention in development and production, and low-quality performance of suppliers.

***Response*: The company's management went forward with a transformation** aimed to reduce quality-related costs (e.g., warranty costs and claims) while increasing capacity.

1. The implementation included a reorganization of the quality function as well as the design and launch of four major process improvements: *design for reliability*—addressing McKinsey's 2013 recommendation (1), a key *manufacturing*

Fig. 4 Security built into QMS

process change—addressing (2); *in-market product performance monitoring*—also addressing (2); and s*upplier quality oversight*—addressing Recommendation (3).

2. The supplier also conducted benchmarking of *quality systems and processes*—addressing (4) with other industries.
3. Key to the success of the company's transformation finally were the introduction of *a* ***proactive quality mind-set—***addressing McKinsey's recommendations *(5–7)* throughout the company, a system for tracking, conducting performance dialogues around key indicators, and disciplined root-cause problem solving.

Results: There was a reduction in cost of quality (with reduced warranty costs, and increased capacity) by 35%; and improved profit by 2.5% of revenues.

Case Studies [26] *from* **Kaiser Permanente (KP) [Note**: where the author as a national ***Clinical Engineering*** leader worked from 1992–2016; the following Case Studies & figures presented in the public domain by the author with KP content permission during those years.]

4.1.3 Large USA HDO Case Study: *Infusion Pump Systems*

Overview: KP replaced Baxter recalled devices with 17,000 CareFusion Alaris large volume infusion pumps (LVP) used for inpatient and clinic care across KP Regions in 2011–2012. KP on average has an LVP 'Brain' (PC Unit) and 1.5 Modules for each patient care set-up. See Fig. 5 for KP LVP IT Infrastructure.

Clinical Requirements were met by: utilizing *Guardrails* Drug Error Reduction System (DERS) with downloadable clinical quality information (CQI) per pump

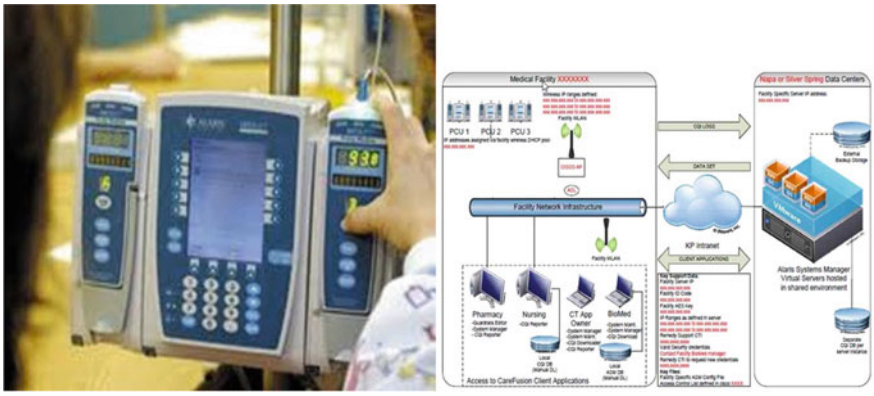


Fig. 5 KP LVP Photo and KP IT Infrastructure

and programmable profiles per use area to monitor quality of use, and Drug Library data sets with 2500 programmable drugs across all settings. A supporting ***Clinical Engineering*** (called ***Clinical Technology-CT***)/IT infrastructure was developed, with the ability to later integrate LVP into KP's EHR.

Quality Challenges: Several FDA alerts for design, SW/firmware, cleaning and infection control, equipment preventive maintenance, and other issues; over-infusion Incidents supplier follow-up; warranty and post-warranty support concerns; and alarms, e.g., such as tubing setup and artifact interference in certain clinical settings.

Other HIT Challenges included:

- wireless challenges for CQI downloads and SW change management
- the two years it took the manufacturer to re-design and correct the wireless card
- eventually hitting the limit and needing to exceed the 2500 programmable drugs for all clinical use cases
- security protocols for all device use cases

4.1.4 KP Case Study 2: USA Alarm Management Systems (AMS)

Overview: Emergin (a Philips product) AMS was integrated with patient monitors, nurse call, and various tele-communication systems across several KP hospitals in 2011–2012. KP Nursing developed a comprehensive approach to AMS during 2013–2014, resulting in alarm alerts being reduced. However, there were some challenges in deployment.

Clinical Requirement Met: In 2011, KP began using Emergin's *IntelliSpace* Event Management, an alert notification solution with an enhanced platform for expanded clinical support, to manage disparate care system alerts. For various clinical settings of higher acuity, the tool helped hospital clinical staff in determining the optimal mix

of people / process / technology (near-term, long-term), e.g., what alarms should be monitored by nurses or monitor technicians and at what patient-to-technician ratios.

Quality Challenges: Initially, scalable solutions were not fully developed, causing server overloads and intermittent system shutdowns. The supplier had purchased a smaller company (Philips and Emergin) to gain this functionality but had not fully assessed the current product and its capabilities. A reduction of monitoring technicians by KP staff occurred before the alarm response protocols were fully developed, which became a patient safety issue. This also occurred when the accreditation body (The Joint Commission) was issuing related National Patient Safety Goals and alerts, happening across the country. AMS was jointly supported by KP ***Clinical Engineering*** & IT.

Other HIT Challenges included:

- recognizing that the AMS was a secondary alarm notification tool and was not optimized for primary notification.
- readily monitoring and adjusting individual device AMS configurations.

KP conducted end-to-end testing and invested significantly to build up IT infrastructure to support an enterprise-wide approach using the tool. See Figs. 6 and 7 for KP's AMS IT infrastructure and strategy.

4.1.5 KP Case Study 3: USA Integrated (Digital) Operating Room (OR) Systems

DOR: KP began deploying Integrated or Digital OR (DOR) systems along with its High-Definition (HD) Rigid Endoscopes via its national Surgeon & Perioperative Nursing leaders purchasing group in 2006. By 2015, there were over 200 DOR systems in place whose images were able to be integrated with PACS and EHR (called KP HealthConnect-KPHC). See Figs. 7 and 8 for a view of KP's Integrated OR Systems and its IT infrastructure.

Clinical Requirements met include: (1) Superior image quality of surgical video (HD), with easy-to-use system features for staff, and supportable by KP ***Clinical Engineering*** and IT. (2) Surgical images and video are able to be seamlessly integrated with PACS systems and EHRs. (3) DOR functionality is able to keep pace with latest computer/tele-communication technologies, e.g., streaming video, e-consult Interfacing/interoperability of various image sources with DOR systems, e.g., C-Arms, ultrasound, and digital microscopes.

Quality Challenges include: (1) Device interoperability ensuring image quality when using different DOR and Rigid Endoscopy suppliers; (2) Storage and retrieval of surgical images with appropriate privacy and security compliance; and (3) Reliability, reprocessing, and durability of surgical video Endoscopy.

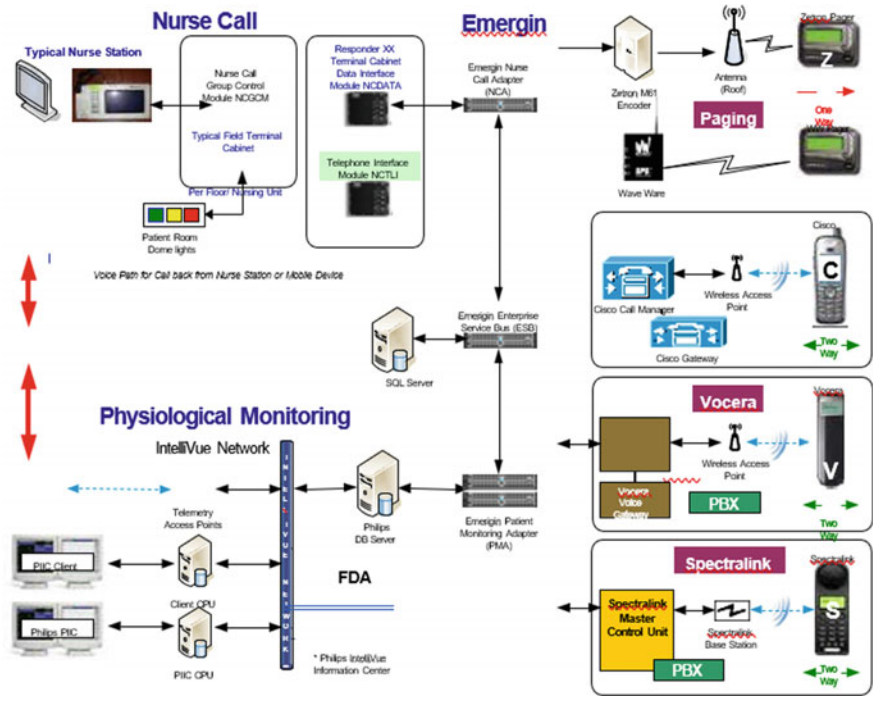


Fig. 6 KP's AMS IT infrastructure. *Source* Lewis MD & T. Judd, *Simulation: Enabling Biomedical Device Assessment, Integration, & Adoption,* AAMI 2011

Other HIT Challenges included: (1) Different image capture and management strategies for different surgical sub- specialties; (2) Sending images to mHealth platforms, e.g., SmartPhones, Tablets while meeting needed privacy and security; (3) Wireless image transfer and fidelity; and (4) Ongoing testing of image quality (Fig. 9).

Source: J. Lewis MD & T. Judd, Simulation: Enabling Biomedical Device Assessment, Integration, & Adoption, AAMI 2011.

4.1.6 Observations Re PMS, November 2022-Present

1. ***AAMI News*, December 2022** [26]: Historically, manufacturers have recognized the value in following up with complaints and concerns from users. Now, however, the bar has been raised with recent regulatory and international standards updates. According to a working group convener for the International Organization for Standardization's ISO/TC 210, the 210 technical committee establishes standardization of requirements and guidance for the QMS and corresponding general aspects for medical devices. Their work recently has zeroed in on PMS.

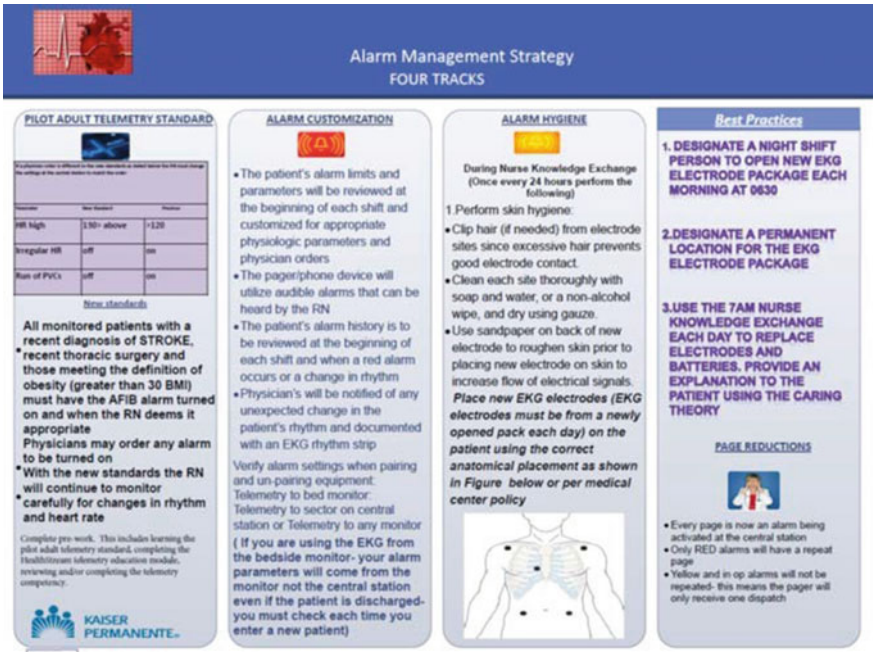


Fig. 7 KP's AMS IT strategy. *Source* Lewis MD & T. Judd, *Simulation: Enabling Biomedical Device Assessment, Integration, & Adoption,* AAMI 2011

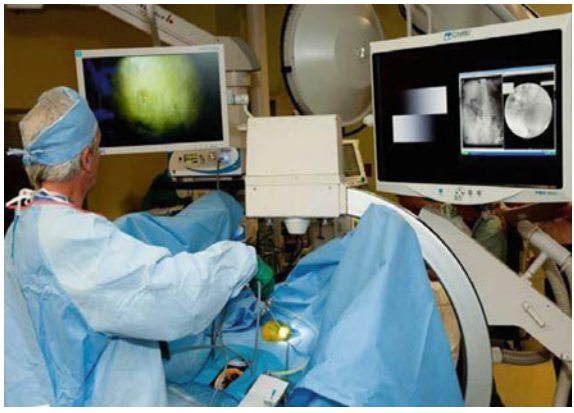


Fig. 8 KP integrated OR system

There is a renewed emphasis on "active engagement for these post-market activities so that you're no longer just sitting there waiting to receive the information," the ***biomedical engineer*** convener explained. "You're going out there and asking the users, 'is our product performing how it was intended? Does it meet your expectations?'" "We don't often talk in the medical device world about customer satisfaction,

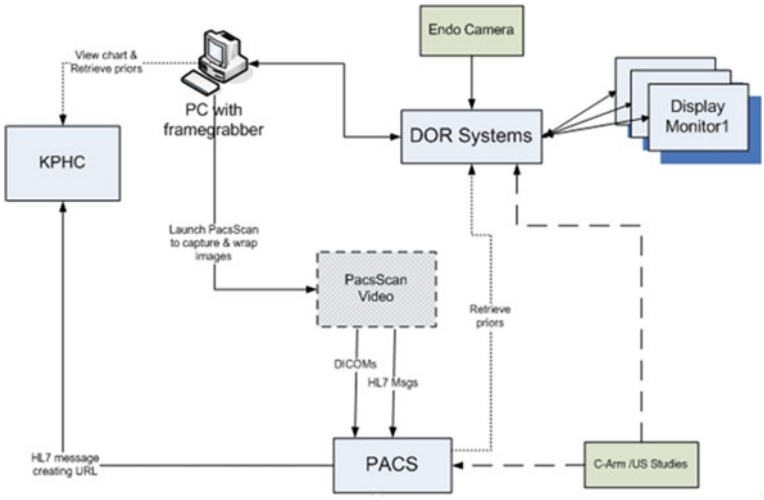


Fig. 9 KP integrated OR IT infrastructure

because it's really about the safety of the product, but obviously, you have satisfied customers if it is performing to the requirements that ensure it's safe!"

Some ongoing work involves assessing the influence ISO/TR 20416:2020 has had on a changing international market. This technical report (TR) provides guidance on the PMS process consistent with relevant international standards, in particular ISO 13485 and ISO 14971. "It's funny. We're essentially doing post-market surveillance on the post-market surveillance guidance!" ISO 13485, the international standard for QMS of medical devices throughout their entire life cycle, "says that you have to actively gather this information. But it also states that you have to do this within the applicable regulatory requirements." This ultimately means that those regulatory requirements can change from region to region. Fortunately, the convenor and his colleagues sought to help manufacturers create and understand the processes of collecting post-market data "whether it's literature review, or conducting user surveys, or launching a focus group—doing those types of things to gather data." "And we can also help them understand the processes and statistical techniques to analyze that data. So, we've focused TR20416 on those two aspects: the collection and analysis of post-market data."

"With this kind of guidance, manufacturers can be better prepared to meet a potentially wide gamut of different regulatory requirements while fueling other quality management, such as product improvement." The ***biomedical engineer*** convener went on to describe how an additional major benefit of effective collection and analysis of post-market data is the ability to confirm if risk management strategies implemented in the past "are actually achieving the goals that those risk management activities were designed to do." He encouraged manufacturers to assess the guidance document for themselves and to answer future user surveys, so the document itself can improve just as the medical devices they influence improve for patient safety.

FDA *draft* Guidance Document [27]**, December 2022**, *Voluntary Malfunction Summary Reporting Program for Manufacturers. An expert Clinical Engineer's Commentary on this proposed document*: "Here is my brief perspective: It won't do much good all. Why? Well, the (USA) Medical Device Reporting Act, regardless of prior versions, was impotent, based on my experience as a medical device manufacturer AND large fleet owner/servicer/manager from 1990-2000. The process of device problems and complaints for manufacturers involved internal and external legal review that shields a lot of incidents and details from formal FDA reporting. Many incidents and malfunctions are attributed to user or use errors, sidelining such items from any formal reporting."

"The manufacturers have to tread a fine line that is, in reality, not so fine. Yes, they have an ethical and legal obligation to report issues under GMP, MDR, and perhaps eventually this new process. On the other side of the equation are huge potential risks, including the costs of device recalls, loss of market share, AND potentially massive liability litigation and awards."

"The huge Philips CPAP recall illustrates the current scale and scope of costs & complexities. https://www.drugwatch.com/news/2022/12/13/recalled-philips-cpap-injuries-fda/. This product is an interesting case, because it is a consumer product crossover, and consumer use errors add to incident assessment complexities. The Steris (Sterisgenics) ETO lawsuits are another example that spreads across many manufacturers https://www.medtechdive.com/news/device-companies-lawsuits-ethylene-oxide-sterigenics/632545/."

"In my opinion and experience, manufacturers infrequently and inconsistently comply with the mandatory regulations (MDR or GMP) until such problems are publicized by the press. Yes, some CEOs and companies risk being forced into very onerous FDA Consent Agreements that are so bad they force the companies towards bankruptcy or sale unless they are part of a huge global conglomerate with deep pockets. Oh, and then there is the whole wide-open space of electronic medical record systems, AI, and related innovations that continue to dance on the edge of "we are not a medical device; we are merely a replacement for the good old fashioned paper records..." I hope I am wrong, but to me, FDA's idealist notion that manufacturers will voluntarily self-report malfunctions will be useless from Day 1."

2. **Technology and Health Care, November 2022** [28]**, *Post-market surveillance of medical devices: A review.* Lead authors, 2 European *Clinical Engineers***: Although the regulatory framework prescribes PMS of medical devices, the process itself is not harmonized with international standards. Particularly, conformity assessment of medical devices (MDs), as an important part of PMS, is not measured and managed in a traceable, evidence-based manner. The lack of harmonization within PMS results in an environment of increased adverse events involving MDs and overall mistrust in medical device diagnosis and treatment results.
3. **Technology and Health Care, January 2023** [29]**, *Evidence-based maintenance of medical devices: Current shortage and pathway towards solution*,**

same *CE* lead authors as item 2 above*:* The introduction of standardized conformity assessment method for testing of safety and performance of medical devices will produce traceable, accurate, complete, verified, unbiased and standardized data. With this, existing digital databases will serve its purpose. Standardized conformity assessment method requires medical device quality testing by independent third-party bodies and/or manufacturers/distributors, but the evidence produced during these activities must be complete, accurate, verified, traceable and unbiased. With this approach two challenges would be solved. Firstly, safety and quality of medical devices would be inspected with calibrated etalons by independent parties introducing more transparency into the overall process. Secondly, standardized data, when entered into existing databases, would result in ready-for-analysis databases using various techniques. The more analysis ready data is created the more data mining can be done.

4. **Technology and Health Care, Jan. 2023** [30]**, *A novel method for conformity assessment testing of mechanical Ventilators for post-market surveillance purposes, ECGs, Dialysis machines: same CE lead authors as item 2 above***. A standardized approach in conformity assessment testing of mechanical ventilators, ECGs, and dialysis machines during PMS, besides increasing reliability of the devices, is the first step in digital transformation of management of these devices in healthcare institutions, opening the possibility for use of artificial intelligence. Previous similar documents were published earlier for Infusion and Perfusion Pumps, Infant Incubators, Anesthesia Machines, and Defibrillators.

5 Conclusions

It was noted from the Case Studies of a large USA health system [31] of 40 hospitals and 600+ clinics that manufacturers (suppliers/industry) were often not prepared for the rising complexity of devices and user environments. The case studies demonstrate that typical pre- and post-marketing surveillance would not be enough to ensure safety. ***Clinical Engineers*** would have to be more deeply involved in several aspects of life-cycle management and a closer partner with industry. Here are several examples of how that closer partnership might occur:

- Device testing and ensuring device integration functionality can be assured via supplier and purchasing controls.
- The use of UDI, eMDR, and clinical registries could improve industry and customer visibility for rapid identification and resolution of quality, PMS, and QMS issues.
- Ongoing recognition of available tools to improve QMS, PMS and related processes, e.g., testing of software components.
- Helping industry to better understand customer clinical requirements, particularly as they relate to customer measures of quality and device to EHR interfaces.

- Closer partnerships of ***clinical engineers*** with industry during design and development of critical Quality & QMS metrics, and post- production and deployed device monitoring, and ongoing training.
- To determine strategies not only for initial but ongoing Customer training and use of clinical best practices to modify quality, QMS, and PMS processes where needed.
- To partner closer with customers for equipment support (e.g., ***clinical engineers***), for early warning about emerging clinical requirements.

There are other ongoing attempts to improve PMS. Examples include:

- Doing post-market surveillance on the post-market surveillance guidance; typically conducted by ***Clinical Engineers***
- Considering Manufacturer Voluntary Malfunction Self Reporting
- Harmonizing PMS with relevant International Standards; an effort often led by ***Clinical Engineers***
- Considering standardized conformity assessment method for testing of safety and performance of medical devices approaches, typically conducted by ***Clinical Engineers***
- Considering digital transformation of management of medical devices in healthcare institutions opening the possibility for use of artificial intelligence, typically conducted by ***Clinical Engineers.***

It will be interesting to see how these approaches move forward in the coming years. Global Clinical Engineering groups, who partner regularly with the World Health Organization (WHO) could lead various efforts with industry and other healthcare stakeholders. These include the ***Global Clinical Engineering Alliance*** [32] (GCEA) and the ***IFMBE Clinical Engineering Division*** [33] (CED), with their combined network of over 600 global CE and HT leaders from over 210 countries.

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Application of Artificial Intelligence for Management of Maintenance and Prediction of Performances

Lejla Gurbeta Pokvić, Amar Deumić, Adna Softić, and Almir Badnjević

Abstract The application of artificial intelligence (AI) in the field of management, maintenance and performance prediction has been increasingly present in recent years. AI is used to automate various tasks and processes, improve decision-making and increase overall efficiency. This paper explores the various ways in which artificial intelligence is being applied to manage, maintain and predict performance in healthcare. Specifically, the paper discusses the use of AI-powered predictive maintenance systems, real-time performance monitoring, and data analytics to optimize operations and reduce downtime. Furthermore, the document highlights the potential benefits of artificial intelligence, including improved security, cost savings and improved user experience. Although there are some challenges associated with the implementation of artificial intelligence in these areas, the paper concludes that the advantages of using artificial intelligence for management, maintenance and performance prediction outweigh the potential disadvantages, and that artificial intelligence will continue to play an increasingly important role in these areas in the future.

1 Introduction to the Application of Artificial Intelligence in Maintenance Management and Performance Prediction

Activities related to medical devices in the European Union were regulated by the Medical Device Directive (MDD) published in 1994 [1]. This directive defined all aspects of design, production, testing, approval, certification and surveillance of medical devices. MDD covered all medical devices that were intended for use in the European Union whether they were made inside the European Union or made for import in the market of the European Union. It was an important directive that provided a framework for medical devices to ensure they comply with European

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standards. However, it lacked some beneficial points such as unique identification for every device, directions for single-use medical devices, ancillary medical products, implantable medical devices and devices that incorporate the human tissues. Also, MDD lacked the defined processes for pre-market and post-market surveillance of medical devices used across the European Union. These shortcomings resulted in the creation of new, improved regulations published in 2017.

Two new regulatives named "European Union Regulation 2017/745 on Medical Devices (MDR)" [2] and "European Union Regulation 2017/746 on In-Vitro Diagnostic Devices (IVDR)" [3] were published in May 2017. After its publication, the transition period from the old MDD to the new MDR was set to three years, but with the unexpected outburst of COVID-19 virus, it was prolonged for another year. Finally, the new MDR became fully applicable on 26th May 2021, and the IVDR became applicable on 26th May 2022, after a five-year transition period. Regular inspection of medical devices that have measurement functionality is essential to ensure their proper functioning, a fact that has been emphasized by the COVID-19 pandemic [4].

New regulations represented considerable development and strengthening of the current regulatory system for medical devices in the European Union. When it comes to management and maintenance of medical devices, the biggest difference is seen in the process of post-market surveillance of medical devices. In the old MDD, both pre-market and post-market surveillance were covered, but not in depth. Pre-market processes were addressed more comprehensively compared to post-market surveillance processes. Pre-market processes are harmonised by related standards, which were adopted internationally. These standards are classified as basic safety standards such as ISO 13485 Medical devices—Quality management, group safety standards such as IEC 60601-1 Medical electrical equipment, and product safety standards such as ISO 80601-2 Medical electrical equipment. By the Medical Device Directives, PMS is defined in Chapter I, Article 2, (40a), as the action MD manufacturer's procedure to review experience that was gained from their devices in the post-production phase. This resulted in an obligation of the manufacturer to report a device-associated incident after it occurred. Despite this directive, the PMS process is not clearly defined and is left on the manufacturer to perform. System like this implies a passive reactive way of managing incidents. PMS is a collection of processes and activities used to monitor the performance of a medical device. These activities are designed to generate information regarding use of the device to expediently identify device design and/or usage problems and accurately characterise the real-world device behaviour and clinical outcomes. The need for PMS arises immediately upon commercialization of the device. The previous edition of the book "Inspection of Medical Devices" provided valuable information on how the development of medical devices affects the delivery of healthcare, highlighting the significance of effectively managing health and dealing with the challenges that come with it [5].

Over the years, post-market surveillance relies on manufacturer obligation to report incidents involving their medical devices to relevant regulatory bodies. They are obliged to provide user and service manuals and training of professionals who conduct service activities. All conformity assessment standards, including ISO

Table 1 Estimated number of medical device failures during a 10-year period based on manufacturer and user facility device experience (MAUDE) database [6]

Medical device	Death	Injuries
Infusion and perfusion pumps	>800	>1300
Defibrillators	>700	>1000
Mechanical ventilators	>300	>500
Therapeutic ultrasound	>200	>400

13485:2016, now require manufacturers to maintain a PMS system regardless of how their medical device is classified. However, this approach has its limitations. Even though this type of data gathering generates some valuable information, it still does not prevent injuries and deaths that occur with usage of MDs. This information can be seen from Table 1, where a number of reported incidents (injuries and deaths) associated with use of MDs are presented. According to the EU MDR Article 83: "Post-market surveillance system of the manufacturer", it is stated that the system of reporting and documenting information about each MD must be an integral part of the manufacturer's quality management system. With this said, it is seen that this results in rather confusion and mess introduced into already unclearly defined processes.

Global Harmonization Task Force (GHTF) [7] discussed post-market surveillance in 2005 and conclusions were drafted in a report, which defined the specific tasks needed for post-market surveillance in the industry and discussed how the requirements for each task could be harmonised across regulatory environments. This report was later updated by the International Medical Device Regulators Forum (IMDRF) [8] to elaborate on reporting guidelines for adverse events. The Global Harmonization Task Force (GHTF) is an international organization that is dedicated to improving the safety and effectiveness of medical devices through the development of guidelines and standards. Established in 1992, the GHTF is comprised of regulatory authorities from around the world, and its work is focused on promoting the harmonization of regulatory requirements for medical devices. One of the key areas of focus for the GHTF is the development of guidelines and standards for the testing and evaluation of medical devices. These guidelines and standards aim to ensure that medical devices are safe and effective for use, and to provide a common framework for the regulatory approval of medical devices around the world. The GHTF has developed a number of guidelines and standards on topics such as clinical evaluation, risk management, and post-market surveillance, which are designed to support the regulatory authorities that are responsible for the approval and oversight of medical devices (GHTF 2011). In addition to its work on guidelines and standards, the GHTF is also involved in a number of other activities that are aimed at improving the safety and effectiveness of medical devices. These activities include the promotion of best practices for the development and testing of medical devices, the sharing of information and expertise between regulatory authorities, and the development of training and education programs for professionals working in the medical device industry (GHTF 2012). The International Medical Device Regulators Forum (IMDRF) is an international organization that is dedicated to improving the safety and effectiveness of medical devices through the development of guidelines and standards. Established in 2011,

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The MDR addresses the recognized problem of post-market surveillance and emphasises the importance of standardisation and harmonisation of the system for supervision of medical devices that are already in use. The MDR obliges stakeholders to monitor the quality, performance and safety of a device throughout the product lifecycle and to apply corrective or preventive actions when necessary. Post-market surveillance is the process of monitoring the performance and safety of medical devices after they have been placed on the market. It is an important aspect of ensuring the safety and effectiveness of medical devices, as it allows regulatory authorities to identify and address any issues or risks that may arise after a device has been approved for use.

The European Medical Device Regulation (MDR) is a framework that is designed to ensure the safety and effectiveness of medical devices in the European Union (EU). The MDR addresses the recognized problem of post-market surveillance by establishing a number of requirements and provisions that are designed to support the ongoing evaluation and monitoring of medical devices. One of the key provisions of the MDR related to post-market surveillance is the requirement for manufacturers to establish and maintain a post-market surveillance system (PMS). Under the MDR, manufacturers are required to have a PMS in place that is capable of collecting and analyzing data on the performance and safety of their devices, and that is capable of identifying and addressing any issues or risks that may arise. In addition to the requirement for manufacturers to establish a PMS, the MDR also establishes a number of other provisions related to post-market surveillance. These provisions include the requirement for manufacturers to report any adverse events or incidents related to their devices to regulatory authorities, and the requirement for regulatory authorities to conduct periodic reviews of the safety and effectiveness of medical devices that are on the market.

PMS as defined in Article 2 (60) by MDR. It is one of the topics specifically called out for monitoring by the person responsible for regulatory compliance (new Article 15). Article 83 suggests that the PMS system is to be used to update the clinical evaluation, update the benefit-risk determination, update the instructions for use and labelling etc. Article 84 requires that a PMS plan has to be developed for each device. The conclusions which result from the review of the PMS data for the device have to be summarised in a report. In the case of Class I devices (new Article 85), the report must be kept available for any Competent Authority who wishes to examine it. However, neither the content of the PMS report, nor the frequency with

which has to be updated are defined. In contrast for Class IIa, Class IIb and Class III devices (new Article 86), the main outputs of the new Periodic Safety Update Report (PSUR) are prescribed. They include the current benefit-risk determination and the current findings of the Post Market Clinical Follow-up (PMCF) activities. The frequency with which the PSUR must be updated is also defined; for Class IIa devices the PSUR must be updated at least every two years. For Class IIb and Class III devices the PSUR must be updated at least annually. Additionally, in the case of Class III devices and implantable devices, the PSUR must be submitted annually to the Notified Body, and the Notified Body's evaluation report has to be made available to the Competent Authorities through the EUDAMED system.

The European Commission has developed EUDAMED [9] (European Databank on Medical Devices) in order to supervise medical devices already in use, which is part of the standardisation and harmonisation of the system. This is the IT system developed by the European Commission to implement Regulation (EU) 2017/745 on medical devices. It functions as a registration system, a collaborative system, a notification system and a dissemination system (open to the public) and will be interoperable. EUDAMED acts as a central hive for the exchange of information between national competent authorities and the European Commission. EUDAMED is the European Union's (EU) database for medical devices. It is a centralized database that is designed to support the EU's regulatory framework for medical devices, and is an important resource for regulatory authorities, manufacturers, and other stakeholders involved in the medical device industry. One of the main functions of EUDAMED is to provide a single, centralized source of information on medical devices that are available on the market in the EU. The database contains information on the characteristics, performance, and safety of medical devices, and is an important resource for regulatory authorities, manufacturers, and other stakeholders who need to access this information. EUDAMED also plays a key role in supporting the EU's regulatory framework for medical devices. The database is used to support the registration and certification of medical devices, and contains information on the status and history of medical devices in the EU. This information is used by regulatory authorities to ensure that medical devices are safe and effective for use, and to support the ongoing evaluation and monitoring of medical devices. In addition to its regulatory functions, EUDAMED also serves as a platform for the exchange of information between stakeholders in the medical device industry. Manufacturers, regulatory authorities, and other stakeholders can use the database to share information on the performance and safety of medical devices, and to collaborate on issues related to the development and use of medical devices.

According to the available information every economic operator—EU and non-EU manufacturers, authorised representatives, system/procedure pack producers and importers has to register as an actor in EUDAMED and provide the required information. As it can be seen, although the EUDAMED specifies a module for vigilance and post-market surveillance, this module is not based on evidence but it still relies on the data provided by manufacturers and distributors. Global digital revolutions are having an impact on the medical device management industry, necessitating data gathering and usage for informed evidence-based decision making [10–13].

The problem was identified in paper by Badnjević et al. (2021) where a systematic review was conducted on the EU and non-EU regional post-market surveillance of medical devices [14]. This paper concluded that post-market surveillance mechanisms lack harmonisation and standardisation that is unique for the whole region of the European Union. In order to achieve a goal of post-market surveillance and to improve patient care, key elements of post-market surveillance like the medical device registry, adverse event reporting, and post-market performance evaluation should be harmonised using the same strategy as it was done for pre-market processes.

The gap in management of maintenance of medical devices opens up space for a lot of opportunities today's technology provides. Development of technology and informatics introduced the world to artificial intelligence. Artificial intelligence provides valuable resources that can be used in this field. However, its power has not yet been used to the full extent. The gap of management of maintenance of medical devices could be filled with application of artificial intelligence. When it comes to maintenance of medical devices, another topic that can be covered is the application of artificial intelligence for prediction of performance of medical devices. This system can be based on sophisticated artificial intelligence that would improve the safety and reliability of medical devices used in healthcare institutions. It can use inputs from data collected during post-market surveillance. Those data contain all the information about a specific device including: name of the manufacturer, model of the device, year of production, number of working hours, information about its previous maintenance, information about malfunctions of the device. Apart from these, the data would contain the information about the electrical safety tests in the past, as well as performance of the parameters from each device. Based on safety and performance measurement data with established traceability, this system predicts device performance and failure in the near future.

Application of artificial intelligence is already in use in some fields of medicine. Artificial intelligence techniques imitate human decision-making but with a huge advantage of great precision. When applied on the properly prepared database of information, it outperforms the speed and accuracy of any human being. One of the main pillars for further developments in the industry is the use of AI in healthcare, which has the potential to increase efficiency while reducing costs. Regulators from all over the world have realised the value of artificial intelligence for enhancing healthcare, transforming hospital-centred systems into integrated care, enhancing health promotion and disease prevention, and adopting customised medicine. To encourage the study, creation, and acceptance of these techniques and technologies, many nations have created or are creating national artificial intelligence strategies and policies. A range of medical gadgets for everyday use in daily life are now available as a result of the integration of this technology in medicine, including wearable medical equipment, electronic health records, and remote patient monitoring systems (EHR). The potential of artificial intelligence applications is enormous, ranging from clinical decision-making and public health to biomedical research and drug discovery, health system administration, and service redesign, given the expanding amount of data created in the healthcare industry. Presence of artificial intelligence can be seen in great results achieved in diagnosis and therapy administration on patients. Its already

been used in the field of diagnostic medical imaging [15], diagnostic of meningitis [16], diagnostic of neonatal sepsis [17], diagnostic of prostate cancer [18], diagnostic of pulmonary emphysema [19].

Predictive maintenance using artificial intelligence has also been used in different industries than medicine. Such cases are reported in sustainable industry [20], aircraft industry [21], production lines and fabrication industry [22] and automotive industry [23]. However, field of clinical engineering in scope of prediction of failure of medical devices has not been covered. Since clinical engineering represents a field that medical industry relies on heavily, there is clearly a present gap that needs to be investigated.

2 Overview of the Different Types of Maintenance Management

Medical devices provide critical insight in a patient's health. It enables medical staff to diagnose, treat or monitor patients. To ensure these services are provided in a safe and effective way, the management system must be properly led and maintained. Management staff must address all related policies including equipment financing, deployment, tracking and utilisation of medical devices, training and access to manufacturer's instructions and follow through the whole device's life cycle. These policies ensure that every device used in healthcare institutions suits the specific needs for the proper treatment, ensure that every device is used properly according to the manufacturer's instructions, and ensure that it is traceable and maintained in a safe condition. Proper quality management system means keeping records of the processes. Records obtained from the management system of devices includes keeping records about the purchase price of the devices, keeping its whole history through instalment and its operation in institutions [24].

Management of medical devices is a plan that usually includes several steps that should be followed. First step in the management system is planning. This process is essential because it provides insight into the needs of institutions provided mostly by medical and technical staff. Planning is focused on getting information on what kind of devices are needed and what they should fulfill. Needs and benefits obtained through this step are beneficial to ensure both compliance with regulations and adequate given treatment.

After plans are created the next step is acquisition of the device. When it comes to acquisition, the financial situation must be taken into consideration as well. An institution opts for acquiring a device with as lowest price as possible with the possibility to improve clinical outcomes.

When the device is shipped to the institution, it must be thoroughly inspected. Every device must contain the existence of accessories, user manuals, compliance with given specifications and electrical safety. Before putting the device in operation, it must be properly installed. After being placed in work, information about the device

must be properly documented. Those include all information about the device. Since medical staff is the one using the device most of the time, they would be first in the line who recognize the problem or deviation with the device. If there is a problem with the device, medical staff file a report to the technical department. Technical department takes this report into consideration and makes a decision on how to proceed.

2.1 Corrective Maintenance

The type of maintenance called corrective maintenance, also known as run-to-failure, is employed when a machine fails unexpectedly during production. It is necessary for prompt restoration of the operation of the machine. Unfortunately, this type of maintenance is accompanied by some major drawbacks. Machine failures often occur without any warning signals and at inconvenient times, causing an unexpected halt in the manufacturing process and leading to additional production costs. Moreover, corrective maintenance is time-consuming and can be expensive [25].

2.2 Preventive Maintenance

Preventive maintenance, also known as use-based maintenance, involves performing maintenance activities after a predetermined amount of time or machine usage, regardless of the actual wear and tear. This type of maintenance relies on probabilities that certain components will fail within a specified period. Preventive maintenance has advantages such as reduced likelihood of equipment failure and increased equipment lifespan. However, it has the disadvantage of requiring production interruptions at scheduled intervals for maintenance work, as well as potentially replacing components that still have useful lifetime remaining [26].

2.3 Predictive Maintenance

When maintenance is performed based on real-time operational data instead of a fixed schedule, it is called predictive maintenance. This type of maintenance, also known as condition-based maintenance or monitoring, is initiated in response to a specific equipment condition. Diagnostic equipment is used to measure various physical conditions of the equipment, such as temperature, vibration, noise, lubrication, and corrosion. Maintenance work is only undertaken when one of these indicators reaches a pre-specified level, indicating that the equipment's condition has deteriorated. The ultimate goal of predictive maintenance is to estimate the remaining useful lifetime of the equipment, providing the user with information to plan maintenance work and avoid unplanned equipment downtime [27, 28].

3 The Role of Artificial Intelligence in Optimizing Maintenance Management Strategies

3.1 Application of Machine Learning Algorithms for Predictive Maintenance

Predictive maintenance refers to a systematic approach of monitoring a machine's actual condition, operating efficiency, and other indicators at regular intervals, with the aim of minimizing unplanned downtime and maximizing the interval between repairs. This method can significantly enhance productivity, product quality, and overall effectiveness of production. To apply predictive maintenance effectively, several tools such as vibration monitoring, thermography, and tribology can be used to gather actual data on maintenance activities and determine the actual condition of the system. The approach relies on the machine's current state rather than general statistics like mean time to failure for scheduling maintenance activities. By implementing predictive maintenance, companies can reduce costs associated with machine repairs and maximize operational efficiency.

Machine Learning (ML) is a subfield of artificial intelligence that has become a valuable tool for constructing intelligent predictive algorithms in various domains. ML techniques are capable of processing large and complex datasets with multiple variables and uncovering intricate patterns and relationships within them. As a result, ML is an effective method for developing Predictive Maintenance (PdM) applications, particularly in challenging and dynamic settings such as industrial environments. Nonetheless, the success of PdM applications using ML approaches depends on the careful selection of the most suitable technique for the problem at hand [29].

Types of models in machine learning that are useful for PdM are:

1. Supervised learning—where knowledge on the happening of failures is there in the dataset;
2. Unsupervised learning—where logistic or process knowledge is there, but maintenance related data does not exist;
3. Deep learning—constructed from multiple simple machine learning algorithms [30].

Supervised learning involves using a dataset consisting of labelled examples of a particular outcome. For instance, if we want to determine whether a component is faulty or functioning correctly, these two states are the potential labels. The aim of supervised learning is to develop a model using this dataset that can take a feature vector x as input and provide output information that helps us identify the label for that feature vector. Logistic Regression, Support Vector Machines, and Decision Trees are some popular models used in supervised learning.

Unsupervised learning involves a dataset that consists of a feature vector x, but there are no labeled outcomes associated with it. The objective of this type of learning is to build a model that can take the feature vector x as input and convert it into another vector or value that can be utilized to address the problem at hand. This approach is

beneficial in gaining insights into the data, rather than making direct predictions. It is often employed in classification models and can also be used to identify various health stages of a degradation pattern. The most widely used algorithms for unsupervised learning are K-means clustering and Nearest Neighbor algorithms.

Deep learning is a unique type of learning that doesn't fit neatly into any of the other traditional learning types. These algorithms are made up of multiple simpler machine learning algorithms, which are organized into complex networks that resemble the structure of the brain. They are capable of learning from large sets of data and can be used for both supervised and unsupervised learning. Some examples of deep learning models include Artificial Neural Networks, Recurrent Neural Networks, and Autoencoders. While machine learning models like Support Vector Machines, Logistic Regression, and Decision Trees performed well with limited data, deep learning models worked better when there was an abundance of data, but didn't perform as well with reduced amounts of data.

3.2 Use of AI-Based Tools for Real-Time Performance Monitoring and Diagnostics

The use of AI-based tools for real-time performance monitoring and diagnostics has gained significant attention in various fields such as manufacturing, healthcare, and transportation. This approach involves the integration of artificial intelligence and machine learning techniques with monitoring and diagnostic systems to enable real-time analysis and prediction of performance and system behavior.

One of the key advantages of using AI-based tools for performance monitoring and diagnostics is their ability to handle large amounts of complex data generated by various sensors and monitoring devices. These tools can analyze data in real-time, identify patterns, and make predictions about system performance. This capability can help organizations to quickly identify and address issues before they become critical, thus improving system uptime and reducing maintenance costs. AI-based tools can also provide insights into the root cause of performance issues, helping organizations to optimize their processes and improve overall efficiency. For example, in a manufacturing plant, AI-based tools can analyze data from various sensors to identify the factors that are contributing to reduced production output. This information can then be used to optimize the production process, resulting in improved efficiency and increased throughput.

3.3 The Role of Natural Language Processing and Computer Vision for Maintenance Management and Performance Prediction

Natural Language Processing (NLP) refers to the ability of computers to understand and interpret human language. This technology has many applications in maintenance management and performance prediction, including analyzing maintenance logs, identifying trends and patterns, and predicting equipment failures [31]. NLP can also be used to extract information from unstructured data sources such as emails, social media posts, and customer feedback, which can help identify areas for improvement and optimize maintenance schedules.

Computer Vision (CV), on the other hand, involves the analysis of visual data to extract information and make predictions. In maintenance management and performance prediction, CV can be used to monitor equipment and detect anomalies or defects. For example, CV can analyze images of machinery to detect signs of wear and tear, corrosion, or other signs of damage. This information can then be used to schedule maintenance or repairs before a failure occurs.

The application of NLP and CV in maintenance management and performance prediction can lead to cost savings, improved safety, and increased efficiency. By automating many of the manual tasks involved in maintenance management, these technologies can free up resources and reduce the risk of human error. Additionally, by predicting equipment failures and scheduling maintenance proactively, it is possible to avoid costly downtime and reduce the risk of accidents.

3.4 Challenges and Limitations of AI-Based Maintenance Management and Performance Prediction, Including Data Quality and Privacy Concerns, and Ethical Considerations

AI-based maintenance management and performance prediction have become increasingly popular due to their ability to analyze vast amounts of data and identify patterns that are difficult for humans to detect. However, despite their many advantages, there are several challenges and limitations associated with these technologies that must be taken into account.

One of the main challenges of AI-based maintenance management and performance prediction is the quality of the data used to train the algorithms. The accuracy of the predictions made by AI systems depends on the quality of the data used to train them. Data quality issues can arise due to missing or incorrect data, or due to biases in the data. It is crucial that organizations ensure that the data used is of high quality, and that they take steps to mitigate any biases present in the data.

Many AI systems are opaque, making it challenging to understand how a particular decision was reached. This can make it difficult to audit or challenge decisions made by these systems, particularly in safety–critical industries.

Privacy concerns are another limitation of AI-based maintenance management and performance prediction. As organizations collect and use data to train and test AI algorithms, they must ensure that they comply with data protection regulations and that personal data is handled securely. Organizations need to obtain informed consent from individuals before collecting their data, and they need to provide transparency about the use of this data.

Ethical considerations are also an important limitation to AI-based maintenance management and performance prediction. There is a risk that algorithms could perpetuate biases present in the data, resulting in discriminatory outcomes. Additionally, the automation of maintenance decisions could result in a loss of control for workers or a dehumanization of the workforce. Organizations need to ensure that AI systems are used ethically and in a manner that respects the rights of workers and individuals.

3.5 Future Directions and Potential Developments in the Field of AI-Based Maintenance Management and Performance Prediction

As AI technology continues to advance, there are numerous potential directions that the field could take in the coming years.

One of the most important areas for future development in AI-based maintenance management is enhanced predictive maintenance. This involves using AI algorithms to analyze data from various sensors and systems to predict when maintenance is needed, before a breakdown occurs. The goal is to prevent unexpected equipment failures and reduce downtime, which can be costly for businesses. As AI continues to improve, the accuracy of predictive maintenance systems is likely to increase, making them even more valuable to businesses.

Another area of potential development in AI-based maintenance management is intelligent asset management. This involves using AI algorithms to track and manage assets, including equipment, vehicles, and other assets. By using AI, businesses can optimize their asset management strategies, reducing maintenance costs and improving efficiency. For example, AI could be used to schedule maintenance tasks based on usage patterns or to predict when certain components will need to be replaced.

Autonomous maintenance involves using AI algorithms to monitor and maintain equipment automatically, without the need for human intervention. This could include self-diagnosing equipment, ordering replacement parts, and scheduling maintenance tasks. Autonomous maintenance has the potential to reduce labor costs and improve equipment uptime, but it will require significant investment in AI technology and infrastructure.

Augmented reality (AR) is technology that has the potential to transform the field of AI-based maintenance management. AR could be used to provide technicians with real-time information about equipment and maintenance tasks, allowing them to work more efficiently and effectively. For example, technicians could use AR to see a 3D model of a piece of equipment and identify the location of specific components that need to be repaired or replaced.

Big data analytics—by analyzing large amounts of data from sensors and other sources, AI algorithms can identify patterns and correlations that humans might miss. This could lead to more accurate predictive maintenance systems, better asset management strategies, and more efficient maintenance operations overall.

4 Maintenance of Medical Devices

Activities of maintenance should be covered in the policy of the quality management system of a healthcare institution. Maintenance can be scheduled in specific intervals for regular maintenance or can be performed extraordinarily when a failure occurs. The main goal of proper maintenance is to reduce downtime of medical devices. Regular maintenance includes activities required to check whether the device is still functioning in a proper manner, to check if it performs in functioning limits based on the specification criteria.

Preventive maintenance is performed to prolong the working life of a device by preventing the possible failures. These failures are often not visible by staff operating the device, but are present inside the device. By performing regular preventive maintenance services, operating intervals between failures are prolonged. The intervals of these services are determined by manufacturer and stated in the device's specification.

Corrective maintenance are procedures performed by service bodies on a service request. Those include larger problems and failures with the device, and they are performed after the device has encountered a problem.

Medical devices are essential tools in the healthcare industry, and their proper maintenance is crucial for ensuring their effectiveness and safety. However, there is currently a shortage of evidence-based guidelines for the maintenance of medical devices, which can lead to inconsistencies and potential risks for patients.

One of the main challenges in maintaining medical devices is the lack of standardization in the industry. Different manufacturers may have different guidelines for maintenance, and there may also be variations in the frequency and types of maintenance required for different devices. This can make it difficult for healthcare professionals to properly maintain and troubleshoot issues with the devices.

To address this shortage of evidence-based maintenance guidelines, the healthcare industry can turn to a number of solutions. One approach is to develop and implement standardized protocols for the maintenance of medical devices. This could involve establishing minimum requirements for maintenance and establishing a system for tracking and documenting maintenance activities.

Another potential solution is to increase the use of predictive maintenance technologies, such as sensors and algorithms that can monitor the performance of medical devices and alert maintenance personnel when issues are detected. These technologies can help to prevent issues from occurring and reduce the need for unscheduled maintenance.

Additionally, there is a need for more research and analysis on the maintenance of medical devices. This could involve collecting data on the performance of different devices and identifying best practices for maintenance. The results of this research could then be used to develop evidence-based guidelines and standards for the industry.

Overall, the shortage of evidence-based maintenance guidelines for medical devices is a significant issue that needs to be addressed. By implementing standardized protocols, leveraging predictive maintenance technologies, and conducting more research and analysis, the healthcare industry can work towards a solution and ensure the proper maintenance of these vital tools.

5 Evidence-Based Performance Testing

The gathering of data regarding the usage and actual behavior of the gadget is the third essential element of a PMS system. The significance of obtaining information and signals about the functionality of medical devices available on the market is emphasized by Kumar et al. [32]. This aspect of the PMS process is a formal duty of the manufacturer/distributor under current regional/national law. Only 22 of the 47 manufacturers who were required to approach performance inspection of their MDs did so, or less than 50%, according to the study by Ross et al. [33]. This report should serve as a warning because it demonstrates that manufacturers do not always evaluate MD performance once the MDs are installed in healthcare facilities. If the healthcare facility is not performing preventative maintenance "in-house," it is done during corrective maintenance, which is performed after potential damage has already been done. Additionally, it is more difficult to gather data on how a product is used and behaves in real-world situations because manufacturers have different distributors in various nations. The lack of a standardized, evidence-based methodology that will permit the collection of medical device performance data once they are used regularly in healthcare institutions in order to evaluate the behavior of the device in use and across a variety of environments is highlighted as a significant issue in the PMS mechanism by this study. The professional community has already acknowledged this. For instance, Tarricone et al. [34] reviewed MD PMS methodologies and came to the conclusion that well-developed PMS strategies would greatly lower the risks associated with medical devices.

According to the study by Badnjevic et al. [35], 30% of the mechanical ventilators and infant incubators that were evaluated were found to be malfunctioning and in need of maintenance, recalibration, or removal from daily use. According to Gurbeta et al. [36], 13.84% of tested anesthesia machines and 14.91% of tested defibrillators

performed improperly and should be taken out of service or scheduled for corrective maintenance. On the other hand, report on dialysis machines [37] demonstrate that 12.6% of inspected devices either perform below specifications or do not exceed electrical safety criteria. More specifically, 2% of the evaluated devices failed the IEC 60601 safety examination. Heating system problems were found in 22.64% of the devices that did not fulfil performance requirements. Additionally, although malfunction was not reported, 11.32% of the devices in this group performed inconsistently with their specifications.

These particular studies on the performance evaluation of MDs that have been used and managed within healthcare institutions best demonstrate how much the devices actually deviate from the reference values and how crucial it is to develop a unified evidence-based methodology that will allow collection of MD performance data once they are used in healthcare institutions on a regular basis in order to assess the device behavior in practice and in different environments and prevent future incidents.

The following gaps were realized:

- The current function of medical device registries, which solely serves to facilitate registration and import of medical devices;
- The procedure for reporting adverse events is handled differently around the world, and stakeholders' reactions vary;
- Evaluation of medical device performance demonstrates a large variance in MD performance;
- Since data collection and performance evaluation are not done uniformly across healthcare facilities, the use of medical devices and their performance evaluation currently cannot be examined with great precision.

The PMS mechanism is therefore a potential area for development, but it will directly affect patient safety and the standard of care provided by healthcare facilities.

Evidence-based performing testing of medical devices is a critical aspect of ensuring their effectiveness and safety for use in healthcare settings. There are several key considerations for conducting this testing, including the selection of appropriate test methods, the use of representative samples, and the importance of standardization and reproducibility.

One of the most important aspects of performing testing on medical devices is the selection of appropriate test methods. It is important to choose methods that are relevant to the specific device and its intended use, and that are capable of accurately evaluating the device's performance. For example, the testing of a new type of heart valve may require the use of in vitro and in vivo testing methods to assess its functionality and durability.

Another important consideration is the use of representative samples when performing testing on medical devices. It is important to ensure that the samples used in testing are representative of the population of devices that will be used in practice. This may involve testing multiple samples of the same device or using a variety of devices to ensure that the results of the testing are accurate and relevant.

Standardization and reproducibility are also crucial considerations when performing testing on medical devices. It is important to establish clear protocols and guidelines for conducting the testing, and to ensure that the testing is conducted in a consistent and controlled manner. This can help to ensure that the results of the testing are reliable and can be reproduced by other researchers.

6 AI Based Computerized Maintenance Management System

Term of artificial intelligence has first been used by Alan Turing in the late 1950s with the computer game made to "communicate" with humans [38]. The first use of artificial intelligence seen its light in the MADALINE which was officially the first neural network that imitated the "brain" and solved a maze while learning from its mistakes in the process [39]. Along the way, artificial intelligence came to the point of literally replacing the humans in processes that they wouldn't even be able to perform with such accuracy and precision. This technology makes a real impact on today's industry and of them is certainly its application in the field of predictive maintenance and prediction of performances.

Predictive maintenance is a topic that's been around for some time. Main benefit of this approach of maintenance is reduced downtime of equipment and working processes which represents a high cost for the industry. It is also one of the fastest-growing applications of artificial intelligence in industry that can deliver real value to end-users. Insight in the equipment or processes allows for taking actions to prevent negative outcomes and downtime. Different data can be used for developing systems for predictive maintenance. They can be based on data already collected in the past that give valuable information which can be used for development of the AI-based system, or the data can be gathered through real-time monitoring. Real-time monitoring can be more difficult to implement since it mostly consists of sensors (air sensors, sound sensors, switch sensors), but although it takes great complexity, they allow for huge amounts of data that is constantly gathered and can be put to good use. All this appoints one thing—systems for predictive maintenance are able to identify mistakes/errors, separate noise from valuable data, and predict breakdowns to help advise future decisions.

Artificial intelligence and machine learning techniques are applied on the gathered data to deliver a model whose output is the predicted outcome. Model itself is made to learn different patterns from the previous events and enhance itself based on the learnings.

An example of such a system is reported by McKinsey & Company [40] where artificial intelligence based predictive maintenance implemented on the industrial sector in Germany achieved great results. They concluded that by implementing a predictive maintenance system based on artificial intelligence they can boost availability up to 20% while inspection costs were reduced by 25% and the total yearly maintenance

costs were reduced by up to 10%. Another similar system was implemented for detection of errors in artificial auditory cortexes. This model was developed by company Neuron Soundware and helped identify the causes of breakdown of their devices. Along with data gathered from sensors, valuable information can also be taken from the variety of data such as logs of maintenance, outputs of quality measurement, data from weather and environmental conditions, all which could not be used before all together. McKinsey reports that such a system needs several months for it to be fully functionable.

Another interesting approach has been reported by Blue Yonder company which implemented an internal solution based on artificial intelligence used in their asset management. They managed to predict the market demands based on previous history, and ensure that their inventory never goes low if the demand increases. Such a system helped reduce the costs of lost sales up to 65% and manage to keep the inventory filled with the necessary goods.

In manufacturing, artificial intelligence is used to analyse data, optimise processes and improve their efficiency. In this field, artificial intelligence allows for detecting automation failures which results in maintaining machines with high-performance used constantly [41, 42]. Such systems can use real-time intelligent video analytic technology which detects malfunctions or misaligned connections that are sometimes missed by the human eye. These solutions are already present on the market and provided by 3ds company.

Cardoso and Ferreira [43] in their work reported the process of implementing a predictive maintenance system based on machine learning algorithms. They used data about more than one hundred machines that contained information gathered through telemetry, logs from errors, maintenance records and malfunctions history and were able to create a predictive system.

Previous examples show that it is possible to implement artificial intelligence for predictive maintenance in several industries. When it comes to healthcare and medical devices, traditional ways of management maintenance are still mostly used. A way of management of medical devices is by using standard computerised maintenance management systems (CMMS). All CMMSs provide services of management in healthcare institutions by providing them with an insight into actual and real information about their devices. They may provide the information such as the assessments of the service bodies, user training for the devices, the scheduled maintenance timelines. However, this system is still manually operated and needs a human input to provide information about the service and maintenance scheduling. To overcome this and to keep up with other industries, an artificial intelligence approach needs to be taken into consideration in this field too.

An example of this approach was reported by Shamayleh et al. [44], where they introduced an innovative predictive maintenance system based on artificial intelligence. Source of their data was information gathered with IoT sensors which gathered logs of their medical equipment. After analysis of gathered data, it was processed by applying artificial intelligence. They reported a cost decrease of maintenance of 25% to 50% with predicted extension of life of equipment by 36%. Sancandi and Gruosso [45] proposed a framework for predictive maintenance of medical devices.

They proposed a thesis for roller bearing and roller pump devices by monitoring their vibration.

The application of artificial intelligence (AI) in the management, maintenance, and prediction of device performance has the potential to revolutionize the way that medical devices are used and maintained in healthcare settings.

To create AI based systems for management maintenance and prediction of failures, we need data. In order for data to be valuable and usable, all parameters used in development of this database must be the same. As mentioned in previous chapters, there are two types of surveillance of devices in their lifetime. Pre-market surveillance include tests to see whether the certain device complies with international standards such as **ISO 13485:2016**—"Medical devices—Quality management systems—Requirements for regulatory purposes for production and manufacturing of medical devices" and **IEC 60601-1-11:2015**—"Medical electrical equipment — Part 1–11: General requirements for basic safety and essential performance".

After the device is placed on the market, it is a subject of post-market surveillance processes, required by EU MDR. According to both MDD and MDR, preventive and corrective maintenance actions are prescribed to perform. Those actions result in reports about the performed procedures and they are meant to be inputted into one of the databases, EUDAMED for region of European Union, and MAUDE for the region of the United States. EUDAMED must also be filled with the information gathered through post-market surveillance of the medical device. Every report fed into the EUDAMED database comes from either a manufacturer itself, notified body or from a third inspection body as shown in Fig. 1.

As all sides create their own reports and fill the same database with the different information about devices, a great confusion arises. The problem arises when it comes to comparing different reports or using them for further analysis such as implementing an evidence-based maintenance of medical devices or implementing AI solutions

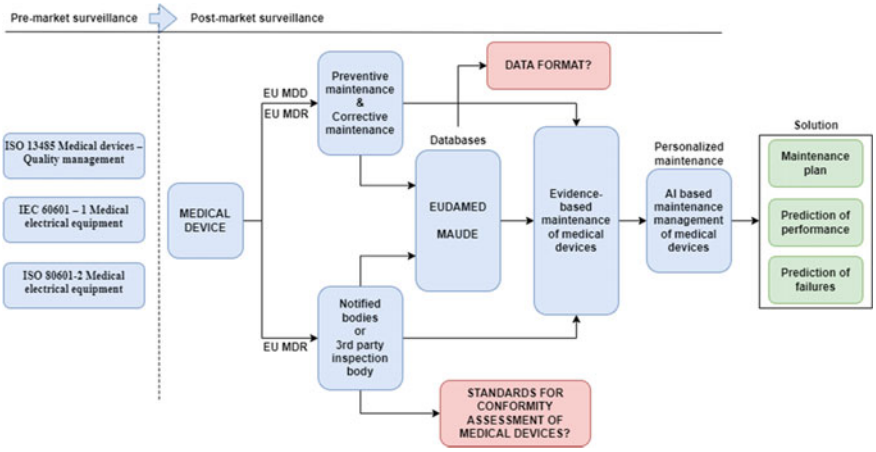

Fig. 1 Pre-market and post-market surveillance frameworks

for development of maintenance management of medical devices. Evidence-based maintenance cannot be proposed taking in consideration every party generates reports on non-standardised and not-harmonised way. Same way implies to development of artificial intelligence-based maintenance management of medical devices. In order to create these systems, all data must be gathered in the same manner. Main missing elements for developing a proper evidence-based maintenance of medical devices are the proper **data format** of all the information gathered through services and maintenance, and harmonized **standards for conformity assessment of medical devices**. Only then a proper system can be created and results in solutions like maintenance plan, prediction of performance and prediction of failures of medical devices.

To address this problem, legal metrology framework for conformity assessment of medical devices has been established in Bosnia and Herzegovina [46]. This framework includes assessment of all medical devices with measuring function: defibrillators, electrocardiographs, patient monitors, infusion and perfusion machines, mechanical ventilators and anaesthesia machines, neonatal and paediatric incubators, therapeutic ultrasounds and blood pressure devices. According to this legal framework, all healthcare institutions in Bosnia and Herzegovina are obliged for post-market surveillance of their medical devices. This chapter presents a procedure intended to inspect medical devices having measuring function [47]. Every assessment is performed in the same manner for every device individually, according to Rulebook on metrology requirements for medical devices published in Official Gazette of Bosnia and Herzegovina No. 75/14. Conformity assessment is performed annually for every device. Every assessment consists of visual inspection, inspection of electrical safety and inspection of performance of device. During assessment all information about the device are gathered, including name of manufacturer, model, serial number and environmental conditions. All this information is put into an online eLab software as shown in Fig. 2. This framework ensures that every report is harmonized and performed by an ISO 17020 accredited inspection body. With harmonized reports, every result from the same group of devices is the same and then can be used for implementation of system development for evidence-based maintenance of medical devices, as well as development of artificial intelligence-based systems for management of medical devices. Similar legal metrology framework has been established in Serbia as well.

The application of artificial intelligence (AI) in the management, maintenance, and prediction of device performance has the potential to significantly improve the efficiency and effectiveness of medical devices in healthcare settings. In addition to the benefits described in the previous response, AI can also be used to support post-market surveillance efforts, which involve monitoring the performance and safety of medical devices after they have been placed on the market.

In Bosnia and Herzegovina and Serbia, post-market surveillance is regulated by laws and frameworks that ensure the safe and effective use of medical devices. These frameworks include the legal metrology frameworks that are enforced by law, which establish standards and requirements for the testing and measurement of medical devices.

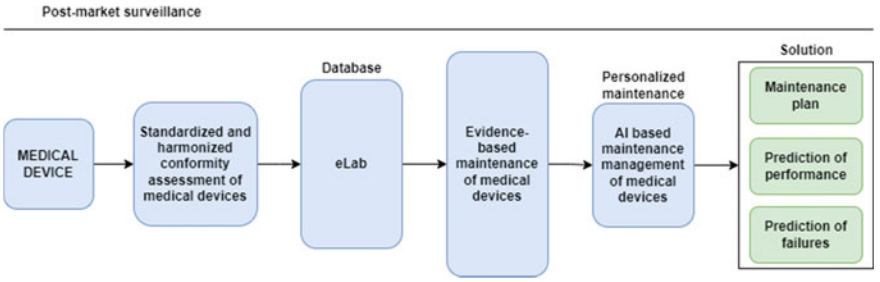

Fig. 2 An example of post-market surveillance in Bosnia and Herzegovina and Serbia

AI can be used to support post-market surveillance efforts in Bosnia and Herzegovina and Serbia by analyzing data on the performance and safety of medical devices, identifying patterns and trends, and providing insights that can help to optimize device performance and identify potential issues or risks. This can help to ensure that medical devices are safe and effective for use in these countries, and can support the regulatory frameworks that are in place to protect patients and healthcare professionals.

6.1 CMMS in Healthcare

A Computerized Maintenance Management System (CMMS) is a software application that includes a computer database of information related to an organization's maintenance activities. Within the context of Healthcare Technology Management (HTM), a CMMS is utilized to automate the documentation of all activities related to clinical equipment, including equipment planning, inventory management, corrective and preventive maintenance procedures, spare parts control, service contracts, and clinical device inspections and alerts. The collected data can be analyzed and used for technology management, quality assurance, work order control, and scheduling of clinical equipment.

The decision to automate an HTM system or replace an existing CMMS depends on the individual circumstances of the healthcare facility, including operating procedures, information technology (IT) infrastructure, and available budget. In order to effectively assist in the management and maintenance of clinical equipment, a CMMS must comprehensively address the needs of the user. Although major vendors strive to develop a system that adequately addresses the needs of all HTM managers, no available system provides a complete solution. However, most systems can be customized to meet the specific needs of the healthcare facility. Alternatively, an IT firm can be contracted to develop a CMMS package tailored to local requirements. A customized CMMS package is generally more expensive but, if well-designed and maintained, will often provide a more satisfactory solution that addresses local problems.

A CMMS can be used to: (a) standardize and consolidate information within an HTM program; (b) facilitate the planning and monitoring of inspection and preventive maintenance, as well as schedule and track repairs; (c) monitor equipment performance indicators, such as mean time between failures, downtime, and maintenance costs for individual or equipment groups of the same model, type, or manufacturer; (d) monitor clinical engineering staff performance indicators, such as repeated repairs by the same staff member for the same issue, average sick time related to individuals, and productive work time for individuals or groups; (e) generate reports that can be used to plan user training programs based on equipment failure trends in specific departments or healthcare facilities; (f) have libraries of regulatory requirements and safety information; (g) generate the appropriate documentation for accreditation by regulatory and standard organizations; and (h) generate reports to assist in the monitoring and improvement of the HTM program [48].

7 Conclusion

Application of artificial intelligence is very valuable in sector of medical devices. However, its potential has not yet been fully realized. Artificial intelligence could be used to address the gap in medical equipment maintenance management. However, lack of standards for conformity assessment of medical devices and lack of defined data format for reports that are put into EUDAMED and MAUDE database lead to non-uniformed information that are not usable on wider aspect. Today, manufacturers, notified bodies or third-party inspection bodies all create reports of surveillance or maintenance based on their internal procedures. In order for this information to be valuable and can be used in development of systems for evidence-based management maintenance or development of artificial intelligence-based systems for maintenance plan, prediction of performance or prediction of failures, every created report must have the same criteria and the same testing sequences. Such a system has been established in Bosnia and Herzegovina and Serbia where medical devices with measuring functions are put into a legal metrology framework.

Artificial intelligence (AI) has the potential to significantly improve the maintenance and management of medical devices in healthcare institutions. By analyzing data on the performance of medical devices and identifying patterns and trends, AI can help to optimize device performance and predict when maintenance is needed, improving the efficiency and cost-effectiveness of device management. The use of AI for prediction in the maintenance and management of medical devices is particularly beneficial for patient safety. By identifying potential issues with medical devices and proactively addressing them, healthcare institutions can reduce the risk of devices failing or experiencing issues, ensuring that patients receive the best possible care. In addition to improving patient safety, the use of AI for prediction in the maintenance and management of medical devices can also increase the confidence of medical staff in the devices that they are using. By knowing that devices are being regularly monitored and maintained, and that potential issues are being identified and addressed in

a timely manner, medical staff can have greater confidence in the effectiveness and safety of the devices they are using.

The use of AI for prediction in the maintenance and management of medical devices is a crucial development that has the potential to significantly improve the safety and effectiveness of these devices in healthcare institutions. It is an important tool that can help to ensure that patients receive the best possible care, and that medical staff have the confidence they need to use medical devices effectively.

The use of artificial intelligence (AI) in the maintenance and management of medical devices can bring a number of benefits to healthcare institutions. One of the key benefits of using AI for prediction in the maintenance and management of medical devices is that it can improve the efficiency and cost-effectiveness of these processes. By analyzing data on the performance of devices and identifying patterns and trends, AI can help to optimize device performance and predict when maintenance is needed, allowing healthcare institutions to plan and schedule maintenance activities in a more efficient manner. This can help to reduce the need for unscheduled maintenance, which can be time-consuming and costly, and can improve the overall performance and availability of medical devices. Another benefit of using AI for prediction in the maintenance and management of medical devices is that it can improve patient safety. Medical devices are an essential part of the healthcare system, and ensuring that they are functioning properly is crucial for patient safety. By using AI to identify potential issues with medical devices and proactively addressing them, healthcare institutions can reduce the risk of devices failing or experiencing issues, ensuring that patients receive the best possible care. In addition to improving patient safety, the use of AI for prediction in the maintenance and management of medical devices can also increase the confidence of medical staff in the devices that they are using. By knowing that devices are being regularly monitored and maintained, and that potential issues are being identified and addressed in a timely manner, medical staff can have greater confidence in the effectiveness and safety of the devices they are using. This can help to improve the overall quality of care that patients receive, and can increase the trust that patients have in the healthcare system.

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Inspection and Testing of Electrocardiographs (ECG) Devices

Ratko Magjarević and Almir Badnjević

Abstract Due to its considerable importance in the diagnosis of a wide range of diseases and disorders, electrocardiographs (ECG devices) are currently a routine component of diagnostic procedures in healthcare systems. Since the creation of the initial prototype, these devices have undergone evolutionary changes due to advancements in technology, particularly electronics. These devices can now measure several factors simultaneously and do automatic diagnostics. The entire life cycle of a medical device of this type, from creation to disposal, is defined by numerous international standards and regulations. Yet, because of their current level of sophistication, ongoing legal framework changes their accuracy and safety during usage is largely considered. In addition to providing an overview of the criteria in the area of safety and performance inspection of these devices, this chapter discusses the fundamental concepts of electrocardiography and ECG devices. Lastly, a novel method for safety and performance inspection during usage of ECG devices based on their metrological characteristics is introduced.

1 Introduction

Electrocardiography (ECG) is the method of measuring electrical potentials of the heart in order to discover heart related health problems. The recordings of the potentials of the heart (on paper or on other media) are called the electrocardiogram and the medical devices used for the recording are electrocardiographs (the same abbreviation ECG is used for all three terms). The potentials of the heart are recorded against time. The procedure is undertaken from the body surface during standard check-ups, with only a few seconds of the ECG printed on paper or viewed on a monitor. However, in cases of patients suffering from a heart disease, recordings

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may be taken for a much longer period, e.g. during emergency or in intensive care. In case an abnormality in the heart potential appears rarely, over a period of time longer than a few hours, the ECG is recorded by an ECG Holter monitor, typically for 24 h. Digitised signals are stored in a memory, for further computerised analysis. For the recording, electrodes are placed in standardised positions on a patient's body. An ECG is an important part of every preventive medical check-up and it is mandatory for the assessment of patients who are suspected to have a heart related problem. The ECG is considered an extremely safe procedure, without any risk involved. Adverse effects reported in rare cases deal with skin irritation from the electrode adhesive. Though ECG is an important procedure in evaluation of cardiac patients, additional examinations are undertaken to get the full picture of symptoms and the disease. In some cases, normal recordings are obtained in patients with heart disease, or some recorded parts of ECG may be recognised as pathological despite the heart's normal condition. The ECG provides information about the heart's electrical activity and has a great value in finding the causes of symptoms like chest pain or pressure. It is used for interpretation of the severity of a heart attack, inflammation of the pericardium, angina or other symptoms of heart disease like shortness of breath, dizziness or even fainting, and of arrhythmias. By ECG interpretation, physicians may infer some physical dimensions of the parts of the heart, e.g. the thickness of the heart chambers walls. Furthermore, ECG reflects the efficiency of medication and enables finding of their side effects. Surface ECG is also used in regular control of implanted devices for heart management, like pacemakers and cardioverters—defibrillators (though modern implantable devices enable telemetric measurement of intracardiac ECG). It is also used for the assessment of the heart's health in the presence of other diseases or conditions, e.g. high blood pressure, high cholesterol, diabetes, a family history of early heart disease or history of smoking [1, 2].

An electrocardiograph is a type of medical device with a measuring function (MDMF) that measures the electrical activity of the heart to look for any abnormalities [3]. Medical device sensors or measuring tools are used to perform measurements on the devices. How well the sensors and measuring tools function on the MD directly affects the overall level of product quality [4].

Each pre-programmed heart rate and ECG voltage signal amplitude setting has a specific purpose. The patient will undoubtedly suffer harm from any anomalies that occur because the ECG is used to swiftly detect cardiac problems and monitor general heart health. Due to the fact that the electrocardiogram's effectiveness is based on the evaluation of the heart rate and voltage signal amplitude, post-market surveillance is focused on the precision of the calculated values of the aforementioned measuring quantities as well as the overall safety of the medical device.

Each ECG instrument is rigorously tested and assessed before being released on the market to ensure that it is free from functional flaws. Yet, once a product is placed on the market, regulatory control becomes uncoordinated and there are no guidelines describing how it should be carried out [5]. A technique for performance assessment of all ECG devices used in healthcare facilities must be designed and developed in order to guarantee accuracy and safety [6].

2 Historical Aspects of Electrocardiography

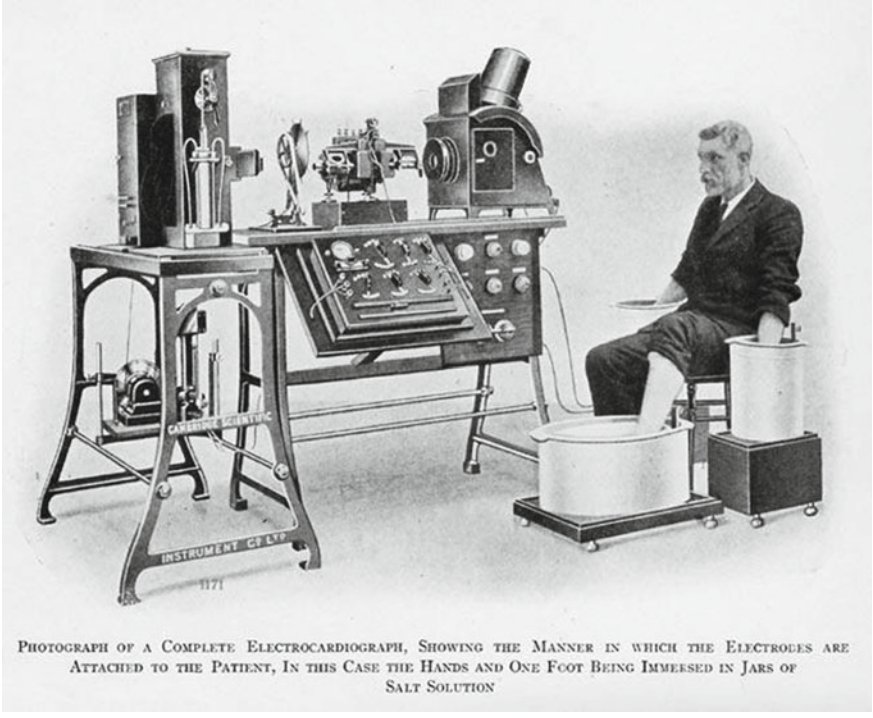
Luigi Galvani (1737–1798) was an Italian physician and physicist known for his groundbreaking work in electrophysiology, or the study of the electrical properties of biological cells and tissues. Luigi Galvani's most famous experiment, which he conducted in the late eighteenth century, involved the use of frogs' legs to demonstrate the relationship between electricity and muscle contractions. He began by removing the skin from the frogs' legs and dissecting out the nerves and muscles. He then used a copper wire to suspend the legs from a brass hook. The copper wire was then touched to a scalpel that was in contact with the frog's leg muscles, causing them to twitch. Galvani noticed that the legs twitched even when they were not in direct contact with the scalpel, but were just close to it. He deduced that this was because the frog's body contained a natural electrical charge. Galvani went on to conduct additional experiments, such as electrically stimulating the legs using an electrical generator, and discovered that the muscles contract in response to electrical stimulation. This resulted in the discovery of "animal electricity" and the advancement of bioelectromagnetism, which is the study of the interaction of electric and magnetic fields in biological systems. A very sensitive device for measurement of small voltages and currents is called a "galvanometer" in his honour. Galvani's discovery of the electrical nature of muscle contractions was one of his most significant contributions to the development of electrocardiography (ECG) devices [7].

Alessandro Volta (1745–1827), an Italian physicist, was Galvani's contemporary and a critic of his "animal electricity" theory. Volta believed that the electrical current was generated by the contact of different metals and fluids in the circuit, rather than by the animal tissue. To put his theory to the test, Volta devised a series of experiments involving various metals and fluids, such as zinc and copper disks separated by moistened paper or cloth. Volta's invention of the battery allowed researchers to study the effects of electrical stimulation on various tissues such as the heart, muscles, and nerves, laying the groundwork for the development of electrotherapy and electrodiagnostics. The conflict between Volta and Galvani became known as the Galvani-Volta controversy. Despite their differences, both Galvani and Volta made significant contributions to electrophysiology, and their work established the foundation for modern electrical stimulation techniques in medicine [8].

Willem Einthoven (1860–1927), a Dutch physician and physiologist. The invention of the string galvanometer, an extremely sensitive instrument capable of detecting very small electrical signals produced by the heart, was Einthoven's most notable contribution. This instrument was used to record the electrical activity of the heart, resulting in the first accurate and detailed ECG recordings. Nowadays, the practicality of that device, shown in Fig. 1, would be questionable, since it had a mass of approx. 270 kg and for the recording, and the examinee was asked to immerse his hands and a leg into containers with salt water which were serving as electrodes. This formation is actually the standard ECG lead system, another Einthoven's immense contribution, which specifies where electrodes should be placed on the body to produce a standard ECG recording. It is still used in routine ECG recording, with the I, II and III

standard limb leads, while the imaginary triangle these measurement points build is named Einthoven's triangle. This standardisation has allowed clinicians to compare ECG recordings across patients and over time, allowing them to better interpret and analyse ECG data. Einthoven introduced the letter nomenclature for those five deflections which can be recognised in the ECG: P, Q, R, S and T (and later also the U wave). In his publication from 1906, Einthoven described normal and abnormal electrocardiograms recorded by the string galvanometer. In 1924, he was awarded the Nobel Prize in Physiology or Medicine for his discovery of the mechanism of the electrocardiogram [9].

St. Mary's Hospital in London, England, was the first to use an electrocardiogram (ECG) machine for clinical purposes, with Willem Einthoven's original string galvanometer installed in 1906. This was done by the first mass producer of electrocardiograms (ECGs), an American company—the Cambridge Instrument Company, which was founded in 1893. In the early 1900s, the company began producing Einthoven's string galvanometer on a larger scale. Following Einthoven's initial development of the ECG, other hospitals quickly began to adopt the technology for clinical use, with the Mayo Clinic in Rochester, Minnesota being the first in the United States to use the ECG for diagnosing heart disease in the early 1910s. ECG machines



Photograph of a Complete Electrocardiograph, Showing the Manner in which the Electrodes are Attached to the Patient, In this Case the Hands and One Foot Being Immersed in Jars of Salt Solution

Fig. 1 An early commercial ECG machine, built in 1911 by the *Cambridge Scientific Instrument Company* [10]

were widely used in hospitals around the world by the 1920s and 1930s. During this time, other companies also began to produce ECG machines, including the American companies Hewlett-Packard and General Electric, as well as the German company Siemens [11].

In order to make ECG recording practical, a lot of technological improvements were necessary. Amplifiers with vacuum tubes were introduced in 1928 by Ernstine and Levine [12] and later, the cathode ray tube for displaying the potentials on the screen. Electrocardiographs designed in the analogue technology era were equipped with chart recorders, with first models which wrote with ink on grid paper and later ones using hot wire on temperature sensitive paper. Containers with salt water were replaced with dry electrodes only in 1930s by silver plate electrodes and by suction electrodes, normally used for recording the precordial leads [13]. Early ECGs used vacuum tubes and were therefore heavy, unreliable and they had large power consumption. Invention of the silicon transistor in 1954 enabled production of smaller and more practical ECG devices and facilitated diagnostic use of the ECG, Fig. 2.

Dr. Robert Bruce and his colleagues at Bellevue Hospital in New York City performed the first cardiac stress test using an electrocardiogram (ECG) machine in 1937. The patient walked on a treadmill while being hooked up to an ECG machine, with the treadmill's speed and incline gradually increasing over time. The stress test was designed to assess the heart's response to physical exertion and to look for any abnormalities in the ECG waveform that could indicate the presence of heart disease. The test was considered revolutionary at the time because it allowed doctors

Fig. 2 The Cambridge Simpli Scribe, manufactured from 1945 to 1960. Vacuum tube technology [14]

to non-invasively diagnose heart disease and determine the severity of the condition. Norman J. Holter invented the first ambulatory electrocardiogram (ECG) device, also known as a Holter monitor, in 1949. Holter was a biomedical engineer who wanted to create a portable device that could continuously monitor a patient's heart activity outside of the clinical setting for an extended period of time. The first Holter monitor was a large device that used a reel-to-reel tape recorder to record ECG signals. It weighed almost 40 kg and was carried in the patient's backpack, as seen on Fig. 3. The device could record up to 24 h of ECG data, which could then be analysed by a technician or physician after the recording period was over. Despite its limitations, the Holter monitor presented a significant advancement in cardiac monitoring because it enabled doctors to collect more comprehensive and accurate data on a patient's heart activity than a traditional ECG could. Ambulatory ECG devices are now widely used in clinical practice, particularly for diagnosing and managing arrhythmias and other cardiac conditions. They provide valuable insights into a patient's heart activity over time, allowing doctors to make more accurate diagnoses and treatment decisions [15].

Computerised ECG machines were introduced in the 1960s, and digital signal processing in the 1970s has been used for more accurate interpretation and analysis. Wireless technology enabled real-time ECG monitoring and transmission in the 1990s, while machine learning and artificial intelligence were used for automated ECG interpretation in the 2000s. Advances in mobile technology have now enabled the development of smartphone-based ECG devices that patients can use

Fig. 3 The first Holter monitor [15]

at home. The global ECG market has grown significantly over the years, owing to factors such as rising cardiovascular disease prevalence, an ageing population, and technological advancements. As ECG devices become more affordable, accessible, and user-friendly, the market is expected to expand further [16].

3 Medical Aspects

To understand electrocardiograms, we firstly need to understand the electrical system of the heart. The heart is a hollow muscular organ with four chambers. It is filled with blood, and through regular, rhythmic contractions, it allows blood to circulate throughout the cardiovascular system. Figure 4 shows how the heart draws blood from the veins and pumps it into the arteries. The atrium and the ventricle, which make up each of the two chambers that make up the right and left halves of the heart, are situated on either side of the septum, a muscle. The largest and strongest muscle in the heart, the left ventricle, pumps blood to the aorta, the largest blood conduit in the body, via the tricuspid valve. The rhythmic contractions of the chambers, firstly synchronous contraction of the atria and secondly the synchronous contraction of the ventricles, control the directed blood flow in the cardiovascular system. Four heart valves prevent the backflow (reflux) of blood from ventricles to atria and from arteries to ventricles. In the right heart, the tricuspid valve is located between the atrium and the right ventricle, and the pulmonary valve is located between the right ventricle and the pulmonary arteries. In the left heart, the mitral valve is located between the left atrium and ventricle, and the tricuspid valve is located between the left ventricle and the aorta [17].

Systole and diastole are the names given to the pumping and resting phases of the heart cycle, respectively. The exact electrical activity of the heart's specialised conduction system controls how tightly the heart muscles contract. Special cells located in the sinoatrial node (SA), at the top of the right atrium, start the typical cardiac cycle (Fig. 5). The heart's natural pacemaker consists of these cells. The entire atria experiences depolarization from the SA node, which causes atrial tissue to contract. The atrioventricular (AV) node is where the electrical depolarization from the atria reaches the ventricles because the atria and ventricles are separated by a fibrous ring with low conductivity, which causes a brief delay in the propagation of the depolarization. The depolarization moves from the AV node through the left and right bundles of His to the left and right ventricles. When the heart is beating normally, the left and right hearts contract simultaneously, allowing the heart to efficiently pump blood into the arteries. The heart is situated in the thorax, between the lungs, and is covered by the skin, a thin layer of breathing muscles, and the pericardium, as well as by the breastbone and ribs. The electrical characteristics of these tissues vary from one another, but taken collectively, they function as a low pass volume filter, causing a large difference between the potentials recorded at various locations on the heart and the surface ECG (Fig. 5) [17].

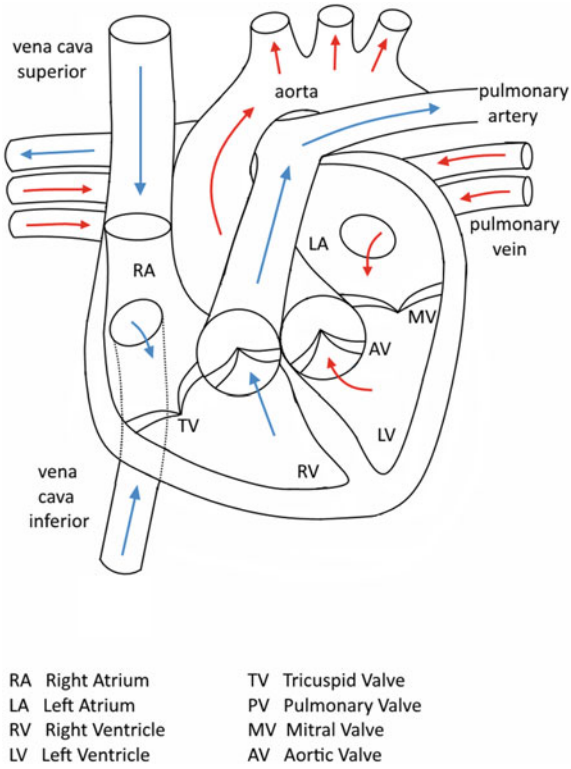


Fig. 4 Cross-section and blood flow of the heart [18]

More diagnoses can be made from the ECG than from any other bioelectric potential, which is why measuring and analysing the heart's potentials has such great diagnostic value. The P-wave, QRS complex, and T-wave are the three regular portions of the typical ECG waveform that can be identified in time in almost every standard lead record. Although the ECG signal varies from person to person, it behaves in a nearly steady manner. The five distinctive components of the ECG spectrum are primarily identified by their shapes, their timings within the cardiac cycle, and the variability of the heart rhythm. Most cardiac muscle abnormalities and arrhythmias can be identified with ECG analysis. The surface ECG (Fig. 6) depicts how the myocardium (cardiac muscle) is electrically active. The depolarization of the atria is represented by the P-wave in a normal ECG, and the depolarization of the ventricles is represented by the QRS complex, where the repolarization of the atria is obscured by the considerably greater signal of ventricular depolarization. The repolarization of the ventricles is represented by the T-wave. The S-T segment plays a crucial role in the interpretation of the ECG because its waveform, particularly the divergence from the baseline, may indicate significant heart muscle damage. For example, the elevation of the ST-segment suggests an acute myocardial infarction. The heart rate is frequently calculated using the R-R interval, which is the reciprocal value of the

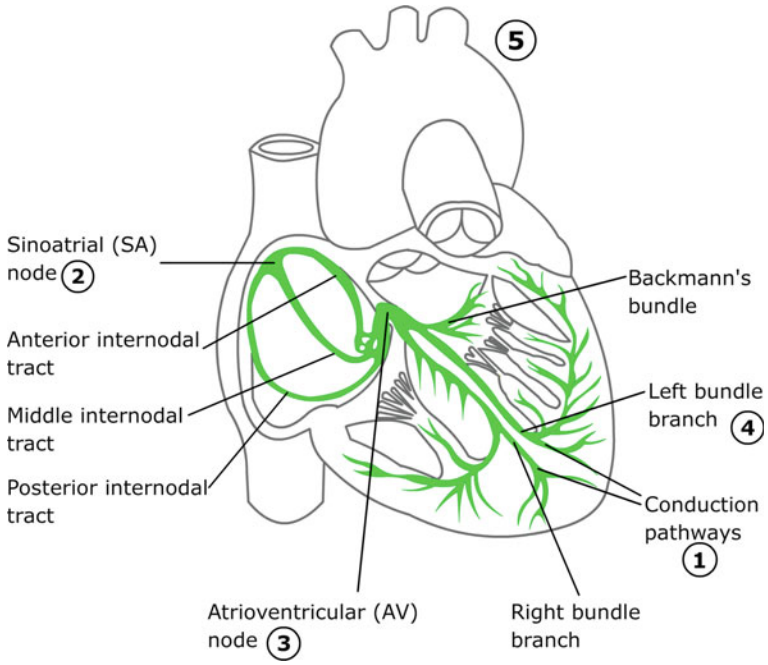


Fig. 5 Conduction system of the heart [19]

interval between two R peaks. Normal heart rate in rest varies a little, and the variation is larger since it adapts to the activity of the person (Fig. 7). Arrhythmias are variations in the heart's normal rhythm; bradycardia and tachycardia are terms for slow and fast heart rates, respectively. Long-term sustained tachycardia has the potential to progress to ventricular fibrillation, which, if not treated promptly, can be fatal. The blood flow ceases and the brain's oxygen supply is cut off in ventricular fibrillation because there is no regular, synchronised contraction of the muscle fibres. Ectopic beats, produced by myocardial cells with lower excitation thresholds, which fire asynchronously in comparison to normal heart rhythm and do not contribute to the heart output because they are premature, are another common variation from normal heart rhythm. Interruption in conducting of the pulses from atria to ventricles is called atrioventricular block and leads to absence of ventricular contraction. It can be recognised as missing R peak after a P-wave [20].

3.1 ECG Electrode Placement

Electrodes are the necessary interface for connecting the human body to medical electronic instrumentation. In case of ECG recording, the electrodes can be attached to

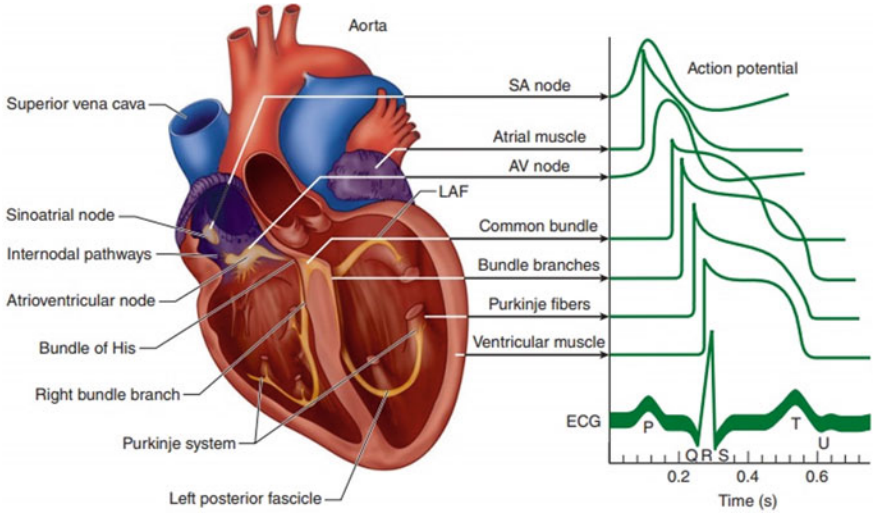


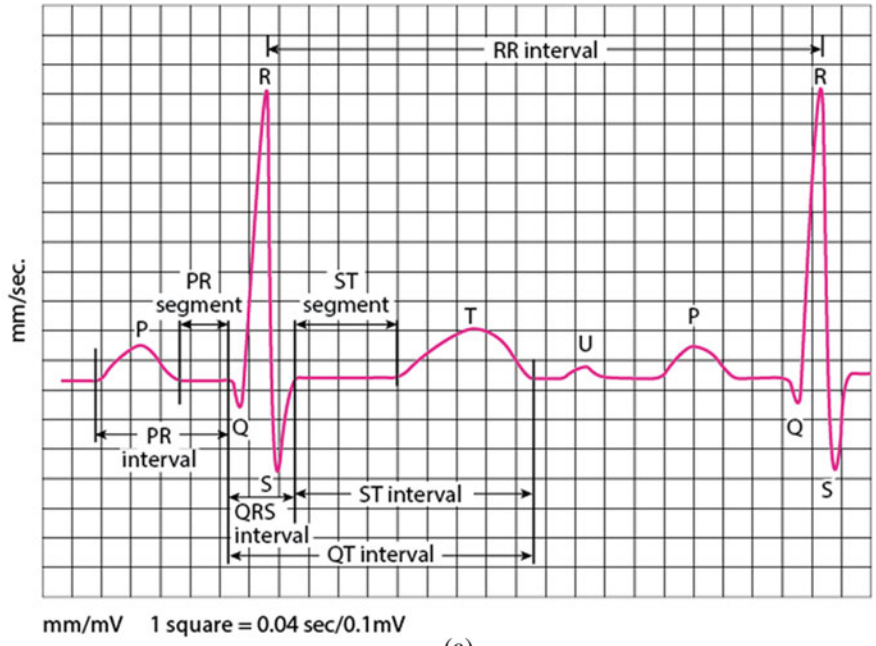
Fig. 6 Action potentials at different positions within the heart [21]

the surface of the body or implanted. In this chapter, authors only consider recording of surface ECG, so only surface electrodes will be described.

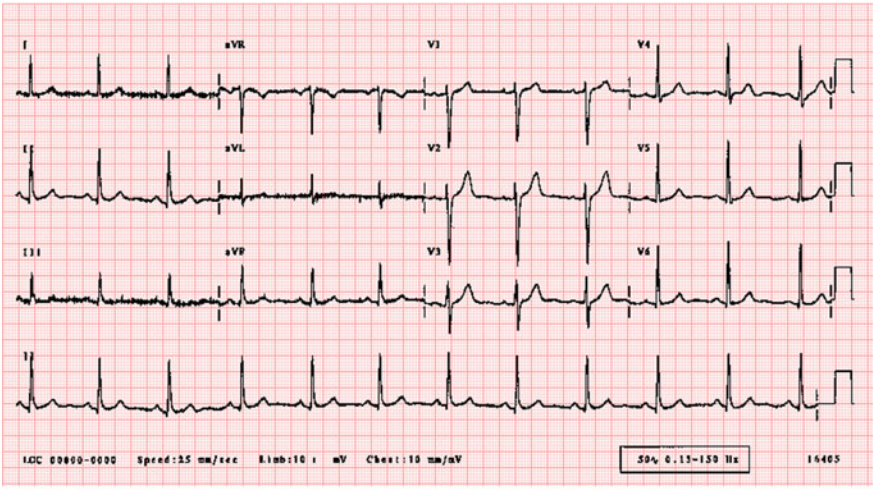
ECG electrodes are transducers which enable exchange of charge carriers in the system consisting of the human body and the medical device. In the body, charge carriers are ions of both polarities, and in the electronic equipment, the carriers are electrons. Though electrodes seem to be simple in their design, they may cause a lot of interference and noise at the interface. More on technical characteristics of electrodes is presented in the technical description of the ECG equipment later in this chapter.

From the point of interpretation of the ECG, physicians evaluate the recorded curves by comparing them to the recordings they have previously seen and used in their training, and from the experience they got practicing medicine. The American College of Cardiology Foundation stated that it takes 3500 supervised ECG reads to become an expert [23]. Since the ECG records vary between individuals, a lot of skill is necessary to observe the common ECG features. Placing the recording electrodes always in the same position on the patient's body establishes a reference for observing those common characteristics that lead to accurate diagnostics. For practical reasons, the electrodes for standard ECG recording are positioned on human extremities being easily accessible and the housing of electrodes is colour coded so that they enable rapid connection to a medical device for e.g. recording in emergency cases, Fig. 8.

Standard ECG recording presents bioelectric potentials of the heart recorded in 12 traces and by 10 electrodes positioned on the body [1]. The potentials measured in-between the electrodes are called leads. The leads can be explained as projections of the heart vector to different planes on the body, as shown in Fig. 8. All leads together represent the heart vector projection in practically all directions, which means that the



(a)



(b)

Fig. 7 Characteristic ECG wave shape: **a** symbolic and **b** measured [22]

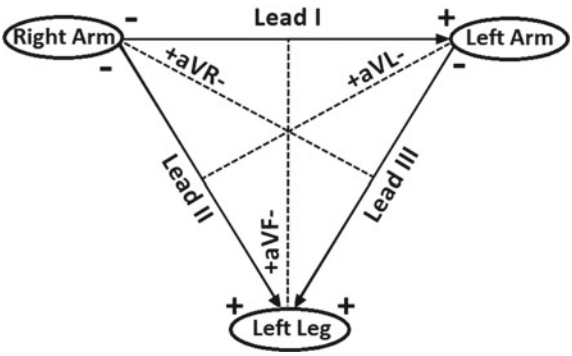


Fig. 8 Standard electrode placement

information on electrical activity of the heart is acquired with high spatial resolution. Those 12 leads are organised as follows:

- Three bipolar limb leads,
- Three augmented limb leads,
- Six precordial or chest leads.

Four electrodes are placed on the all four extremities of the human body (therefore also called limb electrodes) on predefined places slightly proximal to the hand and the ankle. These positions are designated by:

- LA standing for left arm,
- RA standing for right arm,
- LL standing for left leg and
- Ground for the reference electrode.

The limb electrodes are used for bipolar or differential measurement of the potentials between them and they form the I, II and III standard leads of the ECG with the orientation of the polarity as shown in Fig. 8. These leads are also called Einthoven leads since they are based on the first, historical ECG measurement performed by Einthoven.

The same limb electrodes are used for augmented leads which are unipolar measurements where the potential present at a particular electrode is measured against the average value of the potentials from the other two electrodes. The augmented leads are also called Goldberger's leads in honour of Emanuel Goldberger who introduced the leads to electrocardiography in 1942 in order to increase the voltage of Wilson's leads. The principle of operation of augmented leads is shown in Fig. 8. The augmented leads are marked aV_R, aV_L and aV_F.

Precordial or chest leads measure the potential of the electrodes positioned on the rib cage of a patient in a predefined way against the potential of a reference electrode. The potential of the reference electrode is defined by connecting each of the three limb electrodes through a resistor of 5 kΩ into the reference node which is considered to have 0 potential. The reference node is called Wilson's electrode and the precordial leads got the name Wilson's leads and are labelled as V_1–V_6.

3.2 Bipolar Leads and Einthoven's Law

The potentials measured between the limb electrodes are projections of the heart vector to the Einthoven equilateral triangle. Einthoven's Law states that the electrical potential of any limb equals the sum of the other two. The electrodes and the polarity when the ECG is measured by the standard limb leads is the following (Fig. 8):

- Lead I—The negative terminal of the ECG amplifier is connected to the right arm, and the positive terminal is connected to the left arm.
- Lead II—The negative terminal of the ECG amplifier is connected to the right arm, and the positive terminal is connected to the left leg.
- Lead III—The negative terminal of the ECG amplifier is connected to the left arm, and the positive terminal is connected to the left leg.
- Einthoven's Law states that the electrical potential of any limb equals the sum of the other two (+ and − signs of leads must be observed).

3.3 Cardiac Vector

Vectors are used to describe depolarization and repolarization events of the heart muscle. Cardiac vector shows the direction of charge spread in the heart muscle as they happen in time and the magnitude of the electrical activity (Fig. 9). Each lead of the ECG represents a projection of the cardiac vector into a different plane. The standard three leads and the augmented leads each show the projection of a cardiac vector into a plane, which is 60° rotated from the previous lead (Fig. 8). In case there is no electrical activity of the heart, the projection is zero and the ECG shows the baseline, a horizontal line.

Standard record of an ECG is on paper or on the screen of a monitor. In order to adapt it for measurement in time (duration of ECG waves, segments etc.) the printing is calibrated so that 1 mm equals 40 ms at standard paper speed 25 mm/s. In case better time resolution is needed for diagnostics, paper speed is increased to 50 mm/s. The electrical axis of the heart is a sum of all vectors activated in a particular chamber of the heart. In such a way, each part of the ECG has its own respective vector.

3.4 Recording of an ECG

Since the ECG is one of the most informative diagnostic examinations of the heart and cardiovascular system, it became a routine procedure in screening patients.

The routine procedure is taken with the patient lying on a bed. The patient's skin is cleaned in positions provided for electrode placement on the chest and the extremities, followed by the attachment of electrodes. In standard procedure, suction electrodes are attached to the chest and clip electrodes to the arms and legs. The electrodes

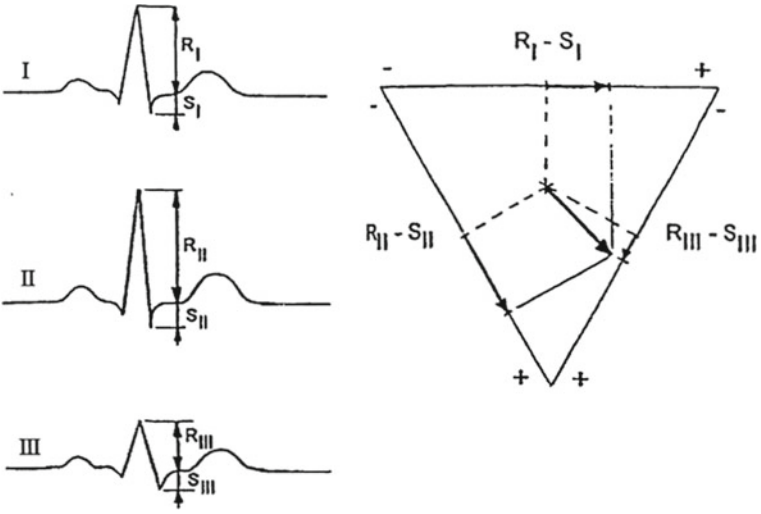


Fig. 9 Calculation of the heart vector

are connected to the cables of the electrocardiograph and, after the patient calms down, the recording begins. The patients have to remain still during the recording. They may be asked to hold their breath for a few seconds. Any movements during the recording may introduce artefacts which degrade the potentials of the heart. In some patients, the diagnostic procedure is specified as a stress test, and then it is recorded under controlled exercising. The recorded electrocardiograms are reviewed by physicians.

Patients taking any kind of medication should inform the physician. They should not be physically active before the test. The procedure itself is comfortable and patients feel well during and after the test.

The diagnostic value of the ECG primarily in screening of cardiac arrhythmias and abnormalities of the conduction system of the heart, as well as in detecting myocardial ischemia. The ECG is used for monitoring of drug intake and the performance of implanted devices like pacemakers. The ECG is also used in interpretation of hypertension, cardiomyopathy, valvular disease, metabolic diseases and many others.

4 ECG Devices—Technical Description

ECGs are categorised as Class IIa medical devices under the Medical Device Regulation (MDR) of 2017 [24]. Class II denotes that a medical device is of moderate to high risk and requires particular controls, and it also reflects the regulatory scrutiny that devices are exposed to before being placed on the market.

An electrocardiograph (ECG) is a measuring device and it is designed as an open measurement channel. The main parts of the ECG are: a set of electrodes, a lead selector, an amplifier, filters, a printer and/or a display unit (Fig. 10).

The ECG may be designed as a 3 channel, 6 channel or a 12 channel device, though for a number of years 12 channel devices dominate since they match to 12-lead standard in ECG interpretation. The device is able to record bipolar, augmented precordial leads. Many multichannel electrocardiographs acquire and analyse the ECG signals since they have embedded microprocessors with ECG signal processing software. The signals recorded at the surface have a range of magnitude of 1 mV and the spectrum between 0.05 and 150 Hz [26]. The block diagram of an analogue front end of an electrocardiograph is presented in Fig. 11. In Fig. 12 a block diagram of an integrated circuit with ECG capabilities is presented. Immediately after amplification, the signals are digitised and further processed digitally. Front-end sampling may be performed at rates from 1000 to 2000 samples per second. Active right leg drive (RDL) is integrated to the circuit as well. Detailed descriptions of the functionalities of the ECG integrated circuits may be found at the Internet sites of leading integrated circuits producers, Fig. 12.

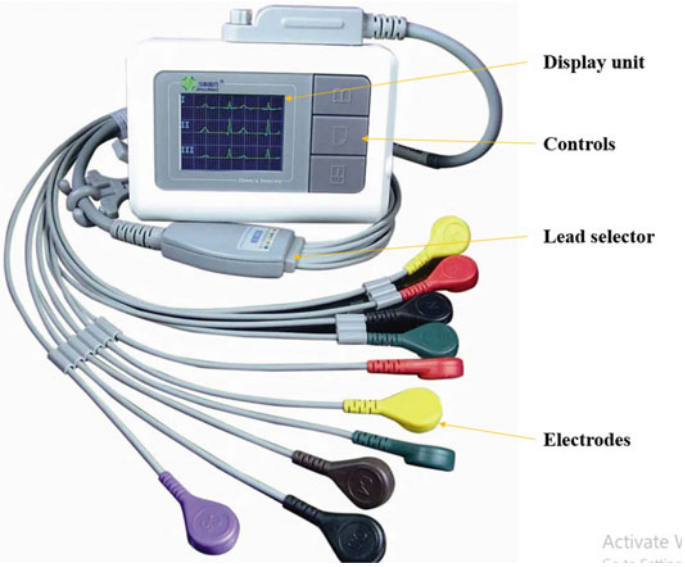


Fig. 10 Parts of a modern ECG device [25]

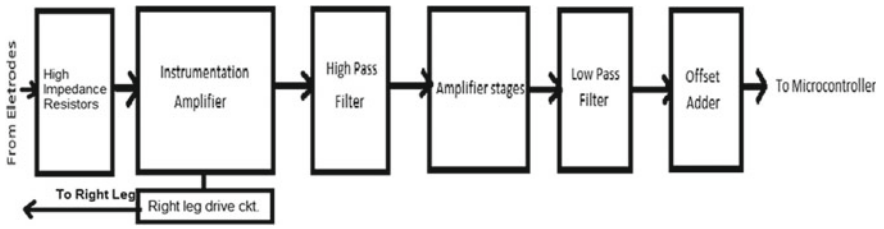


Fig. 11 Block diagram of an electrocardiograph with analog front end [27]

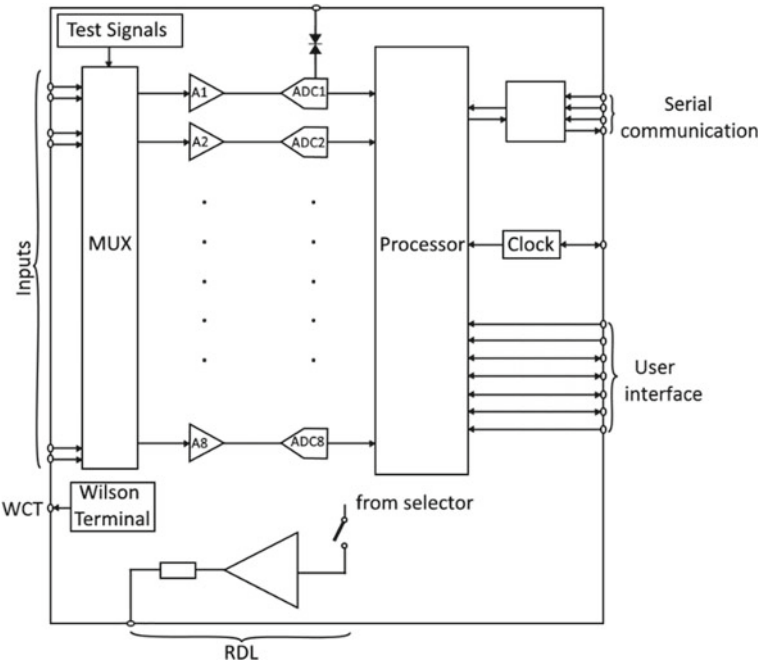


Fig. 12 Block diagram of an integrated circuit comprising many functionalities of an electrocardiograph

4.1 Electrodes

Electrodes for recording biopotentials are usually produced from an inert metal. In ECG, most commonly silver–silver chloride (Ag–AgCl) or stainless steel are used due to their biocompatibility and chemical stability. Each metal electrode that is in contact with electrolyte (which is always present in biological tissue), produces a double layer where positive ions are attracted to the electrode surface and negative ions form adjacent to it. The potential drop over the double layer is called half cell

potential, which changes in time with changes of ion concentration and temperature. The characteristic of Ag–AgCl electrodes is a constant half cell potential of approximately 0.8 mV. Clip and suction electrodes are usually reusable while self adhesive ECG electrodes are expendable. They carry a conductive gel soaked sponge under the snap which is applied to the skin once the electrodes are attached into the position for recording. The conductive gel lowers the resistance of the skin under the electrode which contributes to the quality of the recording because it is lowering the sensitivity of the input stage to interference. Conductive gel may be applied to the skin after cleaning for the same reason [28].

4.2 Lead Selector

Electrodes are connected to the input stage of the ECG by shielded cables with a standardised electrode snap on the electrode end. In the input stage of the device, an overvoltage protection circuit is built-in immediately at the front end. The selector has the function to connect the signals from the electrodes to the input of the particular amplifier, directly or through a resistor network so that the selected leads are amplified, processed and displayed according to the number of channels of the ECG. The functionality of the selector is realised by a multiplexer. An important part of the input stage is a calibrator which has to be connected to the input stage in order to ensure that all parts of the measurement channel are calibrated. The calibration of ECG devices is provided by connecting a 1 mV step function to the input of each measurement channel. For devices with printers and paper with millimetre grid, the deflection for 1 mV input voltage should be calibrated to 10 mm [28].

4.3 Amplifier

Amplifiers for bioelectric signals must have high sensitivity due to low amplitudes of the original signals. High amplification is achieved by multiple stages of amplification in the measurement channel, though the realisation of these stages is mainly within integrated circuits. For amplification of ECG signals, in the input stage, instrumentation amplifiers are used most commonly. Instrumentation amplifiers have very high amplification (100–120 dB), very high input impedance (10 MΩ) and a symmetrical structure of the input stage, which all enables the realisation of a high common mode rejection ratio (CMRR) of the amplifier. CMRR is a measure of suppression of common mode voltage, compared to amplification of the useful bioelectric signals and should be above 100 dB for biopotential amplifiers. The bioelectric signals are prone to electromagnetic interference, especially from the electrical power lines (230 V/50 Hz in Europe) which are superimposed to the useful ECG signal [2].

The signal at the input of the ECG measurement chain consists of four fractions:

1. The measured bioelectric potential (ECG), considered to be the useful signal, with an input range from 50 μV to 1.5 mV.
2. Polarisation voltage which is the difference between the half-cell potentials of two electrodes, ergo, a DC voltage up to 300 mV. The appearance of the polarisation voltage is avoidable whenever the skin is in contact with metal electrodes.
3. Interference from the AC mains frequency (50 Hz or 60 Hz) from line voltages appears as a common mode signal with amplitudes up to 100 mV. Human body, electrodes and connection cables act as an antenna also for signals with higher frequencies but those signals are usually much easier to filter out due to the limited frequency range of ECG amplifiers.
4. Interference high voltages that appear at the input of an ECG device are mainly caused by defibrillator shock voltages or by RF surgery equipment. The defibrillator shock can be treated as a single event and the energy of the shock is always known—up to 400 J. The voltages generated by the defibrillator may reach a few thousand volts, but have limited duration. However, the shocks may be repeated several times. Electrosurgical RF devices produce voltages up to a few hundred volts at a frequency between 500 and 5 MHz, but the duration of the application of the voltage through the body is much longer as compared to the defibrillator shock [29]. The protection circuits that are built into the input stage of the ECG protect the internal circuits and the patient from those potentially dangerous voltages.

From the above analysis of the complex signal that can appear at the input of the ECG measurement chain, it is easy to conclude that the bioelectric signal is the weakest and therefore the processing strategy for the input stage has to be well deliberated.

In order to protect the patient from the mains voltage and the other potentially dangerous voltages coming from the mains, and also to protect the device from overvoltage potentially appearing at the patient side e.g. due to defibrillation, the ECG amplifier is in many designs realised as an isolation amplifier. The isolation circuit separates the patient side and the device side with an isolation barrier which can withstand an electrical shock up to 7.5 kV.

4.4 Filters

The frequency range of diagnostic ECG signals spans from 0.05 to 150 Hz thus the instrumentation in the signal processing channel has to band-pass those parts of the ECG spectrum. The electronic filtering circuits for low-pass and high-pass filters are designed separately. The high-pass filter is applied to remove the polarisation voltage (DC component) which may be two orders of magnitude larger than the ECG itself and could drive the input amplifier into saturation, and the very slow components of the signal which correspond to baseline wandering. The low-pass filter removes artefacts from muscle activity and any high frequency interference. Some parts of

the myoelectric spectrum overlap with the spectrum of ECG so that remains of the EMG signal can be observed in the records. Also some of the movement artefacts cannot be efficiently removed from the ECG since their spectrums overlap.

The interference from the mains voltage may be eliminated by a notch filter with the central frequency at 50 Hz or 60 Hz. However, due to the narrow frequency range of notch filters, analog notch filters have a pronouncedly non-linear phase characteristic, and may change the wave shape of the ECG trace significantly, which may lead to wrong interpretation in reading of the ECG record [29]. Filtering of power noise from ECG is performed mainly by high order linear phase digital filters where the design keeps flatness of the band pass characteristic.

4.5 Display Device

Contemporary electrocardiographs have low power displays and in most cases an embedded printer or wireless connection to a network printer. Digital records may be stored in an appropriate database as a part of the electronic health record of the patient. Electrocardiographs equipped with only paper printers are very rare today.

4.6 Final Assembly

The components of the electrocardiograph are assembled and placed into an appropriate metal frame. The finished devices are then put into final housing along with accessories such as spare electrodes, printout paper, and manuals. They are then sent out to distributors and finally to customers.

5 Safety and Performance Requirements During the Usage of ECG Devices

Legal and technical requirements for all those who manufacture and design electromedical devices are numerous and may be dependent on the particular requirements in different regions. In Europe, the legal aspects are regulated by the Medical Device Directive (Council Directive 93/42/EEC of 14 June 1993) [30]. The Directive intends to harmonise the national laws that relate to medical devices within the European Union and it is a “New Approach” Directive which means that safety aspects rely on Harmonized Safety Standards for the products, including medical electrical equipment. Devices meeting “harmonised standards” are considered to meet the conformity to the Directive which is confirmed by issuing of the CE mark by a EU Notified Body. The Directive was amended by the 2007/47/EC and the revised

directive became mandatory in the EU on March 21, 2010. In April 2017, a new regulation on medical devices was adopted in the European Parliament—Regulation (EU) 2017/745. The Commission claims that Regulation brings more consistency into legislation covering safety of medical devices but also adaption of significant technological and scientific progress occurring in the sector in recent past. The new regulation on medical devices will be applied after a transitional period of three years, i.e. in 2020. The COVID-19 epidemic has brought to light how vital it is to do periodical inspections on medical devices with measuring functions to ensure their correct operation [31].

The "New Approach" takes standards, which are technical specifications defining requirements for products, production processes, services or test-methods as the measure for safety of products. The specifications are voluntary, but they were developed by stakeholders and they are following the same principles: consensus, openness, transparency and non-discrimination. The standards ensure not only the safety but also interoperability, so important in todays' connected health services.

The preceding edition of the book "Inspection of Medical Devices" provided valuable perspectives on how the progress of medical device technology influences healthcare delivery. It stressed the significance of healthcare management and addressed the challenges that come with it [32].

The European Committee for Standardization (CEN) and the European Committee for Electrotechnical Standardization (CENELEC) closely collaborate with the International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) in order to promote the benefits of the international standardisation for trade and market harmonisation. The organisations cooperate based on the Vienna Agreement signed by CEN and ISO and the Frankfurt Agreement between CENELEC and IEC. Many of standards in safety of medical equipment created by these European and International organisations are mutually adopted which can be recognised by e.g. IEC/EN marking in the specification of the particular standard.

The Technical Committee (TC) 62 of the IEC, Electrical equipment in medical practice, prepares international standards concerning electrical equipment, electrical systems and software used in healthcare and their effects on patients, operators, other persons and the environment. IEC 60601 series of technical standards deals with the safety and effectiveness of medical electrical equipment. First standards in this series were published in 1977. In the series, there is a general standard IEC 60601-1 that applies to all electrical medical equipment, some 10 collateral standards which are applied more selectively depending on the topic and about 60 particular standards which apply to specific medical equipment, e.g. electrocardiographs. When designing and testing the equipment standardised by a particular standard, both, general and particular standards have to be obeyed [30–42].

The standard IEC 60601-1:2005 *Medical electrical equipment—Part 1: General requirements for basic safety and essential performance*, describes requirements for basic safety and essential performance applicable generally to all medical electrical

equipment. A collateral standard, take IEC 60601-1-2:2014 *Medical electrical equipment—Part 1–2: General requirements for basic safety and essential performance—Collateral Standard: Electromagnetic disturbances—Requirements and tests*, as an example, describes as well basic safety and essential performance of medical equipment but in the presence of electromagnetic disturbances as well as electromagnetic disturbances emitted by medical equipment. Particular standards from 60601 series that deal with electrocardiographs are:

- IEC/EN 60601-2-27 Medical electrical equipment—Part 2–27: Particular requirements for the basic safety and essential performance of electrocardiographic monitoring equipment.
- IEC/EN 60601-2-47 Medical electrical equipment—Part 2–47: Particular requirements for the basic safety and essential performance of ambulatory electrocardiographic systems.
- IEC/EN 60601-2-51 Medical electrical equipment—Part 2–51: Particular requirements for safety, including essential performance, of recording and analysing single channel and multichannel electrocardiographs.

5.1 Calibration of ECG Devices

Even though different international standards and regulations prescribe all steps in a device's life cycle, nowadays more attention is given to safety and performance inspections or verifications of these devices during normal usage. These procedures consist of visual inspection of the device, safety inspection in accordance with IEC 60601 and performance evaluation also in accordance with IEC 60601 and manufacturer's recommendations. The purpose of these inspections/verifications is to ensure that device performance during usage is still in stated limits. At this point, metrology as a science of measurement is introduced into medical device management. These inspections should be periodical, recommendations are once a year, like preventive check-ups that are basic practice of medical device management in most of the healthcare institutions in the world.

Electrocardiographs must pass through the procedure of examination and approval type, and before letting it into work, they must pass the procedure of first verification and have certificates of verification. Examination of type is done based on documentation which producer or his agent must contribute along with application for approval. Documentation must have general, technical and other documentation and instructions for usage. First verification includes visual examination and is done by specific instruments. Maximum mistake allowed when done in regular verifications cannot be bigger than maximum allowed done by first verification. Periods of verification are defined [42]. ECG devices must have a visible place tile with an accurately written label. These labels and marks should be written in a country's official language.

A qualified technician should calibrate ECG devices using a reference signal generator that has been tested. The National Institute of Standards and Technology

(NIST) in the United States or the International System of Units (SI) are two examples of national or international standards that the reference signal generator should be traceable to. The ECG device should undergo accuracy, linearity, frequency response, noise, and other pertinent parameter testing during the calibration procedure. The calibration procedure should be carried out at various input signal amplitude levels, and the outcomes should be documented in a calibration report. The following details ought to included in the calibration report:

- Identifying the ECG instrument that is being calibrated
- Used calibration process, encompassing tools and techniques
- The calibration's results, including any modifications made to the device
- Reference signal generator's ability to be tracked back to a national or international standard
- Name of the technician that carried out the calibration.

For performing verification/inspection of devices, etalons should be used. Etalons are standards utilised to calibrate equipment, including ECG machines, in many different fields. The way that etalons for ECG calibration function is by offering a reliable reference signal that can be used to check the accuracy and dependability of ECG equipment. ECG calibration can be done using a variety of etalon types, such as:

- High-precision resistors are used to create resistive etalons, which are used to generate a stable reference signal. A high-precision multimeter measures the etalon's resistance, and the output voltage is then employed as the calibration reference signal.
- Capacitive etalons are used to produce a stable reference signal and are constructed of high-precision capacitors. A high-precision capacitance metre is utilised to measure the etalon's capacitance, and the voltage output obtained serves as the calibration reference signal.
- Electronic gadgets called "signal generator etalons" are intended to produce a reliable reference signal. Because they offer a more flexible and precise reference signal than resistive or capacitive etalons, they are frequently employed in ECG calibration. They may be programmed to generate various waveforms and frequencies.

The etalon is connected to the ECG equipment that is being calibrated during ECG calibration, and the output signal produced is compared to the anticipated reference signal. Any variations between the reference signal and the measured signal are noted and utilised to modify the ECG device as appropriate. For the calibration process to be accurate, the etalon's precision is crucial.

For safety inspection there are electrical safety analysers available in the market that allow safety inspection according to IEC 60601, but also in accordance with a vast number of electrical safety standards. These analysers are portable and easy to use, and usually they have software support. Together with a number of safety probes and sensors used to assess electrical characteristics including ground leakage, insulation resistance, and patient leakage, the electrical safety analyzer normally comes with

a set of test leads that are connected to the ECG device being checked. The ECG equipment is subjected to a variety of electrical signals during electrical safety testing, and the electrical safety analyzer then examines the resulting electrical parameters to make sure they are within permissible bounds. Before the ECG equipment can be approved as safe for use, any irregularities or failures that were found during testing are reported and must be fixed.

For performance inspections, various analysers can be used also. Generally these analyser's comprise of slots for connecting ECG leads, casing, battery, power supply, user interface. They are often supported with software that enables generation of different performance ECG tests.

The accuracy of the ECG depends on the condition being tested. ECG devices must be constructed and made in a proper way so that in normal working conditions there is protection from electric shock, too high temperature, dust and water into the housing of instrumentation. Reference conditions for ECG:

- Voltage 220–240 V AC, 50 Hz
- Battery of 12 V
- Working time minimally 1 h
- Input impedance >10 MΩ
- Calibrational voltage 1 mV ± 2%.

Every part of an electrical medical device that comes into contact with the patient's body has some risk of electrical shock caused by unsafe leakage currents. The electrical safety inspection involves testing of ground wire resistance, chassis leakage, patient leakage currents and mains on applied parts.

During the verification of ECG by etalon, range of measuring which must be controlled are next:

- Amplitude of voltage signal identified by ECG in mV is 0.5, 1.0, 1.5 or 2.0 mV
- Speed of beats in a time frame of 1 min is: 30, 40, 60, 80, 90, 100, 120, 140, 150, 160, 180, 200, 210, 220, 240, 260, 270, 280, 300.
- Limits of allowed mistakes are:

  In case of measuring amplitude of voltage signal is ±5%
  In case of measuring speed of beats in time frame of 1 min is ±2%.

Performance inspection is performed in order to determine measurement error of the device under test. If the error is in any of these cases bigger than maximum allowed error, ECG cannot be used and it must be serviced and verified again.

6 A Novel Method for Conformity Assessment Testing of ECG Devices for Post-market Surveillance Purposes

The methodology proposed for assessing the conformity of ECG devices involves several steps. Firstly, legal requirements must be established, including technical and metrological standards that the devices must meet to be considered suitable for diagnosis or therapy. After identifying these requirements, a testing method must be established that involves using calibrated reference instruments to measure the crucial parameters of the device. Finally, the results of the measurements should be presented in a report that allows for an analysis of the device's performance, leading to a conclusion about whether or not the device meets the previously established requirements.

Safety and performance inspection during usage of ECG devices has been developed and validated by Badnjevic et al. [43]. The developed methodology takes into account the International Organisation of Legal Metrology (OIML) approach established for other classes of measurement-capable medical devices while in use.

The reported method has the following coherent structure:

1. Definition of technical requirements for ECGs,
2. Definition of metrological requirements for ECGs,
3. Description of method for visual inspection,
4. Description of method for electrical safety inspection,
5. Description of method for performance inspection,
6. Summary and expression of test results.

The method is performed using calibrated etalons for electrical safety analysis and performance analysis.

Technical and metrological requirements are established in accordance with regulatory specifications included in directives and regulations, manufacturer technical specifications, and international standards defining the performance and safety of medical equipment. This chapter outlines a procedure that is tailored for inspecting medical devices that come with a measuring function [44–46].

6.1 Technical Requirements

The routine examination of ECGs' technical specifications is crucial for ensuring their safety and dependability once they are sold and put to use in clinical settings. Labels and marks must be clear, readable, and permanent in order to assure the devices' traceability. They must also be impossible to remove without causing lasting harm. The technical specifications for the ECG are formalised in the following way.

The technical requirements refer to the:

- Label and marking
  - name and/or trademark of manufacturer;
  - production mark (basic type)
  - year of fabrication;
  - unique serial number;
  - CE mark of appropriate administrative marking;
- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz; Battery supply (12 V);
  - Working time on battery for ECG devices is a minimum of 1 h.
  - Input impedance >10 MΩ.
  - Calibration voltage 1 mV ± 2%.
- Compliance with IEC 60601-2-25 Medical electrical equipment—Part 2–25: Particular requirements for the basic safety and essential performance of electrocardiographs [42].

A testing procedure must be used to inspect all of the requirements listed above. According to OIML recommendations, IEC 60601-compliant visual inspection and electrical safety inspection should be used to test these kinds of requirements [42].

6.2 Metrological Requirements

Medical device reliability can be demonstrated by looking at how well it complies with metrological standards. Metrological characteristics, which are quantitative parameters that are unique to each device and show the reliability of the instrument, include inaccuracy, accuracy, and uncertainty. Each measurement device's manufacturer defines some specifications, such as the measurement unit, range, division, and accuracy. The metrological requirements for ECGs are formalised in the following way in accordance with the OIML guideline:

- Measurement unit
  - Amplitude of voltage signal identified by ECG is set and measured in millivolts (0.5–2.0) [mV].
  - Heart rate in a time interval of 1 min is set and measured in beats per minute [bpm].

The volt is a derived unit of electric potential, electric potential difference (voltage), and electromotive force in the International System of Units (SI) (NIST

2019). A millivolt is 1/1000 of a volt (0.001 V or 10^{-3} V). One volt is defined as the electric potential between two points of a conducting wire when an electric current of one ampere dissipates one watt of power between those points (SI base units: kg m^2 s^{-3} A^{-1}).

Beats per minute (heart rate), the number of heartbeats detected during one minute.

- Measuring range and division
  - Amplitude of voltage signal identified by ECG is set and measured in millivolts (0.5–2.0) [mV].
  - Heart rate in a time interval of 1 min is set and measured in beats per minute (30–300) [bpm]
  - Outside this working range no energy reading and no measurement result shall be displayed.
  - Division:

    Amplitude of voltage signal identified by ECG in millivolts: 0.5, 1.0, 1.5 and 2.0 [mV]
    Heart rate in a time interval of 1 minute: 30, 40, 60, 80, 90, 100, 120, 140, 150, 160, 180, 200, 210, 220, 240, 260, 270, 280, 300 [bpm]

  - Performance accuracy stated by the manufacturer in the technical specification.

A testing procedure must be used to inspect all of the requirements listed above. According to OIML recommendations, performance inspection, as shown in Sect. 6.4 of findings, should be used to test these kinds of requirements. A test report must be written in accordance with findings Sect. 6.4. Testing for metrological compliance assessment is done using a performance inspection approach. According to OIML recommendations, the metrological compliance assessment testing requirement can be expressed as follows:

- For any set of conditions within the ambient temperature range of 21–26 °C, the maximum permissible error for the measurements is as follows:
  - Amplitude of voltage signal ±5% of reading,
  - Heart rate in a time interval of 1 minute ±2% of reading.

6.3 Method of Test

6.3.1 Visual Inspection

(a) Equipment

The prerequisites for performing visual inspection are:

- Device under test / ECG;
- Manufacturers specification;

Table 1 Technical requirements and pass/fail criteria

No.	Criteria technical requirements	Result	Conformity assessment testing
1	Prescribed labels and markings on the device under test	• Name and/or trademark of manufacturer • Production mark (basic type) • Year of fabrication • Unique serial number • CE mark of appropriate administrative marking	Pass/fail
2	Construction of the device	• The integrity of the device under test in respect to the manufacturer's specification • The functionality of the device under test in respect to the manufacturer's specification	Pass/fail
3	Performance of the device	• Measurement range • Measurement unit	Pass/fail

(b) *Procedure*

Checking label/marking and construction integrity are steps in the process of visual inspection for a device that is being tested. The device's functioning and auxiliary components must meet the manufacturer's specifications.

(c) *Summary and expression of test results*

The results are expressed as Pass/Fail answers to the criteria which have been tested (Table 1).

6.3.2 Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

– Device under test/ECG;
– Reference electrical safety testing equipment /analyser;

(b) *Procedure*

Choose measuring points to cover the whole measuring range based on the device's measuring range. Attach the ECG electrodes to the testing device's designated places (Fig. 13). In each measuring point, check the heart rate and voltage signal amplitude every minute. Choose the desired settings on the reference testing device to test these two parameters. The signals will be simulated as a result, and the DUT will interpret them.

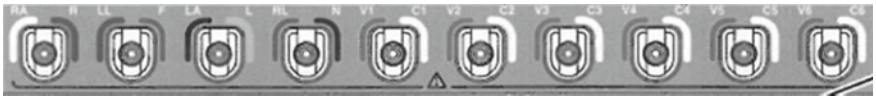


Fig. 13 Connection sites for the ECG electrodes on the reference testing device

(c) *Summary and Expression of Test Results*

The choice to undertake conformity assessment testing is made following the study of the test findings. The OIML suggests presenting the results in tables as a summary. As can be seen, a qualitative analysis is used to report on visual inspection. The conformance assessment testing is stated in simple YES/NO responses to the criteria. The findings of the performance inspection are shown in terms of error. Absolute error or relative error can both be used to indicate inaccuracy in metrology. The relative inaccuracy between the specified values of the device under test and the corresponding readings of the calibrated reference testing apparatus might be given as the performance inspection result in the case of ECGs.

6.4 Performance Inspection

Relative error calculation:

$$\Delta X = X_{\text{set}} - X_{\text{measured}}/X_{\text{set}} * 100 \quad (1)$$

The value of this error determines the conformity assessment testing in performance inspection [43]. It was created using the same worldwide standards that were used to produce the ECG. This requirement's basis is used to formulate the conformance error as follows:

- If the error is less than the greatest allowed limit, then the device is compliant with metrological requirements.

All of the ECGs in this study were examined for the qualitative features listed below that affect their performance in addition to the quantitative testing suggested by this methodology, such as chassis integrity (technical requirements) in terms of strain reliefs, electrodes, connectors, switches, displays, alarms, and battery. Additionally, tests were performed on the instrument and control accuracy, charging duration, and internal electrical power source.

It is evident that the percentage of faulty ECGs varied most significantly over the first two years of technique implementation in practice. Even though it is less evident, the negative trend is still present throughout time. Most healthcare facilities have already submitted their ECGs for performance evaluation in previous years, and any non-compliant equipment from those evaluations has either been taken out of service or has been repaired and inspected again.

The OIML metrological standards-based medical device inspection technique is the most effective way to stop the use of inaccurate ECGs in clinical practice, which is another finding supported by this. In the absence of performance inspection, healthcare professionals would not be aware of the non-compliance of the output values of the measured heart rate and the amplitude of the voltage signal, hence the majority of erroneous ECGs would continue to be used.

This underlines the need for independent periodic evaluation of the technical and metrological requirements for the currently in use ECGs. The performance test found performance deviations that were not identified during usage or routine preventive and corrective maintenance. Comparable to the suggested equipment examination in this study, Serhani et al. [47] evaluation testing of ECGs at adjacent hospitals. The significance of ECG usage inspection in healthcare facilities is highlighted in both the study by Serhani et al. [47] and the study detailed in this publication.

The medical device management industry is presently being impacted by the worldwide digital revolution, which necessitates the gathering of data and its utilization for informed, evidence-based decision making [48–50]. Only traceable measures produced from standardised conformity assessment testing methodologies may be used by artificial intelligence (AI)-based systems for individualised prediction of medical device performance and potential problems [51].

7 Conclusion

The significance and impact of the ECG since its invention in the nineteenth century is practically immeasurable. 'The person behind the machine', Willem Einthoven, was even awarded a Nobel in 1924 for his prominent achievement. ECG allows us to observe the complex electrical activity of the heart, and through its recordings, make deductions about a person's health. In fact, the device had been a literal life for more than a century. Naturally, its spread in use grew over time, bringing more and more updates to the design. Moreover, we have discovered numerous applications for it, especially in the blooming field of preventive medicine. Currently, the main cause of death worldwide is heart disease, particularly heart attacks. Many lives can be saved if doctors have access to reliable ECG equipment that can identify impending cardiac arrest. Furthermore, its usage is not only for those with cardiac problems. The ECG and its properties can be used to diagnose, prevent, and treat a wide range of ailments and diseases. Regardless of whether we are discussing youthful athletes or the elderly, men or women, ECG determines the type of treatment, food, or any other significant aspect of a person's lifestyle. Yearly controls should be implemented, as it would lead to prevention of diseases. People should get familiar with its fundamentals, including how it operates, why it is used, and how to use it appropriately, given its obvious relevance. Also, a large portion of the population should always have access to it, therefore its availability should be very high. For instance, the availability of current ECGs in every drugstore and the ability for consumers to self-test at any time would likely reduce the need for doctor visits. It might become commonplace in a

few years, just like taking a person's body temperature, arterial blood pressure, or blood sugar level. ECG usage could become routine.

Each ECG is subject to regulations, which ensure its proper functioning. Every parameter, from physical dimensions to reading range is well defined, and must be verified before it arrives at the healthcare facility where it is meant to be used.

Another way to increase patient safety and trust in healthcare is to ensure the traceability of ECGs output values according to international standards. The presented novel method for post-market surveillance is based on a metrological approach that produces verifiable proof of device performance. The work of two inspection bodies for medical devices operating within the legal metrology framework, which has been implemented for medical devices in Bosnia and Herzegovina and Republic of Serbia, demonstrates the legitimacy of this procedure. This innovative approach can be addressed for future global standardisation of post-market surveillance of ECGs used in healthcare institutions, in accordance with the OIML recommendations.

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Inspection and Testing of Noninvasive Blood Pressure Measuring Devices

Igor Lacković

Abstract The main purpose of the present chapter is to provide an overview of noninvasive blood pressure measuring devices and their inspection and testing. The chapter first introduces systematic classification of methods for blood pressure measurement. Strengths and weaknesses of each method are discussed. Devices for noninvasive blood pressure measurement are described. Several international standards for evaluating the accuracy of blood pressure monitors (AAMI/ANSI SP10, BHS, DIN, IEC, etc.) are compared. This is followed by a section on the inspection and testing of non-invasive blood pressure measuring devices as recommended by the latest guidelines from the International Organization for Legal Metrology (OIML). At the end of this chapter a short summary is given emphasizing the importance of accuracy testing of noninvasive blood pressure measuring devices.

1 Introduction

The measurement of blood pressure is important in the diagnosis and monitoring of a wide range of clinical conditions. The blood pressure in the circulation is principally due to the pumping action of the heart and other determinants including peripheral vascular resistance, the blood volume and viscosity. The pumping action of the heart generates pulsatile blood flow, which is conducted into the arteries, across the microcirculation and back via the venous system to the heart. Blood pressure usually refers to the arterial blood pressure in the systemic circulation. Arterial blood pressure is the force blood exerts per unit area on the walls of the arteries as the heart pumps it through the arterial tree. It is one of the vital signs, along with heart rate, oxygen saturation, respiratory rate and body temperature. Blood pressure is usually expressed in terms of the systolic pressure (maximum during one heart beat) over diastolic pressure (minimum in between two heart beats). Illustration of idealized arterial pressure waveform with indication of characteristic point pressures is given in Fig. 1. For a more detailed introduction to cardiovascular anatomy and physiology refer to [1].

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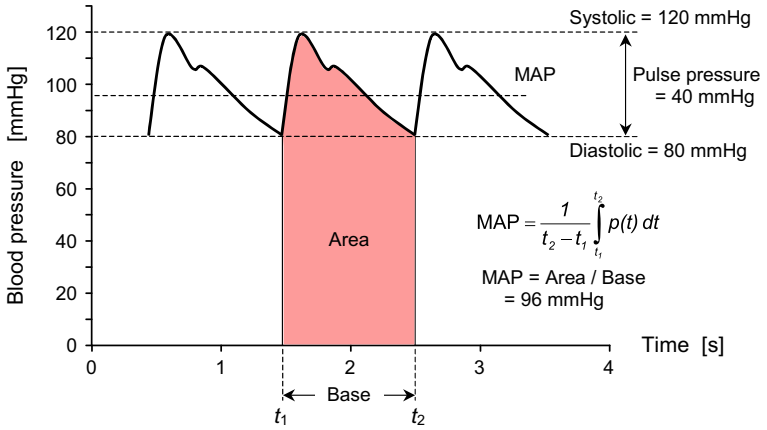

Fig. 1 Idealized arterial pressure waveform. When the left ventricle ejects blood into the aorta, the aortic pressure rises. The maximal aortic pressure following ejection is termed the systolic pressure (Psys). As the left ventricle is relaxing and refilling, the pressure in the aorta falls. The lowest pressure in the aorta, which occurs just before the ventricle ejects blood into the aorta, is termed the diastolic pressure (Pdia). MAP indicates mean arterial pressure. MAP ≈ 2/3(Pdia) + 1/3(Psys)

Normal blood pressure at rest for adults is within the range of 100–140 mm of mercury (mmHg) systolic and 60–90 mmHg diastolic. Hypertension, or high blood pressure is present if the resting blood pressure is persistently at or above 140/90 mmHg for most adults. Table 1 gives one of the most widely used classifications of blood pressure for adults [2]. As of 2015, approximately one billion adults or ~22% of the population of the world have hypertension [3]. Arterial hypertension is a major risk factor for heart disease and could lead to severe organ damage. It is often called a "silent killer", because there are usually no warning symptoms before hypertension strikes a person in the form of a stroke, heart attack, heart failure, eye problems (hypertensive retinopathy) or kidney disease. Therefore, it is important to measure blood pressure regularly especially if any of risk factors (family history, smoking, obesity, high sodium intake, stress, etc.) is present.

Auscultatory method using aneroid or mercury sphygmomanometers is commonly used for manual blood pressure measurements. For automated noninvasive blood pressure monitors oscillometric method has become the de facto standard. Public awareness of risks associated with high blood pressure and the availability of embedded microcontroller-based systems have resulted in the development of numerous automated devices for noninvasive blood pressure measurement and their widespread use not only in medical facilities, but also in homes and public places. The only way to determine whether someone has high blood pressure is to have it checked regularly. The key to blood pressure control is "good blood pressure measurement". From the engineering point of view "good" means accurate and reliable. Both medical professionals and general public users require accurate, safe and reliable blood pressure measuring. A standardized set of recommendations for blood

Table 1 Classification of blood pressure for adults (JNC7) [2]

Category	Systolic pressure, mmHg[a]	Diastolic pressure, mmHg
Normal	90–119	60–79
High normal (prehypertension)	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	160–179	100–109
Stage 3 hypertension (emergency)	≥180	≥110
Isolated systolic hypertension	≥140	<90

[a] A millimeter of mercury is a manometric unit of pressure, formerly defined as the extra pressure generated by a column of mercury one millimetre high and now defined as precisely 133.322387415 Pa. Although not an SI unit, the millimeter of mercury is still routinely used in medicine, meteorology and some other scientific fields

pressure measurement in humans, that, if followed, should lead to accurate estimation of blood pressure, are summarized in [4].

2 Survey of Methods for Blood Pressure Measurement

Methods for arterial pressure measurement are usually classified into direct and indirect methods [5]. The first being invasive and the only that measure the "true" pressure. All other methods belong to the group of indirect methods since the pressure is measured noninvasively from outside the body.

2.1 Invasive Method

Invasive methods imply the insertion of an arterial cannula into a suitable artery and then displaying the measured pressure waveform on a monitor. The arterial cannula is connected to tubing filled with saline, which acts as a coupling medium between the blood in the artery and the external pressure transducer. The liquid within the tubing is in contact with a diaphragm that moves in response to the transmitted pressure wave. The movement is converted to an electrical signal by a transducer. In that way the complete arterial pressure waveform is measured and it is easy to determine systolic and diastolic pressure on a beat-to-beat basis.

Invasive method is the gold standard of blood pressure measurement giving accurate beat-to-beat information. Due caution is required regarding the frequency response of the system (i.e. damping, resonant frequency, etc.) as it affects the accuracy of intraarterial pressure monitoring. Arterial pressure waveform is a complex waveform composed of many individual sine waves. It is therefore important that the natural frequency of the measuring system (the catheter and column of saline

etc.) does not correspond to any of the frequencies of the arterial pressure waveform. This is achieved by making sure that the natural frequency of the measuring system is raised high enough i.e. above any of the frequencies of the arterial pressure waveform. Therefore, arterial catheter must be short and with the maximum gauge possible; column of saline must be as short as possible; the catheter and tubing must be stiff walled; the transducer diaphragm must be as rigid as possible. Also, a potential source of error may be the incorrect positioning of the catheter or the pressure transducer positioned at the different level to the patient's heart. The drawbacks of direct methods are that they are invasive and uncomfortable for patients and in long-term use could lead to risks associated with infection, air embolism or thrombosis. Therefore, invasive measurement of blood pressure is performed only in clinical environment in patients who are likely to display sudden changes in blood pressure (e.g. vascular surgery), in whom close control of blood pressure is required (e.g. head injured patients), or in patients receiving drugs to maintain the blood pressure.

2.2 Noninvasive Methods

Noninvasive measurement of arterial pressure is based on the detection of certain characteristic physical phenomena that can be registered at the surface of the body and correlating these phenomena to the arterial pressure. In the majority of noninvasive methods an occlusive cuff is used to obstruct the blood flow normally in the brachial artery. Then during cuff deflation, occurring phenomena are being recorded (e.g. Korotkoff sounds, cuff pressure oscillations, etc.). In some methods systolic and diastolic pressure can be determined not only during cuff deflation but also during cuff inflation. The process of cuff deflation (or inflation) can be continuous or incremental (stepwise).

Noninvasive methods may be classified according to different criteria. A widely used criterion is whether the method enables continuous or intermittent measurement. Main feature of intermittent methods is that systolic and diastolic pressures are obtained during the time interval that encompasses many heartbeats. Continuous methods provide either absolute, continuous pressure waveform similar to intraarterial recording (from which characteristic pressures are easily determined) or give only the systolic and diastolic pressure on a beat-to-beat basis. The main advantage of continuous methods is their ability to track beat-to-beat variations of blood pressure. The principal disadvantage of all continuous noninvasive methods is a relatively large measurement error that depends on the calibration method being used. Continuous noninvasive methods have great importance in long-term physiological monitoring, e.g. for studies of sleep disorders or nocturnal hypertension, or in polygraphic recordings.

Noninvasive methods can also be classified upon the use of cuff. We can distinguish cuffless methods, methods that use partially inflated cuff and methods that use a cuff for complete occlusion of the arterial blood flow (cuff pressure is raised above

Table 2 Characteristics of noninvasive blood pressure measurement methods

Method	Intermittent/continuous	Cuff/cuffless
Auscultatory method	Intermittent	Occlusive cuff
Oscillometric method	Intermittent	Occlusive cuff
Palpatory method	Intermittent	Occlusive cuff
Ultrasound method	Intermittent	Occlusive cuff
Pulse-wave velocity method	Continuous	Cuffless
Vascular unloading method	Continuous	Partially inflated cuff
Arterial tonometry	Continuous	Cuffless although the artery is partially occluded

systolic pressure). If occlusive cuff is used at least ~2–5 min are required between successive measurements to allow for restoration of normal blood flow.

Based on the physical principle noninvasive methods for blood pressure measurement are divided into one of the following categories [5, 6]:

- Auscultatory method (Riva-Rocci method, Korotkoff method)
- Oscillometric method
- Palpatory method
- Ultrasound method
- Pulse-wave velocity method (Transit-time method)
- Vascular unloading method
- Arterial tonometry.

Among these, the most widely used are the auscultatory method and the oscillometric method. Other methods are not routinely used. They are either used only in research settings or were used in the past and have been replaced by other methods.

Some characteristics of noninvasive methods for blood pressure measurement are disclosed in Table 2.

It is important to stress that each method has its own algorithms (criteria) to determine characteristic pressures that will be discussed in the forthcoming sections. Therefore, the accuracy of any particular method cannot be established without knowing the characteristics of the algorithms used to identify systolic and diastolic pressure. That is especially important for the oscillometric method since numerous algorithms have been developed over the years, and also for the auscultatory method due to the disagreement whether Phase IV or Phase V of Korotkoff sounds should be used as the indicator of diastolic pressure.

2.2.1 Auscultatory Method

The auscultatory method (Riva-Rocci method, Korotkoff method) is still the most widely used noninvasive method for blood pressure measurement. For routine arterial

pressure measurement, physicians prefer the manual auscultatory method. Automatic devices based on the use of one or several microphones were also developed.

Occlusive cuff, typically 12 cm wide is wrapped around the upper arm and rapidly inflated to the supra systolic pressure in order to completely stop the blood flow distal to the cuff. To avoid erroneous results, due caution is required to the choice of proper cuff width (standard 12 cm cuffs are usually inappropriate for obese, or generally always when subject's arm circumference considerably deviates from average population), as well as to the proper cuff positioning and the degree of tightening. The cuff deflation rate should be around 3 mmHg per beat or approximately 3 mmHg/s. As the cuff pressure is decreased, a stethoscope placed over the artery distal to the cuff will detect a sequence of sounds (the Korotkoff sounds) that suddenly appear (Phase I), change in character and intensity (Phase II, Phase III, Phase IV) and then gradually disappear (Phase V), Fig. 2. The appearance of sounds (Phase I) is taken as the indicator of systolic pressure, and the disappearance of sounds (Phase V) is usually used as the indicator of diastolic pressure. Mean arterial pressure cannot be determined, and if needed, a suitable empirical formula is used to calculate it from systolic and diastolic pressure.

The phenomenon known as auscultatory gap, which is characterized by disappearance and then reappearance of Korotkoff sounds, can lead to an erroneous indication of diastolic pressure (see Fig. 2). To avoid errors due to auscultatory gap cuff pressure should be allowed to fall below the gap, where sounds return. Rapid cuff inflation and increased interval between successive measurements can also help, since auscultatory gap frequently occurs due to high venous pressure distal to the cuff.

In some subjects, during cuff deflation, the sounds do not disappear after Phase IV (Phase V does not exist). Instead, they persist to well below diastolic pressure (see Fig. 2). In that case the beginning of Phase IV is recommended as the indicator of diastolic pressure.

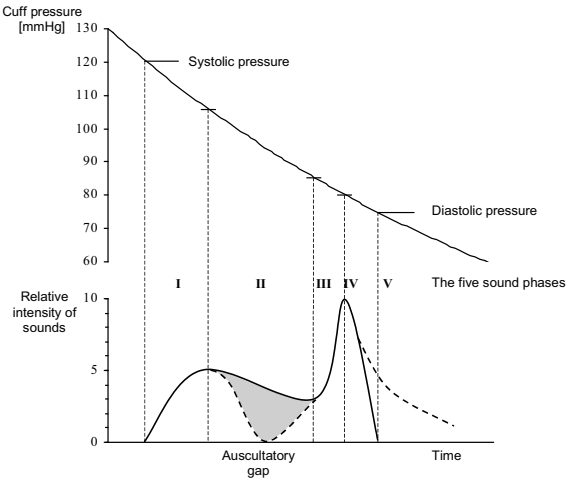

Fig. 2 Relative intensity of Korotkoff sounds, along with the estimate of systolic and diastolic pressure

The origin of Korotkoff sounds is in two physically different phenomena—rapid movement of the arterial wall and turbulent flow of blood through partially opened artery [7]. Clearly, the contribution of each is not equal and dominant mechanism changes during phases.

Auscultatory method can be automatized in a way that cuff is automatically inflated and slowly deflated and that systolic and diastolic pressure are measured electronically. In that case instead of stethoscope, one or more microphones are used, and an electronic system for signal processing is needed. The limitation of that approach is high sensitivity to external noise that can lead to large errors. Techniques to reduce the effects of artifacts and external noise include the application of more microphones and ECG-gating or oscillometric-pulse-gating (OP-gating) techniques. Identification of Korotkoff phases can be performed either in time or in frequency domain. Frequency spectrum of Korotkoff sounds covers frequency range from 20 to 300 Hz, but the majority of energy content lies below 50 Hz. The Korotkoff sounds represent only the audible portion of a broader range of arterial vibrations that also spread to inaudible range.

Some of the most important factors that influence the accuracy of auscultatory method are: cuff width, observer's ability to identify the phases, choice of Phase IV or Phase V as indicator of diastolic pressure, manometer accuracy, cuff deflation rate, cuff location (influence of hydrostatic pressure), etc.

Comparison of auscultatory method with direct intraarterial recording performed by London and London, showed that Korotkoff method underestimates systolic pressure by 5–20 mmHg and overestimates diastolic pressure by 12–20 mmHg [8]. Average error estimates were -2 mmHg for systolic and $+4$ to $+10$ mmHg for diastolic pressure. Another study showed similar results [9].

In summary, the average error of blood pressure measured by auscultatory method is around 10 mmHg when compared to intraarterial recording. Auscultatory method tends to underestimate systolic pressure and to overestimate diastolic pressure. Measurement error is larger for diastolic than for systolic pressure.

2.2.2 Oscillometric Method

The oscillometric method is based on characteristic physical phenomenon—cuff pressure oscillations (oscillometric pulses) generated by the pulsatile displacement of the artery that occur during cuff deflation from supra systolic to sub diastolic pressures. With decreasing cuff pressure the amplitude of the oscillations increases at first, reaches its maximum and then begins to decrease, Fig. 3. These phenomena are used to calculate characteristic pressures [6, 10, 11].

Mean arterial pressure is easiest to determine—it corresponds to oscillations' maximum. Systolic and diastolic pressure are determined indirectly, since oscillometric method provides clear indicator only for mean arterial pressure. There are two types of criteria used to determine systolic and diastolic pressure: height-based criteria (amplitude ratio approach) and slope-based criteria (derivative oscillometry).

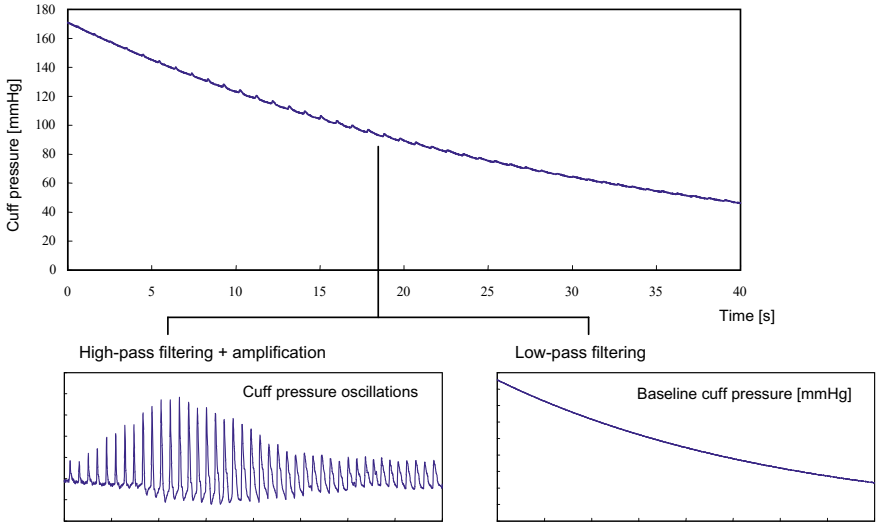

Fig. 3 Cuff pressure signal (top) contains small oscillations superimposed on gradually decreasing pressure. After high pass filtering and amplification dynamics of cuff pressure oscillations is clearly observed. Low-pass filtering removes oscillometric pulses to obtain baseline cuff pressure (bottom)

Criteria for systolic, diastolic and mean arterial pressure determination can be graphically demonstrated when the oscillations' envelope is plotted against the corresponding baseline cuff pressure, Fig. 4.

In the height-based approach (amplitude-ratio approach), the systolic pressure is determined as the baseline cuff pressure that is greater than the mean arterial pressure and at which the ratio of the oscillometric pulse amplitude A_s over the maximum pulse amplitude A_{max} is equal to a certain predetermined value—the systolic ratio. Similarly, the diastolic pressure is determined as the baseline cuff pressure that is lower than the mean arterial pressure and at which the ratio of the oscillometric pulse amplitude A_d over the maximum pulse amplitude A_{max} is equal to another predetermined value—the diastolic ratio. These ratios depend on cuff compliance, cuff deflation rate, etc. and have to be determined empirically on a population of subjects. Systolic ratio is usually around 0.5 and diastolic ratio around 0.7, although literature values range from 0.4 to 0.75 for systolic and from 0.6 to 0.86 for diastolic ratio.

In the slope-based approach the baseline cuff pressure at which the pulse amplitude increases rapidly is taken as systolic pressure, while that at which the amplitude decreases rapidly is taken as the diastolic pressure. Mathematically, these two points may be defined as the points at which the slope of the envelope is maximum or minimum (inflection points of the envelope). Equivalently, time derivative of the oscillations' envelope can be used to determine characteristic pressures. Therefore, slope-based approach is also known as derivative oscillometry. Mean arterial pressure can be easily identified as the point where the derivative passes through zero. The

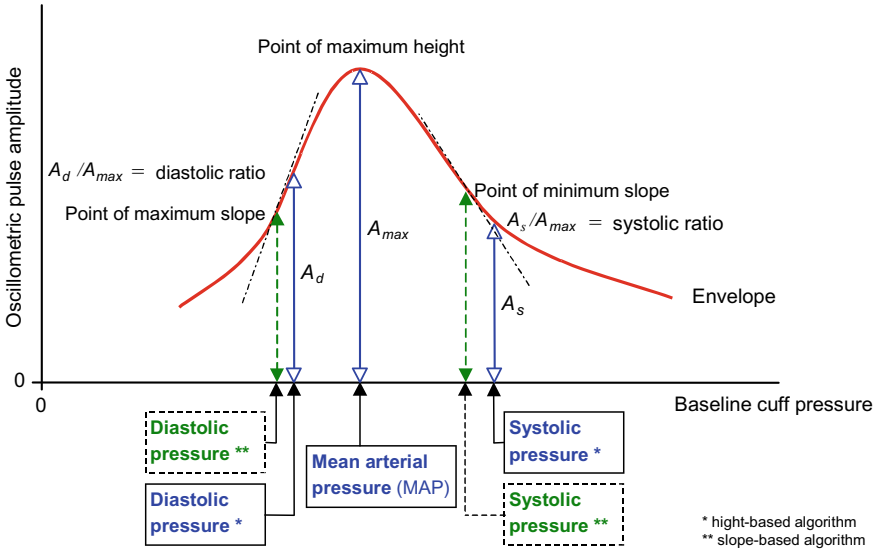

Fig. 4 Envelope of cuff pressure oscillations (oscillometric pulses) with the illustration of two algorithms for detection of systolic and diastolic pressure. One asterisk—height based approach (amplitude ratio approach), two asterisk—slope based approach

baseline cuff pressure at which the derivative reaches maximum is taken as the systolic pressure, while the baseline cuff pressure at which the derivative reaches minimum is taken as the diastolic pressure.

Different variations of oscillometric method have been reported both regarding the algorithms, the application of more than one cuff etc., but many technical details used in commercial oscillometric devices are proprietary and patent protected. Very similar to oscillometric method is the volume-oscillometric method. The only fundamental difference is that volume-oscillometric method is based on artery volume oscillations. Consequently, photoplethysmographic or similar volumetric sensor is used for detecting arterial volume changes.

The key point to understanding limitation of oscillometric method is that it provides only mean arterial pressure directly. Both systolic and diastolic pressure are calculated using empirical criteria. Also, motion artifacts, presence of arrhythmias, increased arterial stiffness due to aging, etc. can lead to envelope distortion and erroneous measurement of blood pressure.

2.2.3 Other Methods

The palpatory method (return-to-flow method) can provide a good estimate of systolic pressure [5, 6]. During cuff deflation, an artery distal to the cuff is palpated. The appearance of palpable beats indicates systolic pressure. Instead of manual palpation,

an electronic sensor can be used. Electronic palpation is more sensitive than manual and enables more accurate determination of systolic pressure. Usually electronic palpatory methods use arm cuff and transcutaneous Doppler flowmeter or other plethysmographic sensor (typically photoplethysmographic) that is placed at the wrist or finger. As long as the cuff pressure is above the systolic pressure, blood flow distal to the cuff is obstructed and the sensor cannot detect any changes of blood volume. When the cuff pressure falls below the systolic pressure, blood starts to flow through the partially opened artery to the distal part of the limb. That moment can be detected by a distal sensor as appearance of pulses and indicates systolic pressure. However, diastolic pressure cannot be determined by palpatory method since there is no indicator in the distal pulse when cuff pressure passes through diastolic pressure.

The ultrasound method is based on the ultrasonic detection of the arterial wall motion during cuff deflation. Two piezoelectric transducers, one that serves as transmitter and generates ultrasound waves, and the other that receives the reflected waves are embedded in the distal part of the occlusive cuff. Systolic and diastolic pressure are determined from the frequency shift of the reflected waves to the transmitted waves due to the Doppler effect [5]. As long as the cuff pressure in greater than systolic pressure, artery is fully occluded and the transmitted waves reflect without the change of frequency. When the cuff pressure falls below the systolic pressure, the artery wall moves rapidly what is manifested with the appearance of high frequency and immediately after by the low frequency due to the closing of the artery. As cuff pressure decreases, time between opening and closing increases causing the increase of time interval between frequency shifts. Finally closing and next opening coincide and frequency shift disappears. That indicates the diastolic pressure. Although ultrasound method has a relatively small error, complicated measuring system and the need for contact medium between the transducers and the skin renders this method unsuitable for clinical practice or home use.

The pulse-wave velocity method proceeds from the fact that pulse-wave velocity (the velocity of pressure wave along the arterial tree) increases with the increase of arterial pressure [6]. Theoretically, this relationship can be used to derive arterial pressure waveform, without a need for a cuff, which if calibrated against measurements made by a reference method, yields absolute continuous arterial pressure waveform. However, measurement of pulse-wave velocity is indirect-pulse wave velocity is computed from the measured pulse-transit time between two different sites of the arterial tree during the same cardiac cycle and the estimated distance between these two sites. Although the pulse-wave velocity method is theoretically capable of measuring continuous arterial pressure waveform, it typically provides only beat-to-beat point pressure. To obtain continuous pressure waveform multiple measurements of the pulse-transit time during the same cardiac cycle would have to be made for each and every heartbeat. That problem is still not solved. In order to measure pulse-transit time, two photoplethysmographic sensors are used. Typical peripheral measuring sites include forehead, finger and wrist. Instead of using two photoplethysmographic sensors it is also possible to measure the time between the occurrence of the R-wave of ECG and the arrival of the pulse wave at the peripheral site that is detected by a photoplethysmographic sensor [12]. Modifications of

pulse-wave velocity method include the application of occlusive cuff. In that case the pulse-wave velocity depends on the degree of artery occlusion. When the cuff pressure is just below the systolic pressure, the pulse-wave velocity is low, and consequently the measured pulse transit time to the distal sensor is large. As the cuff pressure decreases the transit time gradually becomes shorter reaching a steady state near the cuff pressure value that is near the diastolic pressure. This modified pulse-wave velocity method provides only intermittent pressure measurement.

The vascular unloading method (also known as Penaz method, or FINAPRES method) belongs to the group of continuous measurement methods and is usually performed at a finger. The method is based on the following theory [13]. If an external pressure applied to the artery is continuously changed as to be equal to the arterial pressure, the artery will be continuously unloaded meaning that the transmural pressure (difference between intraarterial and external pressure) across the artery wall is zero. In that state the artery has maximal compliance what corresponds to the maximal arterial volume oscillations. These volume oscillations are detected by a photoplethysmographic transducer. By applying the mechanical control loop, cuff pressure is continuously adjusted to support the continuous unloading of the arterial wall. In that way the cuff pressure continually follows and is equal to the intraarterial pressure meaning that complete pressure waveform is obtained and systolic and diastolic pressure can be easily determined.

The method of arterial tonometry is based on the fact that if a superficial artery, close to an underlying bone is partially flattened or applanated with a flat rigid surface, and kept in that state, the force exerted to the surface is proportional to the arterial pressure [6, 14]. This relationship can be used to derive the arterial pressure waveform, which if calibrated yields absolute continuous arterial pressure. Tonometer is usually placed at the wrist and radial artery pressure is measured. The instrument consists of a pressure transducer (an array of piezoresistive sensors), an electropneumatic system to applanate the artery and an electromechanical positioning system. However, these devices are difficult to position, and maintaining the proper contact is a challenge [14].

3 Blood Pressure Measurement Equipment

Devices for noninvasive blood pressure measurement, usually known as NIBP monitors (NIBP stands for noninvasive blood pressure), can be classified into three groups. One of them is the group of ambulatory monitors for 24 h recording of arterial pressure during normal activities, similar to ambulatory ECG. These are designed to record the patient's blood pressure at pre-defined intervals over a 24-h period during normal activities and store the data for future analysis. These devices help physicians to diagnose blood pressure disorders and to manage and optimize antihypertension therapy. Ambulatory devices are also important to assess the prevalence of "white-coat" hypertension (elevated blood pressure when measured in the physicians' office due to emotional excitement or fear). The second group comprises of

bedside and transport monitors. The blood pressure measurement module is usually a part of multiparameter physiological monitor that enables measurement of ECG, SpO_2, respiration, body temperature, etc. These make repetitive measurements at set time intervals and often incorporate vital sign parameter alarms. They are designed for bed-side monitoring in a clinical environment and are an expensive option. The third group of blood pressure measuring devices is the largest one comprised of the so-called self-taking NIBP monitors. The characteristic of this group is that these devices are intended for routine measurement at home, office or in public places either by a subject himself or by a physician. These devices are usually very simple and are widely available for an attractive price.

According to the way the systolic and diastolic pressure are determined and the way the cuff pressure is controlled three categories of NIBP monitors can be distinguished: non-automatic devices (manual cuff inflation, observer determines characteristic pressures), semiautomatic devices (manual cuff inflation, automatic determination of characteristic pressures) and fully automatic devices (automatic cuff inflation, automatic pressure determination). Typical non-automatic device is mercury sphygmomanometer, typical semi-automatic devices are some older oscillometric blood pressure monitors with manual cuff pump, and the example of the automatic devices are the majority of oscillometric NIBP monitors available nowadays at the market. Combined auscultatory-oscillometric monitors are also available.

3.1 Devices for Use with the Manual Auscultatory Method

The auscultatory method relies on inflating an upper arm cuff to occlude the brachial artery and then listening to the Korotkoff sounds through a stethoscope whilst the cuff is slowly deflated. The patient's systolic (phase I) and diastolic blood pressure (phase V) is recorded from the reading on the sphygmomanometer. Devices for use with the manual auscultatory method, Fig. 5 [15]:

Fig. 5 Devices for use with the manual auscultatory method (from left to right: mercury sphygmomanometer; aneroid sphygmomanometers (hand-held model and wall-mounted model); electronic sphygmomanometer)

- **Mercury sphygmomanometer**

  This includes a mercury manometer, an upper arm cuff and a hand inflation bulb with a pressure control valve; requires the use of a stethoscope to listen to the Korotkoff sounds. The mercury sphygmomanometer has always been regarded as the gold standard for clinical measurement of blood pressure. In principle, the simplicity of the design means that there is negligible difference in the accuracy of different brands and that there is less to go wrong with mercury sphygmomanometers than with any other type of manometer.
- **Aneroid sphygmomanometer**

  As above, with an aneroid gauge replacing the mercury manometer. In these devices, the pressure is registered by a mechanical system of metal bellows that expands as the cuff pressure increases and a series of levers that register the pressure on a circular scale. The aneroid gauge may be wall or desk mounted or attached to the hand bulb.
- **Electronic sphygmomanometer**

  As above, with a pressure sensor and electronic display replacing the mercury manometer. Blood pressure is taken in the same way as with a mercury or aneroid device, by an observer using a stethoscope and listening for the Korotkoff sounds. The cuff pressure can be displayed as a simulated mercury column, as a digital readout, or as a simulated aneroid display. Battery powered.

3.2 Automated Devices, Generally Using the Oscillometric Method

The majority of non-invasive automated blood pressure measuring devices currently available use the oscillometric method. The oscillometric method relies on detection of variations in pressure oscillations due to arterial wall movement beneath an occluding cuff. Empirically derived algorithms are employed, which calculate systolic, mean arterial and diastolic blood pressure. Manufacturers develop their own algorithms by studying a population group and may have validated the stated accuracy by performing a clinical trial in accordance with one of the standards (AAMI/ANSI SP10, BHS, DIN, etc.). Automated devices, generally using the oscillometric method, Fig. 6, [15]:

- **Automated (spot-check) device**

  This includes an electronic monitor with a pressure sensor, a digital display and an upper arm cuff. An electrically-driven pump raises the pressure in the cuff. When started, the device automatically inflates the cuff to the appropriate level (usually about 30 mmHg above an estimated systolic reading), then deflates the cuff and displays the systolic and diastolic values. Some devices may have a user-adjustable set inflation pressure. The majority calculate these values from

Fig. 6 Automated devices for noninvasive blood pressure measurement (from top left to bottom right: automated spot check devices, wrist device, finger device, spot check NIBP monitor, cycling NIBP monitor, multiparameter patient monitor, ambulatory blood pressure monitor)

data obtained during the deflation cycle, but there are some that use data from the inflation cycle. The pulse rate may also be displayed. These devices may also have a memory which stores the last measurement and previous readings. Battery powered.

- **Wrist device**

  This includes an electronic monitor with a pressure sensor, an electrically-driven pump attached to a wrist cuff. Function is similar to the automated (spot-check) device above. Battery powered.

- **Finger device**

  This includes an electronic monitor and a finger cuff, or the device itself may be attached to the finger. Battery powered. Uses oscillometric, pulse-wave or plethysmographic methods for measurement.

- **Spot-check non-invasive blood pressure (NIBP) monitor**

  This is a more sophisticated version of the automated device above and is designed for routine clinical assessment. There may be an option to measure additional vital signs, such as oxygen saturation in the finger pulse (SpO_2) and body temperature. Mains and battery powered.

- **Automatic-cycling non-invasive blood pressure (NIBP) monitor**

  This is similar to the spot-check NIBP monitor, but with the addition of an automatic-cycling facility to record a patient's blood pressure at set time intervals. These are designed for bed-side monitoring in a clinical environment where repetitive monitoring of patients and an alarm function is required. These devices may incorporate the ability to measure additional vital signs. The alarm limits can usually be set to alert nursing staff when one or more of the measured patient parameters exceed the pre-set limits. Mains and battery powered.

- **Multi-parameter patient monitors**

  These are designed for use in critical care wards and operating theatres and monitor a range of vital signs including blood pressure. May be possible to communicate with a Central Monitoring Station via Ethernet or Wi-Fi.

- **Ambulatory blood pressure monitor**

  This includes an upper arm cuff and an electronic monitor with a pressure sensor and an electrically-driven pump that attaches to the patient's belt. The unit is programmed to record the patient's blood pressure at pre-defined intervals over a 24-h period during normal activities and stores the data for future analysis. Battery powered. Uses electronic auscultatory and oscillometric methods.

4 Sources of Error, Type of Hazards and Other Issues

Sources of error for blood pressure measuring devices could be manometer related, cuff related, patient related and observer related. For automated devices errors could be also algorithm related.

As stated previously, the mercury sphygmomanometer has always been regarded as the gold standard for clinical measurement of blood pressure, but nowadays these are being removed from clinical practice because of environmental concerns about mercury contamination. In principle, the simplicity of the design means that there is negligible difference in the accuracy of different brands and that there is less to go wrong with mercury sphygmomanometers than with any other type of manometer. Even in most recent International protocol for the validation of blood pressure measuring devices by the European Society of Hypertension (from 2010) mercury sphygmomanometers are still used as reference standards. However, one hospital survey found that 21% of devices had technical problems that would limit their accuracy [16]. In another study just under 500 mercury sphygmomanometers and their associated cuffs were examined and more than half had serious problems that would have rendered them inaccurate in measuring blood pressure [17]. In an aneroid sphygmomanometer, aneroid gauge is used replacing the mercury manometer. This type of system does not necessarily maintain its stability over time, particularly if handled roughly (shocks, drops, etc.). Aneroid sphygmomanometers therefore are inherently less accurate than mercury sphygmomanometers and require calibrating at regular intervals. Recent developments in the design of aneroid devices may make them less susceptible to mechanical damage when dropped. Wall-mounted devices are less susceptible to mechanical shocks and are generally more accurate than mobile devices [18]. Surveys conducted in hospitals have examined the accuracy of the aneroid devices and have shown significant inaccuracies ranging from 1% [18, 19] to 44% [16]. The accuracy of the manometers varies greatly from one manufacturer to another. Some studies have focused on the accuracy of the pressure registering system and have identified that small dials used in many of the devices limit their accuracy. Another survey of the accuracy of the absolute static pressure scale of aneroid, mercury and automated sphygmomanometers in clinical use in primary care revealed that 17.9% of all surveyed devices gave errors exceeding the ±3 mmHg threshold [20].

Apart from the before mentioned issues related to the accuracy of manometer or pressure registering system, it is also important to recognize that all manual techniques may suffer from observer bias including differences of auditory acuity between observers [15]. Also digit preference is common, with observers recording a disproportionate number of readings ending in five or zero. The observer may also be influenced by the knowledge that they have of the patient (i.e. earlier readings, expected effect of drug therapy, gender, age, race and weight). However, formal training in blood pressure measurement can improve this situation.

Automated methods are also not error free. Users should be aware that for patients experiencing muscle tremors, abnormal heart rhythms, weak pulse or very low blood

pressure due to shock, some automated blood pressure devices may fail to obtain a reading and will either indicate an error code or give unreliable results [15]. It is important to recognize the limitations of automated oscillometric devices in certain groups (e.g. those with cardiac arrhythmias, pre-eclampsia and some vascular diseases).

Incorrect cuff size (i.e. cuff width) is also a source of error for both manual sphygmomanometers and automated blood pressure measuring devices. An under-sized cuff tends to over-estimate blood pressure, while an over-sized cuff may under-estimate. This is especially critical when measuring blood pressure in children or obese. Incorrect cuff placement can also be a source of error. The cuff should be placed on the arm with the centre of the bladder over the brachial artery. The optimum bladder size is considered to be: width 40% of limb circumference, length 80–100% of limb circumference at the centre of the range for each cuff size [15].

5 Standards and Protocols for Evaluation of Blood Pressure Measuring Devices

From the 1990s different national and international associations and standardization organizations (ANSI/AAMI—American National Standards Institute/Association for the Advancement of Medical Instrumentation, BHS—British Hypertension Society, European Society for Hypertension, ISO—International Organization for Standardization, IEC—International Electrotechnical Commission, etc.) have set up standards and testing protocols for evaluation of blood pressure measuring devices [21–39]. Some of these standards and protocols are shown in Tables 3 and 4. Apart from those specific standards for blood pressure measuring devices general standards for medical electrical equipment safety and performance (i.e. IEC 60601-1) also apply.

Since automatic noninvasive blood pressure monitors are widely used both in clinical environments and homes, and are probably the most interesting to the readers, some details on the evaluation of these devices according to AAMI (1992), BHS (1993) and DIN (1995) protocol are listed in Table 5.

Considering the number and characteristics of subjects, there is not much difference between them. Minimum 85 subjects is required if manual auscultatory method is used as reference and minimum 15 subjects if direct intraarterial recording is performed. Also, sex and age is mainly left to chance. The AAMI (1992) gives special hints to some groups of patients (elderly, diabetic persons) while both AAMI and BHS (1993) protocol require testing of the device on a prescribed number of persons with particular blood pressure values. Different well-trained observers should perform comparative measurements. There is also much agreement between the three protocols concerning the allowable error of the systolic and diastolic pressure. The AAMI (1992) and DIN (1995) limits are identical, while BHS (1993) protocol requires different report of results.

Table 3 Some standards and protocols for evaluation of blood pressure measuring devices

Blood pressure measuring device	Standard or protocol
Noninvasive non-automated blood pressure measuring devices	ANSI/AAMI SP9 (1994), Non-automated sphygmomanometers ISO 81060-1:2007 Non-invasive sphygmomanometers—Part 1: Requirements and test methods for non-automated measurement type
Noninvasive automated blood pressure (NIBP) monitors	ANSI/AAMI SP10: (1992) for electronic or automated sphygmomanometers and its revisions IEC 80601-2-30:2009 + AMD1:2013 CSV Consolidated version Medical electrical equipment—Part 2–30: Particular requirements for the basic safety and essential performance of automated non-invasive sphygmomanometers The British Hypertension Society (BHS) protocol (1993) for the evaluation of blood pressure measuring devices and its revisions DIN 58130 (1995) Nichtinvasive Blutdruckmeßgeräte - Klinische Prüfung which has been replaced by DIN EN 1060-4:2004-12, and more recent DIN EN ISO 81060-2:2014-10
Invasive blood pressure measuring devices	IEC 60601-2-34:2011 Medical electrical equipment—Part 2–34: Particular requirements for the basic safety and essential performance of invasive blood pressure monitoring equipment ANSI/AAMI BP22:1994/(R)2011 Blood pressure transducers

AAMI Association for the Advancement of Medical Instrumentation; *ANSI* American National Standards Institute; *BHS* British Hypertension Society; *DIN* Deutsches Institit für Normung; *IEC* International Electrotechnical Commission; *ISO* International Organization for Standardization

Table 6 gives the comparison of the British Hypertension Society Protocol BHS (1993), the International Protocol of the European Society of Hypertension ESH IP (2002) and revised International protocol ESH IP (2010).

Tables 5 and 6 should not be used without knowledge of the full protocols. They are intended solely as a quick comparison between protocols.

EN 1060-1 [35] states that for both increasing and decreasing pressure, the maximum error for the measurement of the cuff pressure at any point of the scale range shall be ±3 mmHg. This applies to the 'static calibration' of the cuff pressure in manual and automated devices. This belongs to legal metrology inspection (more details in Sect. 6 Inspection).

ISO 81060-2 [26] states for systolic and diastolic blood pressures, the mean value of the differences of the determinations shall be within or equal to ±5 mmHg, with a standard deviation not greater than 8 mmHg. This applies to the results from a clinical trial protocol when evaluating the accuracy of the blood pressure algorithm in a population of subjects and is not part of regular inspection.

Table 4 Standards, validation protocols, recommendations

Standard/validation protocol	References
Sphygmomanometer Standards	European Standard EN 1060-1:1996. Specification for Non-invasive sphygmomanometers. Part I. General requirements. 1995. European Commission for Standardisation. Rue de Stassart 36, B-1050 Brussels European Standard EN 1060-2:1996. Specification for Non-invasive sphygmomanometers. Part 2. Supplementary requirements for mechanical sphygmomanometers. 1995. European Commission for Standardisation. Rue de Stassart 36, B-1050 Brussels European Standard EN 1060-3: 1997. Non-invasive sphygmomanometers. Part 3. Supplementary requirements for electro-mechanical blood pressure measuring systems. European Committee for Standardization. Rue de Stassart 36, B-1050, Brussels
International Protocol of the European Society of Hypertension	O'Brien E, Atkins N, Stergiou G, Karpettas N, Parati G, Asmar R, Imai Y, Wang J, Mengden T, Shennan A; on behalf of the Working Group on Blood Pressure Monitoring of the European Society of Hypertension. European Society of Hypertension International Protocol revision 2010 for the Validation of Blood Pressure Measuring Devices In Adults. Blood Press Monit 2010;15:23–38 O'Brien E, Pickering T, Asmar R, Myers M, Parati G, Staessen J, Mengden T, Imai Y, Waeber B, Palatini P with the statistical assistance of Atkins N and Gerin W on behalf of the Working Group on Blood Pressure Monitoring of the European Society of Hypertension. International protocol for validation of blood pressure measuring devices in adults. Blood Press Monit 2002;7:3–17
British Hypertension Society Protocol	O'Brien E, Petrie J, Littler WA, de Swiet M, Padfield PL, Altman D, Bland M, Coats A, Atkins N. The British Hypertension Society Protocol for the evaluation of blood pressure measuring devices. J Hypertens 1993;11(suppl 2):S43–S63 O'Brien E, Petrie J, Littler WA, de Swiet M, Padfield PL, Altman D, Bland M, Coats A, Atkins N. Short report. An outline of the British Hypertension Society Protocol for the evaluation of blood pressure measuring devices. J Hypertens 1993;11:677–679 O'Brien E, Petrie J, Littler W, De Swiet M, Padfield P, O'Malley K, Jamieson MJ, Altman D, Bland M, Atkins N. The Britisih Hypertension Society protocol for the evaluation of automated and semi-automated blood pressure measuring devices with special reference to ambulatory systems. J Ambulatory Monitoring 1991;4:207–228 O'Brien E, Petrie J, Littler W, de Swiet M, Padfield PL, O'Malley K, Jamieson M, Altman D, Bland M, Atkins N. The British Hypertension Society Protocol for the evaluation of automated and semi-automated blood pressure measuring devices with special reference to ambulatory systems. In Blood Pressure Measurement. Eds. E. O'Brien and K. O'Malley. Handbook of Hypertension. Eds. W.H. Birkenhager and J.L. Reid. Elsevier. Amsterdam. 1991. pp. 430–451 O'Brien E, Petrie J, Littler W, de Swiet M, Padfield PL, O'Malley K, Jamieson M, Altman D, Bland M, Atkins N. The British Hypertension Society Protocol for the evaluation of automated and semi-automated blood pressure measuring devices with special reference to ambulatory systems. J Hypertens 1990;8:607–619

(continued)

Table 4 (continued)

Standard/validation protocol	References
Association for the Advancement of Medical Instrumentation (USA)	Association for the Advancement of Medical Instrumentation. American National Standard. ANSI/AAMI/ISO 81060–2:2013 Non-invasive sphygmomanometers—Part 2: Clinical investigation of automated measurement type. 4301 N. Fairfax Drive, Suite 301, Arlington, VA 22203-1633, USA: AAMI; 2013 Association for the Advancement of Medical Instrumentation. American National Standard. Manual, electronic or automated sphygmomanometers ANSI/AAMI SP10-2002/A1. 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598, USA: AAMI; 2003 Association for the Advancement of Medical Instrumentation. American National Standard. Manual, electronic or automated sphygmomanometers ANSI/AAMI SP10-2002. 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598, USA: AAMI; 2003 Association for the Advancement of Medical Instrumentation. American National Standard. Electronic or automated sphygmomanometers ANSI/AAMI SP10-1992/A1. 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598, USA: AAMI; 1996 Association for the Advancement of Medical Instrumentation. American National Standard. Electronic or automated sphygmomanometers ANSI/AAMI SP10-1992. 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598, USA: AAMI; 1993 Association for the Advancement of Medical Instrumentation. American National Standard. Electronic or automated sphygmomanometers ANSI/AAMI SP10-1987. 3330 Washington Boulevard, Suite 400, Arlington, VA 22201-4598, USA: AAMI; 1987
Other Protocols	Normenausschuß Feinmechanik und Optik (NaFuO) im DIN Deutsches Institut für Normierung e V: Non-invasive sphygmomanometers—Clinical Investigation. Berlin: Beuth Verlag; 1996
International Organization of Legal Metrology (OIML) recommendations	OIML Recommendation R 16 Part 1 Non-invasive mechanical sphygmomanometers; 2002 OIML Recommendation R 16 Part 2 Non-invasive automated sphygmomanometers; 2002

Table 5 Comparison of ANSI/AAMI SP10, BHS and DIN 58130 protocol for the evaluation of noninvasive blood pressure monitors if manual auscultatory method is used as reference

Evaluation method	ANSI/AAMI SP10 (1992)	BHS (1993)	DIN 58130 (1995)
Reference method	Manual auscultatory	Manual auscultatory	Manual auscultatory
Subjects			
Number	≥85	85	≥85
Sex	Not applicable	Not applicable	Not applicable
Age	Elderly included	Not applicable	Not applicable
Systolic pressure	<100 mmHg, >10% of subjects >180 mmHg, >10% of subjects	<90 mmHg, 8 subjects 90–129 mmHg, 20 subjects 130–160 mmHg, 20 subjects 161–180 mmHg, 20 subjects >180 mmHg, 8 subjects	80–180 mmHg
Diastolic pressure	<60 mmHg, >10% of subjects >100 mmHg, >10% of subjects	<60 mmHg, 8 subjects 60–79 mmHg, 20 subjects 80–100 mmHg, 20 subjects 101–110 mmHg, 20 subjects >110 mmHg, 8 subjects	60–110 mmHg
Circumference of the upper arm	<25 cm, 10% of subjects >35 cm, 10% of subjects		<24 cm or >32 cm, 25% of subjects
Number of observers	2	3	2
Stethoscope with double pairs of earpieces	Yes	Yes	Optional
Comparative measurements (no. of meas. per subject)			
Simultaneous, single arm	Preferably (≥3)	Preferably (3)	(≥3)
Simultaneous, dual arm	3. Option	Less suitable	($\geq 3 + 2 \times 3$)
Sequential, single arm	2. Option	2. Option	Less suitable

(continued)

Table 5 (continued)

Evaluation method	ANSI/AAMI SP10 (1992)	BHS (1993)	DIN 58130 (1995)
Sequential, dual-arm	Less suitable	Less suitable	Less suitable
Maximal allowable error (for systolic and diastolic pressure treated separately)	The mean ($\overline{\Delta}$) and standard deviation (s_Δ) of the difference between the monitor's and reference measurements must satisfy the following limits: -5 mmHg $\leq \overline{\Delta} \leq 5$ mmHg $s_\Delta \leq 8$ mmHg	The percentage of monitor's measurements that differ from the corresponding reference measurements as follows: 50% of meas., $\leq$5 mmHg 75% of meas., $\leq$10 mmHg 90% of meas., $\leq$15 mmHg	Same as for the ANSI/AAMI SP10

It is recommended that only those devices that have passed validation tests of ANSI/AAMI, BHS or ESH should be used in practice. However, the fact that a device passed a validation test does not mean that it will provide accurate readings in all patients [4].

Rigorous methods such as those of the ANSI/AAMI, BHS and other standards are time consuming and impractical in the development stage of a new device or routine performance testing and may or may not be effective. A useful resource of results of validation studies which were published in peer-reviewed journals and other general and specialized journals is available at the website http://www.dableducational.org/ launched by the Working Group of the European Society of hypertension in 2004 [40].

Although validation protocols for BP measuring devices developed by ANSI/AAMI, BHS, ESH and other organizations are widely accepted, it is recently recognized that all stakeholders (science, patients, consumers and manufacturers) would be best served if all BP measuring devices were assessed for accuracy according to an agreed single validation protocol that had global acceptance. Therefore, an international initiative was taken by AAMI, ESH and ISO experts who agreed to develop a universal standard for device validation [41]. Table 7 summarizes the most important methodological and clinical issues affecting the validation procedure and consensus reached by AAMI/ESH/ISO representatives.

An alternative method to various protocols for clinical validation of BP measuring devices is the use of a noninvasive blood pressure simulator or the so-called "surrogate arm" (arm phantom) [42, 43]. The cuff of a monitor under test is wrapped around the surrogate arm that simulates the physiological properties and characteristics of blood flow and blood pressure in the upper arm, in a way that artificial Korotkoff vibrations and oscillometric pulses are generated in an artificial artery (surrounded by different materials that simulate bone, soft tissues and skin) in response to artery

Table 6 Comparison of the British Hypertension Society Protocol BHS (1993), the International Protocol of the European Society of Hypertension ESH IP (2002) and revised protocol ESH IP (2010)

Evaluation method	BHS (1993)	ESH IP (2002)	ESH IP (2010)
Reference method	Manual auscultatory	Manual auscultatory	Manual auscultatory
Subjects			
Number	85	33 (Phase 1: 15, Phase 2: 18)	33
Sex	Not applicable	≥5 M and ≥5 F (Phase 1) ≥10 M and ≥10 F (Phase 2)	≥10 M and ≥10 F
Age	Not applicable	≥30 years	≥25 years
Systolic pressure	<90 mmHg, 8 subjects 90–129 mmHg, 20 subjects 130–160 mmHg, 20 subjects 161–180 mmHg, 20 subjects >180 mmHg, 8 subjects	Phase 1 90–129 mmHg, 5 subjects 130–160 mmHg, 5 subjects 161–180 mmHg, 5 subjects Phase 2 90–129 mmHg, 11 subjects 130–160 mmHg, 11 subjects 161–180 mmHg, 11 subjects	90[a]–129 mmHg, 10–12 subjects 130–160 mmHg, 10–12 subjects 161–180[a] mmHg, 10–12 subjects Up to 4 recruitment pressures are permitted to be outside these limits
Diastolic pressure	<60 mmHg, 8 subjects 60–79 mmHg, 20 subjects 80–100 mmHg, 20 subjects 101–110 mmHg, 20 subjects >110 mmHg, 8 subjects	Phase 1 40–79 mmHg, 5 subjects 80–100 mmHg, 5 subjects 101–130 mmHg, 5 subjects Phase 2 40–79 mmHg, 11 subjects 80–100 mmHg, 11subjects 101–130 mmHg, 11 subjects	40[a]–79 mmHg, 10–12 subjects 80–100 mmHg, 10–12 subjects 101–130[a] mmHg, 10–12 subjects Up to 4 recruitment pressures are permitted to be outside these limits
Number of observers	3	2 + 1 supervisor	2 + 1 supervisor

(continued)

Table 6 (continued)

Evaluation method	BHS (1993)	ESH IP (2002)	ESH IP (2010)
Comparative measurements	3	3	3
Maximal allowable error (for systolic and diastolic pressure treated separately)	The percentage of monitor's measurements that differ from the corresponding reference measurements as follows: 50% of meas., ≤5 mmHg 75% of meas., ≤10 mmHg 90% of meas., ≤15 mmHg	Phase 1—45 meas. on 15 subjects (min requirements): At least one of 25 meas., ≤5 mmHg 35 meas., ≤10 mmHg 40 meas., ≤15 mmHg Phase 2.1—99 meas. on 33 subjects (min requirements): Two of 65 meas., ≤5 mmHg 80 meas., ≤10 mmHg 95 meas., ≤15 mmHg All of 60 meas., ≤5 mmHg 75 meas., ≤10 mmHg 90 meas., ≤15 mmHg Phase 2.2 At least 22 of the 33 subjects must have at least two of their three comparisons lying within 5 mmHg. At most, three of the 33 subjects can have all three of their comparisons over 5 mmHg apart	Part 1 (min requirements): Two of 73 meas., ≤5 mmHg 87 meas., ≤10 mmHg 96 meas., ≤15 mmHg All of 65 meas., ≤5 mmHg 81 meas., ≤10 mmHg 93 meas., ≤15 mmHg Part 2 At least 24 of the 33 subjects must have at least two of their three comparisons lying within 5 mmHg. At most, three of the 33 subjects can have all three of their comparisons over 5 mmHg

[a] Up to 4 recruitment pressures are permitted to be outside these limits

occlusion. That provides simpler and more controllable testing environment, but the key issue is whether the simulator is capable to precisely simulate in vivo condition [44].

6 Inspection

Blood pressure measuring equipment should be regularly checked and calibrated. Frequency of inspections and calibrations should meet legislative and regulatory requirements and manufacturer's recommendations. Maintenance recommendations vary depending on the type, frequency and location of use (i.e. hand-held devices are likely to receive more shocks and drops than the wall or desk mounted). Faulty

Table 7 A universal standard for the validation of blood pressure measuring devices: Association for the Advancement of Medical Instrumentation/European Society of Hypertension/International Organization for Standardization (AAMI/ESH/ISO)

Methodological and clinical issues	Consensus
Validation study efficacy measure	A device is considered acceptable if its estimated probability of a tolerable error ($\leq$10 mmHg) is at least 85%
Validation study sample size	At least 85 subjects are required for an AAMI/ISO/ESH validation study
Cuff-sizes stratified subgroups	There is a minimum number of subjects to be tested per cuff depending on the number of the test device cuffs. Cuff subgroups are not intended for separate analyses Requirements are set for the distribution of the participants' arm circumference according to the specified range of use of the test device
General population and special populations studies	A general population study should include only subjects older than 12 years Special populations include at least: (i) age < 3 years, (ii) pregnancy including pre-eclampsia, (iii) arm circumference > 42 cm), (iv) atrial fibrillation. Other special populations may be added as special groups Special population studies to include $\geq$ 35 subjects, provided that a general population study has been completed successfully. For special populations BP distribution criteria to differ from those of general population studies. Data to be analyzed independently of general population study data Studies in pregnancy to include 45 women of whom 15 with pre-eclampsia, 15 with gestational hypertension, 15 normotensive. Korotkoff K5 shall be used for reference diastolic BP For devices intended for adults and children, 35 subjects aged 3–12 years can be included and analyzed together with 50 subjects aged >12 years. Mean BP difference and SD shall also be reported separately for age 3–12 and >12 years groups. Korotkoff K5 shall be used for reference diastolic BP
Method for BP data collection	The same arm sequential BP measurement is the preferred method for validation The same arm simultaneous method has been eliminated
Reference BP measurement and validation procedure	Reference BP measurement to be performed with mercury sphygmomanometers or accurate non-mercury devices. The accuracy of non-mercury devices shall be evaluated at the beginning of each study Detailed description of cuffs used for reference BP measurement shall be provided The test device cuffs shall not be used for reference BP determination

(continued)

Table 7 (continued)

Methodological and clinical issues	Consensus
Validation criteria and reporting	The mean BP difference (test versus reference) and its SD, Criteria 1 and 2 of the ANSI/AAMI/ISO 81060-2, to be applied for systolic and diastolic BP The number of absolute BP differences within 5, 10 and 15 mmHg and standardized Bland-Altman scatterplots will be presented
Validation of other BP monitors	Separate validation protocols will be developed for continuous, cuffless and central BP monitors
Quality and reliability of validation study reports	Tools need to be developed to prevent protocol violations and incomplete reporting and to secure appropriate and transparent patient and data selection Detailed forms should be developed to fill in all the data from validation studies that need to be reported

cuffs, hoses, aneroid gauges and mercury manometers can all lead to erroneous blood pressure measurements, with significant effects on patient care [15, 20].

Here we briefly present International Recommendations from the International Organization of Legal Metrology: OIML Recommendation R 148 Non-invasive non-automated sphygmomanometers [38] and OIML Recommendation R 149 Non-invasive automated sphygmomanometers [39] which have been issued in 2020 as separate publications. OIML R 148 and OIML R 149 each have three parts: Part 1: Metrological and technical requirements (OIML R 148-1, OIML R 149-1), Part 2: Test procedures (OIML R 148-2, OIML R 149-2) and Part 3: Test report format (OIML R 148-3, OIML R-149-3). OIML International Recommendations are model regulations that establish the metrological characteristics required of certain measuring instruments and which specify methods and equipment for checking their conformity. The OIML Member States shall implement these Recommendations to the greatest possible extent.

6.1 Non-invasive Mechanical Sphygmomanometers

OIML R 148-1, edition 2020 (E)—was developed by OIML Technical Subcommittee TC 18/SC 1 Blood pressure instruments. It was approved for final publication by the International Committee of Legal Metrology in 2020 and supersedes OIML R 16-1:2002 (E).

OIML R 148-1 specifies general, performance, efficiency and mechanical safety requirements, including test methods for type approval, for non-invasive non-automated sphygmomanometers and their accessories which, by means of an inflatable cuff, are used for the non-invasive measurement of arterial blood pressure.

Included within the scope of this Recommendation are non-invasive non-automated sphygmomanometers with a mechanical or integrated electro-mechanical pressure sensing element and display, used in conjunction with a stethoscope or other manual methods for detecting Korotkoff sounds and for cuff inflation. The basic components of a sphygmomanometer are a manometer for measuring and displaying pressure in the bladder and a pneumatic system for applying and releasing pressure in the bladder. The pneumatic system includes a cuff that can be wrapped around a patient's limb, tubing, connectors, a valve for deflation (often in combination with rapid exhaust valve), transducers and a hand pump or electromechanical pump. For pressure control, electro-mechanical components may be used. Sphygmomanometers typically use either a mercury or an aneroid manometer or another mechanical measuring device for the non-invasive measurement of the arterial blood pressure by means of an inflatable cuff.

Units of Measurement

The units used to indicate blood pressure shall be either the kilopascal (kPa) or the millimetre of mercury (mmHg).

Metrological Requirements

Maximum Permissible Errors of the Cuff Pressure Indication

For any set of conditions within an ambient temperature range from 15 to 25 °C and a relative humidity range from 15 to 85% for decreasing pressure, the maximum permissible error for the measurement of the cuff pressure at any point of the scale range shall be ±0.4 kPa (±3 mmHg) for sphygmomanometers.

OIML R 148-1 also specifies requirements under storage conditions and under varying temperature conditions.

Technical Requirements

Technical Requirements for the Cuff and Bladder

The cuff shall contain a bladder. For reusable cuffs the manufacturer shall indicate the method for cleaning in the accompanying documents.

The bladder length should be approximately 0.80× the circumference of the limb at the midpoint of the intended range of the cuff. The width of the bladder should be at least 0.40× the circumference of the limb at the midpoint of the intended range of the cuff.

Technical Requirements for the Pneumatic System

Air Leakage

Air leakage shall not exceed a pressure drop of 0.5 kPa/min (4 mmHg/min).

Pressure Reduction Rate

The deflation valves in the pneumatic system shall be capable of adjustment to a deflation rate from 0.3 to 0.4 kPa/s (2 to 3 mmHg/s). The deflation valves in the pneumatic system shall be easily adjusted to these values.

Rapid Exhaust

During the rapid exhaust of the pneumatic system, with the valve fully opened, the time for the pressure reduction from 34.7 to 2.0 kPa (260 to 15 mmHg) shall not exceed 10 s.

Technical Requirements for the Pressure Indicating Devices

Nominal Range and Measuring Range

The nominal range shall be equal to the measurement range. The nominal range for the cuff pressure indication shall extend from 0 kPa to at least 34.7 kPa (0 mmHg to at least 260 mmHg). The nominal range for the cuff pressure measurement shall be disclosed in the accompanying document. The measuring and indication ranges of the cuff pressure shall be equal to the nominal range.

Analogue Indication

The scale shall be designed and arranged so that the measuring values can be read clearly and are easily recognized. The graduation shall begin with the first scale mark at 0 kPa (0 mmHg). The scale interval shall be: 0.5 kPa for a scale graduated in kPa; or 2 mmHg for a scale graduated in mmHg. In the case of a scale graduated in kPa, each fourth scale mark shall be indicated by a greater length and each eighth scale mark shall be numbered. In the case of a scale graduated in mmHg, each fifth scale mark shall be indicated by a greater length and each tenth scale mark shall be numbered. For sphygmomanometers with a manometer with elastic or electro-mechanical sensing elements, no graduation is needed within the range from >0 kPa to <2 kPa (>0 mmHg to <15 mmHg) The distance between adjacent scale marks shall be not less than 1.0 mm. The thickness of the scale marks shall not exceed 20% of the smallest scale spacing. All scale marks shall be of equal thickness.

Digital Indication

The digital scale interval shall be 0.1 kPa (1 mmHg). If the measured value of a parameter is to be indicated on more than one display, all the displays shall indicate the same numerical value. Measured numerical values on the display(s), and the symbols defining the units of measurement shall be arranged in such a way so as to avoid misinterpretation. Numbers and characters shall be clearly legible.

Additional Technical Requirements for Mercury Manometers

Portable Devices

A portable device shall be provided with an adjusting or locking mechanism to secure it in the specified position of use.

Devices to Prevent Mercury from Being Spilled During Use and Transport

A device shall be placed in the tube to prevent mercury from being spilled during use and transport (for example: stopping device, locking device, etc.). This device shall be such that when the pressure in the system drops rapidly from 26.6 kPa to 0 kPa (from 200 to 0 mmHg), the time taken for the mercury column to fall from 26.6 kPa to 5.3 kPa (from 200 to 40 mmHg) shall not exceed 1.5 s. This time is known as the "exhaust time".

Quality of the Mercury

The mercury shall have a purity of not less than 99.99% according to the declaration of the supplier of the mercury. The mercury shall exhibit a clean meniscus and shall not contain air bubbles.

Graduation of the Mercury Tube

Graduations shall be permanently marked on the tube containing mercury. If numbered at each fifth scale mark, the numbering shall be alternately on the right- and left-hand side of, and adjacent to, the tube.

Additional Technical Requirements for Aneroid Manometers

Scale Mark at Zero

If a tolerance zone is shown at zero it shall not exceed ±0.4 kPa (±3 mmHg) and shall be clearly marked. A scale mark at zero shall be indicated. Note: Graduations within the tolerance zone are optional.

Zero

The movement of the elastic sensing element including the pointer shall not be obstructed within 0.8 kPa (6 mmHg) below zero. Neither the dial nor the pointer shall be adjustable by the user.

Pointer

The pointer shall cover between 1/3 and 2/3 of the length of the shortest scale mark of the scale. At the place of indication, it shall be not thicker than the scale mark. The distance between the pointer and the dial shall not exceed 2 mm.

Hysteresis Error

The hysteresis error throughout the pressure range shall be within the range 0–0.5 kPa (0–4 mmHg).

Durability of the Manometer

The construction of the manometer and the material for the elastic sensing elements shall ensure an adequate stability of the measurement. When elastic sensing elements are used, they shall be aged with respect to pressure and temperature. After 10,000 alternating pressure cycles from 3 kPa (20 mmHg) to full scale, the change in the pressure indication shall be not more than 0.4 kPa (3 mmHg).

Safety Requirements

Mechanical Safety

Resistance to vibration and shock for handheld sphygmomanometers:

Sphygmomanometers or their parts shall have adequate mechanical strength when subjected to mechanical stress caused by normal use, pushing, impact, dropping and rough handling. Wall mounted sphygmomanometers and mercury manometers are exempt from the requirements of this subclause. Sphygmomanometers shall function normally following a free fall from a distance $d = 25$ cm. A sphygmomanometer that is marked "Shock Resistant" shall function normally following a free fall from a distance $d = 1$ m.

Resistance to vibration and shock for sphygmomanometers used during patient transport: Sphygmomanometers or their parts, intended for use during patient transport outside a healthcare facility, shall have adequate mechanical strength when subjected to mechanical stress caused by normal use, pushing, impact, dropping, and rough handling.

Sphygmomanometers containing a mercury manometer:

A sphygmomanometer containing a mercury manometer shall not leak mercury following a free fall from a distance, $d = 1$ m.

Aborting a Measurement

It shall be possible to abort the blood pressure measurement at any time by activating the manual rapid exhaust valve, which shall be easily accessible.

Unauthorised Access and Tamper Proofing

Means shall be provided to prevent tampering or unauthorised access: for all sphygmomanometers, any adjustment or function that affects accuracy; for mercury sphygmomanometers, the separation of reservoir and scale. Example: Requiring a tool for opening or breaking a seal. It shall be clear to an operator if tampering or unauthorised access has occurred.

Electrical Safety

Regional or national regulations may specify electrical safety requirements.

Tubing Connectors

Luer lock and Luer slip connectors shall not be used on non-automated sphygmomanometers so as to avoid any risk of connecting the output of the sphygmomanometer to intervascular fluid systems as air might inadvertently be pumped into a blood vessel.

Durability of Markings

The markings shall be removable only with a tool or by appreciable force and shall be sufficiently durable to remain clearly legible during the expected service life of the sphygmomanometer. In considering the durability of the markings, the effect of normal use shall be taken into account.

Metrological Controls

Requirements related to type approval, verification (initial and subsequent), sealing, marking the device and manufacturer's information are also prescribed.

For each requirement specified in OIML R 148-1, test procedures are also described (see OIML R 148-2 Part 2: Test procedures). Moreover, test report format is also given (see OIML R 148-3 Part 3: Test report format).

6.2 Non-invasive Automated Sphygmomanometers

OIML R 149-1, edition 2020 (E)—was developed by the OIML Technical Subcommittee TC 18/SC 1 Blood pressure instruments. It was approved for final publication by the International Committee of Legal Metrology in 2020 and supersedes OIML R 16-2:2002 (E).

OIML R 149-1 specifies general, performance, efficiency and mechanical safety requirements for non-invasive automated sphygmomanometers and their accessories which, by means of an inflatable cuff, are used for the non-invasive measurement of arterial blood pressure. This Recommendation only applies to devices measuring at the upper arm, the wrist or the thigh.

The basic components of a sphygmomanometer are a cuff that can be wrapped around a patient's limb, a system for applying and releasing pressure to the bladder in the cuff, and a means of measuring and displaying blood pressure values automatically. *Note 1:* Specific device types included in this category are: sphygmomanometers for self measurement, blood pressure monitors and multi-parameter patient monitors used for home healthcare, or public use. *Note 2:* Components of a sphygmomanometer include: manometer, cuff, valve for deflation (often in combination with the valve for rapidly exhausting the pneumatic system), pump for inflation of the bladder, and connection tubing.

Units of Measurement

The blood pressure shall be indicated either in kilopascals (kPa) or in millimeters of mercury (mmHg).

Metrological Requirements

Maximum Permissible Errors of the Cuff Pressure Indication Under Ambient Conditions

For any set of conditions within the ambient temperature range from 10 to 40 °C and the relative humidity range from 15 to 85%, both for increasing and for decreasing pressure, the maximum permissible error for the measurement of the cuff pressure at any point of the measurement range shall be ±0.4 kPa (±3 mmHg) or ±2% of the reading, whichever is greater.

Maximum Permissible Errors of the Overall System as Measured by Clinical Tests (this is carried out by the manufacturer).

The following maximum permissible errors shall apply for the sphygmomanometer:

Maximum mean error of measurement: ±0.7 kPa (±5 mmHg); maximum experimental standard deviation: 1.1 kPa (8 mmHg).

Recommended protocols for the clinical investigations are BHS [30] and ANSI/AAMI/ISO 81060-2 [26] (see section 5 Standards and protocols for evaluation of blood pressure measuring devices).

Maximum Permissible Errors of the Cuff Pressure Indication Under Storage Conditions

The sphygmomanometer shall maintain the requirements specified in this Recommendation after storage for 24 h at a low temperature of −5 °C, followed by additional storage for 24 h at a high temperature of 50 °C and at a relative humidity of 85% (non-condensing).

Blood Pressure Measurement Range

The sphygmomanometer shall be capable of indicating diastolic blood pressure over at least the range from 2.7 kPa (20 mmHg) to 8.0 kPa (60 mmHg) in neonatal mode, and 5.3 kPa (40 mmHg) to 17.3 kPa (130 mmHg) otherwise.

The sphygmomanometer shall be capable of indicating systolic blood pressure over at least the range from 5.3 kPa (40 mmHg) to 14.7 kPa (110 mmHg) in neonatal mode, and 8.0 kPa (60 mmHg) to 30.7 kPa (230 mmHg) otherwise.

Repeatability of Blood Pressure Indication

For any set of conditions within the ambient temperature range from 10 to 40 °C and the relative humidity in the range from 15 to 85%, the experimental standard deviation of the blood pressure indication of the sphygmomanometer shall not exceed 0.4 kPa (3 mmHg).

Technical Requirements

General

Equipment, or parts thereof, using materials or having forms of construction different from those detailed in this Recommendation shall be accepted if it can be demonstrated that an equivalent degree of safety and performance is obtained.

Technical Requirements for the Cuff and Bladder

The cuff shall contain or incorporate a bladder. The cuff shall be designed and marked (i.e. using permitted circumference indicators) to ensure and restrict the use of the appropriate cuff size corresponding to a given limb circumference.

The bladder length should be approximately 0.80× the circumference of the limb at the midpoint of the intended range of the cuff. The width of the bladder should be at least 0.40× the circumference of the limb at the midpoint of the intended range of the cuff.

For reusable cuffs the manufacturer shall indicate the method for cleaning in the accompanying documents.

Effect of Voltage Variations of the Power Source

Internal Electrical Power Source

Changes in the voltage within the working range specified by the manufacturer shall not influence the cuff pressure indication. Outside this working range no cuff pressure indication and no result of the blood pressure measurement shall be displayed.

External Electrical Power Source

Changes in the voltage within the working range specified by the manufacturer shall not influence the cuff pressure indication. Outside the working range specified by the manufacturer, no cuff pressure indication and no result of the blood pressure measurement shall be displayed.

Pneumatic System

Air Leakage

Air leakage shall not exceed a pressure drop of 0.8 kPa/min (6 mmHg/min).

Pressure Reducing System for Devices Using the Auscultatory Method

The pressure reducing system for manually operated and automated deflation valves shall be capable of maintaining a deflation rate of 0.3–0.4 kPa/s (2–3 mmHg/s) within the target range of systolic and diastolic blood pressure. For devices which control the pressure reduction as a function of the pulse rate, a deflation rate of 0.3–0.4 kPa/pulse (2–3 mmHg/pulse) shall be maintained.

Rapid Exhaust

During the rapid exhaust of the pneumatic system, with the valve fully opened, the time for the pressure reduction from 34.7 to 2.0 kPa (260 to 15 mmHg) shall not exceed 10 s. For the sphygmomanometer having the capability to measure in a neonatal/infant mode, the time for the pressure reduction from 20.0 to 0.7 kPa (150 to 5 mmHg) during the rapid exhaust of the pneumatic system with the valve fully opened shall not exceed 5 s.

Zero Adjustment of a Measuring System

The sphygmomanometer shall be capable of automatic zero adjustment. The zero adjustment shall be carried out at appropriate intervals, at least when the device is powered on. After a zero adjustment, the device shall keep the indication of a gauge pressure of 0.0 kPa (0 mmHg). The sphygmomanometer shall repeat a zero adjustment or shall be switched off automatically when the output of the pressure transducer drifts one scale interval (0.1 kPa or 1 mmHg) or more.

Manometer Test Mode

The sphygmomanometer shall have a manometer test mode that permits static pressure measurement over at least the nominal blood pressure indication range. This mode shall not be available in normal use, but restricted to service/test personnel. When the sphygmomanometer is put into the test mode, all air outlets shall be closed. The manufacturer shall confirm that the test results are identical to the results in the normal use mode.

Maximum Time for Which the Cuff Is Inflated

The total time for which the pressure exceeds 2.0 kPa (15 mmHg) shall be no longer than 180 s in the case of adult patients. The total time for which the pressure exceeds 0.7 kPa (5 mmHg) shall be no longer than 90 s in the case of neonatal/infant patients.

Electromagnetic Compatibility

Immunity

The following requirements apply: electrical and/or electromagnetic interferences shall not lead to degradations in the cuff pressure indication, i.e. the maximum permissible error for the measurement of the cuff pressure shall be ±0.4 kPa (±3 mmHg) or ±2% of the reading, whichever is greater; or if electrical and/or electromagnetic interferences lead to an abnormality, the abnormality shall be clearly indicated and it shall be possible to restore normal operation within 30 s after cessation of the electromagnetic disturbance.

Testing shall be carried out in accordance with 202 of IEC 80601-2-30:2018 Medical electrical equipment—Part 2-30: Particular requirements for the basic safety and essential performance of automated non-invasive sphygmomanometers.

Electrosurgery Interference Recovery

If a sphygmomanometer is intended to be used together with HF surgical equipment, it shall return to the previous operating mode within 10 s after exposure to the field produced by the HF surgical equipment, without loss of any stored data.

Testing shall be carried out in accordance with 202.8.101 of IEC 80601-2-30:2018 Medical electrical equipment—Part 2-30: Particular requirements for the basic safety and essential performance of automated non-invasive sphygmomanometers.

Durability

The change in the cuff pressure indication shall not be greater than 0.4 kPa (3 mmHg) throughout the pressure range after 10,000 simulated measurement cycles.

Technical Requirement for the Pressure Indicating Device

Nominal Range and Measurement Range of the Cuff Pressure Measurement

The nominal range for the cuff pressure measurement shall be specified by the manufacturer. The measurement range of the cuff pressure shall be equal to the nominal range. Values of blood pressure measurement results outside the nominal range of cuff pressure shall be clearly indicated as out of range.

Digital Indication

The digital scale interval shall be 0.1 kPa (1 mmHg). If the measured value of a parameter is to be indicated on more than one display, all the displays shall indicate the same numerical value. Measured numerical values on the display(s), and the symbols defining the units of measurement shall be arranged in such a way so as to avoid misinterpretation. Numbers and characters should be clearly legible.

Technical Requirements for the Display

The display shall be designed and arranged so that all information can be read and easily recognized. If abbreviations are used on the display they shall be as follows: S or SYS: systolic blood pressure (value); D or DIA: diastolic blood pressure (value); M or MAP: mean arterial blood pressure (value). Single letter abbreviations shall be positioned in such a way to avoid confusion with SI units.

Signal Input and Output Ports

The construction of the signal input and output ports (excluding internal interfaces, e.g. microphone signal input) relevant to the non-invasive blood pressure measurement shall ensure that incorrectly fitted or defective accessories shall not result in erroneous indication of cuff pressure or erroneous indication of blood pressure. An error message or a blank display is sufficient.

Safety Requirements

Aborting a Measurement

It shall be possible to abort any blood pressure measurement at any time by single key operation and this shall lead to a rapid exhaust.

Unauthorized Access and Tamper Proofing

All controls which affect accuracy shall be sealed against unauthorized access. Tamper proofing of the instrument shall be achieved by requiring the use of a special tool or breaking a seal. It shall be clear to an operator if tampering or unauthorised access has occurred.

Tubing Connectors

Luer lock and Luer slip connectors shall not be used on sphygmomanometers so as to avoid any risk of connecting the output of the sphygmomanometer to intravascular fluid systems as air might inadvertently be pumped into a blood vessel.

Electrical Safety

Regional or national regulations may specify electrical safety requirements.

Resistance to Vibration and Shock

The sphygmomanometer or its parts not intended for use during patient transport outside a healthcare facility shall have adequate mechanical strength when subjected to mechanical stress caused by normal use, pushing, impact, dropping, and rough handling. A fixed (e.g. wall mounted) sphygmomanometer is exempt from the requirements of this subclause.

After the test for the resistance to vibration and shock, the sphygmomanometer shall comply with the requirements for maximum permissible errors of the cuff pressure indication but only at a temperature of 20 °C ± 5 °C and at ambient humidity.

Durability of Markings

The markings shall be removable only with a tool or by appreciable force and shall be sufficiently durable to remain clearly legible during the expected service life of the sphygmomanometer. In considering the durability of the markings, the effect of normal use shall be taken into account.

Metrological Controls

Requirements related to type approval, verification (initial and subsequent), sealing, marking the device and manufacturer's information are also prescribed.

For each requirement specified in OIML R 149-1, test procedures are also described (see OIML R 149-2 Part 2: Test procedures). Moreover, test report format is also given (see OIML R 149-3 Part 3: Test report format).

In order to speed up the testing procedure in everyday practice blood-pressure simulators are available (e.g. BP Pump 2 NIBP Blood Pressure Simulator by Fluke), as well as Electrical Safety Analyzers to test for IEC60601-1 compliance.

7 Summary

To be suitable for clinical use blood pressure measuring devices must comply with numerous requirements that depend on state legislative. To ensure reliable and accurate blood pressure measurement it is equally important that in hospitals and other medical facilities quality assurance (QA) measures have been implemented. It is also necessary to perform routine inspection and calibration of blood pressure manometers, and all automated blood pressure measuring devices used in hospitals and primary care facilities. How often, by whom, and at what cost remain to be decided by responsible authorities. Training of those who use blood pressure measuring devices must be done and kept up to date.

Devices for home use are rarely thoroughly tested. Especially automatic oscillometric blood pressure monitors that are widely available could in some patients show unreliable and highly inaccurate results. It is therefore important to inform patients of the limitation of these devices. These limitations are also present in oscillometric monitors used in clinics, but physicians and nurses could cope with them if properly trained.

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Inspection and Testing of Diagnostic Ultrasound Devices

Gordana Žauhar, Ana Božanić, and Slaven Jurković

Abstract This chapter provides an overview of the safety aspects of application of ultrasound in medicine. It begins with the short history of ultrasound methods and devices as well as basic principles of ultrasound imaging systems. The application of ultrasound in medicine has highly evolved and nowadays it can be divided into two main areas: imaging and therapy. To assure quality, safe use and responsible application of ultrasound in medicine one should be aware of physical processes which can be produced in tissue by ultrasound such as temperature rise, cavitation, and acoustic streaming. The importance of understanding how these processes can affect the human cell is self-explanatory. To better understand the guidelines for testing and quality control of ultrasonic devices it is necessary to provide an overview of basic output parameters. Only the most important parameters from the point of safe use of ultrasound are described, e.g., acoustic pressure, acoustic power and intensity. To protect the public against inappropriate exposure when ultrasound is used for medical applications, international standards and national regulations are developed. Diagnostic ultrasound imaging is very often the basis for diagnostic decision; therefore, it is also necessary to include such systems into a comprehensive quality assurance programme. Ultrasound systems used for therapy have larger intensities though there are additional safety requirements compared to diagnostic systems. The ultrasound intensity, effective radiation area and beam non-uniformity ratio and are parameters which should be monitored.

1 History of Ultrasound Methods and Devices

The history of ultrasound and ultrasonic waves can be traced back to 1790. At that time, the Italian biologist Lazzaro Spallanzani perceived and described the ability of bats to navigate accurately in the dark by echo-reflection of high-frequency sound.

In 1826, Swiss physicist and engineer Jean-Daniel Colladon used a church bell underwater to prove that sound travels faster through water than through air. By this

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experiment the value of speed of sound in water was almost accurately determined which opened up great possibilities in the field of ultrasound.

A real revolution in this field took place a little later in 1881, when Pierre and Jacques Curie found that electricity was generated in quartz crystal under mechanical stress. This phenomenon was described as the piezoelectric effect and led to the development of ultrasonic probes as they are known today. So, we can say that serious investigation of ultrasound was happening at the end of the nineteenth century, at the same time as the discovery of x-rays, radio waves and radioactivity. This happened approximately half a century before ultrasound started to emerge in medicine as a potential therapeutic agent, followed shortly by its development for diagnosis and imaging [1].

Two events triggered the application of ultrasound to detect objects. These are: the sinking of the Titanic in 1912 and the beginning of World War I. During World War I, French physicist Paul Langevin began work on using ultrasound to detect submarines and icebergs through echolocation. Paul Langevin was a doctoral student of Pierre Curie and is famous for his two U.S. patents with Constantin Chilowsky in 1916 and 1917, which involved ultrasonic detection of submarines [2]. However, World War I was over by the time their invention came into use.

The medical use of ultrasound started for therapy purposes. The destructive power of high-intensity ultrasound was recognized by Langevin as early as 1920. High-intensity ultrasound soon became a tool in neurosurgery. Also, ultrasound effects were widely used in physical and rehabilitation medicine.

Karl Dussik, Austrian neurologist and psychiatrist, was the first one who used ultrasound waves to diagnose brain tumours in the late 1930s. He called the procedure "hyperphonography".

In 1947, George Ludwig and his associates were the first to record and describe the difference in speed of sound waves passing through various tissues and organs in animals. This was a huge progress in the field of medical ultrasound diagnostics.

The Scottish scientist Ian Donald invented and improved a various device that were used in pregnancy diagnostics and pathology. During the World War II he developed the technology of radars and sonars. In the 1950s, he became famous when he met a patient with an inoperable abdominal tumour. Using new technology, he discovered that the tumour was actually an ovarian cyst, and the patient underwent successful surgery. Shortly after that, he became the "father" of gynecological ultrasound techniques. He also invented the B-mode ultrasound.

In the 1950s and 1960s, Douglass Howry and Joseph Holmes further developed the technology of 2D B-mode ultrasound. Until then, the patient had to be placed in a water bath for the examination. The invention of the ultrasound probe in full contact with the patient opened the way for the development of modern ultrasound systems. John Wild and John Reid modified the standard ultrasound systems and developed a hand-held B-mode device to allow different angles of view, which was extremely important for breast imaging.

Although the use of ultrasound in diagnostics began in the mid-1950s, it expanded rapidly in the early 1970s with the introduction of two-dimensional, real-time ultrasound scanners. An additional step forward was the appearance of phased array systems in the early 1980s.

In the 1970s, technology based on the Doppler effect was used to be constructed a device for visualizing blood circulation. A new milestone was the introduction of colour flow imaging systems in the mid-1980s. The first 3D image was acquired by Kazunori Baba in Japan in the 1980s, while 3D devices began to appear in the 1990s. Further improvements led to the introduction of 4D (real-time) capabilities.

Ultrasound elastography is a relatively new technique that evaluates tissue elasticity in real time during ultrasound imaging. It has been used clinically for the last twenty years and has added a new dimension to ultrasound. It is considered the most important advance in ultrasound technology since the introduction of Doppler imaging [3]. Currently, two main types of elastography are used: strain elastography, in which tissue displacement in response to gentle pressure is used to calculate and image tissue strain, and shear wave elastography, in which the speed of shear waves traversing the tissue is measured and used to create an image of tissue stiffness [4]. Both methods will continue to improve and provide increasingly powerful new diagnostic tools.

Also, the use of contrast agents and harmonic imaging should be mentioned as innovative techniques that have been applied recently in ultrasound imaging.

Finally, the growing role of ultrasound is addressed by its current and future directions: innovative diagnostic applications and the growing ultrasound role in interventional therapies.

With the development of electronics and computers, the devices are constantly evolving and become more convenient. Today's ultrasound machines are completely different from the historical ones, but the goal has remained the same—better quality of imaging or therapy [5]. The domain of medical device management is being impacted by the ongoing digital revolution across the world, necessitating the collection of data and its utilization for making informed, evidence-based decision making [6–10].

2 Basic Principles of Ultrasound Imaging Systems

Ultrasound imaging instruments have evolved over the last 50 years from relatively simple hand moved scanners to rather sophisticated imaging systems. In this chapter basic components and principles of a generalized ultrasound imaging system will be presented.

The earlier edition of the book "Inspection of Medical Devices" offered insightful viewpoints on how medical device development has affected healthcare delivery, underlining the relevance of successfully managing health and resolving any issues that may occur in the process [11].

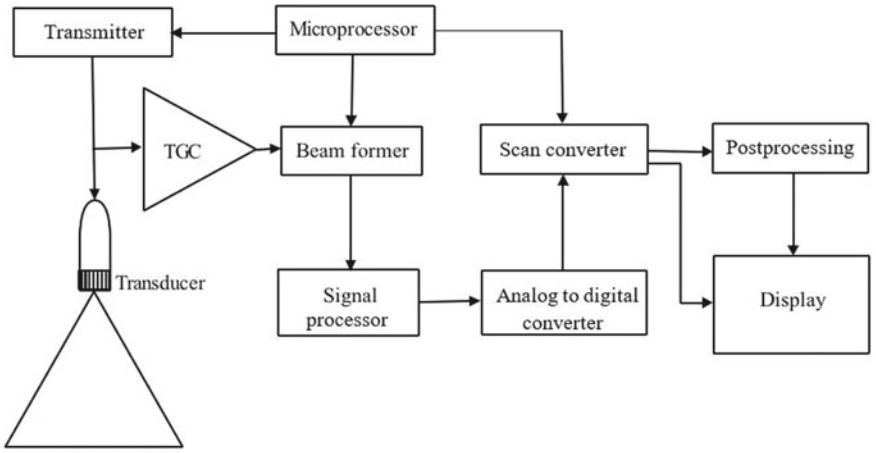

Fig. 1 Block diagram of a typical ultrasound imaging system

A block diagram of a typical ultrasound imaging system is shown in Fig. 1. A primary component of an ultrasound imaging systems is a transducer. Ultrasound transducers employ piezoelectric crystals for the generation of ultrasound. Piezoelectric crystals change size and shape when a voltage is applied and vice versa. AC voltage makes them oscillate at the same frequency and produce ultrasonic sound. The ideal piezoelectric material for medical ultrasound transducers should be both an efficient producer and sensitive receiver of ultrasonic waves. The piezoelectric materials that are commonly used in medical ultrasonic transducers are piezo ceramics such as lead zirconate titanate (PZT) or polymer materials such as polyvinylidene fluoride (PVDF).

A transducer, which converts electrical signals to mechanical forces, generates pulses of ultrasound which are sent through a body. Organ boundaries and different types of tissues produce echoes that return back and are detected by the same transducer, which converts the acoustic signal to an electrical signal. Most medical ultrasound imaging systems uses the same transducer for both generation and reception of ultrasound. The ultrasound imaging system then processes the echoes and presents them usually on a grey scale image on a display. The time of return of these pulses gives information about the location of a reflector. Each point in the image corresponds to the location, and its brightness corresponds to the echo strength (hence the name for the basic ultrasonic imaging mode, B-mode, with B for brightness).

In order to obtain a two-dimensional image, the transmitted beam must be steered (scanned or swept). The transducer can be fabricated in several ways to perform B-mode imaging. In its simplest form, the B-mode transducer is a circular single-element transducer with a fixed geometric focus. Nowadays, this type of a transducer has been mostly replaced by more sophisticated multi-element transducers. Early ultrasound systems used single-element transducers that were manually scanned within a body. Modern systems use either mechanical or electrical means to scan the

beam. With respect to steering methods, the great majority of instruments available today are electronically steered.

The block diagram in Fig. 1 shows the signal processing steps required for B-mode image formation. The actual implementations vary considerably among manufacturers and the types of systems.

The beam former is part of the ultrasound imaging system where the action starts. It consists of pulser, pulse delays, transmit/receive switch, amplifiers, and a summer [12]. The pulser generates voltages that drive the transducer. The frequency of the voltage pulse determines the frequency of the resulting ultrasound which ranges from 2 to 15 MHz for most applications. In order to avoid echo misplacement, all echoes from one pulse must be received before the next pulse is emitted. For deeper imaging, echoes take more time to return, therefore the pulse repetition frequency (PRF) must be reduced. The pulser adjusts the PRF appropriately for the current imaging depth. Beam formation can be considered to be composed of two separate processes: beam steering and focusing [13]. The implementation of these two functions may or may not be separated, depending on the system design. The sequencing, phase delays, and variation in pulse amplitude that are necessary for electronic control of beam steering and focusing must be accomplished. The pulser and pulse delays carry out all these tasks. The transmit/receive (T/R) switches are used to direct the high voltages from the pulser and pulse delays to the transducer during transmission and then direct the returning echo voltages from the transducer to the amplifiers during reception stage.

The time gain compensation (TGC) equalises differences in received echo amplitudes caused by different reflector depths. TGC compensates for the effect of attenuation caused by the propagation of sound in tissue. The dynamic range available from typical TGC amplifiers is of the order of 60 dB.

After amplification the echo voltages pass through analog-to-digital converters (ADC). An ADC converts voltage from analog to digital form.

The signal processor performs filtering, demodulation and compression of echo data. Demodulation is the conversion of echo voltages from radio frequency form to video form. There is a large range of received echo amplitudes from the lowest level that can be detected to the maximum signal level. To display all echoes, it is necessary to reduce the large range of received echoes. Compression is the process of decreasing the difference between the smallest and largest echo amplitude to a usable range.

The main function of the scan converter is to properly locate echo data into image or into video pixel space. The image processor converts echo data from digital to analog form and transfer them to the display. The information delivered to the display can be presented in several ways. The most commonly used is brightness mode (B-mode), but in addition motion mode (M-mode) is sometimes used in echo cardiology, and occasionally amplitude mode (A-mode) in ophthalmology. The development of computers made it possible to obtain three-dimensional ultrasound imaging (3D). Ultrasound 3D imaging is accomplished by acquiring many parallel two-dimensional (2D) images and then post processing this 3D volume of echo information and presenting it in an appropriate way on 2D display. Further development of ultrasound technology led to the so called “4D imaging” which is actually a real-time 3D

imaging. 4D ultrasound imaging allows users to study the motion of various moving organs of the body. It is called 4D because time is considered as the fourth dimension.

3 Safety and Quality Assurance for Ultrasound Medical Devices

Ultrasound medical devices have an important role in diagnostics and treatment of patients. Ultrasound is a non-invasive, real-time, tomographic soft-tissue imaging modality, with a wide range of clinical applications, both as primary modality or as modality complement to other diagnostic procedures. Advancements in the field of diagnostic ultrasound have led to increased use of this modality in many clinical applications.

Ultrasound is often considered the preferred imaging modality because of its ability to provide continuous, real-time images without the risk of ionizing radiation and at significantly lower costs than computed tomography or magnetic resonance imaging. As with any modality, an increase in use is accompanied by an increased requirement for performance testing to ensure the accuracy and repeatability of the results. Since the image is the basis for diagnostic decisions, the image quality produced by a scanner provides the most important information when examine scanner performance.

Testing and manufacturing guidelines for medical ultrasound devices are laid out in the medical devices directive MDD 93/42, as well as the recommendations for electrical medical equipment in IEC 60601-2-5 [14], IEC 60601-2-37 [15], and IEC 60601-2-62 [16]. Most of the guidelines that are being followed are those related to the manufacturing and sales (as well as obtaining the CE mark), while the precision and accuracy of medical ultrasound devices in the subsequent period of use are neither sufficiently monitored nor obligatory.

3.1 The Acoustic Output Parameters of Ultrasound Medical Devices

In order to better understand the guidelines for testing and quality control of ultrasonic devices it is necessary to give an overview of basic output parameters. Although there are a lot of physical quantities and parameters which are used to describe the acoustic field only the most important parameters from the point of safe use of ultrasound will be described. These acoustic output parameters are: the maximum negative or rarefaction acoustic pressure (p_- or p_r), the spatial-peak temporal-average intensity (I_{SPTA}), the temporal-average acoustic power (P), and the temperature of the transducer face (T_{surf}).

3.2 Acoustic Pressure

When ultrasound propagates through a medium, it induces a series of compressions and rarefactions of the particles constituting the medium and because of that acoustic pressure varies with time. Accurate measurements of acoustic pressure are essential for characterisation of ultrasonic sources and for experimental validation of models of ultrasound propagation [17]. Acoustic pressure is normally measured in water using hydrophone. They are generally based on piezoelectric operating principles and require calibration in terms of sensitivity, expressed in units of V Pa^{-1}, to convert voltage waveforms to acoustic pressure. The most common method of measuring ultrasound pressure fields is by scanning a hydrophone through the acoustic field of a source transducer using an automated scanning tank. Acoustic pressure is obtained from the measured voltage waveforms by deconvolution of frequency dependent sensitivity of the hydrophone over the required bandwidth. Common commercially available hydrophone types include piezoelectric probe, membrane type hydrophones and fibre-optic hydrophones [18]. Whilst a range of hydrophone devices exist [19] the choice of which one to use may be dependent upon features of the acoustic field being characterized.

Figure 2 shows a typical pressure waveform obtained by hydrophone. The most important parameters which can be determined directly from the pressure waveform are: maximum positive or peak compression acoustic pressure, p_+ (or p_c) and maximum negative or peak rarefaction acoustic pressure, p_- (or p_r). The largest value of the acoustic pressure is of considerable importance in assessing the risk of a cavitation occurrence. Acoustic cavitation is the formation and collapse of gaseous and vapour bubbles in the medium due to an acoustic pressure field. In particular, the peak rarefaction pressure is strongly related to cavitation events. The peak rarefaction pressure changes with position in the beam and is the largest in the focal region.

3.3 Acoustic Power

When passing through the tissue ultrasound waves carry energy that is gradually absorbed and deposited in the tissue. The power of an ultrasound beam is the total energy passing through the whole cross-sectional area of the beam per unit of time. It is measured in watts (W). Acoustic power is a measure of the rate at which the transducer emits energy. A medium which absorbs the acoustic energy heats up, but it is also subject to a radiation force.

In ultrasound fields of megahertz frequencies, output power is typically determined by measuring the force on a target using a radiation force balance. The principle of the radiation force measurement technique is that a target placed in the path of an acoustic beam will experience a radiation force (F). The target may be of an absorbing or reflecting type. For a plane wave incident on a perfectly absorbing target, the acoustic power (P) is given by:

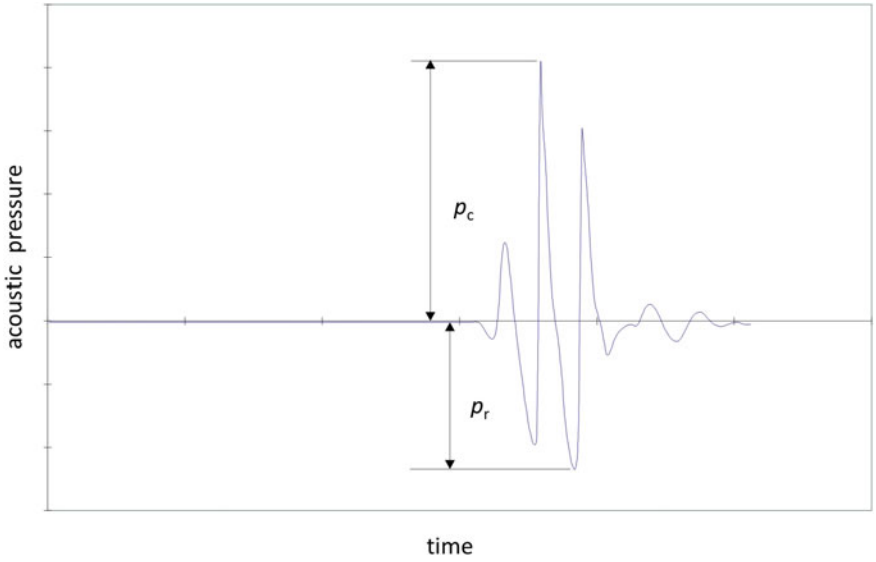

Fig. 2 Acoustical pressure parameters: maximum positive or peak compression acoustic pressure (p_c), and maximum negative or peak rarefaction acoustic pressure (p_r)

$$P = F \cdot c \tag{1}$$

where F is the radiation force, c is the propagation speed of ultrasound in the coupling medium, usually water. However, the relationship between the radiation force and the output power is affected by the focusing or other geometrical aspects of the field, by the type and shape of the target, by the distance of the target from the transducer, by the absorption of high frequency harmonics associated with the non-linear propagation of ultrasound waves in water, and by the acoustic streaming currents. Fortunately, many of these effects are small for typical diagnostic or physiotherapy ultrasound fields and can be ignored in the first approximation.

The radiation force method has become the internationally accepted method for characterizing ultrasonic power. There are a number of variations in the design of power measurement systems. Either the target or the transducer can be kept fixed and the force detected at the non-fixed element. The radiation force is typically determined by measuring the change in weight of an initially buoyant target. It can be calculated that one watt of acoustic power produces a radiation force and the change in weight of approximately 69 mg on an absorbing target. Therefore, measuring of acoustic power requires the application of a sensitive microbalance and measurement should be performed under strictly controlled conditions. Unfortunately, at the present time there is no commercially available form of power measuring device that is both sufficiently sensitive and portable for measurements at hospital sites. However, the two power balances designed by Perkins [20] and Farmery and Whittingham

[21] have been found previously to be satisfactory and suitable for measurements in hospital environment.

Other methods of power measurements include calorimetry and integration of intensity across a plane perpendicular to the beam. Unfortunately, calorimetric methods have lacked sufficient sensitivity while the planar integration method is only suitable as a laboratory-based method.

The recommended measurement method according to IEC 61161 [22] is the radiation force method. Today, several companies manufacture commercial ultrasound power meters that utilize the radiation force balance principle. The time-average ultrasonic power emitted by an ultrasonic transducer is a characteristic quantity which is important under safety aspects and whose declaration is required for medical ultrasonic equipment by IEC 61157 [23] for diagnostic instruments and by IEC 61689 [24] for therapeutic instruments. The COVID-19 pandemic has shown how vital it is to regularly assess medical devices with measuring functions in order to ensure their correct operation [25].

3.4 Intensity

Although acoustic power is important, it is essential to describe how that power is distributed throughout the beam and across a scanning plane. This is measured as the acoustic intensity of ultrasound, which can be described as the power transferred per unit area, where the area is an imagined surface that is perpendicular to the direction of propagation of the energy.

Intensity is not usually measured directly but calculated from the pressure waveform obtained by measurement of pressure using a hydrophone. In plane waves, intensity (I) is related to the square of acoustic pressure (p) with the relation:

$$I = \frac{p^2}{\rho c} \tag{2}$$

where ρ is the density and c is the propagation speed of ultrasound in the medium.

During the passage of an ultrasound pulse through the medium, the pressure in a certain point within the ultrasound beam varies with time (Fig. 2). The maximum or peak value of intensity during the pulse is called the temporal peak intensity I_{TP}. An alternative and more widely used measure of intensity during the pulse is the pulse average intensity, I_{PA}.

The intensity also varies across the beam but it is possible to specify intensity at the position in the beam where it has maximum value. This is called the spatial-peak value. Alternatively, it is possible to calculate a value averaged over the beam cross-sectional area, and this value is called the spatial average value. The most often quoted intensity parameters are the following:

I_{SATA} (Spatial-average temporal-average intensity): The temporal average intensity averaged across the beam cross-section
I_{SPTA} (Spatial-peak temporal-average intensity): The temporal average intensity measured at the location where it is the largest
I_{SPPA} (Spatial-peak pulse-average intensity): The pulse average intensity measured at the location where it is the largest.

3.5 Free-Field and Derated Values

Measurements of acoustic output parameters for ultrasound medical devices are normally performed in water using hydrophones. The values of output parameters obtained in this way are commonly called free-field values. Although everyone agrees that it is good practice to use water as the standard measuring medium, it is not always representative of the real clinical conditions. To estimate pressure values that might exist in soft tissue in the same ultrasound beam the pressure values measured in water are derated, by an amount that depends on the attenuation of the tissue. Derated values are calculated assuming that the attenuation coefficient of soft tissue is 0.3 dB (MHz cm)$^{-1}$. This value of the attenuation coefficient was chosen to be representative of typical low-loss tissue, and this so-called "derating factor" has been used widely for calculations related to the safety. Consequently, all "derated" output parameters of the ultrasonic fields have the index 0.3.

3.6 The Purpose of Acoustic Output Measurements

Over the five decades in which diagnostic ultrasound have been in use, the magnitudes of average intensity and other acoustic output quantities have increased considerably. The need to measure acoustic output was identified very early [26], and values of intensities reported were of the order of the few mW cm^{-2} or few tens of mW cm^{-2} for B-mode, and up to a few hundred mW cm^{-2} for Doppler devices. Reported values of acoustic outputs increased during the 1980s [27] and 1990s [28, 29]. It was demonstrated that both time-averaged intensities and peak pressures have increased considerably. It was also found that B-mode produces the lowest spatial-peak time-averaged intensities I_{SPTA} values because the beam is scanned across a region of tissue. The highest I_{SPTA} values are produced in pulsed Doppler mode, while Colour Doppler modes tend to have I_{SPTA} values intermediate between those of pulsed Doppler and B-mode. Surveys since 1991 demonstrated that peak pressures have increased steadily. The spatial-peak temporal-average intensity (I_{SPTA}) values in B-mode have shown the greatest increase and now overlap with the range of pulsed Doppler values [29, 30].

To protect the public against inappropriate exposure to ultrasound when used for medical applications international standards and national regulations are developed.

Individuals are commonly exposed to ultrasound as patients for diagnostic, therapeutic and surgical purposes. IEC standards for safety and essential performance of all medical electrical equipment are set out in the 60601 series. There are three particular standards in the 60601 safety series concerning medical ultrasound. These are part 2–5 for ultrasound physiotherapy equipment, part 2–37 for ultrasound diagnostic and monitoring equipment and part 2–62 for basic safety and essential performance of high intensity therapeutic ultrasound (HITU) equipment.

4 Protection Standards for Diagnostic Medical Ultrasound Devices

Although the upper limits of the output ultrasonic parameters for diagnostic ultrasound are not defined there is an obligation for equipment manufacturers to provide information about certain acoustic output parameters. Separate regulations regarding this exist in Europe and in the USA.

For example, in the USA, before an ultrasound scanner can be sold, approval must be sought from the Food and Drug Administration (FDA), and its regulations known as 510(k) [31] impose some limits. These regulations had a strong influence in setting and controlling ultrasound output levels. Elsewhere, government departments have established similar legislative processes which use similar safety criteria for allowing market approval.

In the IEC standard for diagnostic medical ultrasonic equipment, there is no upper limit on output intensity, nor any other output exposure quantity. Instead of these an International Electrotechnical Commission standard IEC 61157 requires certain acoustic output parameters to be declared if they exceed certain threshold values. Those parameters are: maximum negative or rarefaction pressure (p_r), output beam intensity (I_{OB}) and time-average intensity (I_{SPTA}). If any of the three above-mentioned parameters exceeds the limit value, manufacturers must provide specific information relating to the acoustic output of their scanners in water under conditions which produce the maximum temporal-average intensity and maximum negative pressure for each mode of operation. In addition to the three parameters mentioned above manufacturers are obligated to declare total acoustic power, frequency, −6 dB beam width where the pulse pressure squared integral (PPSI) is the largest, and the mode and control setting that give maximum acoustic output values. The threshold value for maximum negative pressure is 1 MPa; for time-average intensity it's 100 mW cm^{-2} and for output beam intensity it's 20 mW cm^{-2}. If ultrasound equipment has lower values of acoustic output parameters manufacturers are not obligated to provide such detailed output information.

The IEC 606012-37 standard for ultrasound diagnostic and monitoring equipment specifies how the user should be informed about potential hazards by displayed indices related to exposure and safety. These indices were developed in the USA in the early 1990s, and first were defined in the so-called "Output Display Standard"

(ODS) and published jointly by the American Institute of Ultrasound in Medicine (AIUM) and the National Electrical Manufacturers Association (NEMA) [32].

When ultrasound propagates through a medium, it induces a series of compressions and rarefactions which can produce various physical and chemical effects such as shear forces, acoustic streaming, cavitation, temperature and pressure changes, and radical formation. As heating and cavitation produced by ultrasound in tissue are two main mechanisms which are generally considered, the standard defines the Thermal Index (TI) and the Mechanical Index (MI) as safety indices. This standard requires the display of safety indices only if the ultrasound scanner has the ability of producing a value greater than 1.0 for either MI or TI under any operating conditions. Index value must be displayed whenever it exceeds 0.4. However, the standard allows manufacturers of low output devices to avoid the display of safety indices.

4.1 The Safety Indices

The thermal index (TI) is a relative indicator of thermal risk during an ultrasound examination. Heating occurs due to absorption of ultrasound energy by the tissue. Amount of heat produced by ultrasound passing through the tissue depends on the power and intensity of the ultrasound beam and type of tissue as well. Fluids are weak attenuators and would not be significantly heated as ultrasound passes through them while bone is known to have a larger attenuation coefficient. Consequently, heating would be minimal in fluids and maximal in adult bone. The ultrasound beam cross section is another important parameter because it gives information about the area over which the interaction of the beam with tissue takes place.

TI is defined as:

$$TI = \frac{W}{W_0} \tag{3}$$

where W_0 is the acoustic power required to achieve an increase in temperature of 1 °C in tissue and W is the current acoustic power. As temperature rises strongly depends on the type of the tissue different versions of *TI* are defined. The formulas for *TI* can be divided into two types, those intended to predict temperature rise in soft tissue (Soft Tissue Thermal Index-TIS), and those for bone (Bone at focus thermal index (TIB) and Cranial bone thermal index (TIC)).

In the formula for TIS, it is assumed that the medium is homogeneous with an attenuation coefficient of 0.3 dB cm^{-1} MHz^{-1} and is intended to predict temperature rise in soft tissue. For calculation of soft tissue heating the formula has the expression $TIS = A\,f\,W$, where f is acoustic frequency, and W is acoustic power while constant A takes defined values for the specific scan mode and geometry. Thermal index for bone is independent of frequency but it depends on the place where the temperature rise is estimated. TIB applies when bone is situated near the focus of an ultrasound

beam, while TIC is used to predict temperature rise in bone close to the probe, as in transcranial scanning.

For each of the three thermal indices, two conditions of ultrasound exposure can be considered. Conditions of ultrasound exposure are: scanned and un-scanned exposure. These tissue model parameters differ from those of real tissue, so the TI formulation does not provide accurate measures but presents a relative measure of risk [33].

Mechanical index (MI) is a relative indicator of the possibility of occurrence of mechanical damage in the tissue because of internal cavitation during ultrasound exposure. Acoustic cavitation is the formation and collapse of gaseous and vapor bubbles in a liquid due to an acoustic pressure field. Stable cavitation (non-inertial) is represented by relatively long-lived gas bubbles which results in emissions at subharmonics of the main excitation frequency and can induce bubble-associated microstreaming while transient cavitation (inertial) bubbles exist for a very short period of time and collapse violently. The implosion of cavitating bubbles can generate extreme temperature and pressure conditions under which highly reactive radicals can be generated. The ability of ultrasound to cause cavitation depends on frequency and intensity of ultrasound, medium properties (viscosity and surface tension), and ambient conditions (temperature and pressure).

The formula for MI calculation is based on a mathematical model which assumes the presence of bubble nuclei in the tissue [34]. It predicts that cavitation is more likely to occur if the peak rarefaction pressure (p_r) is large and at lower frequency (f). Mechanical index (MI) is defined as:

$$MI = \frac{p_{r,0.3}}{\sqrt{f}} \tag{4}$$

where $p_{r,0.3}$ is the maximum value of derated peak rarefaction pressure (in MPa) in the beam and f is the centre frequency in the pulse in MHz. The MI is roughly proportional to the mechanical work that can be performed on a bubble in the rarefactional phase of the acoustic field. According to the theory, cavitation production is not likely to occur at values of MI less than 0.7. This threshold applies only to bubble clouds in water while much higher values are required to initiate bubble generation in tissue in vivo [35]. Also, it is not generally possible to compare MI thresholds at different frequencies. Furthermore, application of different contrast agents will influence on MI threshold for cavitation.

The introduction of the safety indices contributes significantly to ensure safe use of ultrasound, but definitions of both the TI and MI experienced much criticism. The MI and TI are output indices because their values are related to specific output parameters, but they are rather relative quantities. It is known that there are some shortcomings in the methods of calculation of indices, such as: the inappropriate assumption that the linear conditions of acoustic propagation apply and lack of consideration of the transducer as a heat source [36], etc. Another criticism has been that the index alone does not inform the user about the related depth at which the index applies. The indices are based on calculation and assumptions which lead

to a maximum value of the index, irrespective of depth at which this may be found. Although the definition of both indices suffered much criticism, if they are properly used, they fulfil their goal of helping to ensure patient safety. By implementing the security index, a higher responsibility is transferred on the user to limit exposures and help to protect patients from inappropriate exposure to ultrasound. Therefore, it is very important that users are well educated and informed about the meaning of safety indices and according to that appropriate use of indices in practice to provide quality of medical procedure and ensure patient safety.

Even though the indices are available on screen, the user still faces the problem of knowing how long a particular tissue can be imaged. General recommendation is restricting the acoustic output to no more than what is actually required to obtain the necessary diagnostic information. In order to help users, the British Medical Ultrasound Society (BMUS) has published guidance [37] which advises on actions to be taken by the user depending on the value of the displayed safety indices. It is emphasized that these are not rules to be rigidly followed but recommended guidelines only. The BMUS guidance gives recommendation for limiting exposure time at TI values higher than 0.7. For obstetric scanning the upper limit for TI is 3.0. The limit on TI of 1.0 for eye scanning is the same as that set by US regulations [31]. More detail can be found in the BMUS Detailed Guidelines.

4.2 Transducer Surface Temperature

In addition to heating due to absorption of ultrasound in the tissue, the temperature of tissue near the transducer is strongly influenced by heating of the transducer itself. Conduction of heat from the transducer surface can result in temperature rises of several degrees Celsius in the tissue close to transducer [36, 38]. Maximum allowable transducer surface temperatures are specified in IEC 60601-2-37 and these limits are presented in Table 1.

According to Table 1, the maximum allowable transducer surface temperature is 50 °C when the transducer is transmitting in air and 43 °C when the transducer is transmitting into tissue. Also, a higher increase in temperature is allowed if the transducer is applied externally in contact with the skin than for those used internally, such as trans-vaginal or intra-rectal probes.

Table 1 Limits on surface temperature and surface temperature rise specified by IEC 60601-2-37 (IEC 60601-2-37) [15]

	In air	On tissue (external use)	On tissue (internal use)
Maximum temperature (°C)	50	43	43
Maximum temperature rise (°C)	27	10	6

5 Quality Assurance for Ultrasound Medical Diagnostic Devices

Quality assurance (QA) programme in diagnostic radiology is an organized effort by the staff operating a facility to ensure that the images produced are of sufficiently high quality so that they consistently provide adequate diagnostic information at the lowest possible cost and with the least possible exposure of the patient [39].

Quality control (QC) is a part of quality assurance programme consisting of observation techniques and activities to be performed to fulfil requirements for appropriate equipment performance.

Ultrasound imaging is very often the basis for diagnostic decision; therefore, it is necessary to implement a QA programme on such systems as well. Ultrasound probes degrade 10–13% per year which can, in absence of quality control, lead to image of inappropriate quality and poor diagnostic value [40].

Several recommendations have been published on diagnostic ultrasound QA [41–46], but there is still no general agreement on a standard protocol to be followed. In 2012 EFSUMB published *Guideline for Technical Quality Assurance (TQA) of Ultrasound devices (B-Mode)* [46] with a goal to develop a standardized protocol for all EU member states. The implementation of quality assurance in some centers is still rather exception than rule. There are many possible reasons for this but the most important is probably the lack of legislative requirement. Other reasons could be: sonography workload and the lack of a medical physicists as well as general view that formal QA is unnecessary [47].

Different approaches for QA have been suggested in these publications, but the tests to be included are mostly the same in all of them. It is up to the user to define and follow their own QC protocol. Basic quality control procedures usually includes: physical and mechanical inspection, evaluation of image uniformity, geometric accuracy, system sensitivity, dead zone, spatial resolution, grey scale evaluation and fidelity of image display. In this chapter, a specific approach for inspecting medical devices with measuring functions is presented [48–50]. Recommended frequencies of testing and acceptability criteria are given in the Table 2.

5.1 Physical and Mechanical Inspection

Physical and mechanical inspection includes a visual check of the main unit, transducers, monitor, printer, and accessories. Ultrasound systems and accessories, including manuals, repair records and QA records should be checked. Monitor, keyboard, knobs, transducers and holders should be checked for cleanliness. Device housing, and then the air filters should be inspected and cleaned if necessary. Scanner, monitor and accessories should be properly checked, especially on portable units. Wheels should be fastened securely and the wheel locks should be working. All wires must be free of cuts and fraying to ensure proper connection.

Table 2 Frequency of quality control testing and acceptability criteria

Test	Frequency	Acceptability criteria
Phyisical and mechanical inspection	Daily/semi-annually	No visual defects
Image uniformity	Semi-annually	≤20% from baseline
Geometric accuracy: vertical	Semi-annually	≤2 mm or 2%
Geometric accuracy: horizontal	Semi-annually	≤3 mm or 3%
System sensitivity	Semi-annually	≤1 cm from baseline
Dead zone		≤10 mm for $f < 3$ MHz ≤7 mm for 3 MHz ≤ $f < 7$ MHz ≤4 mm for $f \geq 7$ MHz
Spatial resolution: axial		≤1 mm
Spatial resolution: lateral		≤1.5 mm from baseline
Gray scale evaluation		≤10% from baseline

5.2 Phantom Based Measurements

Phantoms for QC procedures of diagnostic ultrasound are made of tissue mimicking material with various inserts designed for a certain procedure. The tissue mimicking material within the phantom consists of water-based gelatin in which microscopic particles are mixed uniformly through the volume. The speed of sound in this material is about 1540 m/s, as the same speed is assumed in the calibration of ultrasound scanners. There are several manufacturers providing such phantoms and they are very similar. An example of a general-purpose quality assurance phantom in use is shown in Fig. 3. For analysis either visual or automatic methods can be used, but according to the guidelines of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) automatic image analysis is recommended [46]. When setting up baseline values, scanner presets for each test should be recorded and reproduced periodically.

a. ***Image Uniformity***

Uniformity is defined as the ability of an ultrasound device to display echoes of the same magnitude and depth with equal brightness on display. This procedure is aimed to prove that all crystals within the transducer are functioning similarly. The phantom section for this procedure is the tissue mimicking material of uniform texture similar to that of liver parenchyma which is free of filament and lesions—simulating targets [43]. Uniformity could be evaluated by performing Region of Interest (ROI) measurements (Fig. 4) using an image processing program, for example ImageJ (Research Services Branch of the National Institute of Mental Health, USA). The standard deviation and mean are determined corresponding to the echo level and noise measurements, respectively.

b. ***Geometric Accuracy: Vertical and Horizontal***

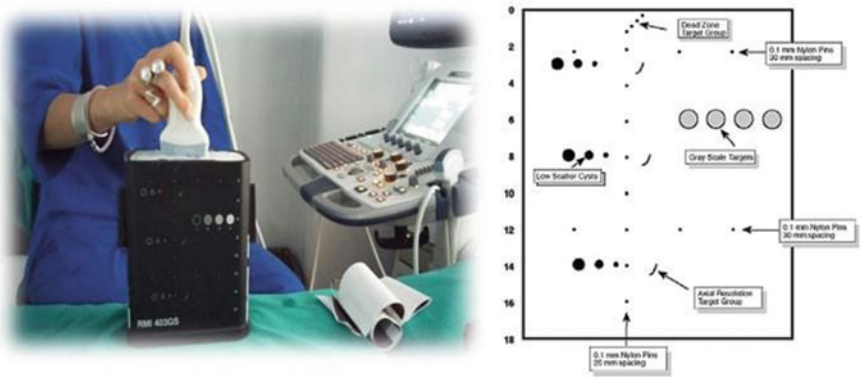

Fig. 3 Example of a general-purpose image quality phantom

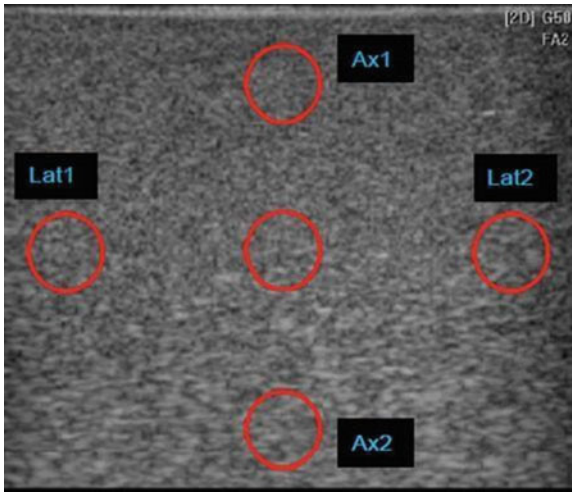

Fig. 4 Image for uniformity evaluation. Red circles represent Regions of Interest (ROIs) for the analysis of echo level and noise

Distance accuracies, both in the direction of the ultrasound beam and perpendicular to the ultrasound beam are contributors to total image quality and are therefore indicators of scanner performance.

Vertical Distance Accuracy

Vertical distance is defined along the axis of the beam. The phantom section for this procedure is the vertical distance target group, vertical column of filament targets equally separated (e.g. 2 cm) in different depths. The distance between the most clearly separated filament targets in the vertical column displayed in the image is determined using the distance tool in the image processing program (Fig. 5).

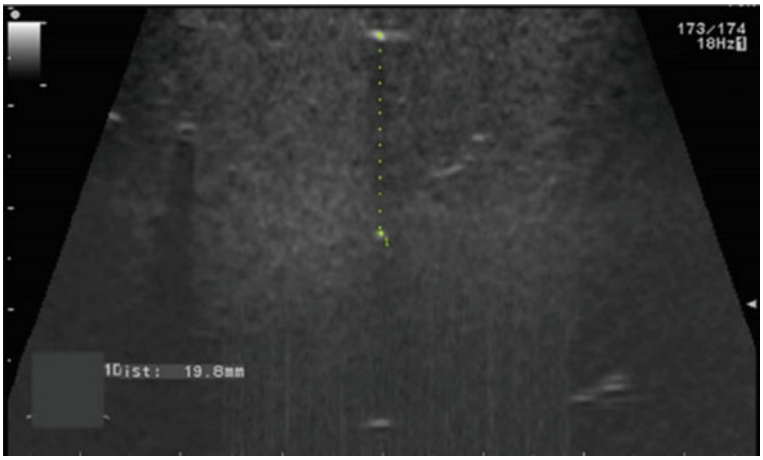

Fig. 5 Vertical distance determination using distance tool

Horizontal Distance Accuracy

Horizontal distance is defined perpendicular to the beam axis. The phantom section for this procedure is the horizontal distance target group, horizontal rows of filament targets equally separated (e.g. 3 cm) in different depths. The distance between the most clearly separated filament targets in the horizontal row displayed in the image is determined using the distance tool in the image processing program (Fig. 6).

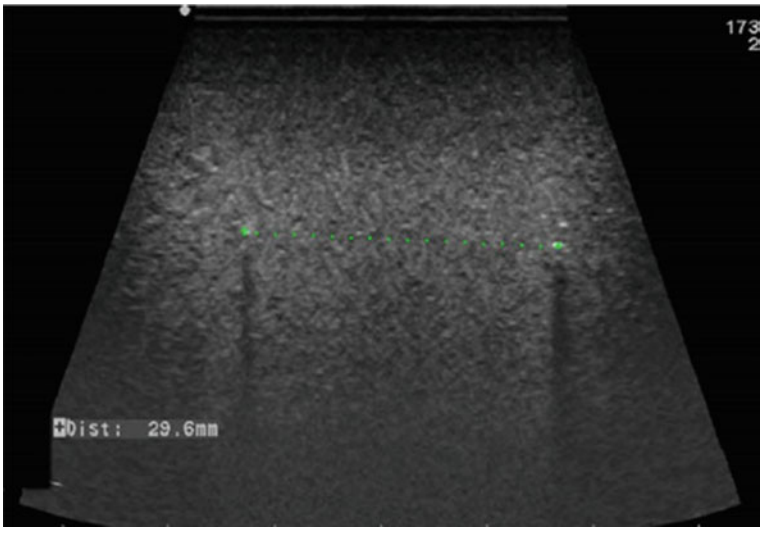

Fig. 6 Horizontal distance measurement using distance tool

c. ***System Sensitivity***

System sensitivity is described by the depth of penetration. This is the largest distance in the phantom for which echo signals from the scatters within the tissue mimicking background material can be detected on the display. The frequency of the transducer, the attenuation of the medium being imaged, and the system settings determine the depth of penetration.

The phantom section for this procedure has the vertical group of filaments, in this case "depth markers" that are equally spaced (e.g. 2 cm) one from another. The point at which the usable tissue information disappears is an indicator of maximum depth of visualization or penetration (Fig. 7).

d. ***Dead Zone***

The ring down or dead zone is the distance from the front face of the transducer to the first identifiable echo. No useful scan data is collected in this region. The dead zone is the result of the transducer ringing and reverberations from the transducer-test object, phantom or patient interface [43]. The phantom section for this procedure is the one containing pin targets in close proximity to the phantom surface at different shallow depths (e.g. 1, 4, 7, and 10 mm) (Fig. 8).

e. ***Spatial Resolution: Axial and Lateral***

Axial resolution is defined as the ability of an ultrasound system to resolve objects in proximity along the axis of the beam. It is proportional to the probe frequency and is approximately double the pulse length. Lateral resolution is a measure of how close two reflectors can be to one another, perpendicular to the beam axis and still

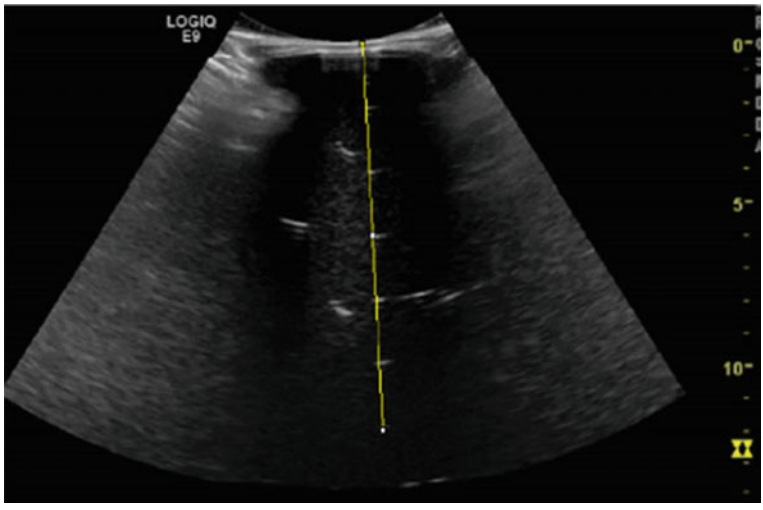

Fig. 7 Measurement of the depth of visualization using distance tool which describes the system sensitivity

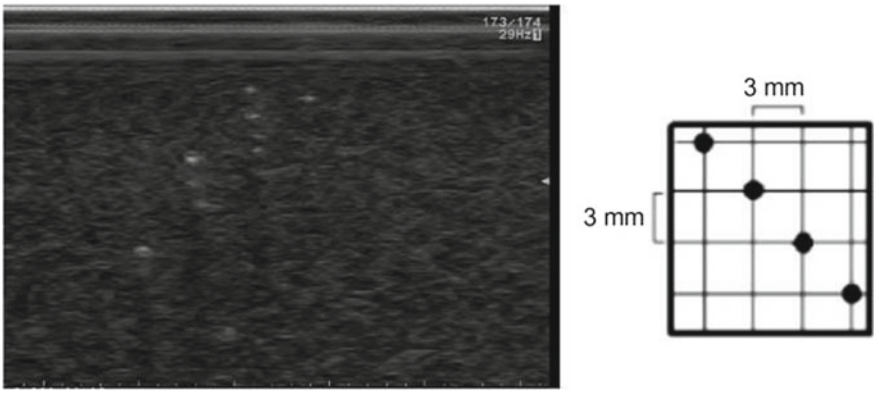

Fig. 8 Image for the visual evaluation of the dead zone and an illustration of the dead zone insert

be distinguished as separate reflectors. It is defined in the direction perpendicular to the beam axis. Lateral resolution is determined by the width of the ultrasound beam and therefore is detected to be at its best within the focal zone.

The phantom usually has three sets of resolution target groups at different depths (e.g., 3, 8 and 13 cm). The target consists of four wires of small diameter vertically and horizontally spaced at known distances (e.g., vertically 2, 1, 0.5 and 0.25 mm and horizontally 1 mm) (Fig. 9). Both axial and lateral resolution are evaluated using the same group. Axial resolution corresponds to the last pair of points identifiable as two separate entities in the target group. Lateral resolution corresponds to the width of a single filament in the focal zone.

f. ***Grey Scale Evaluation***

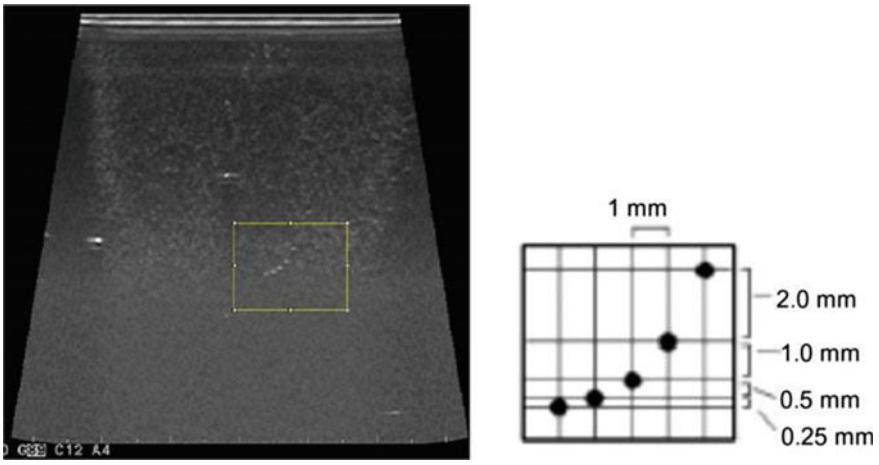

Fig. 9 Image and an illustration of the spatial resolution target group

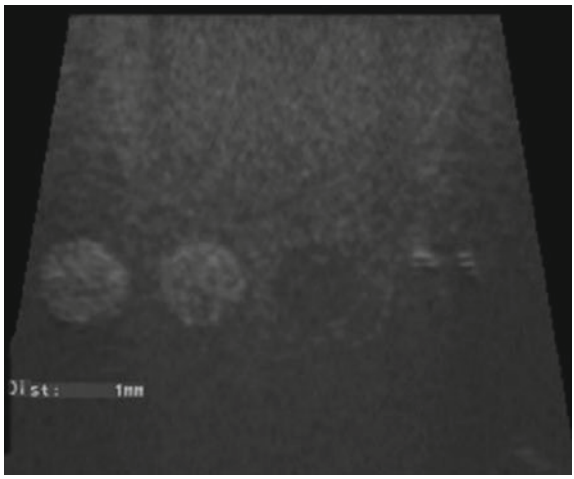

Fig. 10 Image of a grey scale evaluation insert; four spherical objects of different contrast

Grey scale evaluation of an ultrasound image is a very important parameter because clinical differentiation of the various lesions in tissue depends significantly on the grey scale characteristic of the obtained image. The phantom section utilized for this procedure consists of a set of four spherical objects each having the same diameter (e.g. 1 cm), placed at the same depth (e.g. 6 cm) with different contrast (e.g. 0, −6, +6 and +12 dB) (Fig. 10). For the quantitative determination the mean pixel value is computed using the ROI tool.

5.3 Fidelity of Ultrasound Scanner Electronic Image Display

Ultrasound images are viewed on electronic image displays. Therefore, they must be appropriately set up and monitored. Many ultrasound units have "built-in" or internally stored grey scale test patterns that can be used for display setup. A less comprehensive variation of the protocol for QC of diagnostic image display in general can be used. Verification of image displays is in accordance with the AAPM TG18 report [51] and is using TG18 test patterns (Fig. 11). Such patterns should not be the only tool for evaluation. Clinical images should also be examined. Setting up the displays for the first time, to establish the operating levels, is to be performed with the advice of radiologists to ensure that the levels are clinically acceptable.

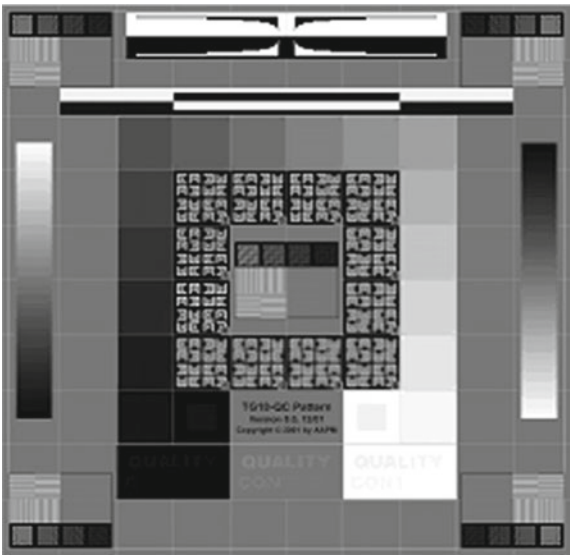

Fig. 11 AAPM TG18-QC pattern used for overall evaluation of image display performance

6 Protection Standards for Ultrasound Physiotherapy Equipment

Ultrasound has been used as a therapeutic technique for physical medicine since the 1950s. The need to measure and calibrate ultrasound equipment for physical therapy was recognised in the early 1960s and specification standards were first published by the IEC in 1963. Requirements for physiotherapy machines are small in number and well defined [52]. The IEC 60601-2-5 standard for physiotherapy equipment includes two limits for the purpose of patient protection.

The first one limits the temperature of the front face of the transducer. It must be less than 41 °C when operated under water with initial temperature 25 °C. According to the standard the equipment must operate for 3 min at the maximum effective ultrasound output power. The treatment head is then removed from water for 15 s and then immediately re-immersed in the water. The above procedure should be repeated three times.

The second protection limit applies to ultrasound intensity. According to IEC standard 60601-2-5 the effective intensity shall not exceed 3 W/cm^2. In the same document the effective intensity is defined as the quotient of the effective ultrasound power and the effective radiating area (ERA).

The ultrasonic beam distribution generated by the treatment head is another important parameter concerning safety. Beam homogeneity can be quantified by the parameter called beam non-uniformity ratio (BNR), which represents the ratio of the highest intensity in the beam to the intensity averaged over the effective radiating area. Sometimes, beam distribution can be non-uniform and can potentially generate regions of

high local pressure, also called "hot spots" [53]. These regions may produce excessive heating in small regions of the tissue. According to IEC standard 61689 [54] transducers with BNR > 8 are considered unsafe.

Since the first introduction of standards and limits for output parameters of the devices used in physiotherapy, numerous surveys have been published [55, 56]. These papers show that lot of physiotherapy devices have significant differences between the indicated and actual output power. Also, some cases of excessive heating because of equipment failure have been cited in literature [57]. All these publications have emphasized the need for measurement and calibration of the equipment used in physiotherapy.

6.1 Measurement of Ultrasonic Power for Physiotherapy Devices

Ultrasound transducer output power is a key safety related parameter. The clinical effects of the ultrasound physiotherapy depend on applied acoustic dose defined as energy deposited by absorption of acoustic wave per unit mass of the medium [58]. If the acoustic dose is too low, there will be no significant clinical effects and if it is too large it can cause tissue injury [59]. Therefore, it is very important to measure and calibrate ultrasonic devices used in therapy, to preserve patient safety.

The most common method for determining ultrasound power includes a measurement of the radiation force by using radiation force balances (RFB). The basic concept of the method has been previously explained. This method is based on the fact that ultrasound exerts a force on a target placed in the path of an acoustic beam that is directly proportional to the total power absorbed or reflected by the target [60]. The small magnitude of the radiation force makes the method difficult to apply within a clinical environment. Another limiting factor for radiation force balances is that it can register only the component of the radiation force which is collinear with the axis of measurement. This fact may cause problems in the measurement of power for divergent or convergent beams.

There are some alternative methods for measurement of acoustic power based on the conversion of acoustic energy into thermal energy such as calorimetry [61] and pyroelectricity [62].

The calorimetric method for measurement of acoustic power is attractive because the principle of measurement is simple. The absorption of ultrasound energy in an absorbing liquid such as castor oil produces a temperature rise. The acoustic power may be then calculated from the resultant increase in temperature. Disadvantages of these methods are that it is time consuming and has low sensitivity. Also, this method will give a good result for acoustic power only if all acoustic energy is converted into thermal energy, and if thermal losses can be ignored. Advantages of the calorimetric method are that it is insensitive to the direction of ultrasound propagation and can be used for measuring power of divergent and convergent beams [52].

Recently, the UK National Physical Laboratory (NPL) has developed a new method for measurement of acoustic power which exploits the pyroelectric effect generated within a thin layer of the piezo polymer polyvinylidene fluoride (PVDF). One side of the membrane is bonded to a very highly acoustically absorbing material. Most of the ultrasonic energy passing through the PVDF membrane is absorbed in the thin layer of backing material, producing a rapid increase in temperature and generation of pyroelectric voltage which is proportional to delivered ultrasonic power. The measurement concept was introduced in the paper [62], with follow up publications addressing the measurement of physiotherapy fields [63] and of diagnostic fields [64, 65].

6.2 Determination of Effective Radiating Area

The effective radiation area (ERA) is the area close to the face of the transducer over which most of the ultrasonic power is emitted. Accurate determination of the effective radiation area of the transducer is particularly important because it effects the calculation of the effective intensity which should not exceed 3 W/cm^2 as mentioned previously. The geometric surface of the piezoelectric crystal itself is not a reliable value for the area over which ultrasound is emitted. Also, ultrasound physiotherapy treatment heads require periodic checks as their performance tends to deteriorate slowly, mainly resulting from minor damage to the transducer probe. Hence, accurate determination of ERA is of particular importance.

Performance of the treatment head can be verified, and determination of effective radiating area can be performed using the standardized method which is based on the scanning of the acoustic field in water tanks using miniature hydrophones. These procedures require a specially equipped laboratory, and they are not convenient for use in clinical environment. Recently, an alternative method based on the use of thermochromics materials was proposed [66] and tested in a clinical environment [67, 68]. This method is useful for quality assurance of physiotherapy ultrasound treatment heads.

There are two specification standards which describe methods for determination of the ERA. According to standard IEC 61689, ERA is evaluated through the derivation of an intermediate quantity called the beam cross-sectional area (BCSA). The BCSA is defined as the minimum area which contains 75% of the total mean square acoustic pressure. It is determined by sorting analysis of the acquired data. ERA of the treatment head is calculated by multiplying the beam cross-sectional area determined at a distance of 0.3 cm from the treatment head's face, by a dimensionless factor F_{AC}. This method allows the determination of real values for ERA.

Prior to the publication of IEC 61689, most manufacturers measured ERA using technique specified by the FDA. This method involved measuring the maximum pressure in the beam and then defining an area within which pressure amplitude exceed 5% of this maximum. This method can result in large measurement uncertainties.

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Inspection and Testing of Electroencephalographs, Electromyographs, and Evoked Response Equipment

Mario Cifrek and Luka Jelić

Abstract This chapter deals with the inspection of neurodiagnostic equipment for measurement of electrophysiological signals in order to detect eventual problems and prevent them from becoming serious safety risks. The first section of the text gives a brief description of the human neuromuscular system, followed by description and short historical overview of considered neurodiagnostic methods: electroencephalography (EEG) including evoked potentials (EP), electromyography (EMG) and nerve conduction study (NCS). Operating principle of a computer-controlled neurodiagnostic instrument is explained using a generic block diagram. The next sections discuss potential harms and hazards associated with the use of neurodiagnostic equipment as well as standards and regulations concerning basic safety and essential performance requirements. A dedicated section follows up with importance of evidence-based post-market surveillance (PMS), while inspection section describes testing and inspection procedures for periodic testing of modern computer-based neurodiagnostic instruments in the field. Following section is a review of recommendations, contraindications, and warnings for use, while the closing section provides a chapter summary.

1 Introduction

To treat disorders of the brain, spinal cord, muscles and peripheral nervous system, neurologists use a variety of diagnostic tests to help identify the specific nature of neurological diseases, conditions, or injuries. The results of these tests can help in planning an appropriate course of treatment. Some of these tests are provided using electroencephalography (EEG)—a method for recording spontaneous as well as evoked (evoked potentials, EP) brain electrical activity, nerve conduction study (NCS) comprising action potential morphology and nerve conduction velocity (NCV)

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measurement, and electromyography (EMG), a method for recording the electrical activity of muscles.

2 Human Neuromuscular System

The human neuromuscular system includes the nervous system and the muscular system. The nervous system is anatomically divided into two parts: the central nervous system (CNS) which is made up of the brain and spinal cord, and the peripheral nervous system (PNS), which consists of 12 pairs of cranial and 31 pairs of spinal nerves along with their associated ganglia [1]. Functionally, the nervous system has two main subdivisions: the autonomic (involuntary) and the somatic (voluntary) nervous system. The autonomic nervous system maintains internal physiologic homeostasis, regulating certain body processes, such as blood pressure and the rate of breathing, which work without conscious effort. The somatic system is made up of two different types of neurons: sensory neurons (afferent neurons), which transmit messages to the central nervous system and motor neurons (efferent neurons) which relay information from the central nervous system toward the peripheral effector organs, mainly muscles and glands [2].

Different parts of the brain are responsible for different tasks. A basic division of the brain is into four lobes: frontal, temporal, parietal and occipital [3]. For example, the visual cortex is situated in the occipital lobe, the primary somatosensory cortex is in the anterior part of the parietal lobe, and the primary motor cortex is in the posterior part of the frontal lobe. A large fissure called the central sulcus separates the primary somatosensory and the primary motor cortex. Different parts of the primary somatosensory and motor cortex are responsible for different parts of the body [4]. The left side of the brain is mostly responsible for movements of the right side of the body and vice versa.

Nerve conduction velocity—the velocity with which a signal (an action potential) propagates through a neuron—depends on the type of the nerve fibre and spans the range from 0.5 m/s (the slowest, type C unmyelinated fibres) to 120 m/s (the fastest, type A myelinated fibres) [2]. Conduction velocities are affected by a wide array of factors, including age, sex and various medical conditions. Studies allow for better diagnoses of various neuropathies, especially demyelinating conditions, as these conditions result in reduced or non-existent conduction velocities.

The muscular system is responsible for the movement of internal body parts as well as the movement of the whole human body. There are three types of muscle tissue: smooth (visceral), cardiac and skeletal. Smooth muscle is found inside of organs like the stomach, intestines and blood vessels, where it makes organs contract to move substances through them. It is known as involuntary muscle because it is controlled by the unconscious part of the brain. The term “smooth muscle” is often used because it has a very smooth, uniform appearance when viewed under a microscope. This uniform appearance contrasts with the banded appearance of cardiac and skeletal muscles. Found only in the heart, cardiac muscle is responsible for pumping blood

throughout the body. Cardiac muscle tissue cannot be controlled consciously, so it is an involuntary muscle. Skeletal muscle, also known as the striated muscle, is the only voluntary muscle tissue in the human body. It is required for every physical action that a person performs consciously (e.g. speaking, walking, or writing). The term "striated muscle" is used because of the banded appearance observed in microscopic images of this tissue.

Skeletal muscles are innervated by alpha-motoneurons, which have heavily myelinated, fast-conducting axons that terminate in motor end plates (neuromuscular junction). In clinical neurology, for motor neurons that innervate the voluntary muscles, the term "lower motoneuron" is used. A single alpha motoneuron and all the muscle fibres it innervates is called a motor unit. The number of muscle fibres within motor units varies from 3 to 8 muscle fibres in the small finely controlled extraocular muscles of the eye to as many as 2000 muscle fibres in postural muscles, for example soleus muscle in the leg. Individual muscle fibres are innervated by neuromuscular junction, usually located near the middle of the cell. The muscle fibres belonging to a motor unit are dispersed and intermingle with those from other motor units.

There are three functional types of muscle fibre: (1) slow-twitch fibres, (2) fast-fatigable twitch fibres and (3) fast-fatigue-resistant twitch fibres. Each motor unit comprises of only one type. The force that slow-twitch fibres produce in response to an action potential rises and falls slowly than the force produced by fast-twitch fibres. The fatigue resistance of slow-twitch fibres results from a reliance on oxidation catabolism in contrast with one subtype of the fast-fatigable-twitch fibres that relies almost exclusively on anaerobic catabolism [5].

3 Diagnostic Methods and Equipment

3.1 Electroencephalography (EEG)

Electroencephalography (EEG) is an electrophysiological method for recording electrical activity of the brain. The EEG is used in the evaluation of brain disorders. Most commonly it is used to show the type and location of the activity in the brain during a seizure. It is also used to evaluate people having problems associated with brain function including confusion, coma, tumours, long-term difficulties with thinking or memory, or weakening of specific parts of the body (such as weakness associated with a stroke).

A thorough history of electroencephalography is given in the book by Niedermeyer and Da Silva [6], while the brief history is summarised in Table 1 [7].

Table 1 A brief history of EEG [7]

1928–1938	First recording of human EEG from the scalp by Berger, Adrian, and Matthews
1937–1945	Studies by Grey Walter, Gibbs, Gibbs, and Lennox show changes related to epilepsy and when the investigation may be used clinically
1950s–1970s	8 or 16 channel hard-wired recordings on paper become incorporated into routine clinical practice
1970s	First use of CCTV linked to analogue EEG
1980s	Analogue 3 or 4 channel ambulatory EEG introduced for long-term monitoring
1990s–2005	Digital EEG gradually replaces analogue recording
2005–current	Digital EEG with simultaneous video for both standard recording and telemetry, and ambulatory monitoring

Electrical activity of the brain can be measured and recorded non-invasively via surface electrodes mounted on the scalp (EEG) or invasively, directly from the surface of the brain (electrocorticography, ECoG). The amplitude of the EEG is from a few μV to 100 μV when measured on the scalp. The bandwidth of this signal is from under 1 Hz to about 50 Hz (Fig. 1). ECoG involves recording electrical signals from the surface of the human brain, typically in patients being monitored prior to surgery. ECoG signals have a much higher signal-to-noise ratio (SNR) than EEG, as well as higher spectral and spatial resolution.

Non-invasive EEG uses cup electrodes made of stainless steel, tin, gold or chloride treated silver disks of 4–10 mm in diameter placed on the scalp surface, and clip electrodes for the earlobes typically used as reference electrode. Most used are silver/silver chloride electrodes because they minimize the contact resistance between electrode and skin surface and guarantee a stable, reliable contact. By means of a special conductive gel, which is applied in the hair between electrodes and scalp, the electrical resistance can be minimized.

Invasive EEG uses subdermal "needle" electrodes, multipole depth electrodes designed for introduction directly into the substance of the brain by a neurosurgeon, and a corkscrew needle electrode. Cortical electrodes are used for recording directly from the surface of the brain (electrocorticography, ECoG). A typical grid has a set of 8×8 platinum-iridium electrodes of 4 mm diameter (2.3 mm exposed surface) embedded in silicon with an inter-electrode distance of 1 cm.

Surface electrodes can be placed on the scalp individually using some sort of adhesive paste or they can be placed using an elastic cap with electrode holders placed at prearranged positions. Electrode caps can be made for up to 256 electrodes. Using a very large number of electrodes does not result in a much better spatial resolution, so in most cases the number of electrodes is limited to 20–30 electrodes. For some clinical applications, just a few electrodes are used. The most frequently used system includes 32 electrodes placed according to the International 10–20 system [8]. The placement of electrodes is based on landmarks on the skull, namely the nasion (Nz), the inion (Iz) and the left and right pre-auricular points (LPA and RPA). Each electrode site is labelled with a letter and a number. The letter refers to the

area of brain underlying the electrode, e.g. F—Frontal lobe, T—Temporal lobe, P—Parietal lobe, O—Occipital lobe, C—border between frontal and parietal lobe. Even numbers denote the right side of the head, and odd numbers the left side of the head. The electrodes that have the letter Z (for zero) as their index instead of a number are positioned at the middle of the scalp. This placement system was devised in order to get comparable data between different laboratories, participants, and experiments. In addition, the system makes sure that all regions of the brain are sampled evenly.

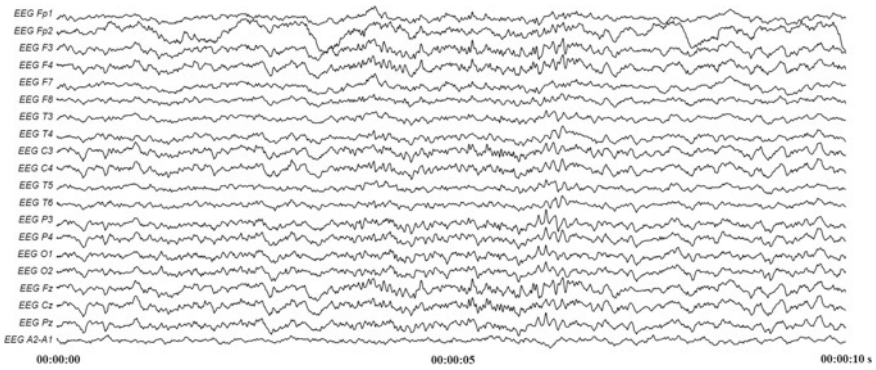

Fig. 1 Standard 20-channel EEG recording [9]

Besides evaluation of spontaneous electrical activity of the brain, EEG is used for evoked potential (EP) measurements. Evoked potential is an electrical potential recorded from the nervous system following the presentation of a stimulus, which can be, for example, electrical, visual, or auditory (Fig. 2). Signals can be recorded from cerebral cortex, brain stem, spinal cord and peripheral nerves. Usually the term "evoked potential" is reserved for responses involving recording from central nervous system structures. Thus, evoked compound motor action potentials (CMAP) or sensory nerve action potentials (SNAP) as used in nerve conduction studies (NCS) are generally not thought of as evoked potentials, though they do meet the above definition. Examples of evoked potentials are visual evoked potential (VEP), somatosensory evoked potential (SSEP), auditory evoked potential (AEP), and auditory brainstem response (ABR). Evoked potential signals are usually below the noise level and thus not readily distinguished, so a train of stimuli and signal averaging must be used to improve the signal-to-noise ratio.

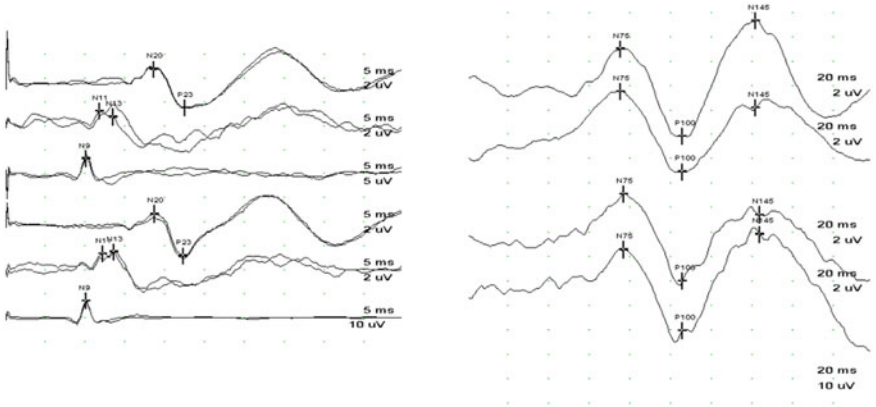

Fig. 2 Examples of somatosensory (SEP) and visual (VEP) evoked potential signals [10]

Along with visual analysis of raw data, modern EEG systems enable quantitative analysis of the digitized EEG (quantitative EEG, qEEG). The qEEG is an extension of the analysis of the visual EEG interpretation which may assist and even augment our understanding of the EEG and brain function. One example of qEEG is brain mapping.

3.2 Electromyography (EMG)

Electromyography (EMG) is an electrodiagnostic method for evaluation and recording of the electrical activity of muscle tissue and its representation as a visual display or audible signal, using electrodes attached to the skin or inserted into the muscle. EMG is performed using an instrument called an electromyograph to produce a record called an electromyogram (Fig. 3). According to IEC 60601-2-40, electromyograph is medical electrical equipment for the detection or recording of biopotentials accompanying nerve and muscle action, either spontaneously, intentionally or evoked by electrical or other stimulation.

EMG can detect abnormal muscle electrical activity in many diseases and conditions, including inflammation of muscles, pinched nerves, damage to nerves in the arms and legs, disc herniation and degenerative diseases such as muscular dystrophy, Lou Gehrig's disease and Myasthenia gravis, among others. The EMG helps distinguish between muscle conditions that begin in the muscle and nerve disorders that cause muscle weakness. The results of this test are often correlated with the results from the Nerve Conduction Study.

After the first experiments dealing with connection between muscles and the generation of electricity by Francesco Redi in 1666, Emil du Bois-Reymond in 1849 discovered that it was possible to record electrical activity during a voluntary muscle

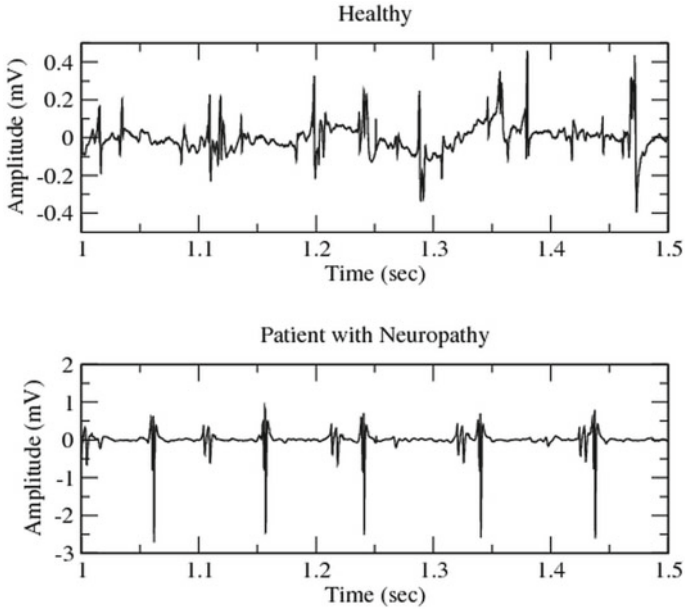

Fig. 3 Examples of healthy and pathological EMG recordings [11]

contraction. The first actual recording of this activity was made by Marey in 1890, who also introduced the term electromyography. In 1922, Gasser and Erlanger used an oscilloscope to show the electrical signals from muscles (according to [12]).

The first application of clinical electromyography was presented in the paper of Buchtal and Clemmesen [13]. A thorough history of electromyography is given in the book by Medved [12], while the brief history of electromyographs is summarised in Table 2 [14].

Table 2 A brief history of electromyographs [14]

1942	The first electromyograph was constructed by Herbert Jasper in 1942 at McGill University, Montreal Neurological Institute
1950	DISA A/S (Denmark) introduced in 1950 first commercially available three channel EMG system (model 13A67)
1950–1973	The era of the analogue EMG systems: EMG signals were recorded, and subsequent analyses were carried out manually on film or paper
1973–1982	The first modular digital EMG systems were introduced. Dedicated analysis modules were introduced, but detailed analysis was still done on paper
1982–1993	Microprocessor-controlled EMG systems
1991–2005	PC-based EMG systems
2001–current	Handheld and wireless EMG systems

There are two types of EMG: intramuscular (needle and fine-wire) EMG and surface EMG. For intramuscular EMG, when the position of the electrode is adjusted so as to give a maximal single fibre action potential, the recorded amplitude is usually between 1 and 7 mV with occasional values of 15–20 mV. Most of the spectral energy is concentrated between 100 Hz and 10 kHz, with a peak value at 1.6 kHz [15]. The amplitude of surface EMG signal is less than 5 mV and the bandwidth of this signal is from about 20–500 Hz [16].

The intramuscular EMG muscle function is commonly studied with concentric or monopolar needle electrodes. The recordings are performed with the muscle at rest, during slight voluntary contraction and during increasing or full contraction. The types of EMG studies include: spontaneous activity (SPA), maximum voluntary activity (MVA), automatic motor unit potential analysis (AMUP), interference pattern analysis (IPA), quantitative EMG (QEMG), and single fibre EMG (SFEMG).

Surface EMG (sEMG) involves placing electrodes on the skin over the muscle to detect the electrical activity of the muscle. It is used in kinesiological studies (gait and movement analysis), fatigue studies [17, 18], mapping of the end-plate area of a muscle [19], and biofeedback devices [20].

3.3 Nerve Conduction Study (NCS)

A nerve conduction study (NCS) is a diagnostic test used to evaluate the electrical conduction of the motor and sensory nerves in the human body. Both the nerve conduction velocity (NCV) and action potential morphology are analysed. Nerve conduction studies are used mainly for evaluation of paresthesias and/or weakness of the arms and legs. Nerve conduction studies along with needle electromyography measure nerve and muscle function and may indicate the pain in the limbs, weakness from spinal nerve compression, or concern about some other neurologic injury or disorder.

Although the first actual recordings of afferent nerve conduction velocity were made by Eichler in 1938 [21], the work of Dawson and Scott led to the clinical development of these methods. They use the high-gain, low-noise amplifiers and a technique of photographic superimposition for recording sensory action potentials [22]. Based on the methods of Dawson and Scott, Gilliatt and Sears pioneered the use of nerve conduction studies in clinical practice. In 1955, they set up a routine recording laboratory, equipped mostly with instruments constructed by Bert Morton (according to [23]). In 1965 they introduce a barrier grid storage tube as an “averager” [23]. In 1965 Data Laboratories Ltd. made “Biomac 500”, one of the first medical averaging computer [24].

NCS are done by placing electrodes on the skin and stimulating the nerves through electrical impulses. To study motor nerves, recording electrodes are placed over a muscle that receives its innervation from the stimulated nerve. The electrical response of the muscle is then recorded in order to determine how fast and how well the nerve

responded. NCS can be performed on any accessible nerve including peripheral nerves and cranial nerves.

There are two categories of nerve conduction studies: motor and sensory nerve conduction testing.

The basic findings are generally twofold: (1) how fast is the impulse traveling? (e.g., how well is the electrical impulse conducted?); and, (2) what does the electrical representation of the nerve stimulation (action potential morphology) look like on the screen? (e.g., does there appear to be a problem with the shape or height that might suggest an injury to some portion of the nerve, such as the axons or the myelin?) [25].

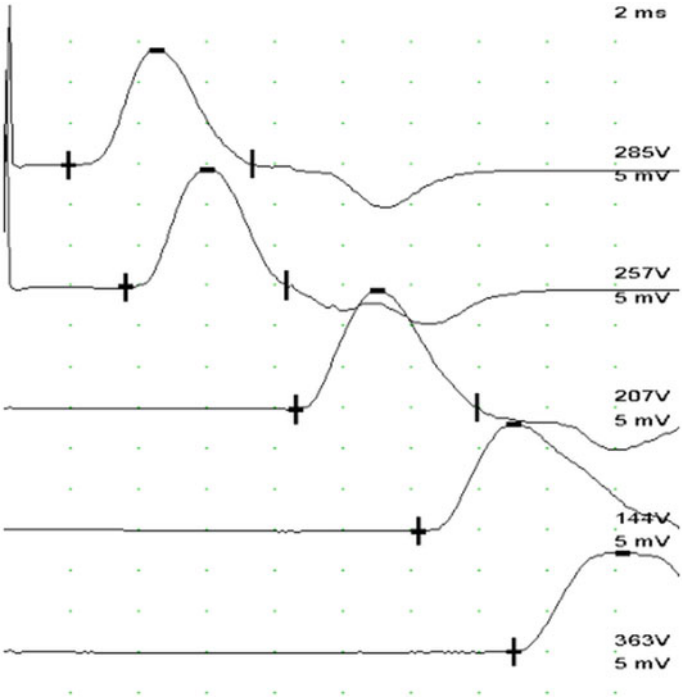

Fig. 4 Example of a nerve conduction study (NCS) [10]

While interpreting NCV, the distance between electrodes and the time it takes for electrical impulses to travel between electrodes are used to calculate the speed of impulse transmission (Fig. 4). Slower than normal speed could indicate nerve damage from direct trauma, diabetic or peripheral neuropathy, viral nerve infection or nerve entrapment diseases like the Carpal Tunnel Syndrome, among other conditions.

3.4 Neurodiagnostic Instruments

The basic neurodiagnostic instrument include data collection, display and storage. The components of these systems include electrodes, connecting wires, amplifiers, a computer control module including software, and a display and printing device. Evoked potential measurements and nerve conduction studies include additional stimulators (Fig. 5).

Electroencephalograph, electromyograph/electromyoneurograph and nerve conduction study systems have similar block diagram. The differences are in: sensitivity and number of input channels, characteristic frequencies of low-pass filters, high-pass filters, and optionally notch-filters, types and output characteristics of stimulators, amplitude and temporal resolution of analogue to digital converter, computer performance and application specific software.

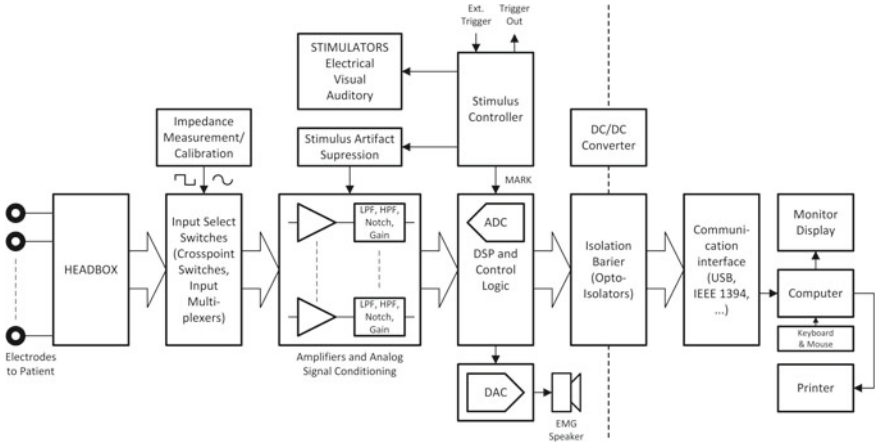

Fig. 5 Generic neurodiagnostic instrument block diagram

Headbox provides an interface between the patient electrodes and input select switches (input multiplexers, crosspoint switches) of the amplifier. Input multiplexers select the proper inputs for recording patient data, conducting an impedance test, or running a calibration procedure. Signal is then amplified by an adjustable gain amplifier to set input sensitivity range from typically 10 μV to 100 mV full scale. Amplified signal is passed through a high-pass filter (HPF) and low-pass filter (LPF). Optionally notch filter reduces amplitude of 50 Hz or 60 Hz line interference. Internally generated calibration pulse is used to check the signal path integrity from the electrode input connectors on the headbox to the host computer.

An impedance measurement circuit lets the user measure the surface electrode impedance and the integrity of the patient-to-electrode connection. Good contacts of the surface electrodes to the skin is one of the important conditions for a good signal. It is necessary to achieve both, low electrode impedance, as well as balanced

electrode impedance. Electrode impedance should be below 30 kΩ, but for good recording impedance should be below 5 kΩ and matched within 1.5 kΩ.

The electrically evoked signals are often contaminated by a stimulus artefact. Stimulus artefact suppression implemented in the amplifier may be used to help counter the effects of electrical stimulus on the measured patient signals. This feature may be applied to individual channels or may be enabled or disabled globally.

The analog-to-digital converter (ADC) converts analog signal to a series of digital samples that represent the data. These samples are processed by a digital signal processor (DSP) and transferred to the host PC via communication interface (usually USB or IEEE 1394). Information for synchronizing the data with stimulus events is placed into the data stream as well. Control and status information from the host PC to the system are exchanged along with the data via the communication interface.

EMG signal may be displayed audibly through a speaker. There are two implementations. In the first, the filtered analog patient signals are mixed and presented to an audio amplifier and speaker. In the second, the digital patient data samples are mixed and presented via an audio digital to analog converter (DAC) to an audio amplifier and speaker for listening.

Stimulators are controlled by stimulus controller (stimulus pulse generator). This block produces the signal that fires the stimuli. The stimulus pulse from this block goes to each type of stimulator. In addition, external trigger outputs along with a trigger inputs may be available for the control and monitoring of externally generated stimuli. The important role of stimulus controller is the synchronization of the stimulus delivery time (MARK) with data collection and processing. If they are present in the system, reflex hammer and footswitch may also be connected to the stimulus controller.

The most commonly used stimulators in neurodiagnostic examinations are electrical, visual and auditory stimulators.

The electrical stimulator is used to provide an electrical signal to the patient, for nerve conduction study (NCS), nerve conduction velocity (NCV), and somatosensory evoked potentials (SEP) recording. There are two types of electrical stimulation: constant current and constant voltage. The constant current amplitude typically ranges up to 100 mA. The constant current stimulator will try to maintain the selected current level, regardless of voltage required to overcome the skin impedance. If the required amplitude of the voltage is higher than the maximum allowable (maximum compliance voltage), the system displays the warning message. The constant voltage stimulator delivers a selected voltage level to the patient. The constant voltage may range up to a few hundred (300–400) volts with the maximum pulse width up to a few milliseconds.

Visual stimulators are used for visual evoked potentials (VEP) and electroretinograms recording. The two types of visual stimulators are pattern reversal in which a black and white checker board is generated (on a computer screen), and a flashing light. Reversing checkerboard pattern produces a short duration evoked response that is better defined than with flash stimuli. This stimulator is used in clinical environments for recording visual evoked potentials and electroretinograms. Flash stimulators, such as the LED goggles or a strobe light, produce a longer duration response

that is less well-defined than checkerboard stimuli, but they can elicit a visual evoked response through closed eyelids. Therefore, LED goggles are primarily used in the operating room or intensive care unit with anesthetized or otherwise unconscious patient.

The auditory stimulators are used for auditory evoked potentials (AEP) and auditory brainstem response (ABR) recording. There are two basic types of stimulation: air (using ear inserts or headphones), and bone conduction (using bone vibrator). The auditory stimulator provides a click or a tone stimulus.

The three types of click polarity are: rarefaction (the earphone diaphragm moves away from the ear), condensation (the diaphragm moves toward the ear), and alternating (the diaphragm will deliver a rarefaction stimulus and condensation stimulus every other stimulus). The variable click parameters are click rate, duration, intensity level and polarity.

The variable tone parameters are frequency and envelope shape. The envelope variables are rise/fall time and plateau time. Output level of each analog channel is adjustable in 1 dB steps up to 140 dB SPL (sound pressure level). The auditory stimulator also provides noise masking. When stimulus levels higher than 95 dB are delivered to the patient, the stimulus can travel by bone conduction to the non-test (contralateral) ear. Noise masking applied to the non-test ear prevents it from contributing to the evoked response.

The auditory transducers convert the electrical signal from the auditory stimulator to sound. Shielded or unshielded headphones, tubal inserts, and bone vibrator are used for auditory evoked potential assessment. The aural headphones and tubal inserts are used to deliver an auditory stimulus to each ear. The bone vibrator delivers an auditory stimulus through the skull, bypassing the eardrum to stimulate the cochlea.

Stimulators may be internal or external. External stimulators are independent of the computer platform and communicate with stimulus controller module via standard communication interface, usually by the AES (Audio Engineering Society) standard, a high-speed serial interface.

Although the system is fully controlled by a personal computer, some controls and indicators are available on the control panel, for example: EMG sound level and Mute switch for the EMG speaker, individual stimulus intensity levels for selected stimulation sites, and stimulator LED (blinking whenever a stim pulse is being delivered).

4 Potential Harms and Hazards Associated with the Use of the Neurodiagnostic Equipment

The main categories of harms and hazards associated with the use of electromedical devices are safety and clinical risks. Safety risks expose patients to potential injury from the equipment. Clinical risks typically relate to misdiagnosis caused by deterioration of characteristics or performance of the medical device over time.

The principles of electrical safety are of great importance in clinical neurophysiology. As with any other electromedical devices with patient applied parts, there is potential risk of electric shock. Furthermore, all of the electrophysiologic studies require the application of electrical connections to equipment that, through connections with the patient, pass small amounts of electrical current to the patient. Although small, there is always an inherent risk to the tissue through which the current passes. When more than one medical device is connected to the patient, leakage currents of the devices are summed together.

From the safety point of view, the critical parts of the neurodiagnostic instruments are those in contact with the patient. According to base safety standard IEC60601-1 [26] and particular requirements for electroencephalographs (Part 2–26), electromyographs and evoked response equipment (Part 2–40), "the applied parts of electrical stimulators, visual stimulators, auditory stimulators and biopotential input parts shall be type BF applied parts or type CF applied parts" [27, 28].

Thus, the most important aspect of device safety is to maintain an electrical isolation barrier between a subject connected to a neurodiagnostic device, and the device (typically a computer) to which the neurodiagnostic device is connected. Figure 5 shows simplified block diagram of typical multichannel amplifier with isolation barrier (opto-isolators) in digital signal path. The isolation barrier can be also implemented in an input amplifier. In both cases, a medical grade DC-DC converter is used for power supply isolation.

In addition to the issues of electrical safety of all biomedical equipment that relate to the electrical supply voltage and leakage currents, clinical neurophysiology studies such as evoked potentials, nerve conduction studies, and transcranial electrical and magnetic stimulation studies, as well as therapeutic devices such as nerve, spinal cord, cortical or deep brain stimulators, involve stimulating neural tissue with electrical currents (or strong magnetic fields), which introduces additional safety considerations related to tissue damage from stimulation and effects on nearby implanted electrical devices such as pacemakers. Besides electrical stimulators, neurodiagnostic equipment may contain visual and audio stimulator whose hazardous output may damage the visual or auditory system. Furthermore, when any part of the neurodiagnostic equipment power supply is interrupted and re-established, all stimulators (electrical, visual, and auditory) shall be disabled upon power reset, and manual intervention shall be required to re-start any stimulation.

Manufacturers of modern, computer controlled electromedical devices, have taken reasonable measures to ensure that software will remain unaffected by the presence of other, third-party software programs. However, given the vast number of software programs available, manufacturers cannot ensure complete immunity, nor can guarantee immunity against software viruses.

5 Standards and Regulations

The base standard for the medical electrical equipment is given by IEC 60601-1 from the International Electrical Commission, which comprises the General requirements for safety and essential performance. Based on this standard, but with regional deviations and adaptions, are the following standards: United States standard UL-60601-1, Canadian CAN/CSA C22.2 No. 601.1, European standard EN 60601-1, in UK known as BS EN 60601-1, Japanese JIS T 0601-1 and Australian/New Zealand AS/NZ 3200.1.0 [29].

Requirements for the basic safety and essential performance of electromyographs, electroencephalographs and nerve conduction devices are provided by two IEC standards that amend and supplement the general standard IEC 60601-1, 3.2 edition [26]: IEC 80601-2-26 Medical electrical equipment—Part 2–26: Particular requirements for the basic safety and essential performance of electroencephalographs, 1st Ed. [27], and IEC 60601-2-40 Medical electrical equipment—Part 2–40: Particular requirements for the basic safety and essential performance of electromyographs and evoked response equipment, 2nd Ed. [28].

Both particular standards refer to some collateral standards. IEC 80601-2-26 amends the clauses or subclauses of the IEC 60601-1-2 Medical electrical equipment—Part 1–2: General requirements for basic safety and essential performance—Collateral Standard: Electromagnetic disturbances—Requirements and tests [30], and the text of this particular standard is additional to the requirements of the IEC 60601-2-27 Medical electrical equipment—Part 2–27: Particular requirements for the basic safety and essential performance of electrocardiographic monitoring equipment [31]. The text of the IEC 60601-2-40 is additional to IEC 60318 (all parts), Electroacoustics—Simulators of human head and ear [32], and ISO 15004-2, Ophthalmic instruments—Fundamental requirements and test methods—Part 2: Light hazard protection [33].

In IEC 60601-2-40 special attention was given to stimulators (electrical, auditory, visual): equipment identification, marking and documents, protection against hazardous output, limitation of stimulator output parameters, and power reset behavior of stimulators (automatic re-start of electrical, visual, or auditory stimulation shall not occur) [28].

6 Post-market Surveillance

One of the more important aspects of the inspection of a medical device is the supervision of the device's functionality after it has been put on market and has reached its end user [34]. While the pre-market activities should ensure the manufacture of a functional and safe medical system, the post-market activities should guarantee that the system remains that way throughout the total product life cycle.

The same applies for neurodiagnostic systems and falls under the general post-market surveillance (PMS) guidelines provided by the International Medical Device Regulators Forum (IMDRF) [35], European Union Parliament and Council [36], and United States Food and Drug Administration [37], among others. These guidelines define processes and activities aimed at monitoring the performance and safety of medical systems and are to be conducted by the healthcare stakeholders. As a part of a global legislation of medical devices, PMS guidelines have also been adopted by the regulatory bodies and included them in their legislations [38]. These regulations require all medical device stakeholders to continuously assess a device's functionality, safety, and reliability, and to take appropriate corrective or preventative action if needed. PMS is aimed at manufacturers, physicians, and patients to report issues involving medical devices, and these reports are then used for evaluation of the device state and condition, and for decision whether any further action is required. Evaluation of the data collected from the medical devices operated in the market is crucial to protect patient safety and to guarantee the intended use of the medical systems [39].

However, there are some shortcomings in proper applications of PMS actions, which mainly stem from technological complexities and insufficient data sharing [40]. Technological management in a form of regular preventive and reactive maintenance processes must be administered according to manufacturer's specifications and international and local regulations. Also, proper technical training should be provided to the medical and technical staff which will be responsible for operating the medical device and PMS reporting. Reports should be introduced as a standard practice to connect stakeholders in proper harmonization of the PMS actions. Full disclosure on all vulnerabilities, potential harm, risks, and malfunctions should be mandatory.

To facilitate data exchange, current digital and artificial intelligence (AI) technologies can be of great help for gathering data and using it to make informed, evidence-based decisions [41–43]. Establishing a medical device database [40] which would be analysed using state-of-art algorithms can help in reducing the potential incidents and can lower the number of malfunctions of patient harm caused by human error.

In the post-market surveillance of neurodiagnostic devices, certain preventive measures can be conducted, which are described in further sections. Similar technology that is being shared among these types of devices might be a good starting point for a shared digital database made by the manufacturers. This database could contain the description of the used components, their expected life cycle, vulnerabilities, and suggested risk management actions. Also, a detailed service log could be created and shared with provided information such as:

- Event/error/malfunction
- Class of the event/error/malfunction
- Date of the event/error/malfunction
- Urgency of the event/error/malfunction
- Date of the servicing event
- Type of the servicing event: preventive/reactive

- Number of clinical/diagnostic procedures done on the system
- Expected lifetime remaining for disposable components
- User authorizations: date, number, level
- Data manipulation
- Firmware and software version.

This information can then be used for evidence-based approach to PMS with, for example, machine learning algorithms that could be used to predict the likelihood of the occurrence of the next event/error/malfunction in the future use of the equipment. An online connection of the device status and constant sharing of this type of information with the manufacturer can help both them and the end user in keeping the device safe and functioning.

7 Inspection of the Equipment

Medical device inspections are aimed to prevent device function deterioration as a potential cause of adverse events and harm to a patient. This chapter presents a particular method for inspecting medical devices with measurement functions [44–46].

The IEC 60601 outlines type-testing in laboratory conditions, but often those conditions are not available or applicable once the device is already in use. To accommodate the needs of in-service device, the standard IEC 62353 Medical electrical equipment—recurrent test and test after repair of medical electrical equipment [47] is introduced. IEC 62353 is specifically designed for testing equipment in the field. IEC 62353 requires testing before initial start-up, after repair, and periodically. The manufacturer is obligated to provide information about the testing of the device, with which the operator of the testing should carefully comply. Inspection must be performed periodically.

According to IEC 62353, the next sequence for electrical safety testing should be followed:

- Visual inspection
- Protective earth resistance
- Leakage current
- Insulation resistance
- Functional test
- Reporting of results
- Evaluation
- Check and prepare for normal use.

Manufacturers of electromedical equipment prescribe in Service Manual detailed system verification procedures, routine backup and maintenance procedures.

As an example, inspection procedure for modern computer-based neurodiagnostic instruments designed to perform electromyography (EMG), nerve conduction studies

(NCS), evoked potentials (EP) and electroencephalogram (EEG) should be as follows [10].

System inspection and cleaning

- In desktop computer systems check board seating in the expansion slots and verify the internal cables are securely connected.
- Check for excessive dust accumulation at the power supply and computer vents, and, if necessary, clean/vacuum dust from ventilation slots.
- Visually inspect external system wiring for any damaged or unseated cables, and replace any damaged cables as needed.
- Clean instrument exterior and the system accessories.
- Power on the system and verify that the ventilation fans are turning on.

Computer (Windows operating system)

- Restart the computer and verify that system boots properly.
- Verify that all devices listed in Device Manager are working properly.
- Check the Application, Security and System logs for pattern of warnings or errors.
- Check disk free space and if it is less than the specified, archive and delete the patient exam files on the hard drive. Run Check Disk and check for any error condition.
- Defragment the hard drive.

Built-in diagnostic programs allow comprehensive testing of the system's amplifier and stimulator modules. The diagnostics run in two modes:

- The Auto-Test mode runs without user interaction, and provides a short Pass/Fail report for each tested unit. When the diagnostic software detects a failure, it provides an error code to pinpoint the failure mode.
- The Manual test mode requires user interaction. Separate tests are provided for individual building blocks (for example: headbox and amplifier, control panel, auditory and electrical stimulator).
  - Manual headbox test checks signal path integrity from the headbox inputs to the host computer. Headbox integrity test and amplifier calibration test require defined calibration signal that is routed via the cable to a headbox or amplifier input. Calibration signal is often available on the dedicated base unit's connector. The software compares acquired data with expected value and if the results are within the allowable tolerances, the calibration test is passed. If a wave shape-related problem is observed, recommendation is to verify all hardware filters. The generic test for hardware filters is to run a square wave calibration pulse through all amplifier channels, and observe the effects of the filter settings on the shape of the waveform. Test starts with High-pass and Low-pass filter settings wide open. Raising the lower cut-off frequency, the waveform shape gradually changes to a form that resembles the charge/discharge current in a capacitive circuit (Fig. 6). Lowering the higher cut-off frequency, the waveform shape gradually rounds off (Fig. 6).

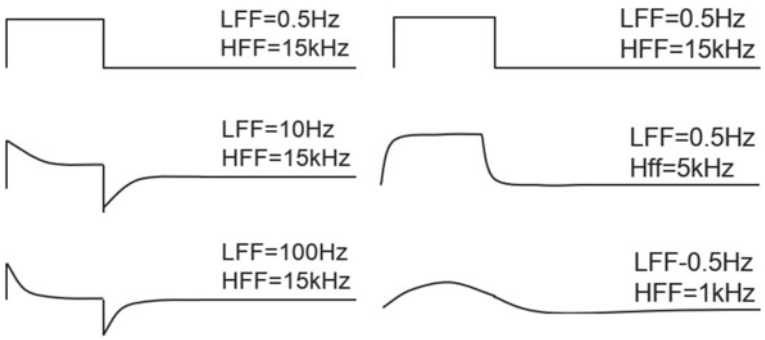

Fig. 6 Effects of lower cut-off frequency (left) and higher cut-off frequency (right) on the shape of the square wave calibration pulse [10]

- Control panel test checks for proper operation of each control panel's potentiometers.
- Auditory test require operator to verify audible click and tone burst signals from the left and right headphones.
- Electrical stimulator test checks electrical stimulus delivery and output level.

To check stimulus delivery, depending on stimulator model, operator may stimulate his or her wrist or thumb muscle, or, if applicable, short the + and − probe tips together and compare delivered current intensity with measured. If an electrical stimulator output does not follow the set value, operator may check the stimulator output using a resistive load and oscilloscope. Instrument itself may be also used as a digital oscilloscope by connecting the stimulator output to a load/attenuator test circuit (Fig. 7) and feeding the attenuated signal to system's amplifier. Using the cursors, voltage levels at the leading and trailing edges of the waveform (peak and droop points, rise/fall times) should be measured and checked for acceptable tolerances.

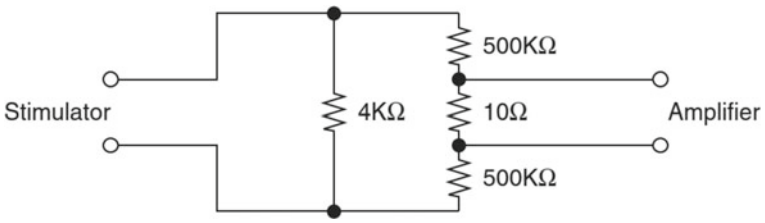

Fig. 7 Loopback test fixture [10]

Miscellaneous Functions—system may contain various functions and user interfaces required by applications. Each of these units requires a periodical inspection.

- LED goggles
  - Using the visual evoked potential (VEP) test, verify that the left and right LED arrays flash and that all LEDs in each array light up.
- Foot switch
  - Enter the test that uses foot switch (for example, nerve conduction study, NCS) and select recurrent stimulation. Press the foot switch a few times and verify that the screen message displayed at the screen switches between RUN and STOP. Assure that no contact bounce occurs.
- Reflex hammer
  - Enter the test that uses reflex hammer (for example, nerve conduction study, NCS) and set the stimulator type to Reflex hammer. Tap the reflex hammer against hand. Each tap should trigger a data sweep in the waveform screen.
- Trigger In
  - Enter the nerve conduction study (NCS) test and set the stimulator type to External. According to user manual, provide the appropriate trigger pulse to Trigger In connector. Each trigger pulse should start a data sweep in the waveform screen.
- Trigger Out
  - Trigger out signal is often a standard TTL logic level pulse. Trigger pulse can be measured using an oscilloscope, but if Trigger Out signal is being used to trigger an external stimulator, the easiest way to test the signal is to perform a functional test using the stimulator.
- EMG speaker
  - Enter the measurement of spontaneous EMG activity and set the amplifier sensitivity to 100 μV, to provide an appropriate level of background noise. Turn the Audio volume knob slowly to verify a linear increase in sound from EMG speaker.
- Electrical stimulator current or voltage compliance
  - The output voltage of the current stimulator cannot exceed a particular maximum value determined by construction of the output stage. Manufacturer specifies parameters of the current pulse and the value of the impedance

connected to the stimulator output in order to perform maximum output voltage test.
– Similarly, the output current of the voltage stimulator cannot exceed a particular maximum value. Parameters of the voltage pulse and the value of the impedance connected to the stimulator output in order to perform this test are specified by manufacturer.

Application verification tests include the steps of generating and printing a report, according to system operator or system user's guide. Common applications include, but are not limited to:

- Auditory evoked potential
- Visual evoked potential
- Somatosensory evoked potential
- Motor nerve conduction
- Sensory nerve conduction
- Spontaneous activity EMG.

Next page gives an example summary report of the inspection and testing of the neurodiagnostic medical device done with test instrumentation specifically designed for this purpose.

EXAMPLE – INSPECTION PROCEDURE REPORT

Test Summary

Status: PASSED
Date: September 20th, 2020
User: John Smith
Test protocol: Version v1.0

Tested Device

Manufacturer: Device Manufacturer
Model: Diagnostic Medical System
Serial Number: 123456
Type: EEG/EMNG/EP
Location: Healthcare Provider Facility

Test Instrumentation

Manufacturer: Instrument Manufacturer
Model: Inspection Device
Serial Number: 999999
Hardware version: v1.0
Software version: v1.0

Test Results

Element	Test Type	Pass (YES/NO)
Mains Voltage	*Mains Voltage*	*YES*
Protective Earth Resistance	*Protective Earth Resistance*	*YES (Value: 0.250 Ohm)*
Earth Leakage Current	*Earth Leakage Current*	*YES*
Patient Leakage Current	*Patient Leakage Current*	*YES*
Live to Neutral	*Mains Voltage* *Live to Neutral*	*YES (Value: 239 V)*
Normal Condition	*Earth Leakage Current* *Enclosure Leakage Current* *Normal Condition*	*YES*

Inspected by:

8 Recommendations, Contraindications, and Warnings

The older version of the book "Inspection of Medical Devices" offered insightful viewpoints on how medical device development has affected healthcare delivery, underlining the relevance of successfully managing health and resolving any issues that may occur in the process [48, 49].

Specific use of medical devices necessitates the user to provide the environment for safe operation of the instrumentation. The COVID-19 outbreak has highlighted the necessity of doing periodic inspections on medical devices with measurement functions to ensure their proper operation. These rules and guidelines range from patient surroundings to correct disposal of medical and electronic waste and are crucial to prevent safety hazards or device malfunctions [50–53]. They are described in detail in the following sections.

8.1 Patient Environment

The patient environment is the area occupied by the patient, and is defined within 2.5 m of the floor, and within 1.5 m laterally from the patient [50, 51].

Before starting the examination procedure, visual inspection should be done to ensure there is no visible impairment of the diagnostic system [50–53]:

- Inspection of physical damage of the medical device
- Inspection of the main electrical supply and connection cables
- Inspection of the patient connections and electrodes.

All patient electrodes should be connected to properly electrically isolated medical device, and not to other devices or any external outlet as it may result in patient injury. Patient should be handled without being simultaneously in contact with the metal or the earth-grounded parts of the system. Patient electrodes should not get in contact to the metal components of the system. Also, to prevent strangulation, no loose cables or electrodes should be in proximity of the patient.

The computer and other hardware (i.e. printer, video camera) that is being used inside the patient environment must be powered through isolation transformer [52], and a network isolator must be used in case the computer is connected to local network.

Simultaneous connection and use of high-frequency surgical equipment with EEG, EMNG, and EP equipment should be avoided, as there is a risk of burns at the location of the recording or stimulation electrodes.

Patient electrodes are not intended for direct cardiac use.

8.2 Electrical Warnings

All electroencephalography, electromyography, and evoked response devices should be connected to fully grounded power outlet only [50–53].

Before powering on the system unit, safety inspection should be done to detect possible damage to cables and components of the system [50, 51]. Failure of the electrical safety verification could lead to electrical shock.

Non-medical equipment which is part of the system must not be connected directly to the power outlet or to the multiple portable socket unit [50–52]. Additional hardware which is not part of the system should also not be connected to the multiple portable socket units or extension cables.

To avoid the summation of the leakage currents when all parts of the systems are connected, only devices connected to the system amplifier may be powered by the isolation transformer. The isolation transformer must have sufficient rating for all the devices connected to it [50, 51].

8.3 Electrostatic Discharge, Conducted Immunity, and Electromagnetic Interference

Certain semiconductor devices can be damaged by the electrostatic discharge. To ensure the protection from potential hazards of static electricity, all cables should be disconnected before moving the system or any of its parts. Cables should be dismantled by only touching the cable connector, and not the cable itself [50, 51]. Before handling the system components, it is advisable to drain the electrostatic charge from the body by touching a known earth ground [50, 51, 53]. Body motions, like lifting the foot from the floor or brushing the clothes together, could generate static electricity which could damage the electrostatically sensitive devices. Sensitive parts should be left in their protective packaging, usually labelled by the manufacturer if there is any static discharge risk.

Connector pins should always be aligned, as damaged cable can cause short circuits and damage the components of the system. Electrical energy from nearby electronic devices can have an effect on functions of the diagnostic system. The high sensitivity amplifiers could be affected by parasitic currents which manifests as noise or channel saturation in the waveforms, as well as values of auxiliary sensors which can be off scale.

Certain medical devices can have incorrect measurement results if they are operated with equipment that has input signals in a range of over ± 10 mV [50, 51].

To increase the conducted immunity of the diagnostic system, and to lower parasitic noise, following steps should be applied:

- All portable multiple socket outlets should be off the floor and in dry location
- Cables of the nearby equipment should be as far away as possible from the main diagnostic system

- Common power source should not be used for the medical system and nearby electronic equipment
- Main power outlet for system power supply must have a protective ground
- When using isolation transformer, diagnostic system should be fully grounded [52]
- Some systems might be affected by the neon lights, as well as noise from the main power disturbances caused by the elevators and similar high-consumption equipment. Medical systems should be installed far away as possible from these interferences.

Medical diagnostic systems should be used with specific precautions concerning electromagnetic compatibility.

Other diagnostic systems such as MRI or CT can affect normal functioning of EEG, EMNG, and EP devices which can result in false results [50, 51].

Portable radio-frequency (RF) communication equipment can disturb medical equipment and proper separation distances should be applied, depending on the frequency of the RF transmitter [50, 51, 53].

8.4 Contraindications for Use and General Warnings

Electroencephalography, electromyography, and evoked response devices must not be operated in environments and use cases providing potential health risks and damage hazards [50–53].

- Medical diagnostic system must not be used in the presence of flammable gases and flammable anaesthetics
- Medical diagnostic system must not be used in the presence of flammable anaesthetics mixture with air, oxygen, or nitrous oxide [50, 51]
- Device amplifier must not be used with defibrillator as defibrillator discharge can damage the diagnostic system [50, 51]
- User manuals should be referred for each medical device individually, when in use for patients who have implanted devices such as pacemakers, defibrillators, or vagus nerve stimulators.

All diagnostic equipment must be operated by trained personnel only, and according to its specific use [50–53]. User instructions should be followed for routine operation as well as for installation of the software and hardware components. Only original parts and accessories must be used to ensure safe and normal functioning of the system. Any component that is missing or is damaged should be replaced or serviced in accordance to the service instructions or by the authorised technicians. Modifications of the original parts of the system can cause serious safety hazards. Malfunctioning parts of the system should be serviced by authorised personnel only.

Third-party software installed on the system computer can interfere with normal functioning of the diagnostic software [50, 51] and should be used with care and

in agreement with the authorised technician. Portable storage drives and internet access should be used with caution as they can be the source of malware software. System upgrades should be done following the manufacturer instructions, or with the assistance from the manufacturer authorised personnel.

Regular cleaning and maintenance should be done with the system disconnected from the power source [50–53]. No liquid should be allowed into any part of the system. If there is a liquid spillage, the system must be immediately disconnected from the power source and not be operated until checked by an authorized technician.

8.5 Environmental Conditions, Storage, and Transport

Specific use of medical diagnostic system requires safe environmental conditions [50, 51]:

- Temperature: 10–30 °C
- Relative Humidity: 30–75%
- Atmospheric Pressure: 700–1060 hPa.

Rooms intended for the use of medical devices should be shielded by conductive material to prevent external electrical and magnetic fields to affect normal functioning of the device. Room floor should be covered with materials preventing static discharge from the physical contact of the personnel or the patient with the floor. If operated in a noisy environment, room walls should have proper sound isolation. Diagnostic systems should be stored in original packaging provided by the manufacturer, ensuring there is no risk of contact with liquid and flammable materials, or risk of falling of the system [50, 51]:

- Storage Temperature Range: −25 to 60 °C
- Storage Humidity Range: 10–95%
- 500–1060 hPa.

Transportation of the equipment should be done with great care, having health safety as a priority. Trained or authorised personnel should manipulate the system during transport, making sure all system components are sturdy and fixed. Both hands should be used when transporting the system, ensuring the wheelbase is aligned to avoid tipping hazard [50, 51].

8.6 Cleaning and Disposal

Systems and all their components should be cleaned and disinfected regularly [50–53]:

- All cables must be disconnected before wiping

- Cloth should be lint-free
- Cleaning solution should have 70% of alcohol
- Petroleum-based and acetone solutions should be avoided as these solvents might damage the system material
- LCD should not be rubbed or pressed with abrasive materials, in order to avoid scratching
- Liquid must not enter any part of the system as it may cause malfunctions
- Amplifiers are not suitable for autoclave use, pressure or gas steriliser
- Reusable electrodes and needle electrodes should be cleaned and disinfected according to the manufacturer's instructions.

When the device and its components are no longer in use, and its service life has expired, all parts and components must be disposed of according to the local laws. Printed circuit boards, metal, and plastic parts should be taken care of separately.

9 Summary

Neurodiagnostic devices inspection and use falls under standard medical devices safety regulations. Individual procedures for the acquisition of EEG, EMG, NCS, and EP signals require specific testing scenarios adjusted for the particular use throughout the total product life cycle. Biggest patient safety threat comes from the patient's contact with the medical system. Diagnostic electrodes are the first line of connection of the patient with the diagnostic system so special care should be put into maintaining electrode integrity and safety. Device housing should be properly grounded, as well as the medical cart used for the device mounting. Amplifier should be regularly inspected and its connectors should be tested for current leakages. Other than the main device unit, amplifier, and the electrodes, users of the neurodiagnostic devices should pay attention to other devices connected to the medical system, such as printers and video equipment. Manufacturer's and regulatory guidelines considering the power supply should be rigorously followed in order to prevent the risk of electrical shock. Device and patient environment should be adapted according to the recommendations for use, keeping in mind the electrostatic and magnetic influences from nearby devices, as well as cleaning and disinfection guidelines. Environmental conditions, storage, and transport recommendations help keep the device functioning, and ensure operator's safety. All healthcare stakeholders involved in the pre- and post-market use of the neurodiagnostic devices should follow the global as well as local regulations and standards. Operating of neurodiagnostic devices should always be done in accordance with the instructions from official user and service manuals to prevent patient harm or device safety hazards.

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Inspection and Testing of Defibrillators

Milan Ljubotina

Abstract Defibrillators are life-saving medical devices that require regular inspection and testing to ensure their functionality and safety. This abstract presents an overview of the inspection and testing process of defibrillators. The inspection includes checking the device's external and internal components, batteries, and electrodes. Testing involves assessing the device's energy output, waveform analysis, and battery endurance. Both inspection and testing procedures are necessary to identify any defects or malfunctions that may affect the device's performance. Regular inspection and testing of defibrillators not only helps to ensure patient safety but also improves the device's longevity and reliability. Therefore, healthcare professionals responsible for defibrillator management must follow the recommended inspection and testing guidelines to maintain the device's effectiveness and safety. In this regard, a method based on the metrological properties of defibrillators is presented for safety and performance inspection while in use.

1 Historical Overview of Defibrillators Invention and Development

Ventricular fibrillation (VF) is a heart arrhythmia caused by stimuli coming from multiple places on the heart muscle, resulting in specific effect on the heart ventricles. They are not contracting normally as they should, but only shivering, or—fibrillating. The absence of normal heart contractions causes the blood circulation to stop. The lack of blood supply to heart arteries and to brain causes death in each case, except for the ones when this lethal arrhythmia was stopped.

This lethal arrhythmia can be stopped by delivering of therapeutic dose of electric current to the heart which is in ventricular fibrillation. A current of approximately 2 A, applied directly to the heart muscle through "spoon" electrodes (used during the open-heart surgery) can be enough to stop the fibrillation effectively. The heart

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will "stop" for a very short period of time, staying in a stage without any electrical activity, an after that phase, a normal rhythm may appear.

In case that the first attempt was not successful, the next one can be repeated, with a higher current. Usually, the current is being increased in three steps, while the fourth and all subsequent trials are being performed with the highest available current.

The process described here is called defibrillation, so, the name defibrillator comes from this source. The increase of current is performed through selection of different (increasing) energy levels on the defibrillator. Increasing may be done either manually or automatically. Output current which will pass through the patient's heart will depend on different factors, including the patient's thorax impedance, which is highly individual and cannot be predicted. Therefore, a modern defibrillator must be able to adapt to different chest impedance values, in order to deliver optimal current value. The relationship between selected energy and output current will be described later in this chapter.

Ventricular fibrillation is the most common cause of cardiac arrest and sudden cardiac death (SCD). The statistics show that the occurrence of sudden cardiac arrest (SCA) in certain human population per year can be as high as 2‰. However, the probability of successful resuscitation of the patient in VF increases if the first defibrillation shock has been delivered to the patients very quickly, in the first minutes after the occurrence of VF. Therefore, the defibrillator used to resuscitate the patient must be ready and completely functional, because any malfunction or other technical issue may postpone or prevent delivery of the electrical shock to this patient. So, finally, it is the question of saving of human life, and consequently there should be zero tolerance on defibrillator technical issues or malfunctions. That is the reason why preventive maintenance and inspection of defibrillators is vitally important, as the defibrillator is a life-saving device [1].

History of the trials of scientists and physicians to resuscitate a dying person (or to establish a normal heart rhythm) by use of electricity is actually much longer than it is generally thought. The oldest recorder trial dates from the year 1774 (published in 1778). Charles Kite, an English physician developed a machine that had a capacitor to store energy, variable output and two electrodes which could be applied anywhere on the body. He applied the machine on a 3-year old girl which fell from a height and looked apparently dead. 20 min after the incident, he started applying electrostatic shocks on different parts of her body, including the chest. After while he noticed that the girl was waking up. However, even Kite suspected that the girl was in coma and not dead, so this was registered only as the first trial to resuscitate the patient with use of electricity.

The real pioneer of cardiac resuscitation with use of the electric shocks is prof. Paul Zoll, MD (1911–1999) a scientist who worked in Beth Israel Hospital in Boston, MA, USA. He was a cardiologist dedicated to work in three parallel areas at the same time; delivering of medical care to patients, scientific work through original research and teaching of students. His scientific work has created the fundaments to saving of thousands of lives every year around the world, because the defibrillators today are using the discoveries from his scientific work.

In 1950, a presentation at a meeting of the American College of Surgeons, in Boston, about stimulating the sino-atrial node via a transvenous catheter, inspired Zoll to develop a technique for pacing the heart through the intact chest during asystole. With an epochal publication in 1952 he described cardiac resuscitation via electrodes on the bare chest with 2-ms duration pulses of 100–150 V across the chest, at 60 stimuli per minute. This initial clinical description launched widespread evaluation of pacing and the recognition by the medical profession and the public that the asystolic heart could be stimulated to beat; it became the basis for future clinical pacing developments. This technique eventually fell from favor, except in an emergency, because of associated pain and the limited mobility it allowed the patient. It was later revised using larger skin electrodes and longer pulse durations, both of which made the shocks less painful and therefore more acceptable.

In 1955, Zoll described a mechanical technique for "stimulating" the asystolic heart. In 1956, he published a transcutaneous approach to terminate ventricular fibrillation with a much larger shock, of up to 750 V, and later described similar termination of ventricular tachycardia. His use of an alternating current shock began clinical cardioversion–defibrillation but eventually was replaced by direct current shock, largely for technical reasons.

From today's perspective it is almost impossible to imagine that Zoll experienced serious critics to his work after he had published the results of his scientific work. The opponents came from certain circles which were claiming that Zoll is playing God by resuscitating "dead" patients. Meaning that death was an act of God, and no man should stand against it. Fortunately, Zoll was able to justify his scientific work in a way that he discovered a way to save human lives, and that has been recognized and appreciated from that time till now [2].

From the early years of use of defibrillators, the devices have evolved, as the technology has developed. On Fig. 1, the development of defibrillators is presented through different models, throughout the years.

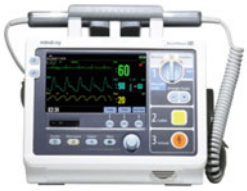
In the last three figures, the latest generation of defibrillators developed and manufactured by *Mindray Medical International Limited* is shown. Modern defibrillators incorporate new functionalities and options, like CPR feedback, or additional parameters available for vital signs monitoring. CPR feedback is important and very helpful functionality which works as guidance through the process of cardio-pulmonary resuscitation and chest compressions. A defibrillator measures frequency rate and depth of chest compressions and helps the user to perform CPR in the most effective way and according to the guidelines.

In the last row of Fig. 1 we see on the left Mindray BeneHeart D60 defibrillator with most advanced features and solutions, which represent the greatest technological step forward after the invention of biphasic defibrillation technology. On top of all well known and standard features for a prehospital defibrillator, a point-of-care ultrasound (POCUS) has been added to this device. Additional option is an infrared ear thermometer, which is wirelessly connected to the main unit.

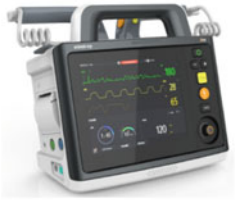
Point-of-care ultrasound has been entering pre-hospital diagnostics more and more rapidly over the last decade. However, it has always been a separate device, until this feature was added to an electronic device which is most often used in the

First portable defibrillator designed by Frank Pantridge in 1965[1]

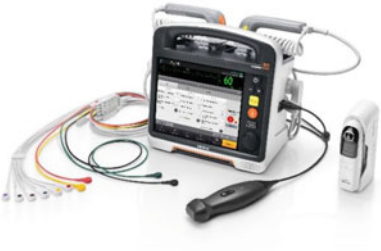
Defibrillator MRL AMB-PAK, used in 1970's[2]



Mindray BeneHeart D3 defibrillator, 2019[3]



Mindray BeneHeart D30 defibrillator, 2023[4]



Mindray BeneHeart D60 defibrillator, 2023[5]

Mindray BeneHeart DX defibrillator, 2023[6]

Fig. 1 Development of defibrillators through the years. *Source* 1, 2 National EMS Museum, http://emsmuseum.org. 3, 4 Mindray Medical International Limited, www.mindray.com. 5, 6 Mindray Medical International Limited, www.mindray.com

emergency medicine ambulance car; multi-parameter patient monitor/defibrillator/external pacemaker. Integration of POCUS functionality to this device not only helps significantly the EMS teams to make more accurate and faster diagnosis, but it also enables data transfer and storage in the integrated format. It means that ultrasound image can be easily stored and transferred together with other patient data and reports. In combination with telemedicine options it can surely bring significant benefits for patients, as well as for the medical teams who are using it.

The last figure shows Mindray BeneHeart DX defibrillator, with especially innovative concept of two detachable devices which can be used together (connected as one device), or separated, as defibrillator and vital signs monitor. This concept enables the user to work in a more flexible way, according to the needs of the patient. If only a vital signs monitor is needed during transport, then, smaller size and weight of a detached vital signs monitor represent great benefit [3].

2 Importance of Preventive Maintenance of Defibrillators

From the previous chapters it is clear that defibrillators are life-saving devices. There are other medical devices belonging to the same group (risk class), but defibrillators are specific in a way that they are used when the patient is dying. Therefore, a defibrillator must be fully functional in that moment, and there is zero tolerance on any technical issue which may postpone or prevent therapy delivery to the patient. It must work first time, every time. In order to understand the importance of proper preventive maintenance of defibrillators, we will review potential risks involved during defibrillation, for user and patient.

The earlier edition of the book "Inspection of Medical Devices" provided valuable perspectives on how the evolution of medical devices has influenced healthcare delivery, highlighting the significance of effectively managing health and addressing challenges that may arise during the process [4].

As the defibrillator is delivering a high-voltage electrical shock, it must be secured that the user or bystanders will not be exposed to that shock, or any other electrical current, coming from a device. There are precaution measures which need to be taken during the resuscitation procedure, but at the same time, the defibrillator must be free from any damages, malfunctions or technical issues which may cause that to happen [5].

American Food and Drug Administration (FDA) has an extensive database with issues caused by technical failures on all medical devices, including defibrillators, and it is publicly available on http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/Search.cfm?smc=1. Some of the cases described there have or could have caused health injury ore lethal consequences on a patient treated with such device. Here are some examples of technical issues which could have been avoided with correct preventive maintenance of defibrillators:

- The customer reported that their device would not power on.
- Device prompted "connect cable" when used on a patient with cardiac arrest. The users had charged defibrillation energy to administer a shock, but when they pushed the shock button, the device prompted to connect the cable.
- The customer reported that his device would continuously reboot on its own when it was powered on. The device may not be able to be used to deliver defibrillation energy if needed.

- The customer reported that during a patient event while monitoring the patient, the display on their device momentarily went blank, which stopped the monitoring capabilities. When the screen returned, the device appeared to be non-responsive and could not be used to continue monitoring. The customer stated that they were initially performing CPR on the patient, but defibrillation was not needed during the call as they only needed to monitor the patient for the remainder of the call. Post transport, at the arrival of the hospital, the customer indicated that they were still unable to power off the device as it was not responding to their button presses.
- The customer contacted the manufacturer to report that their device did not deliver a defibrillation shock during use on a patient. A 200 J defibrillation shock had been administered to the patient, but the hospital crew wanted to deliver a 360 J shock, the device charged defibrillation energy, but did not deliver the shock. CPR was initiated and the device then reportedly shocked without the shock button being pushed.

It has already been described that defibrillator delivers energy shocks in multiple (most often three) escalating energy levels. Each time, the energy level has been selected on the defibrillator, but the actual delivered energy will vary and in most cases will not be exactly equal to the selected value. The variation is a result of different factors, including the impedance in the entire electrical circle, where the patient impedance is the most variable part. Each defibrillator manufacturer will define acceptable tolerance of delivered energy on a certain level. For example it can be $\pm 20\%$ of the selected value.

If the delivered energy is outside that range, it may lead to failure of therapy delivery to a patient. In case that the user fails observe the problem, the consequences may be fatal. Although modern defibrillators will measure and automatically print the values of delivered energy and current, it is essentially important to include the defibrillation simulation in preventive maintenance protocol. It is done by use of defibrillator simulator/tester which will measure and display actual delivered energy on each selected energy level. The testing needs to be repeated on all energy levels available on certain defibrillator. The impedance used is typically 50 Ω, however, certain defibrillator testers will enable the user to change the impedance value, too.

Failure to deliver the shock may come from a depleted battery (in out-of-hospital resuscitation), or a faulty charging circuit which may deliver not enough or zero energy. Further in this chapter, a full protocol for defibrillator preventive maintenance will be explained. Following such protocol in each annual service process minimizes the risk of unwanted issues for user or patient [6].

3 Principles of Operation

Basic construction of a defibrillator is shown in Fig. 2.

A high voltage transformer is used to transform the voltage from 220 V to a high voltage of desired level. Further, the voltage generated that way is used to charge

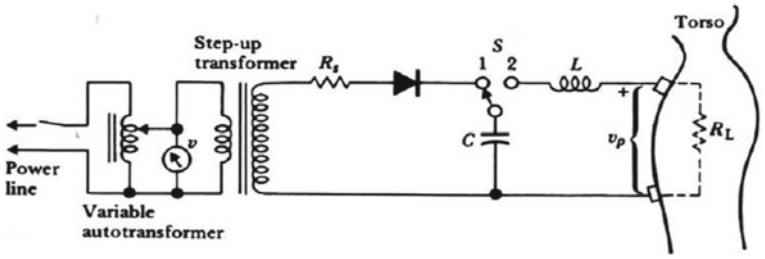


Fig. 2 Electrical diagram of defibrillator. *Source* http://z-diagram.com

a high-voltage capacitor, through the rectifier diode. Instead of single capacitor, an actual capacitor bridge is used. At this point the defibrillator has been charged.

As the "Discharge" buttons on both defibrillation paddles (electrodes attached to patient's bare chest) have been simultaneously pressed, a relay switch which is connected to the capacitor changes its position to connect the capacitor to the second electrical circuit. In that circuit, a capacitor is being discharged through the patient's chest, over the inductance. This way, the electrical impulse passes through patient's chest and heart muscle and performs defibrillation.

A defibrillator can be used also to convert other arrhythmias (like atrial fibrillation), in which the own rhythm of the heart exists, but it is not stable and can develop to a more dangerous arrhythmia, like ventricular fibrillation. In this case, it is necessary to synchronize the defibrillation shock with patient's heart rhythm.

This kind of therapy is called synchronized cardioversion.

In Fig. 3, one QRS complex from patient's ECG is shown. The defibrillator must be able to recognize the R wave, and to mark it with an arrow. The cardioversion shock must be delivered in the interval right behind that point, but prior to the inflexion point between "S" and "T" points on the ECG. The period after that point on the ECG is called vulnerable period. If the cardioversion shock would be delivered during the vulnerable period it would most likely cause a ventricular fibrillation.

In order to avoid that, a defibrillator has a circuit dedicated to enable synchronization for cardioversion. In Fig. 3 it is shown how an ECG amplifier is used to provide input for synchronization circuit. In this case, the synchronization circuit will activate the cardioversion shock delivery in a period after the synchronization marker, before the vulnerable period.

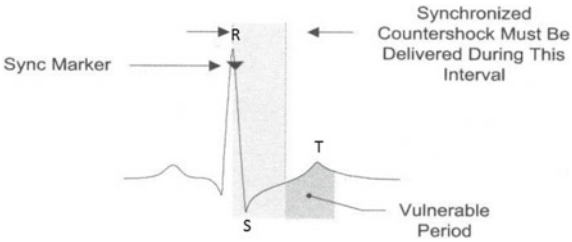


Fig. 3 Synchronization on R-wave. *Source* http://hackettgroup.org

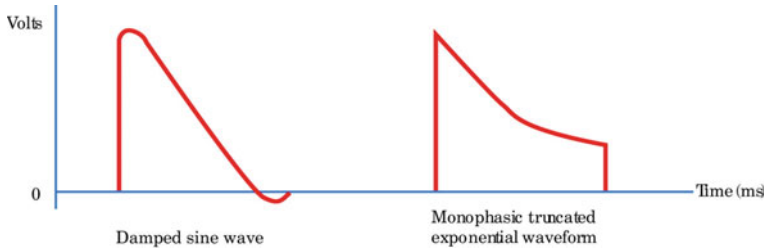


Fig. 4 Monophasic waveform. *Source* British Medical Journal, http://heart.bmj.com

The electric impulse being delivered during the defibrillation has evolved over the years. We will focus here on two most common defibrillation waveforms; monophasic (direct current) and biphasic (alternating current). For many years since their start of use, all defibrillators had monophasic technology. Biphasic defibrillators were first introduced in the late 1980s. At this point, all currently produced defibrillators are biphasic, but there are still monophasic defibrillators being used in healthcare institutions around the world. Here are the descriptions of both waveforms;

Monophasic waveforms: A type of defibrillation waveform where a shock is delivered to the heart from one vector as shown in Fig. 4. It is shown graphically as current versus time.

In this waveform, there is no ability to adjust for patient impedance, and it is generally recommended that all monophasic defibrillators deliver 360 J of energy in adult patients to insure maximum current is delivered in the face of an inability to detect patient impedance.

Biphasic waveforms: A type of defibrillation waveform where a shock is delivered to the heart via two vectors. Biphasic waveforms were initially developed for use in implantable defibrillators and have since become the standard in external defibrillators.

While all biphasic waveforms have been shown to allow termination of VF at lower current than monophasic defibrillators, there are two types of waveforms used in external defibrillators. These are shown in Fig. 5.

The upper waveform is called truncated exponential biphasic waveform, while the lower graph shows rectilinear biphasic waveform.

In order to understand the advantages of biphasic technology, we need to clear the relationship among electrical values involved in defibrillation. It has clearly been established that current defibrillates the heart. But, it can be easy overlook the importance of current in defibrillation because defibrillation settings are labelled with energy, not current. Energy is actually the product of three variables:

$$\text{Energy} = \text{Voltage} \times \text{Current} \times \text{Time}$$

The energy setting on a defibrillator corresponds to how much voltage is charged on the capacitor within the device. This correlation is not the same for every device. One manufacturer may charge 1500 V for a 200 J setting, while another may charge

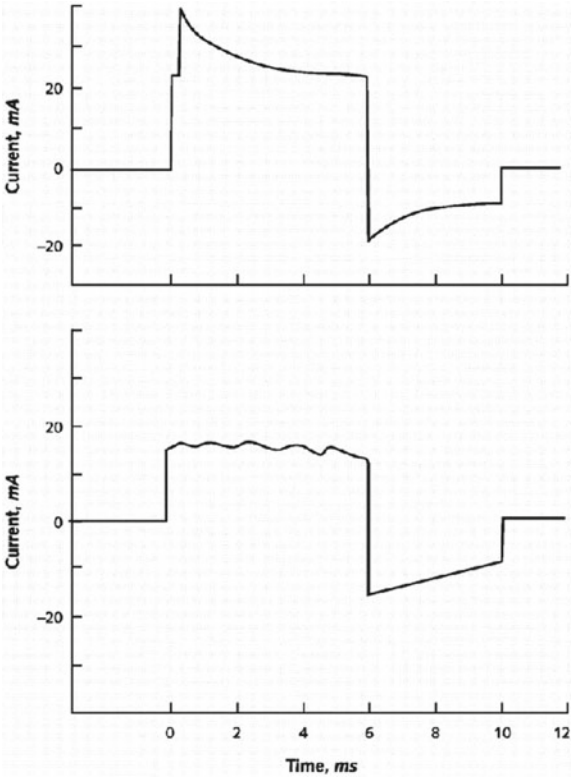


Fig. 5 Biphasic waveforms. *Source* Annals of Internal Medicine http://annals.org/)

2200 V. For this reason, comparison of energy settings between devices is no longer appropriate.

The amount of current delivered to the heart is a function of two factors: voltage and impedance. The amount of current delivered to the heart is determined by Voltage/Impedance. (This relationship is known as Ohm's Law.)

$$\text{Current} = \text{Voltage}/\text{Impedance}$$

So, for a given energy setting, the current depends on (1) the amount of voltage used for a given energy setting on a particular device, and (2) patient impedance.

It is also important to distinguish between two different types of current: average current and peak current. Peak current is the maximum amount of current seen by the heart. Too much peak current can result in electroporation (formation of aqueous pores in the cell membrane caused by a strong external electric field; the basic mechanism of tissue injury on high-voltage electric shock) of the myocardial cells, which may result in myocardial dysfunction. Average current is the mean amount of current seen by the heart over the duration of the shock. This is the component believed to be responsible for successful defibrillation (Fig. 6).

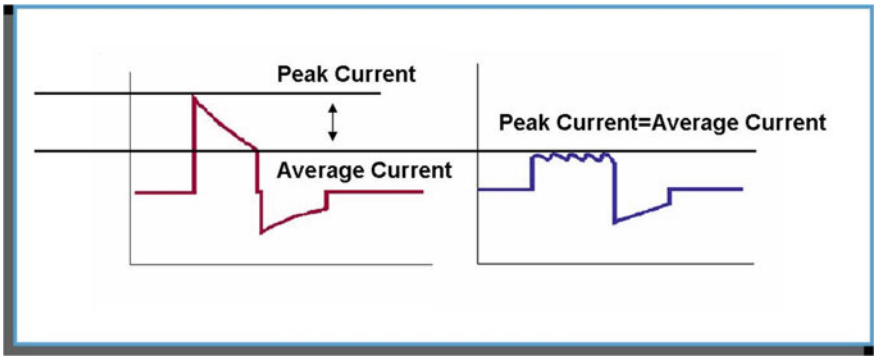


Fig. 6 Peak current and average current. *Source* ZOLL Medical Corporation, www.zoll.com

The goal of a defibrillation shock is to deliver the appropriate amount of average current while minimizing peak current. This is the reason for differences between certain biphasic waveforms, as some of them have developed over time as a result of practical experiences and scientific research.

4 Automatic External Defibrillators (AED)

The scientific research has shown that the time from SCA to defibrillation is crucial in a way that the first defibrillation shock must be delivered to the patient as soon as possible. The optimal time frame is no longer than 3–5 min. But, the chances of survival are higher as the time between SCA and defibrillation is shorter. After 5 min, the victim loses 10% of chances for survival with every minute that passes. So, the obvious question was how to assure availability of a defibrillator everywhere in the shortest time possible.

The answer to that question is an Automatic External Defibrillator (AED). An **AED** is an easy to use, safe and reliable defibrillator that automatically diagnoses ventricular fibrillation and ventricular tachycardia.

In case that either of those 2 rhythms is detected, the AED will automatically charge to an appropriate energy level, and will give a voice and text prompt to a rescuer to deliver the defibrillation shock. Alternatively, so called fully automatic defibrillators will deliver the chock without user intervention.

The most advanced AEDs have the CPR feedback functionality incorporated. Besides that, modern AEDs can communicate through Wi-Fi or GSM networks. Communication options are used to increase safety and readiness of the device for use. In case that a failure of the device occurs in the standby mode, it will communicate that information to a service center, after the first automatic self-check. After use of the AED for resuscitation, stored data will be transferred to chosen remote location, for analysis or training purposes.

Fig. 7 Automatic External Defibrillators (AEDs). *Source* Mindray Medical International Limited, www.mindray.com

Due to their simplicity of design and use (only 2–3 buttons), AEDs are designed to be simple to use for the layperson. AEDs are today widely used and deployed in places where the large groups of people gather, and therefore, the risk of SCA is higher. The most common places for AEDs installation are; public squares, airports, bus and train stations, hotels, swimming pools, beaches, sport halls, office buildings and big companies, etc.

In Fig. 7, 3 different AED models are shown.

There are several reasons why an AED may play a crucial role in resuscitation of an SCA victim; it gives a unique opportunity to a lay rescuer to give a first aid, and to use the defibrillator in a safe and effective way. Without an AED, the first defibrillation shock may be given only when the EMS team comes to the scene. In many cases the EMS cannot come the scene in 3–5 min. So, the use of the AED during the first aid (CPR) performed by the lay rescuer is a "zero step" in resuscitation process, which may be crucial to enable the professional EMS team to proceed with the following steps in resuscitation, and finally, to successfully save the life of a patient.

However, it is important to understand that a lay rescuer, in many cases, has the opportunity to use the defibrillator on the victim, maybe once in his lifetime. Also, an AED can be installed in some public place and not used in resuscitation for many years. But, in that one case, when the resuscitation really happens, the rescuer should do his/her best, and the defibrillator must be fully functional, without any technical issues.

So, the AEDs, as well as professional defibrillators require proper service and preventive maintenance in order to assure full functionality.

5 Networking and Data Management

Although basic principles of defibrillation have not been changed for decades, the biggest progress in development of the latest generation of defibrillators has been achieved in networking and data management.

There are several ways in which data from a defibrillator can be transmitted and utilized:

- Patient data stored for review and analysis
- Some defibrillators support connection to central network system, when device is being used as patient monitor only
- Defibrillators in standby mode can communicate their readiness status or technical issues via wireless network, to hospital technical department or service center
- After resuscitation, recorded data about manual CPR and entire resuscitation process can be used for training purposes
- In case that defibrillator is being used in the ambulance car, it can use telemedicine option to transmit real-time data to a teleconsultation center, where trained and experienced consultant provides support regarding decision making and therapy. One such example is shown in Fig. 8.

There are multiple benefits coming from the possibility to transmit data from EMS to hospital. Besides previously mentioned support by teleconsultation, it can be very helpful for the hospital to prepare for the patient admission if the patient data has been received in advance, during the transport in the ambulance car.

That is especially important in case that the EMS team suspects that a patient has a myocardial infarction (MI). They can send the 12-lead ECG to the hospital and the cardiologist will confirm the diagnosis. In case that it is the MI, the hospital will prepare the intervention team in catheterization laboratory, in advance, before the patient has arrived. That will be a big benefit for patient, because, the shorter time between the MI and intervention is—the better is the outcome for the patient.

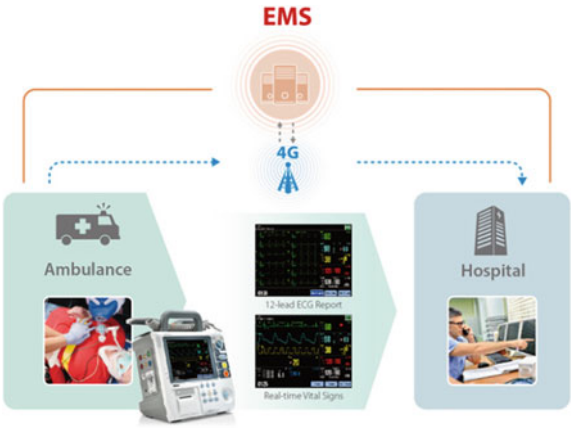


Fig. 8 Telemedicine application enables data transfer between EMS and hospital. *Source* Mindray Medical International Limited, www.mindray.com

During preventive maintenance or servicing of defibrillators, it is important for the service technician to have the complete information what IT and data transition options are being used on a particular device, in order to make sure that those functionalities are properly tested and verified. For example, telemedicine option testing may not be prescribed by the manufacturer as standard part of preventive maintenance, but it must be verified in case that this option is being used on a device.

6 A Novel Method for Conformity Assessment Testing of Defibrillators for Post-Market Surveillance Purposes

The methodology proposed for assessing the conformity of defibrillators involves several steps. Firstly, legal requirements must be established, including technical and metrological standards that the devices must meet to be considered suitable for diagnosis or therapy. After identifying these requirements, a testing method must be established that involves using calibrated reference instruments to measure the crucial parameters of the device. Finally, the results of the measurements should be presented in a report that allows for an analysis of the device's performance, leading to a conclusion about whether or not the device meets the previously established requirements.

Badnjevic et al. designed and verified a system for safety and performance monitoring while using defibrillators [7]. The technique created considers the International Organisation of Legal Metrology (OIML) strategy established for other groups of measurement-capable medical devices while in operation. This chapter provides a method for inspecting medical devices having measurement functions [8–10].

The reported method has the following coherent structure:

1. Definition of technical requirements for defibrillators,
2. Definition of metrological requirements for defibrillators,
3. Description of method for visual inspection,
4. Description of method for electrical safety inspection,
5. Description of method for performance inspection,
6. Summary and expression of test results.

The method is performed using calibrated etalons for electrical safety analysis and performance analysis.

Technical and metrological requirements are established in accordance with regulatory specifications included in directives and regulations, manufacturer technical specifications, and international standards defining the performance and safety of medical equipment [7].

6.1 Technical Requirements

It is crucial to regularly assess the technical requirements of defibrillators to guarantee their safety and reliability, both before they are sold and when they are used in medical environments. Labels and markings on the devices must be easily readable, long-lasting, and cannot be removed without causing permanent damage. The technical requirements for defibrillators are standardized and structured in a specific way.

The technical requirements refer to the:

- Label and marking
  - name and/or trademark of manufacturer;
  - production mark (basic type)
  - year of fabrication;
  - unique serial number;
  - CE mark of appropriate administrative marking;
- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz; Battery supply;
- Compliance with IEC 60601-2-4 Medical electrical equipment: Particular requirements for the basic safety and essential performance of cardiac defibrillators [11].

To ensure that all the requirements mentioned above are met, a testing method must be used. According to OIML recommendations, these requirements should be tested using a combination of visual inspection and electrical safety inspection in accordance with IEC 60601.

6.2 Metrological Requirements

The compliance of medical devices with metrological requirements can demonstrate their reliability. Metrological parameters, including error, accuracy, and uncertainty, are quantitative measures that are unique to each device and serve as evidence of its reliability. Manufacturers define specific parameters for each measurement device, such as the measurement unit, range, division, and accuracy. In accordance with the OIML guideline, the metrological requirements for a defibrillator are standardized and structured in a specific way.

- Measurement unit
  - Output energy of the measuring devices which are part of defibrillators is set and measured in Joule [J].

Joule is a derived unit of energy in the International System of Units (SI) (NIST 2019). It is equal to the energy transferred to (or work done on) an object when a force of one newton acts on that object in the direction of the force's motion through a distance of one metre (1 N-metre or N m).

- Measuring range and division
  - Output energy range: 2, 10, 30, 70, 100, 200, 270, 300, 360 J (depending on the device type):

    Monophasic (2–360) [J]
    Biphasic (2–230) [J]
    Biphasic (2–270) [J]

  - Outside this working range no energy reading and no measurement result shall be displayed.
  - Division: 1 [J], 2 [J], 5[J], 10 [J];
  - Performance accuracy stated by the manufacturer in the technical specification.

To ensure that all the requirements mentioned above are met, a testing method must be used. According to OIML recommendations, the testing of these requirements should be carried out through performance inspection, as presented in Sect. 6.3.3. of the results, and a test report should be prepared according to the same section. Through the performance inspection method, the metrological conformity assessment testing is conducted. The requirement for metrological conformity assessment testing can be formulated in accordance with OIML recommendations as follows:

- For any set of conditions within the ambient temperature range of 21–26 °C, the maximum permissible error for the measurement of the output energy is ±10%.

6.3 Method of Test

6.3.1 Visual Inspection

(a) *Equipment*

The prerequisites for performing visual inspection are:

- Device under test/Defibrillator;
- Manufacturers specification.

(b) *Procedure*

The procedure for visual inspection for a device under test consists of checking label/marking and construction integrity. The device must comply with manufacturers specification in terms of functionality and accompanying parts.

(c) *Summary and Expression of Test Results*

Table 1 Technical requirements and pass/fail criteria

No.	Criteria technical requirements	Result	Conformity assessment testing
1	Prescribed labels and markings on the device under test	• Name and/or trademark of manufacturer • Production mark (basic type) • Year of fabrication • Unique serial number • CE mark of appropriate administrative marking	Pass/Fail
2	Construction of the device	• The integrity of the device under test in respect to the manufacturer's specification • The functionality of the device under test in respect to the manufacturer's specification	Pass/Fail
3	Performance of the device	• Measurement range • Measurement unit	Pass/Fail

The results are expressed as Pass/Fail answers to the criteria which has been tested (Table 1).

6.3.2 Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

– Device under test/Defibrillator;
– Reference electrical safety testing equipment/analyser;

(b) *Procedure*

The procedure starts with connecting the defibrillator to electrical safety testing equipment. Test of the electrical safety of a device under test is performed according to the requirements of IEC 60601-1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [11]. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open neutral, normal condition—reversed mains, open neutral—reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition—reversed mains, normal condition—reversed mains, open earth—reversed mains), patient applied parts leakage current. The procedure for AED is the same as for manual defibrillators.

(c) *Summary and Expression of Test Results*

The results are expressed in terms of requirements of IEC 60601-1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [11].

6.3.3 Performance Inspection

(a) *Equipment*

The prerequisites for performance inspection are:

– Device under test/Defibrillator;
– Reference testing equipment/analyser.

(b) *Procedure*

Based on device measuring range select measuring points to cover the entire measuring range. Test the output energy in every measuring point. To test the output energy in every measuring point select on a device desired energy output level. Initiate charging of the device. Connect the defibrillator to calibrated reference testing equipment. When the device is fully charged, discharge the energy while the pedals of the defibrillator are connected to the calibrated reference testing equipment; Performance inspection of AEDs is performed in a similar manner with the only difference being the fact that AEDs do not allow for setting up the energy level. AEDs were evaluated for their performance by measuring the delivered energy at the same energy level multiple times in order to check for consistency in the delivered energy pulses.

(c) *Summary and Expression of Test Results*

The decision of conformity assessment testing is obtained after the analysis of the results of the conducted tests. The OIML recommends a summary of the results in the form of tables. As it could be seen, visual inspection is reported in the form of qualitative analysis. Simple YES/NO answers to the criteria states the conformity assessment testing. For the performance inspection, the results are expressed using terms of error. In metrology error can be expressed using absolute error or relative error. In case of defibrillators, the performance inspection result can be reported as the relative error between the indicated energy of the device under test and the corresponding readings of the calibrated reference testing equipment.

Relative error calculation:

$$\Delta X = X_{set} - X_{measured}/X_{set} * 100\,[\%] \tag{1}$$

The conformity assessment testing in performance inspection is determined by the value of this error. The allowed performance error is presented in Table 1. It was formulated based on the international standards followed during the production of the defibrillator. Based on this requirement the conformity error is formulated as follows:

- *If the error is less than the greatest allowed limit, then the device is compliant with metrological requirements.*

In the next chapter we will give an example of a regular preventive maintenance protocol for a defibrillator. The preventive maintenance process is oriented to find any technical issues, failures or discrepancies which may affect defibrillator functionality. In order to do that, several measurements need to be done on the defibrillator, using appropriate tools and testing equipment, in order to measure the **output values** on the device and to compare them with limits defined by the manufacturer. On a defibrillator, it will include safety testing (leakage currents) with electrical safety tester (earth, enclosure and patient leakage currents), as well as measurement of output defibrillator energies on all energy levels. Prior to that part a visual inspection needs to be done, and all steps need to be appropriately documented and all measured values recorded.

7 Post-market Surveillance of Defibrillators

Post-market surveillance (PMS) of medical devices (MDs) is a general name for all activities which are being performed after a medical device has been placed in medical institution and a regular use of the MD has been started. The purpose of the PMS is to ensure reliability in performance of the MD. In order to keep PMS on a constant high level, a harmonized evidence-based conformity assessment of MDs is required [12]. PMS is relying on traceability of medical device measurements and it can contribute to higher reliability of diagnosis and treatments.

Although the regulatory framework prescribes PMS of medical devices, the process itself is not harmonized with international standards. The problematic part is a traceable, evidence-based conformity assessment of MDs, which is different from one country to another.

In the European Union (EU) a Medical Device Regulation (MDR) has recently been applied. It has replaced older regulatory document, Medical Device Directive (MDD) [13]. MDR defines pre-market and PMS processes, which include: ideation, design and development phase, testing, approval and certification before the production process, production itself and PMS of medical devices. Globally, there are differences in administrative marking that indicates conformity with health, safety, and environmental protection standards, from country to country. The global digital revolution is having an influence on the field of medical device management, mandating data gathering and use in order to make informed, evidence-based decisions [14–17].

PMS is a collection of processes and activities used to monitor the performance of a medical device once it is placed in healthcare institution. The purpose is to identify quickly device design and/or usage problems and accurately characterize the device behavior in practice. We can generally say that the premarket processes are very well defined, while PMS is conducted by manufacturers or distributors, and therefore less standardized and defined.

The result is the same medical device has different performance levels in different countries, which is noticeable by the number of incidents reported. This indicates possible problems in PMS processes.

One of the ways to address this issue was forming of The Global Harmonization Task Force (GHTF). It's purpose is to discuss PMS and define conformity assessment principles for MDs. That has resulted in procedures which should be performed by manufacturers to maintain a proper function of their devices in the market. A quality management system has been established and final result should be a harmonization of currently non-harmonized processes.

Medical device registries have important role in this process, especially in countries which have an independent inspection body, in charge of performing PMS. For example, in some countries such registry contains information on 11 or 12 different groups of medical devices. The data collected in this way can be analyzed by artificial intelligence tools. This opens the potential for development of medical device registries in the future.

Performance evaluation is a key part of PMS. It can be done during the preventive maintenance, or during corrective maintenance. In the second case, there is a possibility that some damage has already been done. In order to gather true data, both manufacturers and distributors should be involved. MDR defines very precisely the roles of manufacturers and distributors in PMS. The COVID-19 pandemic has shown how crucial it is to do periodical inspections on medical devices with measuring functions to guarantee their proper operation [18].

A good example of data collected in PMS are the results published by Lejla Gurbeta Pokvić et al. in the article *Software solution for tracking inspection processes of medical devices from legal metrology system.* XIV Mediterranean Conference on Medical and Biological Engineering and Computing 2016. Germany. 2016. The authors reported that for 13.84% of tested anesthesia machines and for 14.91% of defibrillators, the device performance was not in accordance with requirements. Such device should either be removed from use or scheduled for corrective maintenance [19].

These results show how much the devices actually deviate from their reference values and how important it is to develop harmonized evidence-based methodology that will allow collection of MD performance data.

In order to reach that goal, some countries have implemented an independent authorized third party body which measures MD performance through periodic inspections. This approach has been applied in Spain, Portugal, Saudi Arabia, Republic of Serbia, Bosnia and Herzegovina, Chezch Republic, etc. Usually the following groups of MDs are being monitored: ECG devices, defibrillators, patient monitors, infant incubators, therapeutic ultrasounds, dialysis machines, anesthesia machines, mechanical ventilators, infusion pumps, perfusion pumps, high-frequency surgical units and blood pressure devices. The results of these inspections are reported in medical device registries.

That is one good example how a harmonized evidence-based conformity assessment of MDs during PMS can be reached. It is reasonable to expect that it will contribute to higher reliability of MD performance.

8 Regular Preventive Maintenance of Defibrillators

Importance of regular maintenance tests on defibrillators has been clearly described in the previous chapters. In this chapter, we will describe standard steps in a regular maintenance test.

A modern defibrillator is actually a multi-functional defibrillator-monitor unit with several optional modules. Most of the options come from the monitoring side of device. During the preventive maintenance process, all modules and functions need to be tested. Here is the list of modules which can be included in a standard defibrillator—monitor:

- Defibrillator (asynchronous / synchronous)
- External transcutaneous pacemaker (asynchronous / synchronous)
- ECG monitor (3/5 lead or 12-lead)
- SpO_2 monitor (pulse oximeter)
- NIBP monitor (non-invasive blood pressure)
- CO_2 monitor (carbon dioxide)
- IBP monitor (invasive blood pressure)
- Temperature monitor
- Memory module (data storage)
- Data communications module (serial, Bluetooth, Wi-Fi…).

In order to assure full functionality of a defibrillator all the time, it is common to define for each defibrillator two checkout procedures: the operator's shift checklist and the extensive 6-month or 12-month maintenance tests checkout procedures. Because the defibrillator must be maintained ready for immediate use, it is important for users to conduct the Operator's Shift Checklist procedure at the beginning of every shift. This procedure can be completed in a few minutes and requires no additional test equipment. Modern defibrillators have built-in self-test module which enables the operator to simulate a defibrillation on each energy level. This way, the functionality of almost all parts which are vital for sock delivery are being checked.

A qualified biomedical technician must perform a more thorough maintenance test checkout every six or twelve months to ensure that the functions of the unit work properly. This chapter describes the step by step procedures for performing such maintenance test checkout.

Preventive maintenance includes the following tests:

– Physical Inspection of the Unit
– Front Panel Buttons
– 3, 5, and 12 Leads ECG
– Leakage Current
– Paddles
– Synchronized Cardioversion
– Shock
– Pacer (External pacemaker)
– SpO_2 Monitor

– $EtCO_2$ Monitor
– NIBP Monitor
– IBP Monitor
– Temp Monitor.

Before start of preventive maintenance testing, following equipment should be prepared:

- Defibrillator Analyzer
- Safety Analyzer
- ECG Simulator; 12 Lead Simulator for 12 Lead test
- An adapter may be required to connect the device to defibrillator analyzer
- Paddles (if used)
- Printer Paper
- Battery
- AC line cord.

Further in this chapter, we will give a description of preventive maintenance testing procedure for one defibrillator-monitor. Exact procedure will vary for different manufacturers and models, but the basic steps are the same. All steps described are intended to check in details each module on the unit, to assure full functionality.

Each performed test needs to be verified in the previously prepared report (document).

Note: The protocol below represents an example of preventive maintenance test of important defibrillator modules. For testing of certain defibrillator model, please refer to original manufacturer's technical documentation, and respect exact values for measured parameters, as well as specific requirements which are result of configuration or construction.

Visual Test

Inspect the equipment for obvious signs of damage. The test is passed if the equipment has no obvious signs of damage. Follow these guidelines when inspecting the equipment:

- Carefully inspect the housing, the display screen and the buttons for physical damage.
- Inspect accessories for signs of damage.
- Inspect all external connections for loose connectors, bent pins or frayed cables.
- Inspect all connectors on the equipment for loose connectors or bent pins.
- Make sure that safety labels and data plates on the equipment are clearly legible.

Power on Test

This test is to verify that the defibrillator/monitor can power on normally. The test is passed if the defibrillator/monitor starts up by following this procedure:

1. Place the external paddles on paddle tray, insert the battery in the battery compartment, and then connect the equipment with AC mains. In this case, both the AC indicator and battery indicator shall light.
2. Turn the Mode Select knob to Monitor. Check that the equipment passes the self test and is turned on properly.
3. Check the display of technical alarm area, prompt area and battery status indicator on the upper right corner of the main screen to judge whether the equipment runs normally.

If a power-on self test error happens, the service indicator is illuminated, and alarm messages are displayed in the technical alarm area.

Manual Defibrillation Test

Test tools:

Defibrillator/pacer analyzer.

Charge/Discharge

1. Remove the batteries and connect the equipment with AC mains. Turn the Mode Select knob to Manual Defib.
2. Connect the external paddles to the equipment and place the paddles on the defibrillator/pacer analyzer.
3. Enter the Configuration-Main screen. From the Record Setup menu set [**Shock Event**] to [**On**] so that shock events can be recorded automatically if happened.
4. Set the analyzer to Energy Measurement mode. In this case, the energy value should be displayed as 0 or blank.
5. Select the energy level to 1 J.
6. Charge/discharge the equipment to verify the energies measured by the analyzer meet the following accuracy:

Selected energy (J)	Measured value (J)
1	0–3
100	85–115
360	306–414

Energy Disarming

1. Run the equipment on fully charged battery. Move the Mode Select knob to Manual Defib.
2. Connect the external paddles to the equipment and place the paddles on the defibrillator/pacer analyzer.
3. Set the analyzer to Energy Measurement mode. In this case, the energy value should be displayed as 0 or blank.
4. Select the energy level to 360 J.
5. Charge the equipment.

6. Verify that the charge tone is issued during charging.
7. Press the "Disarm" soft key to discharge the energy internally.
8. Verify that a prompt "Charge Removed" appears and the charge done tone stops.
9. Verify that the value measured by the analyzer is 0 J or blank.
10. Enter the Configuration-Main menu, select [**Manual Therapy Setup**] and set [**Time to Auto Disarm**] to [**60 s**].
11. Exit "Configuration Management". The equipment restarts automatically.
12. Set the analyzer to Energy Measurement mode. In this case, the energy value should be displayed as 0 or blank.
13. Select the energy level to 360 J.
14. Charge the equipment. Count time after charging is completed.. Verify that the prompt "Shock Removed" appears on the equipment and the energy measured by the analyzer is 0 J or blank after 60 s.
15. Use multifunctional electrode pads. Repeat steps 3 to 14.

Synchronous Defibrillation

1. Connect the external paddles and ECG cable to the equipment. Place the paddles ECG electrodes on the defibrillator/pacer analyzer.
2. Set the analyzer to Measurement Mode and output normal sinus rhythms, e.g. amplitude value 1 mV and HR 60 bpm.
3. Enter Configuration Management. In the [**Manual Therapy Setup**] menu, set [**Sync After Shock**] to [**On**].
4. Adjust the energy setting of the equipment to be 10 J.
5. Press the [**Sync On]** soft key to start synchronous defibrillation. If Remote Sync is switched on, press the [**Sync On]** soft key and select [**Local**] to start synchronous defibrillation
6. Select [Pads] or [Paddles] as the ECG source and begin charging.
7. When charging finishes, press and hold the "Shock" button to deliver a shock.
8. Verify that synchronous discharge succeeds and the delivery energy measured by the analyzer is 10 J $\pm$ 2 J.
9. Verify that the delay time of synchronous defibrillation measured by the analyzer is less than 60 ms.
10. Verify that the synchronous discharge mark appears on the R wave.
11. Verify that the prompt messages are correct during testing.
12. Select lead II as ECG source and perform charging. Repeat steps 7 to 11.
13. Use multifunctional electrode pads. Repeat steps 2 to 12.

Pacing Test

Test tools:

Defibrillator/pacer analyzer.

1. Run the equipment on fully charged battery. Move the Mode Select knob to Pacer. Set [**Pacer Mode**] to [**Fixed**].

2. Connect the pads cable to the equipment and properly place the pads on the defibrillator/pacer analyzer.
3. Set the analyzer to Pacing Measurement mode. Use test load of 50 Ω.
4. On the equipment, set [**Pacer rate**] to [**70 ppm**] and [**Pacer Output**] to [**30 mA**].
5. Press the **[Start Pacing]** soft key. Verify that the pacer rate measured by the analyzer is 70 ppm ± 1 ppm and the pacer output measured is 30 mA ± 5 mA.
6. Press the "Stop Pacing" soft key, and then set [**Pacer rate**] to [**170 ppm**] and [**Pacer Output**] to [**200 mA**].
7. Press the **[Start Pacing]** soft key. Verify that the pacer rate measured by the analyzer is 170 ppm ± 2 ppm, and the measured current is 200 mA ± 10 mA.

The testing protocol described above refers to basic functionalities of defibrillator and external pacemaker only. The protocol for testing of the patient monitor depends on the parameter configuration and is prescribed by the device manufacturer.

9 Conclusion

From all arguments written before, in this chapter, it is clearly visible that defibrillators are life-saving devices which have zero tolerance on technical issues. A failure of a defibrillator during the resuscitation may cause a fatal consequences for a patient.

The issue is especially sensitive due to the fact that the use of defibrillator is random and cannot be planned. Besides, it can easily happen that certain defibrillator (especially an AED in public use) is not used for a long period of time. But, when there is a need for a defibrillator, than it needs to be instantly fully functional, without any technical issues.

It is possible to minimize risk of an incident with unwanted consequences if users and technical service personnel follow the manufacturer's rules for daily checks and 6-months or 12-months preventive maintenance testing. The procedure described before gives an overview of main steps in preventive maintenance testing. If the manufacturer's recommendations given in the service documentation are strictly followed, it will enable successful use and lifesaving with a defibrillator over a number of years.

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Inspection and Testing of Mechanical Ventilators and Anaesthesia Machines

Baki Karaböce

Abstract Mechanical ventilators are used in intensive care units and in operating rooms. It consists of filtering, air compression, and humidifying control board units. A mechanical ventilator is a device that combines the patient's respiratory tract to assist the respiratory system in conditions where the patient has difficulty in breathing or after operations. The device supplies controlled air to the patient by the inner compressor. The breakdown of the oxygen sensor and the heating of the circuit boards (if the filter is not cleaned) are the most common problems in mechanical ventilators. They may not stabilize with required values over time and the tester is used to maintain stability. The device must be calibrated regularly or if the gauge of the test device does not match the standard values of gas flow, volume, pressure and oxygen parameters. The anaesthesia machine delivers pressurised medical gases like air, oxygen, nitrous oxide, heliox etc. and controls the gas flow individually. It composes a known and controlled gas mixture at a known flow rate and then delivers it to the gas outlet of the machine. Therefore, the fresh gas flow is serviced to the anaesthesia circle breathing system in order to make artificial respiration in the patient and monitor vital functions closely. For patient safety, the most important thing is to check out the system regularly and in pre-use and to ensure that there exists a ready and functioning alternative solution for ventilating the patient's lungs. Standards and regulations for the production and post-market surveillance of medical devices, including anaesthesia devices, have been examined. Given the lack of proposed methodology for post-market surveillance of both devices, a new validated method is introduced.

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1 Introduction

Mechanical ventilators are an important topic in the health field. During the SARS-CoV-2 pandemic, ventilators became even more important. The majority of employees have exposure to hazardous gases, vapours, dusts, or mists that require or even suggest the use of a mechanical ventilator. Some employees may be benefited by the use of a particulate mask while doing certain temporary dusty tasks.

A medical ventilator is a mechanical blower system that is designed to transport breathable air into the lungs and then air out of the lungs in order to supply breath for patients who are unable to breathe or insufficiently breathe physically. Wide ranged and certain types of ventilators cover modern ventilators that are computerized machines and simple manually operated bag valve masks. Ventilators are mainly utilized in anaesthesia machines, in intensive care medicine, emergency medicine and home care.

Mechanical ventilators are also called "respirators" which may not represent them correctly. So, ventilators and mechanical ventilators are different functions of medical devices. Ventilators are a machine for helping patients breathe. Mechanical ventilators are protective masks. They are both used to assist with breathing.

The use of mechanical ventilation starts with the various versions of the iron lung which is a type of non-invasive negative pressure ventilator. The iron lung was broadly used during the infantile paralysis epidemics in the twentieth century. The following developments were presented by John H. Emerson in 1931 and the Both respirator in 1937, after the promotion of the "Drinker respirator" in 1928 [1].

There are other types of non-invasive ventilators that are also used extensively for infantile paralysis epidemics patients. These are:

- The rocking bed
- Biphasic Cuirass Ventilation
- Positive pressure machines (somewhat simple).

In 1949, John H. Emerson developed a mechanical aid for anaesthesia with the support of the anaesthesia department at Harvard University. Then mechanical ventilators started to be used widely in anaesthesia and intensive care during the 1950s. Their development was stimulated both by the increasing use of muscle relaxants during anaesthesia and the need to treat infantile paralysis patients. Relaxant drugs paralyze the patient and improve operating conditions during surgery, but also paralyze the respiratory muscles.

The East Radcliffe and Beaver models were early examples as can be seen in Fig. 1 in the United Kingdom [2, 3].

A mechanical ventilator is designed to protect the mask/face piece, hood or helmet that is utilized to protect the patient/user against a various kinds of harmful airborne agents. OSHA's mechanical ventilator standard, 29 CFR 1910.134, requests the use of mechanical ventilators to protect workers from breathing contaminated and/or oxygen-deficient air if efficient engineering techniques and arrangements are not

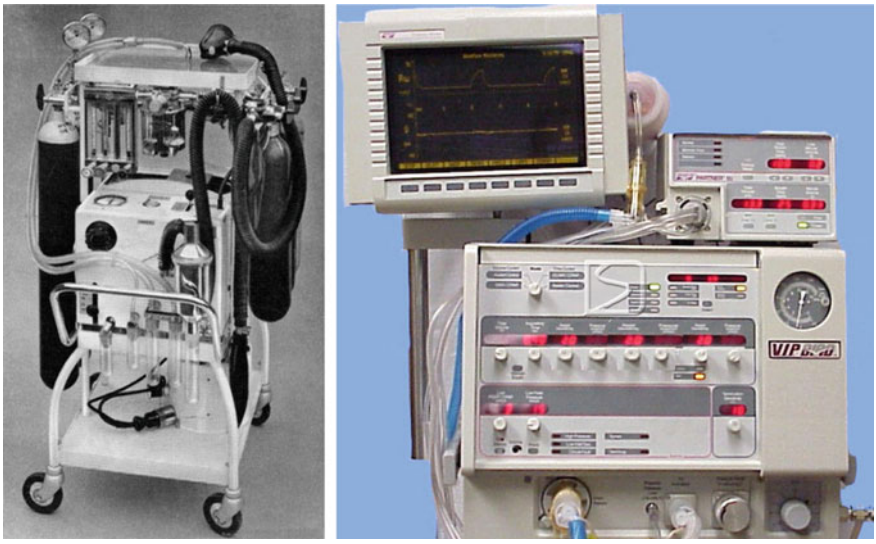

Fig. 1 From the twentieth century, an East-Radcliffe respirator model (left-) and the Bird VIP Infant ventilator (right), (*Source* https://commons.wikimedia.com)

applicable, or while they are being established [4]. Some of the other OSHA regulations also require the use of mechanical ventilators. There is a significant difference between OSHA requirements with regard to particulate masks and mechanical ventilators.

Mechanical ventilators must be chosen on the basis of risks to which the worker is subjected too (i.e., particulates, vapours, oxygen-deficiency, or a combination). OSHA also asks for the use of certified mechanical ventilators. The National Institute for Occupational Safety and Health (NIOSH) certifies mechanical ventilators.

Mechanical ventilators and anaesthesia machines are critically important medical devices that are frequently used in hospitals. Therefore, production, marketing and usage processes are regulated globally and nationally. According to international standards and the definitions and requirements set out in directives and regulations, activities related to such devices can be divided into pre-market processes and post-market surveillance (PMS). In the European Union (EU), pre-market and PMS processes [5–7] have been updated since 1992 by the Medical Device Directives (MDD) and today by the Medical Device Directive (MDR) [8–10]. All aspects from idea generation to design and development due to directives and regulations have been given in detail in [11].

Manufacturers face different challenges in activities to produce ventilators and anaesthesia machines for maintaining quality and compliance when developing products for medical use. Before being placed on the market, the conformity of the products has been evaluated by the notified bodies issued by EU countries. Similar approach is preferred all over the world. For example, in the USA, these processes are carried out by the Food and Drug Administration (FDA).

Different approaches and applications are maintained in each country in terms of ideation, design, development stage, pre-production testing, approval and certification processes of medical devices [12]. Usually, the manufacturer manages the entire process from ideation to market, while independent authorized third parties check the device for conformity and approve for commercialization and certification before it is released. Therefore, it can be said that MDs are produced in a strict process in line with international standards, approved and marked and then released to the market. There are different approaches according to each country in the application of periodic testing and calibration of medical devices.

The chronological evolution of ventilators is summarized below;

In 1952, Roger Manley produced a ventilator which was fully gas driven in Westminster Hospital, London. It was an optimal design and became the most preferred device by European anaesthetists for four decades. It has no independence for electrical power, and induces no explosion hazard.

- In 1955, the "Bird Universal Medical Respirator" was released by Forrest Bird in the United States of America. Mechanical ventilation was realized when a small green box became a well-known part of medical devices. The unit was presented as the Bird Mark 7 Respirator. It was a pneumatic device that does not require an electrical power source for operation.
- In 1971, the Elema-Schönander company released the first SERVO 900 ventilator. It was a revolutionary device around the world for intensive care environments. It was a small, low noise and effective electro mechanic ventilator. This device could supply adjusted volume for the first time.
- In 1979, the Model 500A ventilator was introduced by Sechrist Industries. It was specifically produced to use with hyperbaric rooms.
- In 1991, the SERVO 300 ventilator model was presented. The SERVO 300 series supplied a fully new and unique gas delivery system design with a fast flow-triggering response. The platform of this series enabled to treat all patient categories from neonate to adult.
- In 1999, a compact and a smaller LTV (Laptop Ventilator) model were presented into the medical market. This new design opened up an opportunity of mobility for patients with the same functionality.
- In 2001, a modular concept was introduced with the SERVO-i. It gives an advantageous that the hospital has one model of a ventilator for different user needs. It is possible to select the options/modes, software and hardware required for a particular patient category with this new modular concept.

An anaesthesia machine that delivers gases and inhalation agents has a facility for patient monitoring as well as ventilation and safety features. Safety features of the anaesthesia machine have been adopted step by step within years [13, 14].

In a survey conducted between 1962 and 1991 by ASA, 72 of 3791 malpractice lawsuits were founded to be related to gas delivery equipment within an anaesthesia machine. Death and permanent brain damage have been reported as 76% of all the claims. Improper usage of equipment and use without calibration and test were determined as 3 times more than the common failure of equipment in this survey.

Fig. 2 Old anaesthesia machines from 1920 (left), modern anaesthesia machine (right, (*Source* https://wellcomeimages.org (left)/ and (right)

Surveys indicate the necessity of regular calibration and test of devices for safety use of anaesthesia machines.

General anaesthesia was presented firstly in 1846 by WTG Morton at the Massachusetts General Hospital. Prominent improvements in methods, devices and drugs have made anaesthesia safe over the years. A British anaesthetist H.E.G Boyle, developed a new continuous flow anaesthesia machine in 1917. This anaesthesia machine was eventually patented by the British Oxygen Company as "Boyle's Machine". Several improvements in the simple machine made it easier and safer to control anaesthesia, compared to earlier methods. After significant developments of the Boyle's machine by means of convenience, functionality, mobility and safety, it's being replaced by the "anaesthesia delivery unit" which was also called the "Anaesthesia Workstation" since the 1990s as can be seen in Fig. 2.

An anaesthesia machine that delivers gases and inhalation agents has a facility for patient monitoring as well as ventilation and safety features. Safety features of anaesthesia machines have been adopted step by step within approximately a 100 years period from 1917. Improvements have been made after each problem or accident during application for medical purposes. The developments in anaesthesia machines and systems never stopped within the years by understanding the specifications and features as a point of safety standards every time.

Activities of the anaesthesia may create the risk of complications for the patients. The risks can be the operations of the surgeon and/or the collapse or malfunction of the anaesthesia device [15–18]. In the 1990s from an American report, most of the complications of anaesthesia devices were outlined as 23% death, 21% nerve injury, 9% brain damage etc. [19].

If FDA, MAUDE—Manufacturer and User Facility Device Experience database is searched with the following keywords "ventilator, continuous, facility use" as product class and "death" as event type, 163 events can be found in 2016 [20]. Those events may arise from the device and/or user.

2 The Principle for the Work of Mechanical Ventilators and Anaesthesia Machines

The principle of operation can be outlined as [21];

- an incoming gas flow lifts a weighted bellows unit,
- unit falls intermittently under gravity, and
- it forces to breathe gases into the patient's lungs.

The inflation pressure can be changed by sliding the movable mass on top of the bellows. The volume of the gas supplied is adjustable using a curved slider, which restricts the bellows tour. Residual pressure after the accomplishment of expiration is also configurable by using a small weighted arm that can be visualized on the front panel. This is a robust part and its availability encouraged the introduction of positive pressure ventilation methods into mainstream anaesthetic practice.

A modern positive pressure ventilator mainly consists of;

- a compressible air tank or turbine,
- an air and oxygen supply units,
- valves and tubes set, and
- a reusable and disposable "patient circuit".

The air tank is pneumatically compressed a few times a minute to supply air in the room, or in most conditions, an air-oxygen mixture to the patient. If a turbine is used, the turbine moves air through the ventilator, with a flow valve levelling pressure to provide patient-specific parameters. When excess pressure is released, the patient will exhale passively due to the lungs' elasticity, the exhaled air being released usually through a one way valve within the patient circuit called the patient manifold.

Ventilators may also be furnished with display and alarm systems for patient-related parameters (e.g. volume, pressure, and flow) and ventilator function (e.g., power failure, mechanical failure, and air leakage), backup batteries, oxygen reservoirs, and remote control. The pneumatic system is often replaced by a computer-controlled turbo pump nowadays [22].

Modern ventilators are automatically controlled by a small embedded system to allow precise adaptation of flow and pressure characteristics to an individual patient's requirements as seen in Fig. 3. Fine-tuned ventilator adjustments also serve to make ventilation more tolerable and comfortable for the patient [23, 24]. Respiratory therapists are responsible for tuning these settings while biomedical technologists are responsible for the maintenance in the United States and Canada.

The patient circuit is generally composed of a set of three durable, yet lightweight plastic tubes, separated by function (e.g. inhaled air, exhaled air, and patient pressure). Determined by the type of ventilation required, the patient-end of the circuit may be either invasive or non-invasive.

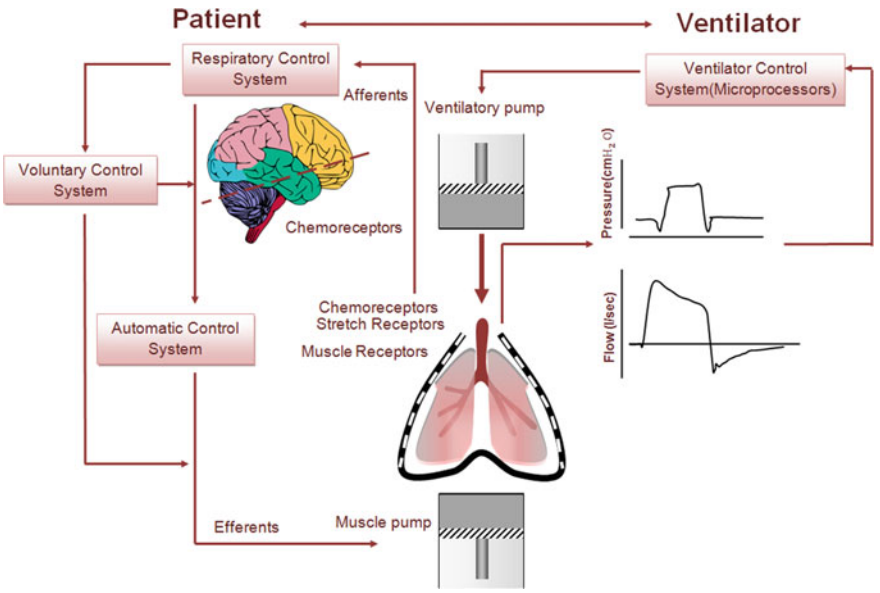

Fig. 3 Modern ventilation system

Non-invasive techniques, which are satisfactory for patients who require a ventilator only while resting and sleeping, mainly employ a nasal mask. Invasive techniques need intubation, which for long-term ventilator dependence will normally be a tracheotomy cannula, as this is much more practical and comfortable for long-term care than larynx or nasal intubation.

A basic anaesthesia machine consists of three fundamental systems;

- Gas supply and control
- Breathing and ventilation
- Scavenging.

Commonly an anaesthesia machine is the continuous flow rebreathing through an anaesthesia device. The exhaled gas from the patient (breath) is supplied back to the patient after it is processed and mixed with a ratio of fresh anaesthetic gases as seen in Fig. 4.

Normally, oxygen and nitrous oxide gases are supplied from the main system of the wall outlets as 345 kPa pressure. Oxygen flows through a check valve (one direction valve) which is reduced to about 110 kPa by the second stage oxygen regulator before it reaches the flow control valve of the oxygen flowmeter as seen in Fig. 5.

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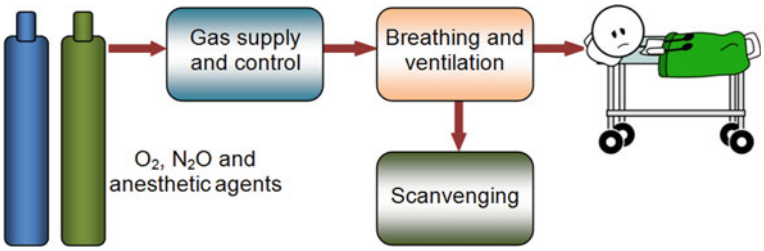

Fig. 4 Block diagram of a basic anaesthesia device

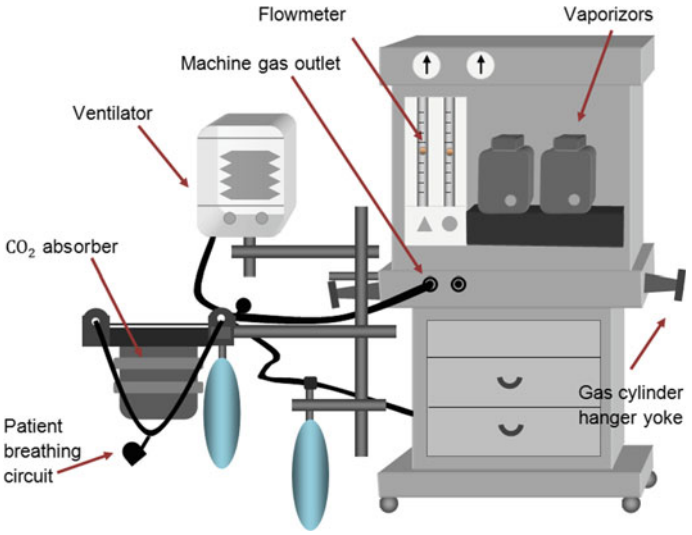

Fig. 5 Basic anaesthesia device

regulator before it reaches the flow control valve of the oxygen flowmeter as seen in Fig. 5.

Nitrous oxide gas from the wall outlet passes through the pressure sensing shutoff valve and reaches the nitrous oxide flow control valve of the nitrous oxide flowmeter. The shut off valve is kept open by the oxygen pressure that is normally at 345 kPa. If the oxygen pressure drops to below 172 kPa, the valve will shut off the nitrous oxide supply to the device. These mechanisms will protect the patient from unknown breathing in a low oxygen level gas mixture in case of supply oxygen failure [25].

Anaesthesia can be adjusted to a suitable mix and flow of oxygen and nitrous oxide gas mixtures by regulating the flow control valves.

The O_2 and N_2O gas mixtures enter the vaporizer from the inlet and split into two flow paths, one into the vaporizing chamber and the other through a bypass into a mixing chamber as seen in Fig. 6. The gas mixture flowing into the vaporizing chamber flows over a reservoir of a liquid anaesthetic agent. Then the gas meets and

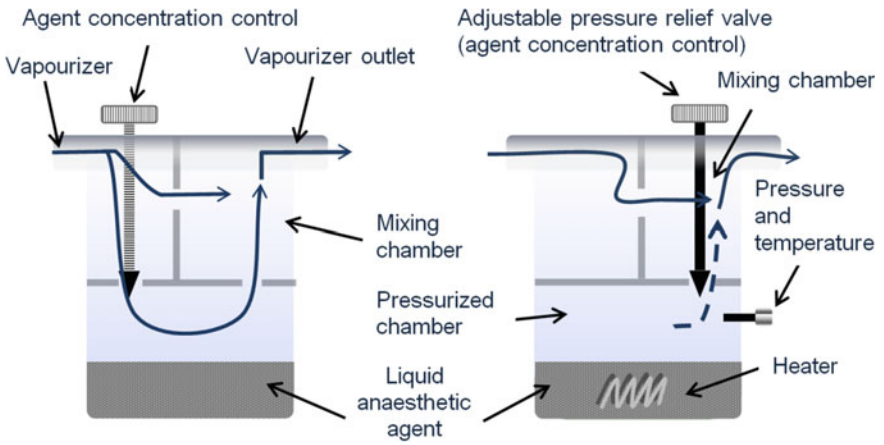

Fig. 6 Bypass variable vaporizer and electronic vaporizer

mixes with the bypassed gas and flows to the vaporizer outlet. The anaesthetic agent is pressurized into liquid state and heated inside the agent chamber in the electronic vaporizer.

The function of breathing and the ventilation subsystem of an anaesthesia system is to deliver the anaesthetic agent gas mixture to the patient. Most anaesthesia machines deliver a continuous flow of anaesthetic gas and oxygen mixture to the patient. Figure 7 shows the circle of the breathing/ventilation subsystem of an anaesthesia machine under ventilator mode. The scavenging subsystem for waste anaesthetic gas removal is also shown in the diagram.

3 Safety and Performance Tests

OSHA regulations obligate that employers who are exposed to harmful levels of hazardous gases or vapours must use mechanical ventilators and apply protocols and procedures. The following work-site for specific items needs to be addressed for a mechanical ventilator application program;

- Medical evaluations for all workers in need of use of mechanical ventilators
- Procedures for choosing mechanical ventilators for different locations
- Fit-testing procedures for tight-fitting mechanical ventilators
- Procedures for convenient mechanical ventilator use during routine check and potential emergency cases
- Procedures for cleaning, disinfecting and inspection of mechanical ventilators.

Normally, a full operational verification procedure maintained by the facility and usually based on the manufacturer's recommendations must be realized periodically. These procedures should be described in a facility's policies and procedures.

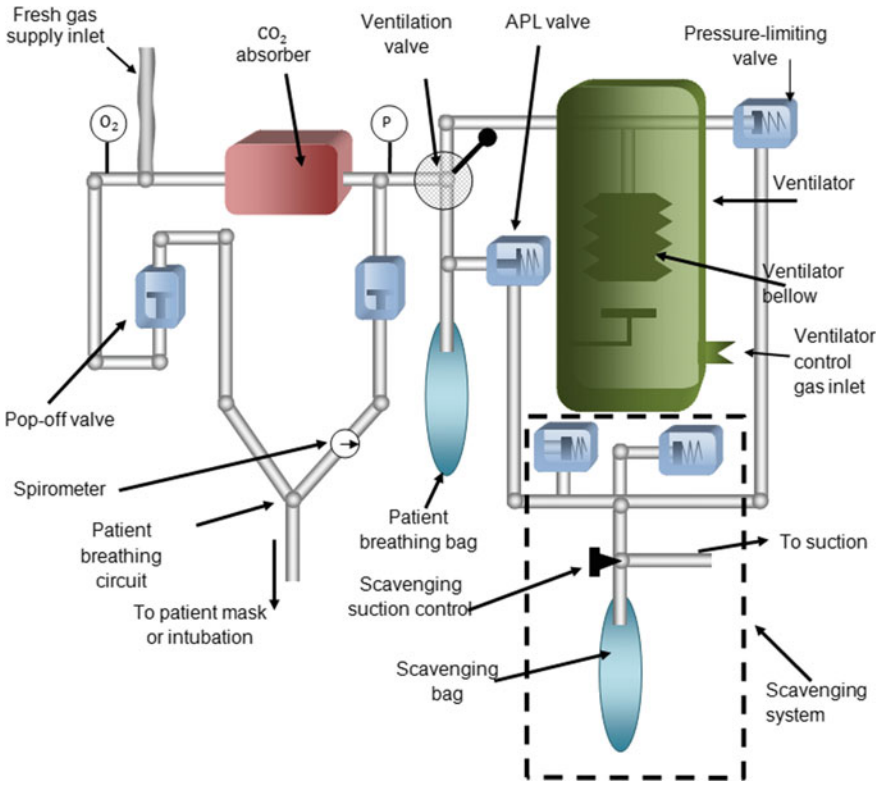

Fig. 7 Breathing/ventilation and scavenging subsystems

The quick tests that should be handled and reported in order to satisfy the safe use of a ventilator are listed below;

- The machine's battery backup and its disconnection alarms should function properly.
- Test lamps must be functioning according to the manufacturer's procedures.
- Appropriate activation of all audible and visual alarms must be tested by using a test lung.
- Proximal airway pressure gauge and positive end expiratory pressure must be controlled.
- Leak tests must be performed either as the machine allows.
- The manometer should be set to the maximum level and the high pressure alarm should activate.
- Plateau pressure should be observed when the ventilator cycles.
- Set the mode to be used for the patient. Verify the proper operation for that mode as the ventilator cycles by using a test lung.

- The number of breaths delivered during a convenient interval must be counted by using a clock.
- Exhaled volume (tidal volume, sigh volume and minute volume) must be measured by using an external device such as a Wright respirometer or equivalent to independently measure exhaled volume.
- Ventilator sensitivity level must be checked in assist mode.
- Expose the oxygen monitor (or analyzer) used with the ventilator to room air and to wall oxygen (100%), and calibrate it.
- Ensure that a high-efficiency particulate-air (HEPA) filter is present on the main inspiratory line.

Numerous international standards are available for specifying the safety features of the anaesthesia machines [26, 27]. Anaesthesia machines are covered by the ASTM (the American Society for Testing and Materials) standards. The most popular ones are;

- the ASA (the American Society of Anaesthesiologists),
- the CAS (Canadian Society of Anaesthesiologists),
- the ABZCA (Australian and New-Zealand College of Anaesthetists).

Most NGOs e.g., AAGBI (Association of Anaesthetists of Great Britain and Ireland) [28] and ASA recommend pre-anaesthesia test procedures that control the proper functioning of all the safety features incorporated in the machine.

Safety features of anaesthesia machine can be divided into the following units:

- **Gas supply unit**: In most of the new type devices, gas supply and monitoring systems can perform as high, intermediate and low-pressure systems. It must be verified from the central pipeline to the machine as well as all cylinders.
- **Flow meter unit**: The risk of oxygen loss because of the oxygen flow meter being positioned upstream from all other gases has been found in the reports. Therefore, the oxygen flow meter is always positioned downstream in a sequence of flow meters in the modern devices. If there is a loss or leakage anywhere upstream of any other gas, still oxygen will be provided in a sufficient concentration to the unit.
- **Vaporizer unit**: A number of errors from the use of vaporizer units have been investigated i.e. filling wrong agents, wrong installation leading to loss of fresh gas flow, using multiple vaporizers simultaneously and filling gas channels with a liquid agent due to inappropriate transport arrangements. All these kind of potential risks have led to addition of safety mechanisms for vaporizers as mandated by the ISO and ASTM.
- **Fresh gas delivery unit for breathing systems and ventilators**: The entire system must be checked to satisfy leak free use and correct gas selection.
- **Scavenging**: It is an ignored part in the anaesthesia machine sometimes due to cost, ignorance, lack of health safety checks etc. Scavenging systems are handled both by ASTM and international standards. Scavenging systems also incorporate

negative and positive pressure relief valves to make sure no dangerous pressures are transmitted into the breathing system in the event of malfunction of the system.

3.1 Comparison of IEC and All Other Manufacturers Testing Procedures and the Suggestion of a New One

Whenever measurements are realized, it is with the objective of generating data. The data is then processed, analysed and compared with requirements so that an appropriate decision can be taken. Reliability and accuracy of all those measurements and controls would be questionable if the devices used were not calibrated. Calibration guarantees that a measuring instrument displays an accurate and reliable value of the quantity being measured. Therefore, calibration is an indispensable action in any measurement process. A measurement must be traceable to the acceptable standard for it to be compared. A measurement result is meaningful only if it is presented with uncertainty value. Uncertainty is a measure of the quality of a measurement. It ensures the means to assess and minimise the risk and possible consequences of poor decisions.

The continuous digital revolution has an influence on the management of medical devices globally, mandating data gathering and use in order to make informed and evidence-based decisions [29–32]. International measurement community establishes documentary standards (procedures) that define how such quantities (flow, pressure etc.) are to be measured so as to provide the means for comparing the quality of goods or providing that safety and health requirements are satisfied. Therefore three elements are required in order to make a traceable measurement:

- Recognised and appropriate definition of how the quantity should be measured
- Calibrated measuring device
- Qualified and trained person who is able to evaluate the standard/procedure, and use the device systems.

The following routine controls should be carried out at the beginning of each operating session. In addition, specified controls should be carried out before each new patient during a session or when there is any change or addition to the breathing system, display or auxiliary equipment. It is the responsibility of the anaesthetist to make sure that all of these controls have been performed correctly.

- Perform machine controls given by manufacturer: Modern anaesthesia workstations may perform many of the following checks automatically during start-up.
- Power supply controls: Ensuring that the anaesthetic device and relevant auxiliary systems are connected to the main electrical supply and switched on.
- Gas supplies and suction controls: Checking that the correct function of the oxygen failure alarm covers the disconnection of the oxygen pipeline on some machines,

whilst on machines with a gas supply master switch, the alarm may be operated by switching off the main switch.

- Medical gas supplies checks: Assign and notice all gases that are being
- provided by a pipeline network, confirming with a -tug test- that each pipeline is properly and accurately inserted into the appropriate gas supply terminal.

  Check that the anaesthetic device is connected to a supply of oxygen and that a sufficient reserve supply of oxygen exists from a spare cylinder.
  Check that sufficient supplies of any other gases intended for use are provided and connected as convenient.
  Check the mechanism and operation of flowmeters, where these are present, ensuring that each control valve smoothly operates.
  Utilize the emergency oxygen bypass control and assure that flow occurs from the gas outlet without significant decrease in the pipeline supply pressure.
  Check that the suction apparatus is functioning and all connections are secure.

- Breathing system and vaporizers controls: Check all breathing mechanisms that are to be used and implement a 'two-bag test' before use, as it is described below. Perform a pressure leak test on the breathing arrangement by occluding the patient-end and compressing the reservoir pocket. Manual leak testing of vaporizers was initially recommended routinely.
- Check that the vaporizer(s) for the required volatile agent(s) are properly fitted to the anaesthetic device. A manual leak test of vaporizer must be performed. Some anaesthetic workstations will automatically test vaporizer integrity. Check the CO_2 absorber and correct gas outlet.
- Ventilator control: Check that the ventilator is configured accurately for intended use. Ensure that the ventilator tubing is securely connected. Set the controls for use and guarantee that appropriate pressure is generated during the inspiratory phase.
- Two-bag test control: A two-bag test should be applied after the vaporizers, breathing system, and ventilator have been checked individually.
- Scavenging control: Examine that the anaesthetic gas scavenging mechanism is switched on and functioning adequately. Provide that the tubing is connected to the appropriate exhaust port of the ventilator, breathing system or anaesthetic workstation.
- Monitoring equipment tests: Inspect that all monitoring devices, particularly those referred to in the AAGBI's Standards of Monitoring during Anaesthesia and Recovery guidelines, are functioning and that appropriate parameters and alarms have been adjusted before using the anaesthetic system.
- Airway equipment control: Check all bacterial filters, catheter mounts, connectors etc.

ECRI (Emergency Care Research Institute) recommends a test procedure as a complete operational verification procedure must be described in a facility's policies/procedures and applied periodically. It should usually be based on the manufacturer's recommendations as follows [33]:

- Verification of the volumetric flow rate(s),
- Checking the efficiency of the system periodically,
- Obtaining the specific information and comparing with design data,
- Setting a baseline for periodic maintenance controls,
- Principles for future installation design where satisfactory air contaminant control is currently being obtained,
- Meets regulatory or governmental requirements for particular types of processes.

3.2 Performance Testing of Ventilators and Anaesthesia Machines

Average air velocity must be measured by means of calculating $Q = V \oplus A$, where V is mean air velocity and A is average cross sectional area.

Three air pressures must be measured at any point in the exhaust system by means of calculating TP = SP + VP, where TP is total pressure, SP is static pressure and VP is velocity pressure in mmH_2O.

Devices used for measurements are the piezometer, U-tube manometer filled with oil or convenient liquid, water gauge and pressure gauge display. It should be noted that an inclined manometer yields increased accuracy and allows reading of lower velocity values.

Measurement methods include the measuring of hood static pressure by means of a U-tube manometer at one or more holes. The manometer is connected to each hole in turn by means of a thick walled soft rubber tube. The difference in height of the water columns is measured. After hood static pressure (SP_h) is known, the volumetric flow rate is determined as $Q = 4005 \oplus A \oplus C_e \oplus \sqrt{SP_{h.,}}$ where Q is flow rate in m^3/s. A is the average cross-sectional area in m^2 sqft, C_e is coefficient of entry loss and SP_h is static pressure in the hood or the duct.

In the velocity pressure and velocity of flow measurements the Pitot tube is used. This device consists of two concentric tubes. One measures the total or impact pressure existing in the air stream, while the other measures the static pressure only. The annular space and center tube are connected across a manometer. The velocity of air stream for standard conditions is determined as; VPe = VPm /df where VPe is equivalent velocity pressure, VPm is measured velocity pressure and df is density correction factor.

In air velocity measurements the rotating vane anemometer, swinging vane anemometer, thermal anemometer, smoke tubes, tracer gas method and Pitot tubes are used. Rotating vane anemometer is used to determine the air flow through large supply and exhaust openings. It is used for either pressure or suction measurements in the range of 10–15 m^3/s. Swinging Vane Anemometer is used for field measurements. It is highly portable and has a wide scale range giving instantaneous readings. Thermal Anemometer consists of a velocity sensor and temperature sensor. The amount of heat removed by an air stream passing a heated object is related to the velocity of the air stream. Tracer gas is metered continuously into one or more

intake ports along with entering air stream in the tracer gas method. Air samples are collected at some point downstream and the concentration of tracer gas in the exit stream is determined. The rate of air flow equals the rate of feed divided by tracer gas concentration.

Several international guidelines are available for anaesthesia machine check. The following protocol was developed based on the existing literature and individual practices, which involves the checking for the pneumatic, electrical, electronic and other components of the machine in a systematic manner [34, 35].

The previous version of the book "Inspection of Medical Devices" provided valuable perspectives on the impact of medical device development on healthcare delivery, emphasizing the importance of effectively managing health and addressing any challenges that may arise during the process [36].

The following recommendations are aimed at providing basic guidelines to anaesthetic practice. They are intended to provide a framework for reasonable and acceptable patient care and should be so interpreted, allowing for some degree of flexibility in different circumstances. Each section of these guidelines is subject to revision as warranted by the evolution of technology and practice.

Gas flow analyzer, ventilator test unit, artificial lung simulator and multi gas analyzer devices are used in performance tests according to EN ISO 80601 given in Tables 1 and 2.

In a study mechanical ventilators were evaluated using the inflated volume as the output parameter [37]. In ventilators, the volume can be calculated as the integration of the flow per unit time, so the test results can give information about pressure and flow. From the literature this seems like the best way to test medical ventilators because volume controlled ventilation (VCV) is the most used mode and is applicable to any type of medical ventilator available on the market [38]. If pressure-controlled ventilation (PVC) is used, the volume changes throughout the breathing cycle because it depends on the patient's airway pressure capacity and the flexibility of the alveoli (i.e., artificial lungs) used in medical ventilator testing) [39]. IMT Medical PF-301 Flow Analyser that measures the flow and the pressure, was used in the tests. In tests with reference volumes of 100 ml, 200 ml and 400 ml, about half of the devices failed [37].

3.3 Electrical Safety Testing of Ventilators and Anaesthesia Machines According to IEC 60,601 Standard

An anaesthetic machine is a continuous flow machine that is designed to provide accurate and continuous supply of medical gases (such as oxygen and nitric oxide), in mixtures with a precise concentration of anaesthetic vapour (such as isofluranyl and sevoflurane (Sevoran)), and deliver it to the patient at controlled pressure and flow.

Table 1 Mechanical ventilator performance tests

Test name	Standart no	Item no
Volume controlled breathing test	EN ISO 80601–2-12	201.12.1.101
Pressure controlled breathing test	EN ISO 80601–2-12	201.12.1.102
Oxygen concentration test	EN ISO 80601–2-12	Sub clause 201.12.1.101-b)3
	2017 ECRI INSTITUTE	Procedure No. 458–20,170,426
Inspiration pause test	EN ISO 80601–2-12	201.107.2
Maximum limited pressure protection (limit pressure) (PEAK) test	EN ISO 80601–2-12	201.12.4.105
Positive end-expiratory pressure test (PEEP)	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Mean airway pressure test (pmean)	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Peak inspiratory pressure	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Tidal volume test	EN ISO 80601–2-12	201.12.4.103
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Respiratory rate test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Inspiration time test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Expiratory time test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Occlusion alarm test	EN ISO 80601–2-12	201.12.4.108
I:E ratio test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19

Table 2 Anaesthesia machine performance tests

Test name	Standart no	Item no
Carbon dioxide test	EN 80601–2-55	201.12.4.103.1
Oxygen test	EN 80601–2-55	201.12.4.103.2
Anaesthetic agent test	EN 80601–2-55	201.12.4.103.3
Exhaled volume accuracy test	EN 80601–2-13	201.12.4.104.1
Anaesthetic respiratory system integrity alarm condition test	EN 80601–2-13	201.12.4.105
Anaesthetic respiratory system continuous positive pressure alarm condition test	EN 80601–2-13	201.12.4.106
Oxygen supply failure alarm system	EN 80601–2-13	201.12.4.107.1
Maximum limit pressure test	EN 80601–2-13	201.105.2.1
	EN ISO 80601–2-12	201.12.4.105
Inspiratory pause test	EN 80,601–2-13	201.105.7.2-f)
	EN ISO 80601–2-12	201.107.2
Positive end-expiratory pressure test (PEEP)	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Mean airway pressure test (pmean)	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Peak inspiratory pressure	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Respiratory rate test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Inspiratory time test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
Expiratory time test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19
I:E ratio test	EN ISO 80601–2-12	201.12.1.101/102-d);1),2)
	2020 ECRI INSTITUTE	Procedure No. 458–20,200,409 COVID 19

Mechanical ventilators and anaesthesia machines must be designed and constructed so that it protects against electric shock, excessive temperature, dust and water under normal operating conditions. All parts of mechanical ventilators and anaesthesia machines that are subject to normal working conditions. Corrosion must be effectively protected. This protection must not be susceptible to damage to handling. Mechanical ventilators and anaesthetic machines must have a name plate on which they are visible and printed in such a way that cannot be deleted or removed during normal use. The name plate shall contain the following elements:

- The manufacturer's name or label
- Serial number and year of production
- Type markers
- Metal type designation.

Mechanical ventilators and anaesthesia machines must undergo the procedure of type approval testing and have type approval certificates.

Mechanical ventilators and anaesthesia machines must meet the following metrological and technical requirements. The verification periods are defined by the regulations. The manufacturer must ensure that these instruments can be used under reference conditions.

Reference conditions for the mechanical ventilator are:

- Input voltage: (100–240) V AC, 50/60 Hz
- (12 - 24) V DC internal battery (when battery operated)

  Charging time: <6 h
  The battery life of the mechanical ventilator and compressor is at least 30 min
  The operation of the battery for the mechanical ventilator is maximally 7 h
  The battery life of the compressor and mechanical ventilator is maximally 2 h

- Concentration of air and oxygen volumes: (18–100) %,
- Current air pressure (if the value is entered manually).

Reference conditions for anaesthesia machines are:

- Input voltage: (100–240) V AC, 50/60 Hz
- Availability of internal rechargeable battery

  Working time is minimum 30 min

- Ambient operating conditions of the system:

  Temperature: (10–40) ° C,
  Relative humidity: (15–95) % rh

Concentrations of anaesthetic gases are:

- CO_2: (0–20) %
- NO_2: (0–100) %
- HAL, ISO, ENF: (0–12) %

- SEV: (0–15) %
- DES: (0–22) %

The measuring ranges for the mechanical ventilator and an anaesthetic machine are as follows:

- Low flow: (−60–40) L/min
- High flow: (−300–200) L/min
- Output pressure of the mechanical ventilator: (−60–140) cm H_2O
- Volume: (−1.00–4.00) L

All measurements must comply with the requirements and guidelines of the standards EN IEC 60,601–1 "General Requirements for Electrical Medical Equipment" [40].

Measurements errors cannot be more than the stated values below:

- Flow rate: ± 10% of reading
- Output pressure of the mechanical ventilator: ± 5% reading
- Volume: ± 10% of the reading
- Deviation of concentration in anaesthetic gases: ± 1% of the reading value.

Certificate of verification must be given and include;

- General, technical and other documentation related to compliance with other standards, which allows conformity of the type of measurement.
- Instructions for use which must include more information and description of the benchmarks with all its parts.
- Information and operation of the software, if the device is equipped with a microprocessor.

3.4 A Novel Method for Conformity Assessment Testing of Mechanical Ventilators and Anaesthesia Machines for Post-Market Surveillance Purposes

The methodology proposed for assessing the conformity of mechanical ventilators and anaesthesia machines involves several steps. Firstly, legal requirements must be established, including technical and metrological standards that the devices must meet to be considered suitable for diagnosis or therapy. After identifying these requirements, a testing method must be established that involves using calibrated reference instruments to measure the crucial parameters of the device. Finally, the results of the measurements should be presented in a report that allows for an analysis of the device's performance, leading to a conclusion about whether or not the device meets the previously established requirements.

The Medical Device Regulation 2017 [41] mandates post-market surveillance (PMS) of medical devices, however there is no specified process for conducting the

surveillance. As a result, there is a considerable disparity in PMS in the medical device market, and the processes for compliance evaluation are not coordinated. So, there is a clear need to develop an efficient PMS approach because there is no effective mechanism for monitoring medical devices.

The accuracy of administered oxygen and anaesthetic gas concentrations is assessed during post-market surveillance of anaesthesia equipment. The safety of anaesthesia machines for both patients and doctors, as well as their functionality and performance, must be guaranteed. Nevertheless, in addition to safety inspections PMS should concentrate on inspecting the device in terms of volume, pressure, flow, and concentration of anaesthetic gases delivered, as it is essential that the device provides a gas mixture of precisely known composition to the respiratory system. The method for assessing medical devices having a measuring function is described in this chapter [42–44].

Safety and performance inspection during usage of anaesthesia machines has been developed and validated by Badnjevic et al. [45]. The COVID-19 pandemic has highlighted how important it is to do periodical inspections on medical devices with measurement functions to ensure their proper operation [46]. The developed methodology takes into account the International Organisation of Legal Metrology (OIML) approach established for other classes of measurement-capable medical devices while in use.

In order to analyze electrical safety and performance, the approach is carried out using calibrated etalons. Technological and metrological specifications are created in compliance with regulatory requirements included in directives and laws, manufacturer technical specifications, and international standards defining the functionality and security of medical equipment.

3.4.1 Technical Requirements

Periodic verification of anaesthetic machines' technical specifications is crucial to ensuring their safety and dependability once they are sold and put to use in clinical settings. Labels and marks must be clear, readable, and permanent in order to assure the devices' traceability. They must also be impossible to remove without causing lasting harm. The technical specifications for anaesthesia machines are formalized in the following manner:

The technical requirements refer to the:

- Label and marking

  name and/or trademark of manufacturer;
  production mark (basic type)
  year of fabrication;
  unique serial number;
  CE mark of appropriate administrative marking;

- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz; Battery supply;
- Compliance with IEC 60,601–2-13: Medical electrical equipment—Part 2–13: Particular requirements for the safety and essential performance of anaesthetic systems [40].
- Concentration of anaesthetic gases:

  CO_2: 0–20%,
  NO_2: 0–100%,
  Halothane, Isoflurane, Enflurane: 0–12%,
  Sevoflurane: 0–15%,
  Desflurane: 0–22%.

A testing procedure must be used to inspect all of the requirements listed above. According to OIML recommendations, IEC 60,601-compliant visual inspection and electrical safety inspections should be used to test these kinds of criteria [40].

3.4.2 Metrological Requirements

Medical device reliability can be demonstrated by looking at how well it complies with metrological standards. Metrological characteristics, which are quantitative parameters that are unique to each device and show the reliability of the instrument, include inaccuracy, accuracy, and uncertainty. Each measurement device's manufacturer specifies some specifications, such as the measurement unit, range, division, and accuracy.

3.4.3 Method of Test

Visual Inspection

(a) *Equipment*

The prerequisites for performing visual inspection are:

– Device under test / Anaesthesia machines;
– Manufacturers specification;
– *Procedure*

The procedure for visual inspection for a device under test consists of checking label/marking and construction integrity. The device must comply with manufacturer's specification in terms of functionality and accompanying parts.

(c) *Summary and expression of test results*

Table 3 List of the permitted performance mistakes in anaesthesia machines

Technical requirements and pass/fail criteria			
No.	Criteria technical requirements	Result	Conformity assessment testing
1	Prescribed labels and markings on the device under test	• Name and/or trademark of manufacturer; • Production mark (basic type) • Year of fabrication; • Unique serial number; • CE mark of appropriate administrative marking;	Pass/fail
2	Construction of the device	• The integrity of the device under test in respect to the manufacturer's specification • The functionality of the device under test in respect to the manufacturer's specification	Pass/fail
3	Performance of the device	• Measurement range • Measurement unit	Pass/fail

The results are expressed as Pass/Fail answers to the criteria which have been tested (Table 3).

Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

– Device under test/Anaesthesia machines;
– Reference electrical safety testing equipment /analyser;
– *Procedure*

The procedure starts with connecting the anaesthesia machines to electrical safety testing equipment. Test of the electrical safety of a device under test is performed according to the requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [40]. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open neutral, normal condition—reversed mains, open neutral—reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition—reversed mains, normal condition—reversed mains, open earth—reversed mains), patient applied parts leakage current.

(c) *Summary and expression of test results*

The results are expressed in terms of requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [40].

Performance Inspection

(a) *Equipment*

The prerequisites for performance inspection are:

– Device under test/Anaesthesia machine;
– Reference testing equipment /analyser;
– *Procedure*

Performance inspection is carried out using direct comparison with the testing etalon at the measured points along the device's whole measurement range to ensure that the requirements are met. A testing etalon is necessary to carry out the performance inspection. Every anaesthesia machine must be separately ready for inspection prior to the actual examination. Hoses for oxygen, air, or any other accessible gases must be appropriately linked to either the oxygen or air bottle or the hospital's central gas system, depending on whatever the equipment is using. Etalon is used for examination and is put on a level, clean surface to ensure accurate results. The etalon is connected to the patient circuit.

To ensure the test is conducted under same conditions every time, defined parameter values are set on the device as follows:

- Inspiratory time (Ti): Expiratory time (Te) = 1:1
- Breaths per min (bpm or f) = 15 bpm
- PEEP = 5
- *Summary and expression of test results*

The choice to undertake conformity assessment testing is made following the study of the test findings. The OIML suggests presenting the results in tables as a summary. As can be seen, a qualitative analysis is used to report on visual inspection. The conformance assessment testing is stated in simple YES/NO responses to the criteria. The findings of the performance inspection are shown in terms of error. Absolute error or relative error can both be used to indicate inaccuracy in metrology. The relative error between the set values of the device under test and the corresponding readings of the calibrated reference testing apparatus can be reported as the performance inspection result for anesthesia machines.

Relative error calculation:

$$\Delta X = X_{set} - X_{measured}/X_{set} * 100 \quad (1)$$

The value of this inaccuracy determines the conformity assessment testing in performance inspection. Table 3 lists the permitted performance mistake. It was

created using the same worldwide standards that were used to create the anesthesia equipment. This requirement's basis is used to formulate the conformance error as follows:

The device complies with metrological criteria if the error is smaller than the maximum permitted limit.

All anaesthesia machines in the study were examined for the qualitative features listed below that affect their performance in addition to the quantitative testing suggested by this methodology, such as chassis integrity (technical requirements) in terms of strain reliefs, connectors, switches, displays, alarms, and batteries [46]. In addition, internal electrical power source, charging time, and instrument and control accuracy.

3.5 Post-Market Surveillance of Mechanical Ventilators

Although there is no established approach for mechanical ventilator post-market surveillance, the disparity in methodologies used globally leads to the lack of traceability of mechanical ventilator performance as well as a sizable gap in the calibre of healthcare services offered globally by mechanical ventilators [11]. A method developed and validated by Badnjević et al. [47] considers the structural integrity, vital safety features, and functionality of mechanical ventilators, as well as the volume, flow, and pressure of air provided to the patient during mechanical ventilation.

The method was developed under OIML recommendation, and the performance assessment testing of mechanical ventilators was done by using two etalons. Technical and metrological requirements are established in accordance with regulatory specifications included in directives and regulations, manufacturer technical specifications, and international standards defining the performance and safety of medical equipment.

3.5.1 Technical Requirements

Periodic evaluation of their technical specifications is crucial to ensuring the safety and dependability of mechanical ventilators after they are sold and utilized in clinical settings. Labels and marks must be clear, readable, and permanent in order to assure the devices' traceability. They must also be impossible to remove without causing lasting harm. The technical specifications for mechanical ventilators are formalized in the following way:

- Label and marking
- name and/or trademark of manufacturer;
- production mark (basic type)
- year of fabrication;
- unique serial number;

- CE mark of appropriate administrative marking;
- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz; Battery supply:
- Charging time < 6 h,
- Working time on battery for ventilator minimum 1 h and maximum 7 h,
- Working time on battery for ventilator and compressor minimum 30 min and maximum 2 h.
- Concentration of oxygen and air (18–100) %
- Compliance with IEC 60,601–2-12 Medical electrical equipment—Part 2–12: Particular requirements for the safety of lung ventilators—Critical care ventilators [40].

According to OIML recommendations, testing for these kinds of criteria should be done using IEC 60,601-compliant visual inspection and electrical safety inspection [40].

3.5.2 Metrological Requirements

Medical device reliability can be demonstrated by looking at how well it complies with metrological standards. Metrological characteristics, which are quantitative parameters that are unique to each device and show the reliability of the instrument, include inaccuracy, accuracy, and uncertainty. Each measurement device's manufacturer specifies some specifications, such as the measurement unit, range, division, and accuracy.

3.5.3 Method of Test

Visual Inspection

(a) *Equipment*

The prerequisites for performing visual inspection are:

Device under test / Mechanical ventilator;
Manufacturers specification;
Procedure

The procedure for visual inspection for a device under test consists of checking label/ marking and construction integrity. The device must comply with manufacturer's specification in terms of functionality and accompanying parts.

(c) *Summary and expression of test results*

The results are expressed as Pass/Fail answers to the criteria which has been tested (Table 3).

Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

– Device under test / Mechanical ventilator;
– Reference electrical safety testing equipment /analyser;
– *Procedure*

The mechanical ventilator is first connected to electrical safety testing apparatus to begin the process. The requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and necessary performance [40]—are followed when testing a device's electrical safety. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open neutral, normal condition—reversed mains, open neutral—reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition—reversed mains, normal condition—reversed mains, open earth—reversed mains), patient applied parts leakage current.

(c) *Summary and expression of test results*

The results are expressed in terms of requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance.

Performance Inspection

(a) *Equipment*

The prerequisites for performance inspection are:

– Device under test / Mechanical ventilator;
– Reference testing equipment /analyser;
– *Procedure*

Performance inspection is carried out using the comparative approach of direct comparison with the testing etalon at the measured points along the device's whole measurement range to ensure that the requirements are met. A testing etalon is necessary to carry out the performance inspection. Every ventilator needs to be separately ready for inspection prior to the examination itself. Hoses for oxygen, air, or any

other accessible gases must be appropriately linked to the oxygen/air bottle or the hospital's central gas system, depending on which the ventilator is using. Etalon is used for examination and is put on a level, clean surface to ensure accurate results. The etalon is connected to the patient circuit, when the device is prepared for testing, its measuring range and measurement points are established. Volume, flow, pressure, and concentration of anaesthetic gases are among the units monitored when an anaesthesia machine is inspected for performance.

The following defined parameter values are established on the device to guarantee that the test is performed under the same conditions each time:

- Inspiratory time (Ti): Expiratory time (Te) = 1:1
- Breaths per min (bpm or f) = 15 bpm
- PEEP = 5
- *Summary and expression of test results*

The choice to undertake conformity assessment testing is made following the study of the test findings. The OIML suggests presenting the results in tables as a summary. As can be seen, a qualitative analysis is used to report on visual inspection. The conformance assessment testing is stated in simple YES/NO responses to the criteria. The findings of the performance inspection are shown in terms of error. Absolute error or relative error can both be used to indicate inaccuracy in metrology. The relative error between the specified values of the device under test and the corresponding readings of the calibrated reference testing apparatus can be used to provide the performance inspection result for mechanical ventilators.

Relative error calculation:

$$\Delta X = X_{set} - X_{measured}/X_{set} * 100\,[\%] \tag{2}$$

The value of this inaccuracy determines the conformity assessment testing in performance inspection. Table 3 lists the permitted performance mistake. It was developed using the same international standards that were used to produce mechanical ventilators. This requirement's basis is used to formulate the conformance error as follows: The device complies with metrological criteria if the error is smaller than the maximum permitted limit.

4 Summary

Production and post-market surveillance of medical devices, including anaesthesia devices need certain standards and regulations. Several mechanical ventilator performance criteria are set to satisfy the physiological requirements of the worker. Filtration principles and the nature of workplace aerosols must also be understood to determine appropriate test conditions for particulate mechanical ventilator filters. A

current filter test criterion assures that significant aerosol penetration will not occur in the workplace.

As can be seen, a mechanical ventilator program is not a simple task, especially if the camp does not have the expertise to evaluate all of the influencing factors. However, it is an important task if the exposure to employees exists. It is perhaps best addressed for most by consulting the regional OSHA office or by using local, qualified vendors who can assist in the selection and fitting of mechanical ventilators as well as in establishing appropriate mechanical ventilator-related procedures and protocols.

The review highlights the fact that problems can occur despite the incorporation of several safety aspects to an anaesthesia machine. Human factors have contributed to greater complications than machine faults. Therefore, better understanding of the basics of the anaesthesia machine and checking each component of the machine for proper functioning prior to use is essential to minimise these hazards. Despite advanced technology, a remote but life-threatening possibility of intraoperative machine malfunction exists. A self-inflating bag appropriate for the patient's age and alternate O_2 source should be present as rescue measures in the event of machine malfunction.

Around the world, there are many medical device regulatory frameworks, but they have all improved recently. Almost all nations today have a set of laws in place that govern the creation of medical devices, manufacturing quality assurance, and testing for conformance before marketing. International organizations like ISO and IEC are working continuously to standardize and harmonize these procedures. Medical device traceability can be guaranteed by applying metrology concepts to the devices and tracking their performance over time. The Badnjević et al. study's findings show that when an efficient methodology, like the one described here, is used, the fraction of defective mechanical ventilators gradually reduces. This innovative method can be evaluated for future harmonization of post-market surveillance of mechanical ventilators and anaesthesia machines used in healthcare institutions all over the world, in accordance with the recommendations of international bodies in charge of standardization of methodologies.

Standards

No.	Standard
1	ISO 8185:2007: Respiratory tract humidifiers for medical use—Particular requirements for respiratory humidification systems
2	ISO 9360–1:2000: Anaesthetic and respiratory equipment—Heat and moisture exchangers (HMEs) for humidifying respired gases in humans—Part 1: HMEs for use with minimum tidal volumes of 250 ml
3	ISO 9360–2:2001: Anaesthetic and respiratory equipment—Heat and moisture exchangers (HMEs) for humidifying respired gases in humans—Part 2: HMEs for use with tracheostomized patients having minimum tidal volumes of 250 ml
4	ISO 10651–3:1997: Lung ventilators for medical use—Part 3: Particular requirements for emergency and transport ventilators

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No.	Standard
5	ISO 10651–4:2002: Lung ventilators—Part 4: Particular requirements for operator-powered resuscitators
6	ISO 10651–5:2006: Lung ventilators for medical use—Particular requirements for basic safety and essential performance—Part 5: Gas-powered emergency resuscitators
7	ISO 10651–6:2004: Lung ventilators for medical use—Particular requirements for basic safety and essential performance—Part 6: Home-care ventilatory support devices
8	ISO/TR 13,154:2009: Medical electrical equipment—Deployment, implementation and operational guidelines for identifying febrile humans using a screening thermograph
9	ISO/PRF TR 13,154: Medical electrical equipment—Deployment, implementation and operational guidelines for identifying febrile humans using a screening thermograph
10	ISO 17510:2015: Medical devices—Sleep apnoea breathing therapy—Masks and application accessories
11	ISO/FDIS 18562–1: Biocompatibility evaluation of breathing gas pathways in healthcare applications—Part 1: Evaluation and testing within a risk management process
12	ISO/FDIS 18562–2: Biocompatibility evaluation of breathing gas pathways in healthcare applications—Part 2: Tests for emissions of particulate matter
13	ISO/FDIS 18562–3: Biocompatibility evaluation of breathing gas pathways in healthcare applications—Part 3: Tests for emissions of volatile organic compounds (VOCs)
14	ISO/FDIS 18562–4: Biocompatibility evaluation of breathing gas pathways in healthcare applications—Part 4: Tests for leachables in condensate
15	ISO 18778:2005: Respiratory equipment—Infant monitors—Particular requirements
16	ISO/DIS 20789: Anaesthetic and respiratory equipment—Passive humidifiers
17	ISO 23328–1:2003: Breathing system filters for anaesthetic and respiratory use—Part 1: Salt test method to assess filtration performance
18	ISO 23328–2:2002: Breathing system filters for anaesthetic and respiratory use—Part 2: Non-filtration aspects
19	ISO 23747:2015: Anaesthetic and respiratory equipment—Peak expiratory flow meters for the assessment of pulmonary function in spontaneously breathing humans
20	ISO 26782:2009: Anaesthetic and respiratory equipment—Spirometers intended for the measurement of time forced expired volumes in humans
21	IEC/NP 60,601–2-83: Medical electrical equipment—Part 2–83: Particular requirements for the basic safety and essential performance of home light therapy equipment
22	IEC 60,601–1-8:2006: Medical electrical equipment—Part 1–8: General requirements for basic safety and essential performance—Collateral standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems
23	IEC 60,601–1-10:2007: Medical electrical equipment—Part 1–10: General requirements for basic safety and essential performance—Collateral standard: Requirements for the development of physiologic closed-loop controllers
24	IEC 60,601–1-11:2015: Medical electrical equipment—Part 1–11: General requirements for basic safety and essential performance—Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment

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No.	Standard
25	IEC 60,601–1-12:2015: Medical Electrical Equipment—Part 1–12: General requirements for basic safety and essential performance - Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the emergency medical services environment
26	IEC/CD 60,601–2-26: Medical electrical equipment—Part 2–26: Particular requirements for the basic safety and essential performance of electroencephalographs
27	IEC/DIS 60601–2-49: Medical electrical equipment—Part 2–49: Particular requirements for the basic safety and essential performance of multifunction patient monitoring equipment
28	ISO 80601–2-12:2011: Medical electrical equipment—Part 2–12: Particular requirements for basic safety and essential performance of critical care ventilators
29	ISO/CD 80,601–2-12: Medical electrical equipment—Part 2–12: Particular requirements for basic safety and essential performance of critical care ventilators
30	IEC/DIS 80601–2-30: Medical electrical equipment—Part 2–30: Particular requirements for basic safety and essential performance of automated non-invasive sphygmomanometers
31	IEC 80,601–2-30:2009: Medical electrical equipment—Part 2–30: Particular requirements for basic safety and essential performance of automated non-invasive sphygmomanometers
32	ISO/FDIS 80601–2-56: Medical electrical equipment—Part 2–56: Particular requirements for basic safety and essential performance of clinical thermometers for body temperature measurement
33	ISO 80601–2-56:2009: Medical electrical equipment—Part 2–56: Particular requirements for basic safety and essential performance of clinical thermometers for body temperature measurement
34	IEC 80,601–2-59:2008: Medical electrical equipment—Part 2–59: Particular requirements for basic safety and essential performance of screening thermographs for human febrile temperature screening
35	IEC/DIS 80601–2-59: Medical electrical equipment—Part 2–59: Particular requirements for the basic safety and essential performance of screening thermographs for human febrile temperature screening
36	ISO/DIS 80601–2-61: Medical electrical equipment—Part 2–61: Particular requirements for basic safety and essential performance of pulse oximeter equipment
37	ISO 80601–2-61:2011: Medical electrical equipment—Part 2–61: Particular requirements for basic safety and essential performance of pulse oximeter equipment
38	ISO 80601–2-67:2014: Medical electrical equipment—Part 2–67: Particular requirements for basic safety and essential performance of oxygen-conserving equipment
39	ISO 80601–2-69:2014: Medical electrical equipment—Part 2–69: Particular requirements for basic safety and essential performance of oxygen concentrator equipment
40	ISO 80601–2-70:2015: Medical electrical equipment—Part 2–70: Particular requirements for basic safety and essential performance of sleep apnoea breathing therapy equipment
41	IEC 80,601–2-71:2015:Medical electrical equipment—Part 2–71: Particular requirements for the basic safety and essential performance of functional Near-Infrared Spectroscopy (NIRS) equipment

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No.	Standard
42	ISO 80601–2-72:2015: Medical electrical equipment—Part 2–72: Particular requirements for basic safety and essential performance of home healthcare environment ventilators for ventilator-dependent patients
43	ISO/DIS 80601–2-74: Medical electrical equipment—Part 2–74: Particular requirements for basic safety and essential performance of respiratory humidifying equipment
44	ISO/CD 80,601–2-79: Medical electrical equipment—Part 2–79: Particular requirements for basic safety and essential performance of home healthcare environment ventilatory support equipment for respiratory impairment
45	ISO/CD 80,601–2-80: Medical electrical equipment—Part 2–80: Particular requirements for basic safety and essential performance of home healthcare environment ventilatory support equipment for respiratory insufficiency
46	ISO 81060–1:2007: Non-invasive sphygmomanometers—Part 1: Requirements and test methods for non-automated measurement type
47	ISO 81060–2:2013: Non-invasive sphygmomanometers—Part 2: Clinical investigation of automated measurement type
48	ISO/NP 81,060–3: Non-invasive sphygmomanometers—Part 3: Clinical investigation of continuous automated measurement type
49	ISO 5362:2006: Anaesthetic reservoir bags
50	ISO 8185:2007: Respiratory tract humidifiers for medical use—Particular requirements for respiratory humidification systems
51	ISO 9360–1:2000: Anaesthetic and respiratory equipment—Heat and moisture exchangers (HMEs) for humidifying respired gases in humans—Part 1: HMEs for use with minimum tidal volumes of 250 ml
52	ISO 23328–2:2002: Breathing system filters for anaesthetic and respiratory use—Part 2: Non-filtration aspects
53	ISO 4135:2001: Anaesthetic and respiratory equipment—Vocabulary
54	ISO 5367:2014: Anaesthetic and respiratory equipment—Breathing sets and connectors

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Inspection and Testing of Dialysis Machines

Dušanka Bošković

Abstract Dialysis machines act as artificial kidney performing extracorporeal blood purification to remove excess water, detoxify the blood and balance the blood composition. The chapter presents development of dialysis from experiments to regular life-saving clinical practice, leading to modern dialysis machine organization and functionality. Function deterioration of a hemodialysis device, as a potential harm for a patient safety, is discussed. Further on, overview of standards related to hemodialysis machines safety and risk management is presented. The chapter ends with a description of a method that relies on the metrological properties of the dialysis machine as a way of assessing safety and efficiency during the use of the machine.

1 Introduction

The dialysis machine is a therapeutic device aimed to provide hemodialysis treatment for patients with renal failure. End-stage kidney disease is among leading causes of morbidity and mortality worldwide, and prevalence of the disease followed with the use of renal replacement therapy (RRT) are expected to rise sharply in the next decade [1]. Kidney disease produces a major effect on global health, not only as a direct cause of global morbidity and mortality, but also as an important risk factor for cardiovascular diseases. [2]

Dialysis machines have a central role as RRT for the majority of patients, because pre-emptive transplantation as an initial modality is not freely available [3]. More than 2.5 million people in the world are receiving the treatment either with dialysis or a kidney transplant, with estimations that this number will rise to 5.4 million people by 2030 [4]. It is also estimated that in many countries, due to a shortage of renal replacement services, 2.3–7.1 million patients have died prematurely from lack of access to the treatment [4].

Hemodialysis is the most commonly used as RRT [5]. In the course of the hemodialysis the blood is taken from the shunt between the veins and arteries of

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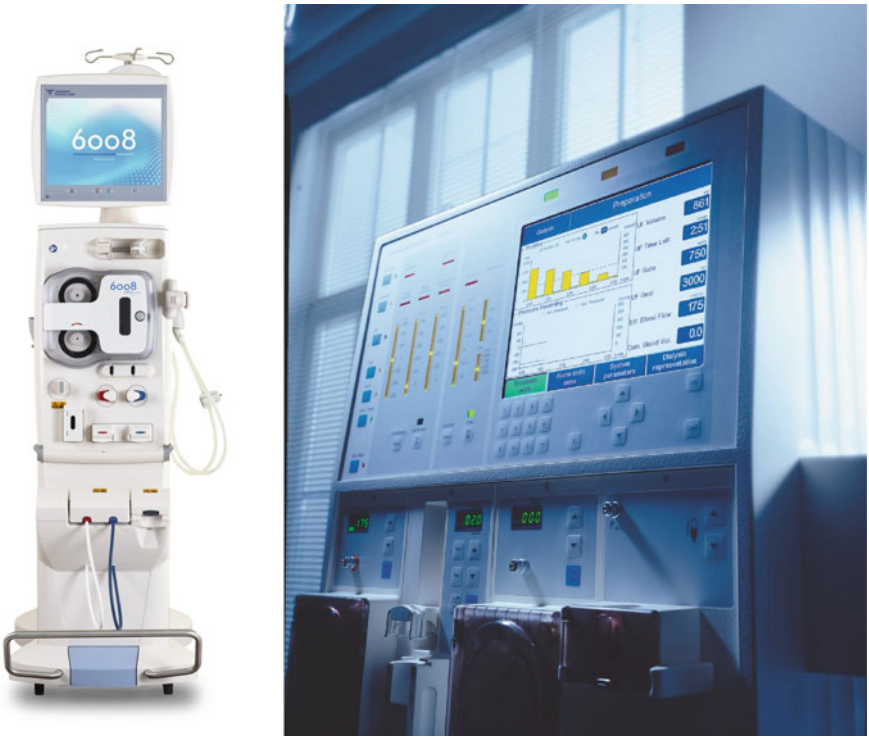

Fig. 1 Hemodialysis 6008 machine (**a**) and online clearance monitor for the 4008H/S (**b**) courtesy fresenius medical care

the patient forearm. The blood is circulated into the dialyzer for excess water and uremic toxins removal; and returned to the patient. Hemodialysis parameters as flow, temperature, blood pressure, blood leaks, etc. are monitored and controlled during the treatment. The developments in design and construction of dialysis machines lead to contemporary devices (Fig. 1) equipped with controls, monitors, and alarms that provide for safe proportioning of dialysate.

2 History of Hemodialysis

The process of dialysis is based on principles of osmosis and diffusion. Thomas Graham (1805–1869), a chemist at the Glasgow University, conducted experiments on separating substances using a semi-permeable membrane made of bladders. Graham described the process in 1854 in his paper "Bakerian lecture on osmotic forces" [6]. He noticed the importance of controlling the rates of transfer through the membrane for successful removal of toxins from the blood, and repeated his experiments with different solutes to measure and compare the rates. Graham was the first

to use parchment membrane, what he described in paper published in 1861 and he was the first to apply the term dialysis "*to the method of separation by diffusion through a septum of a gelatinous matter*" [7].

In 1855 Adolf Fick (1829–1901) provided mathematical description for selective transport processes through a semipermeable membrane caused by concentration gradients [8]. The description would became known as Fick's laws of diffusion. After Fick, who was the first to use collodion membranes, Schumacher in 1860 obtained excellent results with the skins from collodion, and afterwards with collodion tubes [9]. It was not until 1921 that Arnold Eggerth described standardized process for preparation of collodion membranes with controlled difference in water permeability [10].

The first dialysis device was developed in 1914 at Johns Hopkins University School of Medicine by John Abel (1857–1938) and his colleagues, and they named the device "artificial kidney" [9]. Their device used collodion tubes similar to present day hollow fiber dialyzers and was not used on humans, only for experiments on animals. The first hemodialysis device used to treat human patient was performed by George Haas in 1924 [11]. He developed a glass cylinder dialyzer with collodion tubes, and the first treatment lasted for 15 min. Hass performed several hemodialysis procedures in the following years and reported first clinical results. In his work for producing collodion membranes he followed the standards and procedures described by Eggerth [11].

The pioneer of artificial organs, Willem Kolff (1911–2009) from Netherlands, built in 1943 the rotating drum hemodialysis device using cellophane membranes. Kolff was treating patients with the acute renal failure in the following years, and after the series of unsuccessful treatments, in 1945 his hemodialysis treatment saved a patient's life. Kolff continued his work in the USA and he was influential in developing hemodialysis from experimental into standard clinical therapy.

In 1947 Swedish scientist Nils Alwill (1904–1986) described his apparatus for dialysis with improved function for removal of excess water, based on combination of dialysis and ultrafiltration. Alwill was using cellophane membrane with tight fitting container enabling better control of extracorporeal blood volume [11].

Hemodialysis was not seen as a solution for end-stage chronic renal failure, since dialysis treatment damaged patients' veins and arteries. Typical patient with chronic renal failure would need dialysis treatment three times a week, with sessions lasting several hours, so the next important challenge for hemodialysis treatment was development of a suitable vascular access. Scribner and colleagues created in 1960 a shunt between the radial artery and the cephalic vein using an external silicon device [12]. This solution enabled hemodialysis treatments for patients with end-stage renal failure and marked inception of dialysis as a standard clinical treatment. In 1966 Breschia and Cimino proposed a surgical arteriovenous (AV) fistula as a solution to eliminate the external shunt prone to bleeding and infection. AV fistula demonstrated as safe and long-lasting vascular access [12].

The hemodialysis developed significantly since 1960 with modern dialysis machines with improved dialyzer design, volumetric control, embedded monitoring and alarming systems, high flux membranes. In order to ensure no chemical or

bacterial contamination in dialysate, important requirement for dialysis membrane is adsorption capability for bacterial and organic contaminants and inflammatory mediators. In addition, membrane interaction with blood requires blood compatibility and biocompatibility [13]. Significant developments over the recent years are online dialysis monitoring devices and continuous therapy. The modern hemodialysis devices continually measure and record values allowing features as: sodium profiling, ultrafiltration variation based on blood pressure measurement, urea kinetics, etc. [14].

Although dialysis devices are still limited in their functions compared with the complex physiological tasks of the natural kidneys, improvement trends are focused on: maximum removal of uremic retention substances combined with reduced patient exposure to influence of inflammatory stimuli [13].

3 Dialysis Machine Organization and Functionality

The major components of the hemodialysis machine are: (a) extracorporeal blood circuit, (b) dialysate circuit, and (c) dialyzer. The hemodialysis machine provides monitoring and control functions in order to provide safe, efficient and accurate treatment. The basic schematic diagram of the dialysis machine with the relevant parts is presented in Fig. 2.

Basic functions of dialysis machine are: dialysate preparation, dialysate heating to physiological range, monitoring of conductivity and pH, controlling fluid removal, pumping blood and anticoagulant at determined rates, and monitoring pressure in the extracorporeal blood circuit.

The *extracorporeal blood circuit* main function is to provide the continuous blood circulation from the patient through a dialyzer, where waste is removed through a semi-permeable membrane, and returned to the patient. The hemodialysis machine

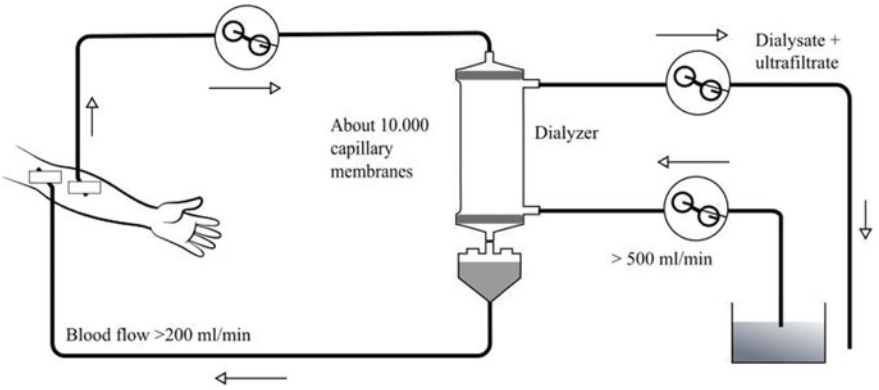

Fig. 2 Hemodialysis machine—schematic diagram

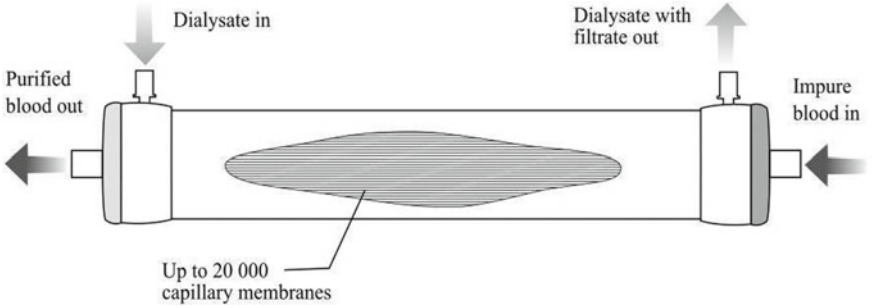

Fig. 3 Dialyzer

administers anticoagulant (heparin) throughout the treatment. The parameters monitored in the blood circuitry are venous and arterial blood pressures, and additional control is air presence detection.

The *dialysate circuitry* is responsible to deliver dialysate fluid and maintain its appropriate temperature, pressure and concentration. Main components of dialysate circuitry are: heating, de-aeration, proportioning, ultrafiltration, and monitoring. Monitoring is used for continual verification of the composition of the dialysate and to detect any abnormal occurrence as blood leak in dialysate circuit.

The blood purification takes place in the *dialyzer*, as presented in Fig. 3. Dialyzer contains about 20,000 hollow membranes imitating the filtering function of the natural kidney unit: the glomerulus. The capillary membranes have an inner diameter of 200 μm. The wall of the capillaries comprises membranes with a thickness of about 40 μm through which material exchange takes place [13].

The space between the capillary membranes are perfused with a dialysis fluid or dialysate in opposite flow to the direction of blood flow. This creates a concentration gradient and various uremic toxins are transferred out of the blood into the dialysate as filtrate, by means of the concentration gradients across the semipermeable capillary membranes. The mass transfer of the solutes is based on principles of diffusion (conduction transfer) and ultrafiltration (convection transfer) [15]. A measure for the efficiency of dialysis is clearance, defined as amount of substance removed from blood over a unit of time, divided by the respective concentration in the blood of a patient [13]. Clearance is calculated as a sum of diffusive and convective portion.

Monitoring devices are responsible to detect and identify hazardous events potentially harmful to patients such as: blood leaks, incorrectly dialysate pressures or temperature, and air in the blood. After detecting adverse event device should trigger an alarm and stop circulation in the blood and/ or the dialysate circuitry.

Control of the blood pump in the blood circuitry is related to the following:

- Monitor for continual measuring of the blood pressure in the extracorporeal blood circuit in the venous segment.
- Air detection in the venous segment before blood is returned into vein.

- Blood leak monitoring by method of detecting hemoglobin in the dialysate circuitry.

Control of the dialysate circuitry is related to monitoring the following parameters:

- Temperature sensor provides a short feedback to heater to maintain body temperature (35–39) ºC; low temperatures can cause shivering and high temperatures can cause protein denaturing or hemolysis.
- Conductivity monitor checks the electrolyte concentrations and prevents any adverse events caused by incorrect dialysate proportioning.
- Measuring pH value, as useful additional parameter for the dialysate proportioning monitoring.

If the concentration of electrolytes changes, the voltage will change, thus increase in electrolytes shall increase the conductivity of the dialysate. Conductivity reflects electrolyte concentration of dialysate and provides for real-time estimate of concentration [16, 17]. This feature of modern dialysis machines support comparison with other important physiological parameters and can help in deciding on appropriate composition of the dialysate what has been one of the central topics in the delivery of dialysis treatment [18]. Alarm limits for conductivity can be adjusted based on set-up concentrate composition and for standard temperature. Conductivity measurements are temperature compensated. Although monitoring display range can be as 10–17 mS/cm, devices have predefined safety alarm limits, as e.g., 12–16.5 mS/cm [19]. Conductivity is also used for modelling sodium mass transfer; calculating differences in conductivity values measured pre and post dialyzer, and conductivity can be used as a surrogate for sodium concentration with one mS/cm conductivity equivalent to 10 meq/L sodium [16].

During the design of a medical device, potential risks and hazards should be identified, and monitoring, control and alerting functions foreseen in order to reduce probability of occurrence of any harm to patient health to a minimum level.

4 Potential Safety Hazards in Dialysis

Safety of a patient is the most important requirement for medical device design and operation. Erroneous hemodialysis device or improper clinical application may cause different serious adverse effects as hemorrhage, low blood pressure, uremia, and etc. The COVID-19 pandemic has brought to light the necessity of periodical inspections of medical devices with measuring functions to guarantee appropriate operation [20].

The previous edition of the book “Inspection of medical devices” presented more important information on the inspection of medical devices, providing comprehensive guidelines and recommendations for conducting inspections to ensure the safety and effectiveness of medical devices [21].

A multidisciplinary task force composed by engineers representing manufacturers of dialysis machines, nephrology clinicians, and dialysis experts published their thorough analysis of hazards and harms related to hemodialysis devices [22]. Based on reviewing adverse events databases, literature and clinical experience, the task force identified and described more than 50 different harms related to a hemodialysis device. The harms are classified in five levels of severity and linked to underlying hazards. The hazards are classified as: biocompatibility, biological, chemical, electromagnetic, mechanical, function deterioration, use error and labelling. Further on hazards are related to physical quantities if adverse event is caused by fault measurement.

Medical device inspections are aimed to prevent device function deterioration as a potential cause of adverse events and harm to a patient. Subset of harms identified in [22] is presented in Table 1, with a following selection criteria: hazards of a type function deterioration, including only hazards related to measurable quantity. With exception of under-dialysis, selected harms are classified with a highest level of severity (5 and 4).

Analyzing quantities in the Table 1, and knowing that conductivity reflects electrolyte concentration, it is possible to conclude that the key parameters for a patient safety are: dialysate temperature, dialysate concentration and extracorporeal blood pressure.

5 Standards and Regulations for Dialysis Machines

With an objective to protect hemodialysis patients from adverse effects, responsible international and national organizations provide standards, regulations and guidelines to the medical equipment manufacturers for the processes of manufacturing and marketing; and to the medical professionals for the use, care, and/or processing of a medical device or system.

Within the European Union the new Medical Devices Regulation (2017/745/EU) –MDR [23] introduced in 2020 replaced the Medical Device Directive (MDD) 2007/47/EC [24]. The new MDR should provide internationally recognized, robust, and transparent regulatory framework, aimed to improve clinical safety. The MDD has introduced medical device classification system [25] and according to the classification dialysis machines are devices with measuring function. With respective to additional rules as duration of contact with the body, degree of invasiveness, and local or systemic effect; dialysis machines are classified as Class IIb medical devices [26].

Standards and regulations for medical equipment, including Dialysis Machines are divided into pre-market processes and post-market surveillance. In the following sections relevant standards supporting the implementation of regulations are listed, and afterwards the post-market surveillance mechanisms including the evidence-based approach for surveillance of medical devices are described.

Table 1 Hemodialysis device hazards related to function deterioration

Harm	Hazardous situation	Related quantity	Severity (min = 1, max = 5)
Acid–base imbalance	High/low bicarbonate in dialysate/substitution fluid	Bicarbonate in dialysate (mmol/L)	4
Hemolysis	Reduced dialysate tonicity	Dialysate conductivity (mS/cm)	5
Hemolysis	Blood exposed to high temperature	Dialysate temperature (°C)	5
Hemolysis	Mechanical stress to red cells as a result of extracorporeal circulation	Extracorporeal BP (negative and positive; mmHg)	5
Hyperthermia	Extracorporeal blood exposed to high temperature	Dialysate temperature (°C)	5
Hypothermia	Extracorporeal blood exposed to low temperature	Dialysate temperature (°C)	5
Plasma electrolyte imbalance	High/low sodium in dialysate/substitution fluid	Sodium in dialysate (mmol/L)	5
Plasma electrolyte imbalance	High/low potassium in dialysate/substitution fluid	Potassium in dialysate (mmol/L)	5
Plasma electrolyte imbalance	High/low calcium in dialysate/substitution fluid	Calcium in dialysate (mmol/L)	5
Underdialysis	Reduced dialysis effectiveness (i.e., inadequate urea removal)	Kt/V	2

5.1 Standards

The International Electrotechnical Commission (IEC) has provided the standard IEC 60,601–1:2005 + AMD1:2012 + AMD2:2020 Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [27], also referred to as IEC 60,601–1 (Edition 3.2).

IEC 60,601 is a series of technical standards for the safety and essential performance that are generally applicable to medical electrical (ME) equipment. The consolidated version is the 3.2 edition IEC 60,601–1 that includes the contents of the corrigenda 1 (2006) and 2 (2007), the contents of the corrigendum to Amendment 1 (2014), as well as the interpretation sheets 1 (2008), 2 (2009), 3 (2013) and

interpretation sheet to amendment 1 (2021). For certain types of medical electrical equipment, these general requirements are either supplemented or modified by the special requirements of a collateral or particular standard. Where particular standards exist, this standard should not be used alone.

IEC 60,601–2-16:2018 is a particular standard for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment. This particular standard takes into consideration the specific safety requirements concerning electrical safety and patient safety, and does not take into consideration the dialysis fluid control system of hemodialysis equipment using regeneration of dialysis fluid and central delivery systems [27].

Dialysis machine design and construction, under referential operating conditions, shall provide for protection against electrical hazard, excessive temperature, and intrusion of fire, dust or water in the device housing. Identification requirements define that dialysis machines shall be marked with the name and trademark of manufacturer, serial number, production year, and model or type reference.

The general standard, IEC 60,601–1 Part 1 is adopted in many countries by their regulatory bodies and recognized as requirement for the commercialization of medical equipment. Some countries also adopted standards or guidelines for further safety testing, inspection and calibration of medical equipment specific for different phases of the medical equipment life cycle. Some examples are: acceptance test, inspections performed in regular intervals, and/or directly following service or repair. Regulations stipulating technical and measurement requirements for medical equipment include following chapters: terms and definitions, general technical requirements, measurement requirements, identification, marking and documents.

The necessary content of a technical documentation for compliance assessment according to the IEC 60,601–1 is as follows:

- A general description of the device/device family, including any variants planned,
- Design and specifications,
- Label and instructions for use,
- Reference to applicable harmonized standards,
- Results of risk analysis,
- Evidence that the essential requirements have been met.

Risk analysis is important for deciding which aspects of a medical device's performance are essential. If variation in a performance may result in injury, then it is considered essential performance. Defining essential performance associated with risk management is crucial for compliance with the IEC 60,601 standards series. Maintaining risk at acceptable levels is responsibility of the alarming functions of medical device, and alarming functions are built upon accuracy and reliability of the key performance parameters measurement.

The IEC 60,601–1 defines that ME equipment shall be marked with the information on supply voltage(s) or voltage range(s) to which it may be connected. ME equipment shall be accompanied by documents containing the instructions for use and a technical description, and also all data that is essential for safe operation, transport and storage, and measures or conditions necessary for installing the ME

equipment, and preparing it for use. It is a common practice that the IEC 60,601–1 standard has been adapted into local national standard for use in specific country. In such cases national standards can introduce additional requirements specific for that environment, such as voltage to which the ME equipment may be connected.

Standard documents provide applicable terms and definitions. Dialysis machine is considered as ME equipment or ME system used to perform hemodialysis, hemofiltration and/or hemodiafiltration.

The IEC 60,601–2-16 provide following definitions:

Hemodialysis (HD) is defined as "process whereby concentrations of water-soluble substances in a patient's blood and an excess of fluid of a patient with renal insufficiency are corrected by bidirectional diffusive transport and ultrafiltration across a semi-permeable membrane separating the blood from the dialyzing fluid." [28]

Hemofiltration (HF) is defined as "process whereby concentrations of water-soluble substances in a patient's blood and an excess of fluid of a patient with renal insufficiency are corrected by unidirectional convective transport via ultrafiltration across a semi-permeable membrane separating the blood from the dialyzing fluid. Ultrafiltrate is simultaneously replaced by an approximately iso-osmolar substitution fluid at a rate such that the difference between the ultrafiltration rate and the rate of substitution fluid addition will lead to removal of the excess fluid over the course of the treatment." [28]

Hemodiafiltration (HDF) is defined as "process whereby concentrations of water-soluble substances in a patient's blood and an excess of fluid of a patient with renal insufficiency are corrected by simultaneous combination of HD and HF." [28]

The scope of the IEC 60,601–2-16 states that the particular requirements in that standard do not apply to: extracorporeal circuits, dialyzers, dialysis fluid concentrates, water treatment equipment, and equipment used to perform peritoneal dialysis.

It is important also to mention the standard IEC 62,353:2014 Medical electrical equipment—Recurrent test and test after repair of medical electrical equipment that applies to testing of ME equipment and ME systems, or parts of such equipment or systems, which comply with IEC 60,601–1:2005 (third edition) and its amendments, before putting into service, during maintenance, inspection, servicing and after repair or on occasion of recurrent tests to assess the safety of such ME equipment or ME systems or parts thereof [29].

International Standard Organization (ISO) provided several standards related to specific aspect of hemodialysis:

- ISO 8637–1:2017 Extracorporeal systems for blood purification—Part 1: Haemodialysers, haemodiafilters, haemofilters and haemoconcentrators
- ISO 8637–2:2018 Extracorporeal systems for blood purification—Part 2: Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters
- ISO 23500–1:2019 Preparation and quality management of fluids for haemodialysis and related therapies—Part 1: General requirements

- ISO 23500–2:2019 Preparation and quality management of fluids for haemodialysis and related therapies—Part 2: Water treatment equipment for haemodialysis applications and related therapies
- ISO 23500–3:2019 Preparation and quality management of fluids for haemodialysis and related therapies—Part 3: Water for haemodialysis and related therapies
- ISO 23500–4:2019 Preparation and quality management of fluids for haemodialysis and related therapies—Part 4: Concentrates for haemodialysis and related therapies
- ISO 23500–5:2019 Preparation and quality management of fluids for haemodialysis and related therapies—Part 5: Quality of dialysis fluid for haemodialysis and related therapies

ISO 8637–1:2017 specifies requirements for haemodialysers, haemodiafilters, haemofilters and haemoconcentrators, hereinafter collectively referred to as "the device", for use in humans [30]. ISO 8637–2:2018 specifies requirements for the blood circuit for devices used in extracorporeal blood filtration therapies and is concerned with the extracorporeal blood circuit manufactured for single use and intended for use in conjunction with haemodialysers, haemodiafilters and haemofilters. The requirements specified in this document for the extracorporeal blood circuit will help to ensure safety and satisfactory function [31].

ISO 23500–1 is the base standard for a number of other standards dealing with water treatment equipment, water, dialysis water, concentrates, and dialysis fluid (ISO 23500 series) and provides dialysis practitioners with guidance on the preparation of dialysis fluid for haemodialysis and related therapies and substitution fluid for use in online therapies, such as haemodiafiltration and haemofiltration [32].

5.2 Post-Market Surveillance

Post-market surveillance (PMS) of medical devices is important topic in the EU MDR that requires establishing of the PMS System including Vigilance—reporting on safety corrective actions as response on adverse events [25]. During the entire lifetime of medical devices in healthcare institutions the PMS system is responsible to systematically collect and analyze relevant data linked to performance and safety. Collected data should drive decisions if preventive or corrective measures are needed.

Systematic review of literature on PMS scoping diverse document sources as medical scientific journals, but also national and international legislation and standard databases is provided in [33], with objective to set a path to harmonization of MD PMS. The review identifies the following key mechanisms for MD PMS: (1) medical device registry, (2) adverse event reporting and (3) medical device performance evaluation. The authors discuss that although the same medical devices are used across different countries, their performance differs according the number of reported incidents, and conclude that "the only cause of such state can be found

in different approaches to management including preventive service and surveillance." The review highlights the lack of harmonized evidence-based methodology to provide data to assess the device behavior in practice and in different environments [33].

Possible approach to solving identified issues is discussed in [34] where author describes how evidence-based methodology for surveillance of MD is integrated in the legal metrology framework based on experiences in Bosnia and Herzegovina and in Republic of Serbia. Further on, all data resulting from the inspections performed by independent appointed body has been recorded in a designated database—eLab what is described in [35].

6 Dialysis Machine as a Measuring Device

At a national level there are national institutes of metrology (NMIs) responsible to establish and maintain reference standards for these metrological requirements, more specific for the following metrology areas: (1) *scientific metrology* through traceability to the International System of Units, or SI; (2) *legal metrology* through regulated measurements and measuring instruments, and (3) *industrial metrology* through confidence in testing and measurement results via certification, standardization, accreditation and calibration. In case of pending national regulations, standards IEC 60,601 and ISO 62353 refer to standardized safety tests and measurement of output parameters of medical devices related directly to patient.

The IEC 60,601–1 addresses risk management stating: "that the technical description provided by the manufacturer shall include characteristics of the ME equipment, including range, accuracy, and precision of the displayed values." Further on it is defined: "that the instructions for use shall identify the parts on which *preventive inspection and maintenance* shall be performed, by service personnel, including the periods to be applied."

Within the scope of patient safety and risk management the *safety performance inspections* of medical devices and corresponding metrological regulations gain importance. The accuracy and reliability of medical measurements are of direct consequences for the health of a patient, and quality assurance of measurement should be ensured by metrological tools, as calibrations, legal metrological inspections and reference measurement methods [36].

The inspection process should be conducted by a medical device inspection laboratory accredited to ISO 17020 [37] with the objective to determine if specified safety requirements and manufacturer specifications are met. The inspection process procedure should be defined with: purpose and scope, frequency, respective standards, required equipment, permissible error range, assessment process description, remedial action, and required documents. The inspection should be documented by an Inspection Report issued by the accredited laboratory and should comprise Work Order, Measurement Report, Calculation of absolute and relative error of device, and Inspection Certificate [38–42].

The key parameters for a patient safety are identified as: dialysate temperature, dialysate concentration and extracorporeal blood pressure. The measurement components for these parameters require periodic inspections to maintain safe and effective hemodialysis systems.

Measurement range for dialysis machine measurements as defined in respective manufacturer technical documentation [19] are:

- Conductivity (10–17) mS/cm
- Temperature (35–39) ℃
- Pressure (−300 to 500) mmHg

Measurement requirements define maximum permissible measurement error as defined in respective manufacturer technical documentation [19] are:

- Conductivity ± 1.5% (average)
- Temperature ± 3 ℃ (calibration conditions for dialysate flow of 500 mL/min)
- Pressure ± 20 mmHg or ± 10% of measurement reading, whichever is greater.

7 Dialysis Machine Inspection Procedure

As identified in previous sections, standardized approach in conformity assessment testing MD within the frameworks of the PMS System is increasing reliability of the devices, but also it is the first step in digital transformation of management of the MDs in healthcare institutions [42]. Globally, the management of medical devices is being impacted by the ongoing digital revolution, which requires data collection and analysis in order to make informed evidence-based decisions [43–45].

Dialysis machine inspection procedure includes (a) visual inspection and (b) verification of measurement error.

Visual inspection, although not defined in the IEC 60,601 series, is an important step for the safety inspections. Visual inspection is a simple procedure confirming that medical device is still in compliance with the manufacturer specifications. Visual inspection include:

- Contamination inspection
- Integrity and functionality inspection
- Markings and labelling inspection.

Integrity inspection is visual examination of device and its mechanical parts including: connectors, tubes, cables, sensors, etc. The examiner shall look for cracks, obstructions and other damages.

Functionality inspection is testing of all device functions performance and visual examination of their status on device monitor. Functional inspection includes testing of the alarm system. If the device is damaged or if it fails to perform the functions, the inspection shall be temporary interrupted, and device shall be sent for repair. This remedy action shall be taken with the consent of the institution under the inspection. After repair is performed, depending on the result of the repair, inspection is either

continued, or if the device is considered defective or malfunctioning, the device shall be taken out of usage and sent for further remedy action.

Device measurement error verification objective is to confirm that the measurement error is smaller than specified maximum permissible error. Modern instrumentation systems used for hemodialysis device verification are portable and modular. Dialysis meters are composed of the main display module and sensor modules for measuring specific parameter as: conductivity, pH, temperature and pressure (Fig. 4) of the dialysate fluids supplied by hemodialysis delivery systems. These physical values are primary parameters indicating safe and accurate operation of hemodialysis systems.

In case the dialyses meter is accompanied with the specific software application, during the inspection process the meter shall be connected to the computer running licensed software application for data upload and processing. Verification is performed to establish indication error for the key dialysis parameters, and verification method shall include range, number of required observations, error type to be calculated, and number of points in calibration curve. Example verification method for the key physical quantities:

- Conductivity: single measurement (10–17 mS/mm), determining relative error,
- Temperature: single measurement (35 ºC–39 ºC), determining absolute error,
- Pressure: six measurements (−300 mmHg, −150 mmHg, 0 mmHg, 150 mmHg, 350 mmHg, 500 mmHg), determining relative error.

Verification process for pressure sensor linearity is in accordance with the measurement experience of collecting measurement data at six points, at equal intervals along the measurement scale.

Maximum permissible measurement error pending relevant international regulations, as defined in respective manufacturer technical documentation [19]:

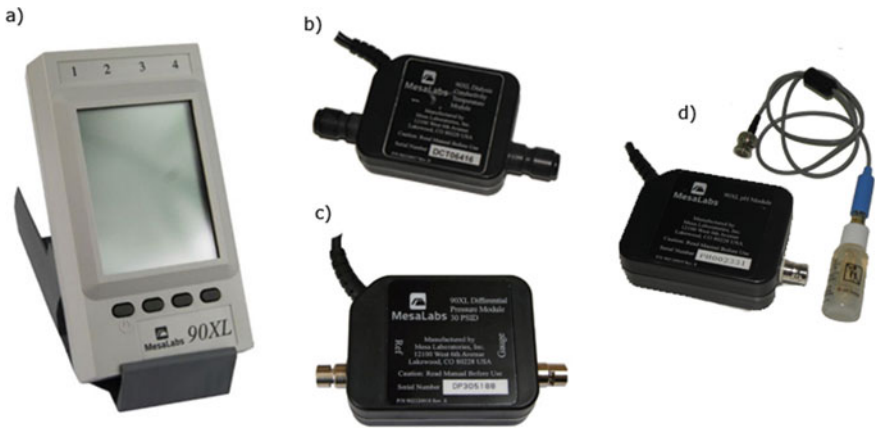

Fig. 4. 90XL™ Meter (**a**) with Conductivity and Temperature (**b**), Pressure (**c**) and pH Module (**d**)

- Conductivity ± 1.5% (average)
- Temperature ± 0.3 ºC (calibration conditions for dialysate flow of 500 mL/min)
- Pressure ± 20 mmHg or ± 10% of measurement reading, whichever is greater.

Verification process is described as follows:

Dialysis machine and dialyses meter shall be connected to power supply as marked on the device. If the dialyses meter is battery powered, the batteries should be recharged prior to verification. The sensor modules needed for the verification shall be attach to the meter device with cables that plug into connectors on the meter.

Conductivity and temperature measurements are taken as the dialysis fluid flows through the dialysate circuitry. If performing sample based measurement the sensor end of the conductivity/temperature sensor module is inserted into the container of test solution. Sample solution steadily flow through the sensor module, and when the display is stable, measurement may be taken. For in-line measurement method, conductivity/temperature sensor module is connected directly to the dialysate delivery system. After the flow is re-established through the sensor module measurement may be taken when the display is stable.

Pressure measurement is performed only after one hour post to attaching a pressure sensor module to the meter device. The pressure sensor module may be used for verification of arterial, venous, negative and differential pressure of the delivery system fluid. Intrusion of fluids into the pressure sensor module is prevented with transducer protectors.

Hemodialysis machine verification include inspection of measurement range and permissible measurement error for defined measurement values. If permissible measurement error is larger than stipulated maximum permissible error dialysis machine shall be ordered for service and verification shall be reiterated. Upon completed inspection procedure the inspection officer shall draft inspection results report and mark the device with the appropriate label.

The authors in [42] propose a novel method for conformity assessment of dialysis machines based on the OIML recommendations [46], and the method was validated by inspection bodies in Bosnia and Herzegovina and Republic of Serbia during the 2018–2021. The authors propose the structure of the inspection results report and provide example for both qualitative—visual and electrical safety inspections and for quantitative performance evaluations. The authors conclude:" The results of method validation confirm the necessity of independent periodical inspection of technical and metrological requirements for the dialysis machines in use, as the performance test revealed the performance variations that were not detected during usage or periodical preventive and corrective maintenance."[42]

8 A Novel Method for Conformity Assessment Testing of Dialysis Machines for Post-Market Surveillance Purposes

The methodology proposed for assessing the conformity of dialysis machines involves several steps. Firstly, legal requirements must be established, including technical and metrological standards that the devices must meet to be considered suitable for diagnosis or therapy. After identifying these requirements, a testing method must be established that involves using calibrated reference instruments to measure the crucial parameters of the device. Finally, the results of the measurements should be presented in a report that allows for an analysis of the device's performance, leading to a conclusion about whether or not the device meets the previously established requirements.

Badnjevic et al., developed and validated a system that can monitor both safety and performance during the use of a dialysis machine [42]. The technique was created in accordance with the OIML recommendations and is presented in a well-structured format, consisting of the following sections:

1. Definition of technical requirements for dialysis machines,
2. Definition of metrological requirements for dialysis machines,
3. Description of method for visual inspection,
4. Description of method for electrical safety inspection,
5. Description of method for performance inspection,
6. Summary and expression of test results.

The procedure involves utilizing calibrated etalons to carry out electrical safety and performance analysis.

The technical and metrological conditions are determined based on regulatory specifications specified in directives and regulations, the technical specifications of the manufacturer, and international standards that define the safety and performance standards for medical equipment. The method for assessing medical devices having a measuring function is described in this chapter [47, 48].

8.1 Technical Requirements

Regular technical inspections of dialysis machines are crucial to guarantee their safety and dependability both before and during their use in clinical environments. The traceability of these devices is ensured by clear, readable, and permanent labels and markings that cannot be removed without causing damage. The technical requirements for dialysis machines are defined as follows:

The technical requirements refer to the:

- Label and marking

name and/or trademark of manufacturer;
production mark (basic type)
year of fabrication;
unique serial number;
CE mark of appropriate administrative marking;

- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz;
- Temperature: 21–26 °C.
- Compliance with IEC 60,601–2-16 Medical electrical equipment—Part 2–16: Particular requirements for basic safety and essential performance of haemodialysis, hemodiafiltration and hemofiltration equipment [49].

To examine all of the requirements mentioned above, a testing approach must be implemented. According to the OIML guidelines, the examination of these requirements should be performed through visual inspection and electrical safety inspection in accordance with IEC 60,601 [49].

8.2 Metrological Requirements

The reliability of a medical device can be established by verifying its conformity with metrological requirements. These requirements include quantitative parameters such as error, accuracy, and uncertainty that are unique to each device and serve as evidence of its dependability. The manufacturer of each measurement device defines specific parameters such as the measurement unit, range, division, and accuracy. In accordance with the OIML guidelines, the metrological requirements for a dialysis machine are specified in the following manner:

- Measurement unit

  Conductivity of the dialysis liquid is set and measured in milisiemens per centimetre [mS]
  Temperature of the dialysis liquid is set and measured in Celsius [°C].
  Pressure of the measuring device is set and measured in millimetres of mercury [mmHg].

Siemens is a derived unit of conductivity in the International System of Units (SI) (NIST 2019). One milisiemens is the electrical conductance equal to 1/1,000 of a siemens, which is equal to one ampere per volt.

Celsius is a unit of temperature in the International System of Units (SI) (NIST 2019). Scale according to which it is defined based on the settings: 0° for the freezing

point of water and 100° for the boiling point of water. Contains 100-degree intervals between defined points.

A millimetre of mercury is a manometric unit of pressure, but not part of the International System of Units (SI). It was previously defined as the extra pressure generated by a column of mercury one millimetre high, and currently defined as exactly 133.322387415 pascals.

- Measuring range and division

  Conductivity (10–17) [mS]
  Temperature (35–39) [°C]
  Pressure (-300 - 500) [mmHg]
  Outside this working range no energy reading and no measurement result shall be displayed.
  Division: Measurement points are defined and taken in one point for every parameter.
  Performance accuracy stated by the manufacturer in the technical specification.

To evaluate all the requirements mentioned above, a testing methodology must be employed. In accordance with OIML recommendations, the testing of these requirements should be conducted through performance inspection, as presented in Sect. 8.3.3 of the results. A test report must be created following part 8.3.3 of the results. With the performance inspection method, the assessment of metrological conformity is carried out. The requirement for metrological conformity assessment testing can be expressed as follows, in accordance with OIML recommendations:

- For any set of conditions within the ambient temperature range of 21 - 26 °C, the maximum permissible error for the measurements is as follows:
  - o Conductivity ± 1.5% of reading,
  - o Temperature ± 0.3 °C of reading,
  - o Pressure ± 10% of reading.

8.3 Method of Test

8.3.1 Visual Inspection

(a) *Equipment*

The prerequisites for performing visual inspection are:

– Device under test / Dialysis machine;
– Manufacturers specification;
– *Procedure*

Table 2 Technical requirements and pass/fail criteria

No.	Criteria Technical requirements	Result	Conformity assessment testing
1	Prescribed labels and markings on the device under test	• name and/or trademark of manufacturer; • production mark (basic type) • year of fabrication; • unique serial number; • CE mark of appropriate administrative marking;	Pass/fail
2	Construction of the device	• the integrity of the device under test in respect to the manufacturer's specification • the functionality of the device under test in respect to the manufacturer's specification	Pass/fail
3	Performance of the device	• measurement range • measurement unit	Pass/fail

The procedure for visual inspection for a device under test consists of checking label/marking and construction integrity. The device must comply with manufacturers specification in terms of functionality and accompanying parts.

(c) *Summary and expression of test results*

The results are expressed as Pass/Fail answers to the criteria which have been tested (Table 2).

8.3.2 Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

– Device under test / Dialysis machine;
– Reference electrical safety testing equipment /analyser;
– *Procedure*

The procedure starts with connecting the dialysis machine to electrical safety testing equipment. Test of the electrical safety of a device under test is performed according to the requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [49]. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open neutral, normal condition—reversed mains, open neutral—reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition—reversed mains, normal condition—reversed mains, open earth—reversed mains), patient applied parts leakage current.

(c) *Summary and expression of test results*

The results are expressed in terms of requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance [49].

8.3.3 Performance Inspection

(a) *Equipment*

The prerequisites for performance inspection are:

– Device under test / Dialysis machine;
– Reference testing equipment /analyser;

(b) *Procedure*

When the device is powered on, has passed a self-test and is ready for a patient connection, connect the tubes to the modules for conductivity, temperature and pressure. Compare the measurement points given on the display of the DUT to the reading values on the reference testing device. Use separate testing modules to test different parameters (temperature, conductivity and pressure).

(c) *Summary and expression of test results*

The decision of conformity assessment testing is obtained after the analysis of the results of the conducted tests. The OIML recommends a summary of the results in the form of tables. As it could be seen, visual inspection is reported in the form of qualitative analysis. Simple YES/NO answers to the criteria states the conformity assessment testing. For the performance inspection, the results are expressed using terms of error. In metrology error can be expressed using absolute error or relative error. In case of dialysis machines, the performance inspection result can be reported as both relative and absolute error between the indicated values, depending on the parameter. Error for parameter of temperature is expressed as absolute error, while errors for conductivity and pressure are expressed as relative errors.

Relative error calculation:

$$\Delta X = X_{set} - X_{measured}/X_{set} * 100[\%] \tag{1}$$

Absolute error calculation:

$$\Delta X = X_{\text{measured}} - X_{\text{set}} \tag{2}$$

The conformity assessment testing in performance inspection is determined by the value of this error. The allowed performance error is presented in Table 2. It was formulated based on the international standards followed during the production of

the dialysis machine. Based on this requirement the conformity error is formulated as follows:

- If the error is less than the greatest allowed limit, then the device is compliant with metrological requirements.

This methodology includes not only quantitative testing but also a qualitative inspection of all dialysis devices to identify features that can impact their performance. The examination focuses on the housing's integrity (technical requirements), assessing components such as strain relief, vanes, connectors, switches, screens, alarms, and battery.

9 Case Study: Legal Metrology and Dialysis Machines

Legal metrology should provide the necessary infrastructure for the traceability of regulated measurements and measuring instruments to SI or national standard, through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty [46]. For medical devices that are applied in the EU but which are not covered by legal metrology in some countries calibration process has to be ensured with an adequate traceability chain.

If medical devices are not covered by legal metrology traceability of results is ensured through calibration procedures with an adequate traceability chain pertaining to the accuracy and correctness of measurement methods. Accordingly, it is necessary to establish adequate traceability chain for measurement results of dialysis machines as medical devices with the measuring function.

For that reason, dialysis meter and verifying sensor modules should be calibrated, according to the ISO 17025:2005 standard [50], and the results of conductivity, pressure, and temperature measurements can be related to national or international standards, through an unbroken chain of comparisons all having stated uncertainties. Therefore, manufacturers in their specifications and manuals for dialysis meters recommend calibration using traceable reference standards before use or whenever inaccurate readings are suspected [51].

Example of inclusion of dialysis machines in national legal metrology system is Bosnia and Herzegovina. Institute of Metrology of Bosnia and Herzegovina (IMBIH) adopted in 2014 the Measurement and Technical Requirements Rule Book for Dialysis Machines, that establish the metrological characteristics, required of dialysis machines, and which specify methods and equipment for checking their conformity [52].

After the inclusion of hemodialysis machines in national legal metrology system is Bosnia and Herzegovina a research was conducted based on the results of electrical safety and performance inspection of 500 hemodialysis machines in public healthcare institutions in Bosnia and Herzegovina [53, 54]. The measurements were made by independent laboratory for inspection of medical devices appointed by the National Metrology Institute of Bosnia and Herzegovina.

The results could be summarized as: 12.6% of inspected devices did not meet electrical safety requirements or have performance outside the specifications. There were 2% devices that did not comply with the safety standards in accordance with the IEC 60,601. Performance verification were not successful for 10.81% hemodialysis machines, with nearly 22.64% of these devices having malfunction of heating systems and pumps [53, 54].

These results in addition to developing awareness among patients and medical personnel about safety and accuracy of devices used in treatment of disease [53] advocates for inclusion of the medical devices in the legal metrology system.

10 Hemodiafiltration: Novel Approach to RRT

Hemodiafiltration (HDF) is mainly used in Europe and Japan, but is not available in the United States because of regulatory restrictions. HDF combines diffusive and convective solute removal, adding the removal of fluid containing larger molecules by convection to the clearance of smaller molecules by diffusion [55, 56]. The basic schematic diagram of the HDF machine with the relevant parts is presented in Fig. 5.

Diffusion is made possible by the difference in the concentration of toxins on both sides of the semi-permeable membrane, and in this way only uremic toxins that have a small molecular mass are removed. The use of HDF is made possible by the use of special high-permeability membranes in dialyzers. The characteristics of high permeability membranes are: ultrafiltration coefficient, membrane surface, adsorption surface and biocompatibility.

Uremic toxins of higher molecular mass are removed by convection, which is made possible by the large flow of liquid that transports these molecules. Thanks to convection, better ultrafiltration is possible. To replace the fluid removed by ultrafiltration in the high-flow procedure, the same volume of sterile substitution fluid is required. The replacement fluid resembles plasma, contains potassium, chlorine,

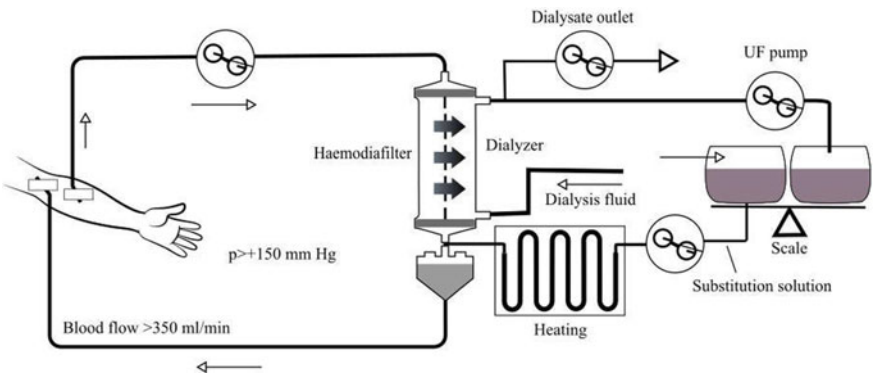

Fig. 5 Hemodiafiltration machine—schematic diagram

calcium, dextrose, and bicarbonates, and can be commercially produced or prepared in the dialysis machine itself online. Considering the type of substitution fluid, HDF devices are divided into conventional HDF and online HDF devices—OLHDF.

The point of entry of the replacement fluid into the extracorporeal circulation can be before or after the dialyzer: which is designated as predilutional and postdilutional OLHDF. With post-dilution OLHDF, the replacement fluid is introduced into the extracorporeal circulation after the dialyzer. In this way, the optimal clearance of small and larger molecules is enabled at the optimal flow of the substitution liquid, and this is the most common way of applying OLHDF.

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Inspection and Testing of Pediatric and Neonatal Incubators

Lejla Gurbeta Pokvić, Lemana Spahić, and Alma Badnjević-Čengić

Abstract Pediatric and neonatal incubators play a critical role in the care and treatment of infants who are born premature or with medical complications. It is imperative that these incubators are thoroughly inspected and tested to ensure their safety and efficacy. This chapter describes the inspection and testing of pediatric and neonatal incubators, which includes a comprehensive examination of the equipment's mechanical, electrical, and thermal systems, as well as its functionality and performance. Also, a review was made on the assessment of the incubator's compliance with the relevant safety standards and regulations. The inspection ensures that the incubator has no defects and can provide a safe and stable environment for newborns. By performing regular inspection and testing of pediatric and neonatal incubators, healthcare facilities can ensure that they are providing the highest level of care to their youngest and most vulnerable patients. The chapter presents a method that uses the measurement properties of pediatric and neonatal incubators to assess their safety and efficiency during use.

1 Introduction

Pediatric and neonatal incubators today are more sophisticated than the first prototypes but basic functions remained the same. They provide controlled environmental conditions needed to treat prematurely born infants who are not able to endure all the conditions outside the womb or infants born with certain diseases or health

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conditions, as explained in the previous version of the book "Inspection of Medical Devices" [1].

Neonatal and pediatric incubators are medical devices that are used to provide a controlled environment for newborns and young children who are critically ill or premature. These devices are designed to maintain a consistent temperature, humidity, and oxygen level to support the development and recovery of the patient. The use of neonatal and pediatric incubators has been demonstrated to improve patient outcomes, especially for premature infants. For example, a study by Badnjević [2] found that the use of neonatal incubators was associated with a significant reduction in mortality rates among premature infants.

However, the proper functioning of neonatal and pediatric incubators is dependent on regular maintenance and repair. In their review of evidence-based maintenance of medical devices, Badnjević [2] highlighted the current shortage of trained personnel and resources for the maintenance and repair of these devices. This shortage can lead to a lack of timely maintenance and repair, which can compromise the function of the incubators and ultimately the care of the patients.

In addition to regular maintenance, post-market surveillance of medical devices is important to ensure their continued safety and effectiveness. As noted by Badnjević Almir [3] in their review of post-market surveillance, monitoring the performance and safety of medical devices after they have been introduced into clinical practice can identify potential problems and inform the development of strategies for improving their use.

Patients in incubators have difficulties in thermoregulation because of the poor thermal insulation, relatively large surface area, a small amount of mass to act as a heat sink and they have no ability to conserve heat by changing body position. There are four different mechanisms of heat loss for patients in incubators that must be taken into account when designing these medical devices. These include radiation, conduction, convection and evaporation. Heat loss through radiation is related to the temperature of the surfaces surrounding the infant but not in direct contact with the infant. Conduction occurs through direct contact with a surface with a different temperature. Heat in an incubator is transferred by convection when air currents carry heat away from the body surface and evaporation occurs when water is lost from the skin.

Neonatal and pediatric incubators are enclosed medical devices that are used to provide a controlled environment for patients who are critically ill or premature. These devices are designed to maintain a consistent temperature, humidity, and oxygen level to support the development and recovery of the patient. The use of neonatal and pediatric incubators can help to protect against temperature fluctuations, dehydration, and other external factors that can be detrimental to the health of these patients.

The use of neonatal and pediatric incubators has been demonstrated to improve patient outcomes, especially for premature infants. For example, a study by Badnjević [2] found that the use of neonatal incubators was associated with a significant reduction in mortality rates among premature infants. Incubators can also help to prevent complications such as hypothermia and respiratory distress syndrome, which are common among premature infants.

When it comes to the concept, design, development stage, pre-production testing, approval and certification processes of medical devices, various methodologies and applications are maintained in each nation [4]. Furthermore, the proper functioning of neonatal and pediatric incubators is dependent on regular maintenance and repair. In their review of evidence-based maintenance of medical devices, they highlighted the current shortage of trained personnel and resources for the maintenance and repair of these devices. This shortage can lead to a lack of timely maintenance and repair, which can compromise the function of the incubators and ultimately the care of the patients. It is therefore important to prioritize the maintenance and repair of neonatal and pediatric incubators to ensure that they are functioning properly and providing the necessary support to patients (Fig. 1).

Incubators, today, differ in design and accessories depending on manufacturer, but main parts of these electrical medical devices, based on various manufacturer specification, are:

- transparent chamber,
- power supply,
- AC powered heater,
- electric fan motor to circulate the heated air,
- water tank for controlling the humidity of air,
- sensors for measuring temperature, relative humidity, sensor of skin temperature, air flow sensor,
- microprocessor-based temperature controller,

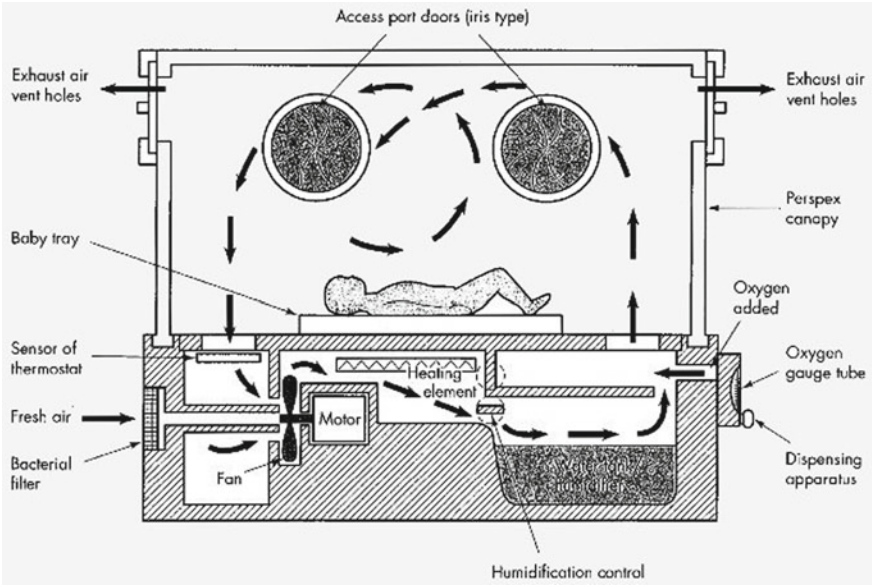

Fig. 1 Schematics of an infant incubator

- sir filters,
- oxygen supply,
- alarms and safety features,
- access ports for nursing care.

Controlled environmental conditions in incubator are achieved by regulation of temperature, humidity, oxygen lever, air flow and sound level. There are two main control modes used in these devices: (1) air temperature control mode and (2) skin temperature control mode.

Incubators can be divided into two groups: (1) stationary and (2) transport incubators. Difference between transport and stationary incubators are mainly concerned about power supply. Requirements for battery for transport incubators are more complex than for the stationary incubators. When designing transport incubators back up power sources need to be ensured, so if external AC is not available that incubator can switch to external DC source and if that is not available that incubator can use external batteries as power supply to provide stable conditions for transport of patient. Also, most of transport incubators only have air temperature control mode and are supported with lifesaving equipment.

The incubator consists of rigid transparent box, called chamber, which has side openings. Transparent material is used for chamber which need to be designed to resist the strains of transportation and to absorb impacts and ensure thermal insulation properties. Most usually chamber is placed on mount which has ability adjust the angle position of the box. The side openings on the box provide accessibility to patient for resuscitation or procedures without jeopardizing thermal stability. Most usually in incubator design, openings on the incubator chamber is provided along one of the longer sides of the incubator and provision is made for convenient displacement of the mattress or other infant support laterally out of and back into the enclosed space of the incubator through the door. At the same time armholes or similar access ports can also be provided, to enable attendants to give attention to the infant within the incubator, without withdrawing the infant support. Longer sides of incubators are intended to be accessible and the one with control panel unit is considered to be front of incubator. Controlled environmental conditions in incubator mean that the air inside the chamber is held on certain temperature with certain percentage of humidity present in the air. Air intake is usually found at the bottom of the device. The fan with motor drive, placed underneath the chamber, takes the room air and blows it over or through the heating element and the humidifier. A heating element made from coiled resistance wire known as the tube type (flat or coiled) heater is used in most incubators. To prevent system from overheating, the power rating of heater used in incubator is much less than in the other devices. Typical power rating of heater in incubators is between 100 and 300 W. The heater is controlled by an electronic temperature control unit. The incubator reading, i.e. reading from temperature sensors and reading of relative humidity of air inside of chamber can displayed digitally on control panel of incubator, or using analog indicators. Humidifier is most usually a water tank. To ensure moisturizing, the heated air flows over the water in the water container and gets moistened. The humidity is often regulated by closing

and opening of valve over the water container closing and opening a deflector plate over the container. Air inlets allow heated and humidified air to enter the chamber, while air outlets take the air from the chamber allowing the air circulation inside the chamber. The humidifier should be filled up only with distilled water only in order to avoid corrosive damage to the incubator. The general requirements for incubators in order maintain the body temperature of the baby between 36 and 37.2 °C, are to be able to create an ambient air between 34 and 38 °C with a humidity of 40–90%. For oxygenation therapy, incubators can be equipped with modules for dosing oxygen into the heated and moistened air. The oxygen concentration is also electronically controlled using microprocessor. If incubator does not pose these modules for dosing the oxygen into the air inside the chamber, oxygen can be applied in chamber through a hose connection from an external cylinder, oxygen concentrator or from the central gas supply. Most oxygenation equipment is compatible with most incubators. Alternatively, the baby gets the additional oxygen directly through a nasal cannula which pipes oxygen directly into the nostrils. Maintaining maximum purity of the air circulated in the incubator is enabled by usage of different filters. Also, the purity of air in the incubator can be achieved by introduction of oxygen into the circulation system in a manner to pass through the filter so that not only the replacement air but also the oxygen, when used, is subject to the filtering action. In this way bacteriological impurities originating even in the oxygen supply are substantially eliminated. Inside the chamber, above the heater and humidifier, cradle for patient is installed. This cradle is most usually equipped with additional scale for measuring the weight of a new-born and can move right, left, up, down. Monitoring and observation equipment is often built into the infant incubator unit which include cardiac monitors, brain-scan equipment, blood-monitoring equipment, thermometers and other instruments for observing vital signs. For treatment of certain medical conditions, medical professionals use UV (ultraviolet) lamps. These lamps can be put over the incubator chamber since the chamber is transparent. When undergoing treatment with UV light, precautions should always be taken to prevent the unnecessary exposure of UV light to healthy skin. In order to ensure safety of the infants, all electronically controlled incubators are equipped with alarming system which tracks the state of the environment within the incubator and alarm the medical staff in case of odd settings. To ensure proper functioning of infant incubators, stable and high-quality delivery of energy is needed to ensure the security of the modern clinical settings. When it comes to an electric failure in the health institution the incubator's internal energy source needs to be able to keep the unit in active mode for few hours in case of power loss. Battery capacity depends on manufacture. In the case of sudden voltage jumps, operation may be interrupted or may result in incorrect operation. For these reasons, units of uninterruptible power supply (UPS) are placed with incubators. Besides, infant incubators with closed chamber and controlled environmental conditions that can be stationary or transport, one additional type can be recognized. It is called infant warmer. This medical device consists of a biocompatible bed on which medical professionals place infant and transparent side panels.

The bed of infant warmer is placed on the rail mounting system. Heater is placed above the bed and delivers radiant heat to the patient inside providing unified heat.

Heaters in infant warmers are typically made from quartz or ceramic. When designing this medical device, type of heater is very important because it has direct impact on time needed for warmer to meet the desired temperature. Each additional minute of cold stress can lead to increased morbidity for an infant. They are characterized by lower power consumption and long life of the heating element lead to considerable cost savings in healthcare institutions. These devices also have air temperature control mode and skin temperature control mode. Skin temperature probe monitors infant temperature. The control unit contains the electronic circuits and controls radiant heater and the observation light. The manual mode of operation (air temperature control mode) allows selecting the level of radiant heat output which is indicated by the percentage power displayed on the control panel. The control circuit maintains the selected level of radiant heat. The manual mode has a preheat setting which allows the warmer to be preheated. In the automatic mode (skin temperature control mode) of operation, the patient's control temperature is chosen. A skin temperature probe is used to monitor the patient skin temperature. The control system modulates the radiant heat to maintain the patient at the selected control temperature. In most cases, the patient temperature, control temperature and elapsed time displays are digital for ease of viewing. Visual and audio alarms are present for safety.

The global management of medical devices is impacted by the ongoing digital revolution, which mandates data collection and usage in order to make educated and evidence-based decisions [5–8]. Performance testing of infant incubators is an important aspect of post-market surveillance to ensure the continued safety and effectiveness of these medical devices. A novel method for conformity assessment testing of infant incubators for post-market surveillance purposes was described in a recent article by Badnjević [9].

The method described in this article involves the use of a test setup that simulates the conditions in which infant incubators are used in a clinical setting. The test setup includes a heated water bath to simulate the body temperature of an infant, as well as sensors to measure the temperature, humidity, and oxygen levels within the incubator [10].

To assess the performance of the infant incubator, the test setup is used to expose the incubator to a range of temperature, humidity, and oxygen levels, and the response of the incubator is measured using the sensors. This allows for the evaluation of the incubator's ability to maintain a consistent and appropriate environment for the patient, as well as its ability to respond to changes in the external environment. For example, the incubator might be tested to see how it responds to changes in ambient temperature or humidity, or to the introduction of external sources of heat or cold [11].

In addition to the performance tests described above, the method also includes a series of inspections and functional tests to assess the physical condition and functionality of the incubator. These tests include checks of the incubator's controls and alarms, as well as an assessment of the incubator's structural integrity and ease of use. These tests are important to ensure that the incubator is in good working order and that it can be safely used by healthcare professionals and caregivers.

Overall, the method described in the article Badnjević et al. [9] provides a comprehensive and systematic approach for evaluating the performance and safety of infant incubators for post-market surveillance purposes. This approach can help to ensure that these devices are functioning properly and providing the necessary support to patients.

2 Preventive Maintenance Qualitative Tests

(a) Chassis/Housing: Examine the exterior of the unit for cleanliness and general physical condition. Be sure that plastic housings are intact, that all hardware is present and tight, and that there are no signs of spilled liquids or serious abuse.
(b) Infant Incubators: Remove any tape adhered to the unit. Check all rubber and plastic gaskets in the unit for signs of deterioration. The condition of the hood is important for power control of the environment. Ensure the hood is free of cracks, warping or other deterioration signs. Verify all parts are assembled correctly. Remove the hood, bed, baffle, main deck and other parts and thoroughly inspect the interior for foreign objects, deterioration or misassembly of internal components that could interfere with performance.
(c) Mount/Fasteners: If the device is mounted on a stand or cart, examine the condition of the mount. If it attached to the wall, or rests on a shelf, check the security of the attachment of every screw on the hood. Operate the iris type port closures to ensure proper function. Examine the iris diaphragms and port sleeves for tears. Verify that disposable irises are b.
(d) Infant Incubators: Check that all nuts and bolts are tightened fully. Use a screwdriver and systematically try to tighten eing replaced after each incubator use, these items are not re-usable.
(e) Casters/Brakes: If the device moves on casters, check their condition. Look for accumulations of lint and thread around the casters, and be sure that they turn and swivel, as appropriate. Check the operation of brakes and swivel locks, if the unit is so equipped.
(f) AC Plug/Receptacles: Examine the AC power plug for damage. Attempt to wiggle the blades to check that they are secure. Shake the plug and listen for rattles that could indicate loose screws. If any damage is suspected, open the plug and inspect it. Should the equipment be placed on a cart that has extra electrical receptacles for other equipment, insert AC plugs into each and verify they are firmly held. Verify that no damage is present in the cart receptacles.
(g) Line Cord: Inspect the cord for signs of damage. If damaged, replace the entire cord or if the damage is near one end, cut out the defective portion. Wire a new power cord or plug on the same polarity. Check the line cords of battery chargers.
(h) Strain Reliefs: Examine the strain reliefs at both ends of the line cord. Be sure that they hold the cord securely. If the line cord is detachable, it is recommend that the cord be affixed to the unit so that it cannot be removed by the operator.

(i) Circuit Breaker/Fuse: If the device has a switch-type circuit breaker, check that it moves freely. If the device is protected by an external fuse, check its value and type against that marked on the chassis and ensure that a spare is provided.
(j) Tubes/Hoses/Bulbs: Check the condition of all tubing, cuff, hoses, and bulbs (if present). Be sure that are not cracked, kinked or dirty. Inspect all oxygen orifices to make sure that they are clear and free of foreign matter. Preventive Maintenance Protocols.
(k) Cables: Inspect the cables of sensors, electrodes, remote control and their strain reliefs and general conditions. Carefully examine cables to detect breaks in the insulation and to ensure that they are gripped securely in the connectors at each end to prevent rotation or other strain.
(l) Fittings/Connectors: Examine all fittings and electrical cable connectors for general condition. Electrical contact pins or surfaces should be straight and clean. Fittings should be tight and should not leak. If keyed connectors are used, make sure that the keying is correct.
(m) Electrodes/Probes: Confirm that special paddles and electrodes are available if appropriate for the area of use. Examine all paddles and probes for physical conditions and cleanliness. Should the equipment have fluids, dried electrode gel or debris on it, inform the clinical staff. Clean paddles and electrode surfaces if needed and ensure they are completely dry before testing. Ensure that probe labels clearly identify the associated units. Improperly interchanged probes of different types or from different manufacturers may adversely affect temperature control. Confirm that any necessary transducers (if applicable) are on hand and check their physical condition.
(n) Filters: If the device has a switch-type circuit breaker, check that it moves freely. If the device is protected by an external fuse, check its value and type against that marked on the chassis and ensure that a spare is provided. Clean filter.
(o) Controls/Switches: Before changing any controls or alarm limits, check their position any settings appear inordinate (e.g., alarm limits at the ends of their range), consider the possibility of inappropriate clinical use or of incipient device failure. Record the settings of those controls that should be returned to their original positions following the inspection. Examine all controls and switches for physical condition, secure mounting, and correct motion. Check that control knobs have not slipped on their shafts. Where a control should operate against fixed-limit stops, check for proper alignment, as well as positive stopping. Check membrane switches for membrane damage (e.g., from fingernails, pens). During the course of the inspection, be sure to check that each control and switch performs its proper function.
(p) Heater: Disassemble the heating unit enough to expose the heating element. Examine the element for severe discoloration or foreign deposits. Heating elements normally change color with use, but dark, distinct surface spotting may indicate that material has come into contact with the element, possibly after falling through the air duct. Foreign matter touching the hot surface could cause a fire or the generation of noxious fumes. If you find such discoloration,

examine the control unit compartment for signs of overheating. If screw terminals connect the heating element to the control circuitry, check that they are tight.

(q) Motor/Fan/Pump: Inspect fan blades for deterioration and damage. Ensure fan is securely attached to drive shaft and that the coupling is present and intact. Check that clearance between the fans and housing are adequate by looking for signs of rubbing. In some cases, an improperly inserted control module and heater assembly in the incubator base has bent and disabled fan. Verify whether if fan requires lubrication or not. Observe the fan in operation to determine if there are excessive vibrations or wobbling.

(r) Fluid Levels: Check all fluid levels, including lead-acid battery levels.

(s) Battery/Charger: Inspect the physical condition of batteries and battery connectors, if readily accessible. Check operation of battery-operated power-loss alarms, if so equipped. Operate the unit on battery power for several minutes to check that the battery is charged and can hold a charge. (The inspection can be carried out on battery power to help confirm adequate battery capacity.) Check battery condition by activating the battery test function or measuring the output voltage. Check the condition of the battery charger and, to the extent possible, confirm that it does, in fact, charge the battery. Be sure that the battery is recharged or charging when the inspection is complete. Some batteries require periodic deep discharges and recharging to maintain a maximum battery capacity. If this is recommended by the manufacturer, verify that it is being performed on schedule.

(t) Indicators/Displays: During the course of the inspection, confirm the operation of all lights, indicators, and visual displays on the unit and charger, if so equipped. Be sure that all segments of a digital display function properly.

(u) User Calibration/Self-Test: Verify operation of these features, if applicable.

(v) Alarms: Operate the device in a way that activates all the alarms. Check that any associated interlocks function. Check action of disconnected-probe alarm, if unit so equipped. If the device has an alarm-silence feature, check the reset method.

(w) Audible Signals: Operate the device to activate any audible signals. Confirm appropriate volume, as well as the operation of a volume control, if so equipped. If audible alarms have been silenced or the volume set too low, alert clinical staff to the importance of keeping alarms at the appropriate level.

(x) Labeling: Check that all necessary labels, conversion charts, and instruction cards are present and legible. Incubators: Since Incubators carry oxygen, a fire hazard sign must be visible. Also a sign warning of the effects of high oxygen concentrations should be present (high oxygen concentration can cause fibroplasias and blindness in infants.)

(y) Accessories: Check the hood thermometer for cracked glasses or separations in the liquid column. If the liquid column has separated, it might be possible to consolidate it by removing the thermometer and carefully dipping it into hot water. If the thermometer has an expanded space at the top, the liquid will pool in the small reserve chamber. When the gap in the column disappears into the

pool, cool the thermometer and recheck it. Repeat the process if necessary. Be careful not to overheat the thermometer, for the liquids in it will expand and crack the glass. If the position of the mattress is adjustable, check the ease of motion and security of lock mechanism. Examine mattress for cleanliness. If the unit is used in the presence of flammable anesthetics, check that a conductive mattress cover is used [12].

3 Preventive Maintenance Electrical Safety Test

a. Grounding Resistance: Using an ohmmeter, electrical safety analyzer, or multimeter with good resolution of fractional ohms, measure and record the resistance between the grounding pin of the power cord and exposed (unpainted and not anodized) metal on the chassis. A maximum of 0.5 Ohms is recommended.
b. Leakage Current: Measure chassis leakage current to ground with the grounding conductor of plug-connected equipment temporarily opened. Operate the device in all normal modes, including on, standby, and off, and record the maxi- mum leakage current. Chassis leakage current to ground should not exceed 300μA.

4 Preventive Maintenance Quantitative Tests

a. Temperature Control: Check the action of the primary and safety thermostats with the incubator fully assembled. Set the temperature to 36 °C. Test the thermostats according to manufacturer's instructions, and record on the form the temperature at which safety or backup thermostats turns off heater.
b. Skin-Temperature Alarms: If the incubator is equipped with high and low skin-temperature alarms, verify alarm function. Adjust skin temperature set point to 36o C. Place sensor in incubator and allow temperature to stabilize. Remove the sensor from the incubator and verify that alarm activates. To verify the high skin-temperature alarm, place sensor near the heaters exit where the temperature is higher than the stabilize temperature throughout the incubator. Note point at which high alarm responds.
c. Safety Thermostat: To test the operation of safety thermostat and high temperature alarm, disable primary thermostat or disconnect from control circuit so heater remains on continuously. In some cases, this can be achieved by turning temperature control to max setting. It's possible to speed up the rise in temperature by supplementing the incubator heater output with a heat gun. Record hood thermometer and the true midhood temperature at which the alarm activates. It is important the air not be heated too quickly, for the mid-hood temperature may increase faster than the hood thermostat temperature and have the alarm go off before expected time.

d. Air-Temperature Alarms: If the incubator is equipped with high and low air-temperature alarms other than those that are controlled by a secondary temperature controller, verify that the alarms are functional. Adjust the air-temperature set point to 36o C and allow the air temperature to stabilize. Verify that low air-temperature alarms activates when the incubator hood opens. To test the high air-temperature, set the point to 36o C and increase temperature inside with outside source (hair blower or heat gun).

Set (°C)	Delivered (°C)
36	
Hi alarm	
Alarm activated	

(Verify other quantitative tests that may apply for Transport Incubators)

5 A Novel Method for Conformity Assessment Testing of Pediatric and Neonatal Incubators for Post-Market Surveillance Purposes

The methodology proposed for assessing the conformity of pediatric and neonatal incubators involves several steps. Firstly, legal requirements must be established, including technical and metrological standards that the devices must meet to be considered suitable for diagnosis or therapy. After identifying these requirements, a testing method must be established that involves using calibrated reference instruments to measure the crucial parameters of the device. Finally, the results of the measurements should be presented in a report that allows for an analysis of the device's performance, leading to a conclusion about whether or not the device meets the previously established requirements.

Preventive maintenance:

a. Clean the exterior and interior
b. Lubricate and clean fan assembly if required
c. Calibrate if needed
d. Replace filter and battery if needed based on Scheduled Parts Replacement Policies.

Since neonatal and pediatric incubators are high risk category devices, their proper functioning needs to be ensured. To ensure this, periodical inspection of electrical safety and performance should be performed, as was particularly evident during the COVID-19 pandemic [13]. The method for assessing medical devices having a measuring function is described in this chapter [11, 14, 15].

5.1 Technical Requirements

In order to ensure safety and reliability of incubators once they enter the market and once they are used in clinical settings the periodical inspection of their technical requirements is very important. In order to ensure traceability of the devices labels and markings shall be visible, legible and indelible, and it is not possible to remove them without permanent damage [9]. In case of the incubators, the technical requirements are formalised in the following manner:

The technical requirements refer to the:

- Label and marking

  name and/or trademark of manufacturer;
  production mark (basic type)
  year of fabrication;
  unique serial number;
  CE mark of appropriate administrative marking;

- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz; Battery supply;
- Temperature: 21–26 °C
- Pressure: 600 hPa–1060 hPa
- Relative humidity 10–95% without condensation
- Compliance with IEC 60,601–2-19 Medical electrical equipment—Part 2–19: Particular requirements for the basic safety and essential performance of infant incubators.

For inspection of all above mentioned requirements, a testing method needs to be adopted. As per OIML recommendations, the testing of these types of the requirements is to be carried out by visual inspection and by electrical safety inspection in accordance with IEC 60,601 [16]. In order to ensure safety and reliability of incubators once they enter the market and once they are used in clinical settings the periodical inspection of their technical requirements is very important. In order to ensure traceability of the devices labels and markings shall be visible, legible and indelible, and it is not possible to remove them without permanent damage. In case of the incubators, the technical requirements are formalised in the following manner.

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5.2 Metrological Requirements

Reliability of medical devices can be proven with its compliance with metrological requirements. Metrological parameters such as error, accuracy and uncertainty are quantitative parameters specific for every device that serve as an evidence of device reliability. For every measurement device specific parameters are defined by its manufacturer such as measurement unit, range and division and accuracy. Following the OIML guideline, in case of the incubator, the metrological requirements are formalised in the following manner:

- Measurement unit:

Air temperature which is set and measured in Celsius [°C].
Skin temperature which is set and measured in Celsius [°C].
Oxygen concentration which is set and measured in percentage [%].
Relative humidity of air which is set and measured in percentage [%].
Weight which is set and measured in kilograms [kg].
Level of sound inside the incubator [dB]
Level of alarms [dB]
Stability of temperature
Uniformity of temperature
Regulator of air temperature
Incubator warming time
Time required for temperature change
Air movement speed.

Celsius is a unit of temperature in the International System of Units (SI) (NIST 2019). Scale according to which it is defined based on the settings: 0° for the freezing point of water and 100° for the boiling point of water. Contains 100 degree intervals between defined points.

The kilogram is a unit of mass in the International System of Units (SI) (NIST 2019). It is defined by taking the fixed numerical value of the Planck constant h to be 6.626 070 15 × 10–34 when expressed in the unit J s, which is equal to kg m2 s-1, where the metre and the second are defined in terms of c and $\Delta\nu$Cs.

The decibel is a relative unit of measurement equal to one tenth of a bel (B). It expresses the ratio of two values of a power or root-power quantity on a logarithmic scale. Two signals whose levels differ by one decibel have a power ratio of $10^{1/10}$ (approximately 1.26) or root-power ratio of $10^{1/20}$ (approximately 1.12).

- Measuring range and division

  Air temperature (13–42) [°C]
  Skin temperature (13–43) [°C].
  Oxygen concentration (18–99) [%].
  Relative humidity of air (10–99) [%].
  Weight (0–10) [kg].
  Level of sound inside the incubator [dB]
  Level of alarms [dB]
  Stability of temperature (32–36) [°C]
  Uniformity of temperature (32–36) [°C]
  Regulator of air temperature [°C]
  Incubator warming time [s]
  Time required for temperature change (32–36) [°C]
  Air movement speed
  Outside this working range no energy reading and no measurement result shall be displayed.
  Division:

  - Air temperature: 30, 33, 34 and 35 °C
  - Skin temperature: 36 and 38 °C.
  - Oxygen concentration 18, 30, 50, 70, 85 and 99%.
  - Relative humidity of air: 80, 90, 95 and 99%
  - Weight:

    for 0–2 kg: 0.5, 1, 1.5 and 2 kg
    for 0–10 kg: 1, 2, 5 and 8 kg

  - Level of sound inside the incubator (1 point) [dB]
  - Level of alarms (1 point) [dB]
  - Stability of temperature: 32 and 36 [°C]
  - Uniformity of temperature: 32 and 36 [°C]
  - Regulator of air temperature: 36 [°C]
  - Incubator warming time: 1 point [s]

- Time required for temperature change: 1 point between 32 and 36 °C
- Air movement speed: 1 point

Performance accuracy stated by the manufacturer in the technical specification.

For inspection of all above mentioned requirements, a testing method needs to be adopted. As per OIML recommendations, the testing of these types of the requirements is to be carried out by performance inspection presented in Sect. 5.3.3 of results. A test report shall be prepared according to part 5.3.3. of results. With a performance inspection method the metrological conformity assessment testing is done. The metrological conformity assessment testing requirement can be formulated as per OIML recommendations as follows:

- For any set of conditions within the ambient temperature range of 21 °C to 26 °C, the maximum permissible error for the measurements are as follows:

  Air temperature ± 0.8 °C
  Skin temperature ± 0.3 °C
  Oxygen concentration ± 3 Vol.%
  Relative humidity of air ± 10%
  Weight:

  ± 2% (for 0–2 kg)
  ± 5% (for 2–10 kg)

  Level of sound inside the incubator: Must not exceed 60 dBa
  Level of alarms: Must be 65 dBa at minimum on 3 m away
  Stability of temperature: Must not exceed 0.5 °C (or 1 °C in case of transport incubators)
  Uniformity of temperature: Must not exceed 0.8 °C
  Regulator of air temperature: Must not exceed ± 1.5 °C
  Incubator warming time: Must not exceed 20% of time needed as specified by manufacturer
  Time required for temperature change: Must not exceed 15 min
  Air movement speed: Must not exceed 0.35 m/s

5.3 Method of Test

5.3.1 Visual Inspection

(a) *Equipment*

The prerequisites for performing visual inspection are:

Device under test/incubator;
Manufacturers specification;
Procedure

Table 1 Technical requirements and pass/fail criteria for infant incubators

Technical requirements and pass/fail criteria			
No.	Criteria technical requirements	Result	Conformity assessment testing
1	Prescribed labels and markings on the device under test	• name and/or trademark of manufacturer; • production mark (basic type) • year of fabrication; • unique serial number; • CE mark of appropriate administrative marking;	Pass/Fail
2	Construction of the device	• the integrity of the device under test in respect to the manufacturer's specification • the functionality of the device under test in respect to the manufacturer's specification	Pass/Fail
3	Performance of the device	• measurement range • measurement unit	Pass/Fail

The procedure for visual inspection for a device under test consists of checking label/marking and construction integrity. The device must comply with manufacturers specification in terms of functionality and accompanying parts.

(c) *Summary and expression of test results*

The results are expressed as Pass/Fail answers to the criteria which has been tested (Table 1).

5.3.2 Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

Device under test / incubator;
Reference electrical safety testing equipment /analyzer;
Procedure

The procedure starts with connecting the incubator to electrical safety testing equipment. Test of the electrical safety of a device under test is performed according to the requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open

neutral, normal condition—reversed mains, open neutral—reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition—reversed mains, normal condition—reversed mains, open earth—reversed mains), patient applied parts leakage current.

(c) *Summary and expression of test results*

The results are expressed in terms of requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance.

5.3.3 Performance Inspection

(a) *Equipment*

The prerequisites for performance inspection are:

Device under test / Incubator;
Reference testing equipment /analyzer;
Procedure

Incubators for neonatal and paediatric patients should first be connected to the power outlet. The reference testing devices are placed in the incubator. Based on device measuring range select measuring points to cover the entire measuring range of temperatures, relative humidity, oxygen concentration and weight. Test all these parameters in every measuring point. To test them, adjust the parameters values on the incubator. When the device is ready and it reaches the desired values of either parameter, read the values from the reference testing devices.

(c) *Summary and expression of test results*

The decision of conformity assessment testing is obtained after the analysis of the results of the conducted tests. The OIML recommends a summary of the results in the form of tables. As it could be seen, visual inspection is reported in the form of qualitative analysis. Simple YES/NO answers to the criteria states the conformity assessment testing. For the performance inspection, the results are expressed using terms of error. In metrology error can be expressed using absolute error or relative error. In case of neonatal and infant incubators, the performance inspection result can be reported as both relative and absolute error between the indicated values, depending on the parameter. Errors for parameters air temperature and skin temperature are expressed as absolute errors, while errors for oxygen concentration, relative humidity and weight are expressed as relative errors.

Relative error calculation:

$$\Delta X = X_{set} - X_{measured}/X_{set} * 100[\%] \quad (1)$$

Absolute error calculation:

$$\Delta X = X_{measured} - X_{set} \quad (2)$$

The conformity assessment testing in performance inspection is determined by the value of this error. The allowed performance error is presented in Table 1. It was formulated based on the international standards followed during the production of the incubator. Based on this requirement the conformity error is formulated as follows:

- If the error is less than the greatest allowed limit, then the device is compliant with metrological requirements.

This methodology includes both quantitative testing and a qualitative inspection of all incubators to identify features that can influence their performance. The inspection focuses on the housing's integrity (technical requirements), assessing components such as strain relief, connectors, switches, displays, alarms, batteries, plastic lids, and holders for distilled water [17].

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Inspection and Testing of Infusion Pumps

Lemana Spahić, Lejla Gurbeta Pokvić, and Almir Badnjević

Abstract Infusion pumps are medical devices used in hospitals and other healthcare facilities to administer medications, fluids, and nutrients to patients. As these pumps play a key role in patient care, it is essential that they are regularly inspected and tested to ensure they are working correctly and safely. The paper describes the inspection and testing of infusion pumps, which usually involves a series of checks and evaluations to ensure that the device is working properly and meeting certain performance standards. Regular inspection and testing of infusion pumps is crucial to maintain patient safety and prevent adverse events such as medication errors, overdosing or underdosing, and device failure. In general, proper inspection and testing of infusion pumps enables quality healthcare, ensuring that patients receive safe, effective and reliable care. This chapter describes a method based on the metrological properties of infusion pumps. The purpose of this unique method is to verify the safety and effectiveness of infusion pumps while in use.

1 Introduction

Fluids, nutrients, or drugs are delivered into a patient's circulatory system using infusion pumps [1]. These days, they are managed by tiny embedded systems that have been carefully created to reduce potential patient injury. Infusion pumps are medical devices used to deliver fluids, such as medications and nutrients, into a patient's body in a controlled manner. These devices have become increasingly popular in healthcare settings due to their ability to deliver precise dosages and reduce the risk of medication errors. There are several types of infusion pumps available, including volumetric pumps, which deliver a specific volume of fluid over a set period of time, and syringe pumps, which use a motor to push the contents of a syringe through a tube [1].

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2 Infusion Pumps

Infusion pumps can be used to deliver a variety of fluids, including electrolytes, blood products, and chemotherapy medications. However, infusion pumps are not without their drawbacks. These devices can be expensive, and their maintenance and calibration can also be time-consuming [1]. In addition, there is a risk of malfunction, which can lead to serious injury or death if not addressed promptly [1]. Medical device faults are prevalent despite the fact that different international and national rules, such as IEC 60,601-Medical electrical equipment: General requirements for fundamental safety and vital performance of medical devices [2], are followed during the production process. Failures in infusion pumps can have a substantial impact on patient safety because they are used to give vital fluids. One potential cause of infusion pump failure is user error, such as incorrect programming or misuse of the device. Other factors that can contribute to infusion pump failures include technical issues, such as malfunction or calibration problems, and environmental factors, such as power outages or extreme temperatures. Infusion pump failures can have serious consequences for patients. In some cases, these failures can result in over- or under-infusion of medications, leading to adverse reactions or inadequate treatment. In other cases, infusion pump failures can cause physical harm to patients, such as burns or tissue damage. Infusion pump issues are a major concern in several nations, including Canada, the US, and the UK, according to The Institute for Safe Medication Practices Canada (ISMP Canada) [3]. Infusion pumps in Canada reportedly failed to reach the intended flow rate in 58% of cases [3]. Infusion device problems accounted for 36% of the accidents in a UK study that looked at 6770 reports of medical device incidents from 1990 to 2000 [4]. The US Food and Drug Administration created the most extensive database of documented incidents and device failures [5]. Numerous reports of infusion pump issues can be found in the Manufacturer and User Facility Device Experience (MAUDE) database [6]. Users of medical devices eventually grow overly dependent on them, which leads to mishaps [7]. Infusion pump-related medication errors made it into the ECRI Top 10 Health Technology Hazards for 2017 [8]. Users should be aware of the electrical, mechanical, and software components of the device that could malfunction and result in subpar performance in order to reduce the likelihood of these faults. The proper management of infusion systems should be established in addition to training. In addition, Chiarizia et al., recommend additional services and mathematical reasoning to guarantee the quality of infusion pumps' functioning in their research [9]. However, despite these potential risks, the benefits of infusion pumps in the delivery of medications and other fluids make them an important tool in the management of patient care.

The previous version of the book "Inspection of Medical Devices" emphasized the importance of effective healthcare management, including overcoming these problems [10]. To mitigate the risks associated with infusion pump failures, healthcare institutions should implement best practices for the use and maintenance of these devices. This may include training for staff on the proper use of infusion pumps, regular maintenance and calibration, and the development of protocols for responding

to infusion pump failures [11]. Moreover, the continuous digital and technological advancements allows informed, evidence-based decision making and data gathering, if the process is implemented correctly [12–16].

Many incident reports indicate that relying solely on safety and performance inspection in accordance with IEC 60,601 is insufficient. At this time, many international projects are being carried out or started, including those with the "Traceability of Medical Measurements" as their main topic by the American National Institute of Standards and Technology (NIST) and the European Association of National Metrology Institutes (EURAMET) [17, 18]. These initiatives seek to build procedures that will improve the precision, accuracy, and dependability of medical measures. Performance inspections of infusion pumps should be conducted regularly to identify and correct any potential issues with the device. This may include checking for physical damage, ensuring that the pump is programmed correctly, and verifying that the pump is delivering the correct amount of fluid at the correct rate. Healthcare institutions should also have protocols in place for responding to infusion pump failures. The metrology concepts can come in handy for these purposes [19]. These inspections are a collection of procedures that demonstrate that a medical device complies with the standards established for that particular device type. While performance inspections take into account testing of output parameter performance of equipment, safety inspections focus on looking for potential electrical risks. For infusion pumps, performance checks can be carried out in accordance with IEC 60,601–2 24 as part of routine device management in healthcare facilities. Specific guidelines for infusion pumps and controllers' safety [20]. The importance of this was especially evident during the COVID-19 pandemic [21].

A recent study by Badnjević et al. [22] presented a novel method for conformity assessment testing of infusion pumps for post-market surveillance purposes. The authors developed a testing protocol that involves simulating real-life scenarios using a combination of mechanical and fluidic tests. This protocol was designed to evaluate the performance of infusion pumps under a variety of conditions, including normal use, fault tolerance, and environmental stress. The results of this study showed that the testing protocol developed was effective at identifying a range of issues with infusion pumps, including incorrect flow rates, inaccurate volume measurements, and pump failure. The methodology is already being used by the inspection body for these purposes. In the past years, inspections according to the methodology in public and private healthcare facilities have been carried out on a variety of device types including infusion pumps [23, 24].

This chapter deals with the methodology for inspection of infusion pumps in healthcare settings according to the published method.

3 History

Infusion pumps have been used in healthcare for several decades, with their development and evolution closely linked to advancements in medical technology. The earliest infusion pumps were simple devices that used gravity to infuse fluids into a patient's body. These pumps were often used for blood transfusions and were limited in their accuracy and precision.

The first infusion device was created in 1656 by Sir Christopher Wren, an Oxford scientist, who used a pig's bladder and a writing quill, earning him the title of Father of Intravenous Therapy. Although successful, Wren found the device to be fragile and difficult to secure.

In 1662, Johann Major became the first to successfully infuse humans with both blood transfusions and medicinal injections. The procedure often resulted in infections at the infusion site, and fatalities.

In 1665, Richard Lower saved an animal's life through blood transfusion, while two years later Jean Baptise Denis successfully infused lamb's blood into a 15-year-old boy who survived, but a subsequent patient died, leading to Denis being tried for manslaughter. The Edict of Chatelet banned all transfusions without the approval of the Paris Faculty of Medicine, and other countries followed suit.

In the 1830s, Dr. Thomas Latta discovered the effectiveness of injecting salty water into a patient's bloodstream to fight cholera, while Dr. James Blundell proved that only human blood could be safely transfused into humans, not animal blood.

In the late nineteenth century, the Luer Company developed the Luer connection, which remains in use today, allowing easy attachment and detachment of the hypodermic needle's head. Karl Landsteiner identified four human blood classifications in 1900, demonstrating that not all human blood is the same.

Infusion therapy advanced rapidly in 1914 when sodium citrate was found to prevent blood from clotting, followed by the use of dextrose as an infusant in 1925. In 1930, vacuum-sealed glass bottles replaced open containers for infusions. Ten years later, nurses were permitted to administer infusions, whereas before 1940, only doctors were allowed to do so.

In 1960, infusion pumps became a standard feature in all hospitals.

During the 1990s, ambulatory infusion pumps grew in popularity as the need for continuous infusion therapy outside of hospitals increased. These pumps were made to be portable, small, and lightweight for patients to wear on their bodies or carry around. They were user-friendly with straightforward controls and alarms to notify patients or caregivers of any issues.

At the start of the 2000s, smart infusion pumps were introduced to help address the common problem of medication errors in healthcare. These pumps utilized advanced technology to automatically calculate the correct medication dose based on a patient's weight. They could also alert healthcare professionals if the dose was too high or too low and be programmed with drug libraries providing medication information and recommended dosages.

In more recent years, wireless infusion pumps were created, offering wireless connectivity to communicate with other devices like electronic health records (EHRs) and remote monitoring systems. This can enable healthcare providers to closely monitor patients and make it easier to track medication administration, ensuring patients receive the right medication doses.

4 Drug Delivery Mechanism

Infusion pumps have revolutionized the way medications and fluids are administered to patients by providing accurate and controlled administration. The drug delivery mechanisms used in infusion pumps allow healthcare providers to deliver medications at a specific rate, over a specific time period, and in precise dosages. This degree of accuracy is especially critical for patients who require medications that must be delivered in a consistent and controlled manner to achieve optimal therapeutic outcomes.

There are multiple drug delivery mechanisms used in infusion pumps, such as peristaltic pumps, syringe pumps, volumetric pumps, and patient-controlled analgesia (PCA) pumps. Each of these mechanisms has its own unique advantages and disadvantages. The selection of the delivery mechanism depends on factors such as the specific medication being administered, the medical condition of the patient, and the desired rate of drug delivery. Despite the differences in the specific mechanisms used, the purpose of all infusion pumps is the same—to deliver medications and fluids safely, effectively, and efficiently. Infusion pumps are indispensable in modern healthcare, enabling precise drug delivery that can improve patients' health outcomes and quality of life.

A peristaltic pump is a type of infusion pump that uses a set of rollers to compress and decompress a flexible tube to move the medication or fluid through the tube and into the patient's bloodstream. The pump typically has a motor that drives the rollers, and the speed and direction of the rollers can be controlled to adjust the flow rate of the medication or fluid. Peristaltic pumps are commonly used to deliver intravenous (IV) medications and fluids, as well as enteral feeding in which nutrition is provided directly to the stomach or intestines via a tube. These pumps are particularly useful for medications that require a consistent and controlled delivery rate, such as chemotherapy drugs, antibiotics, and pain medications. One of the main advantages of peristaltic pumps is that they are less likely to introduce contaminants into the fluid being administered, as the fluid is contained entirely within the tubing and does not come into contact with the pump itself. Additionally, peristaltic pumps are relatively simple to operate and maintain, and can be used in a wide range of settings, from hospitals to home healthcare. However, one potential disadvantage of peristaltic pumps is that the rollers can occasionally cause damage to the tubing or cause small amounts of the medication or fluid to be left behind, which can impact the accuracy of the dose being delivered. Despite this, peristaltic pumps remain a popular and effective choice for drug delivery in a variety of medical settings.

In medical settings, a syringe pump is a type of infusion pump utilized to deliver precise quantities of medication or fluids to a patient during a specific timeframe. Its mechanism consists of a motorized device that controls the plunger of a syringe, which allows for a slow, steady flow of fluid through a small tube or catheter. Syringe pumps are engineered for high accuracy and can provide small, precise doses of medication or fluid over extended periods of time. They are commonly employed in critical care settings, like intensive care units or during surgeries, where the exact delivery of medication or fluids is crucial for patient safety and recovery. One of the benefits of syringe pumps is their ability to maintain a constant infusion rate, despite the reduction in the volume of medication or fluid in the syringe over time. This is achieved by using advanced motor control systems that can adjust to changes in fluid viscosity and other factors that may influence the flow rate. Syringe pumps are usually managed through a user interface that enables the healthcare providers to establish the desired flow rate, volume, and duration of the infusion. Numerous pumps also incorporate safety features, such as alarms that alert the user if the flow rate falls beyond a specified range or if the syringe is empty.

Volumetric pumps, also referred to as positive displacement pumps, are medical infusion pumps that provide accurate delivery fluids in precise volumes. Unlike syringe pumps, which employ a syringe to deliver medication or fluids, volumetric pumps use a reservoir to hold the fluid, which is then pumped out in precise volumes. In medical settings, volumetric pumps are commonly utilized to deliver fluids to patients requiring intravenous therapy, such as antibiotics, chemotherapy drugs, and parenteral nutrition. They are also employed to deliver fluids during surgery and in critical care settings, like intensive care units. One of the benefits of volumetric pumps is their ability to deliver fluids continuously instead of in discrete doses, a feature useful for patients requiring a steady infusion of medication or fluid over a prolonged period. Volumetric pumps have different modes of operation, such as rate-based mode, which delivers a constant flow rate of fluid over a specified period of time, and time-based mode, which delivers a fixed volume of fluid over a specified period. They also come equipped with safety features, such as alarms that alert the user if the fluid flow rate falls outside a specified range, if the fluid volume is low, or if there is an obstruction in the tubing.

Patient-controlled analgesia (PCA) pumps are a type of medical infusion pump that provides pain medication to patients who are experiencing moderate to severe pain. The pumps allow the patient to self-administer the medication in response to pain, offering them greater control over their pain management. Typically used in postoperative settings or in chronic pain management, PCA pumps dispense small doses of opioids through a catheter inserted into the patient's vein or spinal cord. They work by administering small doses of pain medication, mostly opioids such as morphine or fentanyl, through a catheter that is inserted into the vein or spinal cord of the patient. Healthcare providers program the pump in order to deliver a specified amount of medication over a certain period of time, which is known as the lockout interval. The lockout interval is the minimum amount of time that must elapse between doses to prevent the patient from receiving too much medication and experiencing side effects such as respiratory depression. By pressing a button

on the device, the patient can activate the pump when they feel the onset of pain. When the button is pressed, the pump delivers a pre-set dose of medication into the patient's system. If needed, the patient can continue to press the button to receive additional doses of medication, within the limits which are set by the lockout interval. PCA pumps are designed to provide patients with greater control over their pain management, allowing them to receive pain medication when they need it without having to wait for a healthcare provider to administer it. They also help to reduce the risk of medication errors by automating the delivery of medication and minimizing the need for manual calculations and dosing. PCA pumps require careful monitoring by healthcare providers to ensure that patients are not receiving too much medication, which can result in serious side effects such as respiratory depression or even death. Healthcare providers must educate patients on the proper use of the pump and monitor them closely for signs of adverse reactions or complications.

5 Potential Harms and Hazards Associated with the Use of the Infusion Pumps

Although infusion pumps have improved the safety and efficacy of delivering fluids and medications to patients, they can also present risks and dangers.

Infusion errors are a significant potential harm associated with the use of infusion pumps. These errors can occur due to a variety of reasons, such as incorrect programming, device malfunction, or human error. One of the most common types of infusion errors is the incorrect dosage, which may have serious consequences for the patient, including adverse effects or inadequate treatment. In order to prevent incorrect dosages, healthcare providers must ensure that the infusion pump is properly calibrated and programmed with the correct dosing and flow rate. The medication and its dosing must be double-checked before administering it to the patient. Another type of infusion error is wrong medication, which happens if the wrong medication is loaded into the infusion, if the medication is incorrectly labeled, or if the medication is administered to the wrong patient. The consequences can be severe, even lead to adverse effects or death. To prevent this error, all medication must be properly labeled and healthcare providers must verify the medication before loading it into the infusion pump and before administering it to the patient. Rate errors may occur if the pump is not calibrated properly, if the flow rate is programmed incorrectly, or if there is an obstruction in the tubing, leading to under- or over-infusion. This may result in inadequate treatment or overdose, and to prevent this, the pump must be calibrated correctly and the flow rate programmed accurately. Air embolism occurs if air bubbles are introduced into the bloodstream leading to blockages in blood vessels and affecting blood flow to vital organs. This is caused by improper priming of the infusion pump or by disconnection of the tubing. To prevent this, the infusion pump must be properly primed and the tubing must be properly connected. Infusion site errors occur if the infusion site is not properly monitored or if the catheter is

not inserted correctly, which may lead to infection or other complications, including tissue damage or bleeding. Healthcare providers must ensure that the infusion site is properly monitored, and that the catheter is inserted correctly to prevent infusion site errors.

Mechanical failures are another possible risk connected to infusion pumps occurring due to multiple reasons such as malfunctioning of the pump, software glitches, or wear and tear of the pump over the time. It can result in under-infusion, over-infusion, or interruption of therapy, which may lead to serious health consequences for the patient. To prevent this, infusion pumps must be regularly maintained and calibrated. Proper maintenance helps identify possible issues early and prevents the occurrence of mechanical failures. It is crucial to conduct regular inspections of the pump, including the tubing, connectors, and any other accessories used with the pump. If the failure happens, healthcare providers should have a backup plan in place to provide alternative treatment options to the patient. Medical professionals should be trained on how to troubleshoot the infusion pump and take corrective action promptly to minimize any adverse effects on the health of the patient.

The risk of infection occurs when the infusion pump is not maintained correctly or when there is a breach in the skin or sterile field during the insertion of the catheter. Improper disinfection of the pump and its accessories may also lead to infections. Infections can have serious consequences for patients, especially those with weakened immune systems. Infected patients may require additional treatment and extended hospital stays, which can also result in increased healthcare costs. To prevent it, healthcare providers must ensure that the infusion pump and its accessories are properly cleaned and disinfected before each use. The recommended protocols for catheter insertion should be followed, including proper hand hygiene and the use of sterile techniques. Patients must be monitored for signs of infection, such as fever, redness, or drainage at the infusion site. If an infection does occur, prompt diagnosis and treatment are crucial to minimize the risk of complications.

Electrical hazards occur due to problems with the power supply or the electrical components of the infusion pump itself. These hazards can range from minor shocks to serious injuries or even death. To prevent electrical hazards, healthcare providers should follow the manufacturer's instructions for using the infusion pump and ensure that the pump is properly grounded. They should also regularly inspect the pump and its accessories for signs of wear or damage that could lead to electrical hazards. In the event of an electrical hazard, healthcare providers should take immediate steps to disconnect the infusion pump from the power supply and to remove the patient from any potential danger. They should also report the incident to the appropriate authorities and take steps to prevent similar incidents from occurring in the future.

In conclusion, infusion pumps are a critical tool in delivering fluids and medications to patients, but may pose risks and hazards if not used correctly. To prevent these errors, healthcare providers must receive appropriate training on how to use infusion pumps, adhere to established policies and procedures, and double-check their work to ensure accuracy. Infusion pumps should be designed with safety features, such as dose limit alerts and double-check mechanisms. Regular maintenance and monitoring can help prevent mechanical failures, and infection prevention measures

can reduce the risk of infections. By identifying and addressing potential errors in infusion pump use, healthcare providers can help ensure safe and effective patient care.

6 Standards and Regulations

As previously stated, infusion pumps are medical devices used to deliver fluids, such as medication, nutrients, or blood, to patients in a controlled manner. As with all medical devices, there are standards and regulations that must be followed in the development, manufacture, and use of infusion pumps to ensure their safety and effectiveness.

In the United States, the Food and Drug Administration (FDA) regulates the development, manufacturing, and distribution of medical devices, including infusion pumps. The FDA has issued a number of regulations and guidance documents related to infusion pumps, as follow:

- 21 CFR Part 880.5725—this regulation outlines the classification of infusion pumps as Class II medical devices, which are subject to certain regulatory controls to ensure their safety and effectiveness. This means that they are subject to certain regulatory controls to ensure their safety and effectiveness, including pre-market clearance or approval, adherence to good manufacturing practices, and post-market surveillance;
- FDA Guidance for Industry and FDA Staff: Infusion Pumps Total Product Life Cycle—this guidance document provides recommendations for the design, development, and testing of infusion pumps, as well as guidance on post-market surveillance, labeling, and user training. The guidance also includes recommendations for addressing cybersecurity risks associated with infusion pumps;
- FDA Guidance for Industry and FDA Staff: Infusion Pump Improvements—this guidance document provides recommendations for the improvement of infusion pump design and technology, with a focus on reducing the risk of adverse events.;
- FDA Safety Communication: Infusion Pump Use Errors—this communication highlights the importance of proper use and maintenance of infusion pumps to reduce the risk of adverse events, and provides recommendations for healthcare providers and patients.

Additionally, aside from FDA regulations and guidance documents, there are international standards that apply to infusion pumps. These international standards were developed by the International Organization for Standardization (ISO), including:

- ISO 26825:2012—this standard outlines requirements for the design and testing of infusion pumps, including accuracy, reliability, and safety. The standard also includes requirements for software validation and risk management;

- ISO 28620:2010—this standard provides guidance on the use of infusion pumps, including recommendations for user training, maintenance, and safety. The standard emphasizes the importance of proper use and maintenance of infusion pumps, and provides recommendations for addressing common sources of errors and malfunctions;
- ISO/TR 16,142–2:2016—this technical report provides guidance on the integration of infusion pumps into healthcare delivery systems, including recommendations for risk management, interoperability, and system integration The report emphasizes the importance of considering the entire system of care when implementing infusion pumps, and provides recommendations for addressing issues such as communication and data exchange between different systems and devices.

7 Post-Market Surveillance

Post-market surveillance for infusion pumps is the continuous monitoring and evaluation of infusion pumps after they have been authorized for use by regulatory agencies such as the US Food and Drug Administration (FDA). The main goal of post-market surveillance is to detect and evaluate any safety issues or performance problems with the device that may occur during its use in a clinical environment.

Post-market surveillance is a critical aspect of ensuring the safety and effectiveness of infusion pumps, as it enables for the identification of potential problems that may not have been detected during the pre-market testing and evaluation process. By monitoring infusion pumps in real-world clinical settings, manufacturers and regulatory agencies may gain more insight into the performance of the device under various circumstances and can identify any issues that may occur.

One of the key methods used for post-market surveillance of infusion pumps is the reporting of adverse events. Manufacturers and users of infusion pumps are required to report any adverse events associated with the device to regulatory agencies such as the FDA. These adverse events may include malfunctions, device-related injuries or deaths, or other problems that may affect the safety or effectiveness of the device. In addition to adverse event reporting, post-market surveillance may also involve the use of post-market studies. These studies may be required by regulatory agencies as a condition of approval or clearance for the device. Post-market studies are designed to assess the safety and effectiveness of the device in real-world clinical settings and may involve the collection of data on device performance, patient outcomes, and other relevant factors. Another method of post-market surveillance for infusion pumps is data analysis. Manufacturers and regulatory agencies may analyze data from electronic health records, device usage logs, or other sources to identify any trends or patterns that may indicate a problem with the device. This data analysis can help to identify potential safety issues or performance problems with the device and inform decisions about any necessary corrective actions. User feedback is another important component of post-market surveillance for infusion pumps. Manufacturers may solicit feedback from users of their infusion pumps to identify any problems

or issues with the device, and to gather suggestions for improvement. This feedback can be used to make improvements to the device and to inform future regulatory decisions.

Post-approval studies are required by regulatory agencies to assess the long-term safety and effectiveness of medical devices after they have been approved or cleared for use. Manufacturers of infusion pumps may be required to conduct these studies to gather additional data on the performance of their devices in real-world clinical settings. Active surveillance systems involve the continuous monitoring of medical devices in clinical settings to detect any potential safety issues or performance problems. These systems may be used to gather data on the performance of their infusion pumps and to identify any issues that may arise. Collaboration with healthcare providers is an important component of post-market surveillance for infusion pumps, as manufacturers may work closely with healthcare providers to monitor the performance of their devices in clinical settings and to identify any issues that may arise. The collaboration may involve providing training and support to healthcare providers, collecting feedback on device performance, and working collaboratively to identify and address any issues that may arise.

8 A Novel Method for Conformity Assessment Testing of Infusion Pumps for Post-Market Surveillance Purposes

The methodology proposed for assessing the conformity of infusion pumps involves several steps. Firstly, legal requirements must be established, including technical and metrological standards that the devices must meet to be considered suitable for diagnosis or therapy. After identifying these requirements, a testing method must be established that involves using calibrated reference instruments to measure the crucial parameters of the device. Finally, the results of the measurements should be presented in a report that allows for an analysis of the device's performance, leading to a conclusion about whether or not the device meets the previously established requirements.

8.1 Technical Requirements

Once devices enter the market and once they are used in clinical settings the periodical inspection of their technical requirements is very important. In order to ensure traceability of the devices labels and markings shall be visible, legible and indelible, and it is not possible to remove them without permanent damage. In case of the incubators, the technical requirements are formalized in the following manner:

The technical requirements refer to the:

- Label and marking

  name and/or trademark of manufacturer;
  production mark (basic type)
  year of fabrication;
  unique serial number;
  CE mark of appropriate administrative marking;

- Construction of the device that guarantees security against any interference to metrological characteristics.
- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz; Battery supply;

  Charging time < 10 h,
  Working time on battery on maximum flow is 3 h.

- Compliance with IEC 60,601–2-24 Medical electrical equipment—Part 2–24: Particular requirements for the basic safety and essential performance of infusion pumps and controllers.

For inspection of all above mentioned requirements, a testing method needs to be adopted. As per OIML recommendations, the testing of these types of the requirements is to be carried out by visual inspection and by electrical safety inspection in accordance with IEC 60601 [2].

8.2 Metrological Requirements

Reliability of medical devices can be proven with its compliance with metrological requirements. Meteorological parameters such as error, accuracy and uncertainty are quantitative parameters specific for every device that serve as an evidence of device reliability. For every measurement device specific parameters are defined by its manufacturer such as measurement unit, range and division and accuracy. Following the OIML guideline, in case of the infusion pumps, the metrological requirements are formalized in the following manner:

Measurement unit

- Flow of volume is set and measured in milliliters per hour [ml/h].

Millilitre per hour is a derived unit of volume flow in the International System of Units (SI) (NIST 2019). It is defined as the volume in ml divided by the duration in hours.

- Measuring range and division

  Flow of volume range:

Infusion pumps (0.1–999.99) [ml/h]

Outside this working range no energy reading and no measurement result shall be displayed.
Division: Measurement points are defined and distributed evenly on the whole measurement range.
Performance accuracy stated by the manufacturer in the technical specification.

For inspection of all above mentioned requirements, a testing method needs to be adopted. As per OIML recommendations, the testing of these types of the requirements is to be carried out by performance inspection presented in Sect. 2.3.4 of results. A test report shall be prepared according to part 2.3.4 of results. With a performance inspection method the metrological conformity assessment testing is done.

The metrological conformity assessment testing requirement can be formulated as per OIML recommendations as follows:

- For any set of conditions within the ambient temperature range of 21–26 °C in the maximum permissible error for the flow measurements is as follows:

  for infusion pumps ± 5%,

8.3 Method of Test

8.3.1 Visual Inspection

(a) *Equipment*
- The prerequisites for performing visual inspection are:
- Device under test/Infusion pumps;
- Manufacturers specification;

(b) *Procedure*

The procedure for visual inspection for a device under test consists of checking label/marking and construction integrity. The device must comply with manufacturers specification in terms of functionality and accompanying parts.

(c) *Summary and expression of test results*

The results are expressed as Pass/Fail answers to the criteria which has been tested (Table 1).

8.3.2 Electrical Safety Inspection

(a) *Equipment*

The prerequisites for electrical safety inspection are:

Table 1 Technical Requirements and Pass/Fail Criteria

Technical requirements and pass/fail criteria			
No.	Criteria technical requirements	Result	Conformity assessment testing
1	Prescribed labels and markings on the device under test	• name and/or trademark of manufacturer; • production mark (basic type) • year of fabrication; • unique serial number; • CE mark of appropriate administrative marking;	Pass/Fail
2	Construction of the device	• the integrity of the device under test in respect to the manufacturer's specification • the functionality of the device under test in respect to the manufacturer's specification	Pass/Fail
3	Construction of the device	• measurement range • measurement unit	Pass/Fail

Column 1 = Measuring point; Column 2 = Values set on the device under test; Column 3 = Values measured by calibrated testing equipment; Column 4 = Deviation expressed as relative error; Column 5 = Maximum deviation; Column 6 = Conformity assessment testing statement

Device under test/Infusion pump;
Reference electrical safety testing equipment/analyzer;
Procedure

The procedure starts with connecting the infusion pump to electrical safety testing equipment. Test of the electrical safety of a device under test is performed according to the requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open neutral, normal condition—reversed mains, open neutral—reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition—reversed mains, normal condition—reversed mains, open earth—reversed mains), patient applied parts leakage current.

(c) *Summary and expression of test results*

The results are expressed in terms of requirements of IEC 60,601–1:2005—Medical electrical equipment—Part 1: General requirements for basic safety and essential performance.

8.3.3 Performance Inspection

(a) *Equipment*

The prerequisites for performance inspection are:

Device under test/Infusion pump;
Reference testing equipment/analyzer;
Procedure

Based on device measuring range select measuring points to cover the entire measuring range. Test the flow in every measuring point. To test the flow in every measuring point, on a device, select the desired values that are expressed in ml/h. Connect the infusion pump to calibrated reference testing equipment. When the device is connected, initiate the start of the flow on the DUT. All measurements were evaluated for their performance by measuring the delivered flow at the same point multiple times in order to check for consistency in the delivered value.

(c) *Summary and expression of test results*

The decision of conformity assessment testing is obtained after the analysis of the results of the conducted tests. The OIML recommends a summary of the results in the form of tables. As it could be seen, visual inspection is reported in the form of qualitative analysis. Simple YES/NO answers to the criteria states the conformity assessment testing. For the performance inspection, the results are expressed using terms of error. In metrology error can be expressed using absolute error or relative error. In case of infusion pumps, the performance inspection result can be reported as the relative error between the set values of the device under test and the corresponding readings of the calibrated reference testing equipment.

Relative error calculation:

$$\Delta X = Xs - Xm/Xs * 100 \tag{1}$$

The conformity assessment testing in performance inspection is determined by the value of this error. Relative error was formulated based on the international standards followed during the production of the infusion pump. Based on this requirement the conformity error is formulated as follows:

If the error is less than the greatest allowed limit, then the device is compliant with metrological requirements.

This methodology includes both quantitative testing and inspection of qualitative features that can impact the performance of the infusion pumps described in this chapter. These qualitative features include assessing the integrity of the housing, including stress relief, connectors, switches, screen, alarms, and battery. Additionally, the accuracy of the instruments and controls, charging time, internal power source, and device operation after the battery alarm and battery have been tested.

9 Recommendations, Contraindications, and Warnings

When using infusion pumps, it is essential for the user to provide a safe environment for the proper operation of the device. The COVID-19 pandemic has highlighted the need for periodic inspections of medical devices that involve measurements to ensure their correct functioning. These rules and guidelines cover a range of aspects, including patient surroundings and the proper disposal of medical and electronic waste. Adhering to these guidelines is crucial to prevent safety hazards or device malfunctions.

9.1 Patient Environment

The patient environment refers to the physical surroundings of the patient during infusion therapy and includes factors such as the location of the device, the cleanliness of the area, the patient's positioning, and the condition of the surrounding equipment. Creating a clean, organized environment can help reduce the risk of contamination or other safety hazards.

Performing a visual inspection of the infusion pump before use is an important step in ensuring patient safety. This includes checking the device for any signs of damage, leaks, or other malfunctions. The device should also be inspected to ensure that it is clean and free from any debris or foreign material. Any issues should be addressed before beginning infusion therapy.

Proper connection of the infusion pump to the patient is also critical for safe and effective use. The device should be connected to the patient using sterile techniques to prevent infection or contamination. The infusion site should be properly prepared and positioned to ensure that the medication is delivered to the intended area. The healthcare provider should monitor the patient closely during infusion therapy to detect any adverse reactions or complications. Healthcare providers should be aware of the signs and symptoms of potential adverse events and have a plan in place for managing any issues that may arise. In some cases, special considerations may need to be made for patients with specific medical conditions or unique needs.

Healthcare providers should also follow manufacturer recommendations for the use and maintenance of infusion pumps. This may include instructions for device calibration, cleaning, and maintenance, as well as guidelines for patient selection and management.

9.2 Electrical Warnings

Electrical warnings for infusion pumps are an important consideration for patient safety. Infusion pumps rely on electrical power to operate, and any issues with the

electrical system can potentially impact the safety and effectiveness of the device. To minimize the risk of electrical hazards, infusion pumps are typically designed with a variety of safety features, such as grounding wires, fuses, and circuit breakers. Infusion pumps should be regularly inspected for signs of wear or damage, such as cracks or exposed wires. Any issues with the electrical system should be addressed promptly, and the device should be taken out of service if any electrical hazards are identified.

One common electrical warning for infusion pumps is to avoid using the device in the presence of flammable gases or liquids. This is because the electrical current used to power the device can potentially ignite flammable materials, causing an explosion or fire. Additionally, infusion pumps should be kept away from sources of electromagnetic interference, such as other electronic devices, as this can impact the accuracy and safety of the device.

Other electrical warnings may relate to the use of the power cord or battery pack. For example, it may be recommended to only use the power cord provided by the manufacturer, as using an incompatible cord could potentially damage the device or lead to electrical hazards. Additionally, battery packs should be used and stored according to the manufacturer's recommendations, as mishandling or damage to the battery can lead to electrical hazards.

9.3 Electrostatic Discharge, Conducted Immunity, and Electromagnetic Interference

Electrostatic Discharge (ESD), Conducted Immunity (CI), and Electromagnetic Interference (EMI) are important factors to consider when using and testing infusion pumps. ESD is a sudden discharge of static electricity between two objects with different electrical charges, and it can cause damage to electronic devices. CI refers to the ability of a device to withstand electrical interference that may be conducted through the power supply or other electrical connections. EMI occurs when an electronic device emits electromagnetic waves that can interfere with other nearby devices.

In order to prevent ESD, infusion pumps should be properly grounded, and healthcare providers should avoid wearing clothing that generates static electricity while handling the device. Additionally, healthcare providers should avoid using infusion pumps in areas with high electrostatic activity, such as those with high humidity levels. Infusion pumps should be designed to meet appropriate CI standards to ensure that they are not affected by electrical interference from other devices in the clinical setting. Infusion pumps should be designed to minimize EMI emissions, and should be tested to ensure that they do not interfere with other medical devices in the vicinity. Some medical devices within hospitals, such as electrosurgical generators or physiotherapy machines, were recognized as potent sources of interference, but their effects were understood and their use was confined to specific areas. However, the

introduction of new portable communication systems has made the problem of interference more complicated. Implanted therapeutic devices are somewhat shielded by surrounding body tissues, which act as a barrier against electromagnetic interference, but non-implanted devices like ambulatory insulin pumps are more vulnerable and can receive higher doses of interference.

Fortunately, most medical devices have been designed to operate in a "fail-safe" manner, meaning that the device will return to a safe standby state and alert the user if any disruption occurs, regardless of the cause.

Mobile phones and other communication devices should not be used within two meters of medical equipment, especially critical devices like infusion pumps. Patients who use ambulatory pumps outside of the hospital should be provided with guidance on what activities and communication devices to avoid.

Manufacturers should conduct rigorous testing to evaluate the device's ability to withstand ESD, CI, and EMI, in order to ensure that infusion pumps are safe and reliable. Healthcare providers should also be trained on how to properly handle and use infusion pumps to minimize the risk of electrical interference or damage to the device. Healthcare providers should be aware of any potential sources of ESD, CI, or EMI in the clinical setting, and should take appropriate precautions to prevent electrical interference that may impact the safe and effective use of infusion pumps.

9.4 Contraindications for Use and General Warnings

Infusion pumps are widely used in medical settings to deliver medication and fluids to patients. However, there are certain situations in which their use may be contraindicated. For example is a patient has a known allergy or hypersensitivity to a particular medication or fluid that is to be administered via the pump. Additionally, if a patient has a medical condition or is taking a medication that interacts with the medication or fluid being administered, the use of the infusion pump may also be contraindicated. Other contraindications may include conditions that affect the absorption, distribution, metabolism, or excretion of the medication or fluid, as well as conditions that affect the circulation or integrity of the vasculature at the infusion site. It is important for healthcare professionals to be aware of these contraindications and to carefully evaluate each patient's medical history and current condition before using an infusion pump. By doing so, the risks associated with infusion pump use can be minimized and patient safety can be improved.

- The device should be used only as directed and with the correct administration sets and accessories.
- The device should be used only by trained personnel who are familiar with the device and its operation.
- The device should not be used for any purpose other than the one for which it was intended.

- The device should not be used on pediatric patients or in neonatal intensive care units unless specifically approved for such use.
- The device should not be used for the administration of blood or blood products.
- The device should not be used for the administration of drugs that require continuous cardiac monitoring or drugs that are contraindicated for use with the device.
- The device should not be used with drugs that have the potential to cause serious harm if an infusion error occurs.
- The device should not be used with drugs that require special handling, such as those that are cytotoxic or hazardous.
- The device should be inspected before each use to ensure that it is functioning properly.
- The device should be properly maintained and serviced according to the manufacturer's recommendations.
- The device should be stored in a clean, dry, and cool environment, and protected from damage and contamination.
- The device should be used with caution in patients with compromised renal or hepatic function.
- The device should be used with caution in elderly or debilitated patients, or in patients with preexisting conditions that may affect their response to therapy.

9.5 Environmental Conditions, Storage, and Transport

Environmental conditions, storage, and transport are critical factors that must be taken into account when handling infusion pumps because these devices are sensitive to changes in temperature, humidity, and pressure, which can affect their accuracy and reliability. For instance, extreme temperatures can cause the batteries to drain faster, and high humidity can lead to condensation inside the device, which can damage the electronics. As a result, infusion pumps should be stored in a dry and cool place, away from direct sunlight, heat sources, or excessive moisture.

Proper transport of infusion pumps is essential to ensure their integrity and prevent damage during shipping. Pumps should be packaged securely to prevent any jostling or impact during transportation. They should also be clearly labeled as fragile and handled with care. During transport, the pumps should be kept within the manufacturer's recommended temperature and humidity ranges.

The operating temperature for most infusion pumps falls within the range of 10–40 °C (50–104°F). Relative humidity ranges typically fall between 15 and 90%, and atmospheric pressure ranges are between 700 and 1060 hPa. Infusion pumps may also have specific requirements for storage temperature and humidity. The storage temperature range can range from −20 °C to 50 °C (-4°F to 122°F), and the storage humidity range is typically between 10 and 95%.

It is important to note that environmental conditions, storage, and transport can vary depending on the type of infusion pump and the manufacturer's guidelines.

Users should always refer to the manufacturer's instructions for specific guidance on how to handle and transport their device. By following these guidelines, users can ensure that their infusion pumps are stored and transported properly, minimizing the risk of damage and ensuring their safe and reliable use in clinical settings.

9.6 Cleaning and Disposal

Cleaning and proper disposal of infusion pumps are important in preventing the spread of infections and environmental contamination. Infusion pumps should be cleaned and disinfected after each use to remove any traces of blood or bodily fluids that may remain on the device. The cleaning and disinfection process should follow the manufacturer's instructions, including the recommended cleaning agents, concentration, and contact time. It is important to avoid using abrasive cleaners or harsh chemicals that could damage the device.

Before disposing of an infusion pump, it is important to ensure that all the parts are properly disinfected and that the device is no longer functional. Disposal methods for infusion pumps may vary depending on local regulations and guidelines. In some cases, the device may be disposed of in the regular trash, but it is important to remove any batteries or other hazardous materials before doing so. Some facilities may have designated medical waste disposal systems or recycling programs for medical devices, including infusion pumps.

Some infusion pumps may contain sensitive patient information, such as medication dosages and patient identifiers, meaning these devices should be properly disposed of to ensure the confidentiality and security of patient information. Infusion pumps that are no longer needed should be disposed of promptly to prevent the risk of accidental use or theft. Facilities should have policies and procedures in place for the proper cleaning and disposal of infusion pumps, as well as training for staff on how to follow these protocols.

10 Conclusion

Conformity assessment of infusion pumps is an important process in ensuring the safe and effective use of these devices in healthcare settings. The new European Medical Device Regulation (MDR) requires manufacturers of medical devices, including infusion pumps, to demonstrate conformity with the applicable regulatory requirements before placing their products on the market. One aspect of conformity assessment for infusion pumps is post-market surveillance, which involves monitoring the performance of these devices after they have been placed on the market. This includes tracking and reporting incidents involving infusion pumps, as well as conducting regular inspections and testing to identify and correct any issues with the devices.

The importance of conformity assessment and post-market surveillance of infusion pumps cannot be understated. These processes help to ensure the safety and effectiveness of these devices in patient care, and can help to identify and address any potential issues before they cause harm to patients. In addition, compliance with the MDR requirements for conformity assessment and post-market surveillance is essential for manufacturers of infusion pumps to be able to sell their products in the European Union.

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Cost Effectiveness Analysis of Medical Devices in Legal Metrology System

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Abstract Medical device inspection is crucial in ensuring safety and reliability of devices since they are an essential component of patient diagnosis or treatment. Periodical inspection of safety and performance in medical devices decreases risk of errors and injuries caused by device malfunction. Device assessment, management and maintenance is crucial in any industry, not just the healthcare sector, but specifically for healthcare—the COVID-19 pandemic has shown how inadequate the present maintenance techniques are and highlighted the importance of regular device inspections. As we live in the digital age, and data is becoming a currency, investigating the possibility of using the data to update the current medical device maintenance programs is necessary. In order to optimise the maintenance programs, quantifiable factors and good databases are needed which form a good foundation for evidence-based maintenance of medical devices. Evidence-based methodology for surveillance of medical devices has been part of the legal metrology framework in Bosnia and Herzegovina and in the Republic of Serbia. All data resulting from the inspection carried out by independent appointed inspection bodies have been entered in a database specially developed for this purpose. In countries such as these two (third world countries) it is still necessary to improve the system which would lead to superior use of the medical system in the health system. This chapter will outline the role and the importance of the inspection of medical devices in the health system. The data provided from these countries are used in order to determine the cost effectiveness of medical device inspections. The data and analysis will show how the medical devices have affected its accuracy and effectiveness when they have been introduced into the legal metrology of Bosnia and Herzegovina and Republic of Serbia.

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1 Legal Metrology Framework for Inspection of Medical Devices with Measuring Function in Bosnia and Herzegovina and Republic of Serbia

The cost effectiveness analysis presented in this chapter is based on the data extracted from appointed inspection bodies performing periodical inspections of medical devices in healthcare institutions in Bosnia and Herzegovina and Republic of Serbia. From the legislation point of view, there is limited data and details about the laws, rulebooks, regulations, available for both countries.

In Bosnia and Herzegovina, the bylaws published in the Official Gazette of Bosnia and Herzegovina in 2014 (no. 75/14) define 11 types of medical devices to be yearly inspected as follows: *defibrillator, dialysis machine, infusion pumps, perfusor, therapeutic ultrasound, ECG devices, patient monitor, mechanical ventilators, anaesthesia machine, infant incubator and resuscitation warm tables and blood pressure device* [1–3]. In the Republic of Serbia, the bylaws were published in 2020 in the Official Gazette of the Republic of Serbia (no. 92/20) [4] a covering 10 types of medical devices: *ECG devices, infusion and perfusion pumps, anaesthesia machine, defibrillator, dialysis machine, neonatal and paediatric incubators and resuscitation warm tables, mechanical ventilators, therapeutic ultrasound, multifunctional devices for patient monitoring and high frequency surgical knife and equipment.* According to the rulebook published in the Official Gazette of the Republic of Serbia (no. 37/21) [5] all these devices are subject for a control once a year except medical devices for mechanical ventilator and anaesthesia machines. These two types of medical devices are subject to a control twice a year.

The cost-effectiveness analysis was performed on the data about the periodical inspections from Bosnia and Herzegovina covering the period 01.01.2017 until 01.09.2022. For Republic Serbia the data were extracted for the period from 01.01.2021 until 01.09.2022. The collected data analysis is presented in Table 1. Compliant and Non-compliant devices is represented individually as well as for all devices together for each country. In this chapter, a specific approach in analysis of cost-effectiveness of inspection framework for medical devices with measuring functions is presented [6, 7], and the data obtained were used as the basis for all following analyses presented, such as regression and correlation analysis.

Table 1 Compliant and non-compliant defibrillators in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	96.46	98.80	96.26	95.31	96.14	98.21
Non-compliant(%)	3.54	1.20	3.74	4.69	3.86	1.79

1.1 The Data from Bosnia and Herzegovina

Table 1. summarises the percentage of compliant and non-compliant medical devices, as found by independent inspection performed by appointed inspection bodies in Bosnia and Herzegovina.

The research done by Gurbeta et. al [8] in 2017. showed that 14.91% of defibrillators device performance was not in accordance with requirements and should either have its results be verified, or the device removed from use or scheduled for corrective maintenance. Based on the data provided it can be seen that the medical device group: defibrillator has increased its accuracy in each year except in 2020. As the data show there is no decrease each year for the non-compliant devices. In 2018 non-compliant devices were the lowest (Table 2).

The data for the dialysis machine show a tendency of growth in percentages of compliant devices. For the first three years (2017, 2018 and 2019) the growth is very small (approximately the same percentages of devices each year). The significant growth started in 2021. When it comes to the dialysis machine the data show oscillations in the movement of a percentage of non-compliant devices. Only in 2020 there were no non-compliant devices but the highest value for devices was in 2017. Dialysis machine is the only machine that until 2022 had no non-compliant devices among these 11 groups of devices (Table 3).

The percentage of compliant devices for infusion pumps varies from year to year. The smallest percentage of compliant devices was in 2018 and the highest percentage was in 2019. For these devices the higher percentage of non-compliant devices was at the beginning of the collection that i.e., in 2017. After that there were non-compliant devices but the percentage was lower compared to 2017 (Table 4).

When it comes to the perfusor the data show oscillations in the movement of percentages of compliant devices. The highest percentage of compliant devices was for the first year i.e., in 2017. The smallest percentage of compliant devices was in 2018. Also, for these medical devices the percentage of non-compliant devices

Table 2 Compliant and non-compliant devices for dialysis machine in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	94.70	99.31	98.01	100	99.21	100
Non-compliant (%)	5.30	0.69	1.99	0	0.69	0

Table 3 Compliant and non-compliant devices for infusion pumps in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	81.05	84	95.39	90.41	97.31	98.75
Non-compliant (%)	18.95	16	4.61	9.59	2.69	1.25

Table 4 Compliant and non-compliant devices for perfusor in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	89.13	74.53	97.25	92.82	94.97	99.14
Non-compliant (%)	10.87	25.47	2.75	7.18	5.03	0.86

had decreased on a yearly basis until 2020 because in 2020 the percentage of non-compliant devices had increased compared with the previous year. In 2021 the percentage of non-compliant devices had decreased again (Table 5).

The data for the therapeutic ultrasound shows growth in the percentages of compliant devices each year. The highest percentage of compliant devices was in 2021 compared to all years of the period that has been taken into comparison. The movement of the non-compliant devices shows small oscillations because if we take one year to compare it with the previous one the differences are ± 1 or 2 devices (Table 6).

In 2018 there is a decrease in the percentage of compliant devices compared to 2017 but in 2019 the data show growth compared to previous year (2018). After that in the next year (2020) the data show decreases in the percentage of compliant devices. Year 2021 is the year of growth in the percentage of compliant devices with the highest percentage of devices compared to the whole period in which data was collected (2017–01.09.2022). For the first four years (2017–2020) the percentage of non-compliant devices is similar but there is no yearly decrease (Table 7).

Table 5 Compliant and non-compliant devices for therapeutic ultrasound in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	91.67	93.98	96.75	95.27	97.86	96.30
Non-compliant (%)	8.33	6.02	3.25	4.73	2.14	3.70

Table 6 Compliant and non-compliant devices for ECG in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	95.71	95.91	95.95	95.76	97.74	98.67
Non-compliant (%)	4.29	4.09	4.05	4.24	2.26	1.33

Table 7 Compliant and non-compliant devices for patient monitor in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	90.20	97.05	97.67	96.58	98.07	100
Non-compliant (%)	9.80	2.95	2.33	3.42	1.93	0

For this medical device the data show oscillations each year in the percentage of compliant devices. In 2017 there was a higher percentage of compliant devices compared to the year 2018 but after that, the percentage of compliant devices started to increase each year until 2022. From the beginning of the collected data 2017 up to 2019 (including 2019) the percentage of non-compliant devices decreased on a yearly basis in order to increase its value in 2020. Again, after that in 2021 the percentage of Non-compliant devices has started to decrease (Table 8).

According to the research done by Badnjevic et. al [9] in 2017, it was found out that 30% of the tested medical devices were not operating properly and should be serviced, recalibrated and/or removed from daily application. The percentage of compliant devices show growth from year 2017 up to year 2022 except when that percentage was equal in 2018 and 2019. The peak of compliant devices was in the year 2021. In 2018 and 2019 the percentage of non-compliant devices had decreased in order to increase its value in 2020. In 2021 the percentage of non-compliant devices had decreased (Table 9).

The research done by Gurbeta et. al [8] in 2017. showed that 13.84% of tested anaesthesia machine performance was not in accordance with requirements and should either have its results be verified, or the device removed from use or scheduled for corrective maintenance. In 2018 the percentage of compliant medical devices was higher compared to the previous year 2017 but in the next year (2019) that percentage had decreased. After that it had increased again for the rest of the years of the period taken into account. The percentage of Non-compliant devices for anaesthesia machines varies from year to year with the trend of yearly decrease for the first three years (2017, 2018 and 2019). Again in 2020 there is an increase in the percentage of non-compliant devices compared to the previous year and decrease in 2021 compared to the 2020. The percentage of Non-compliant devices was the same in 2019 and 2021 (Table 10).

From the obtained data it can be seen that the percentage of compliant medical devices grows annually. The highest percentage of compliant devices is obtained in the year 2021. The obtained data show a yearly decrease for the first three years

Table 8 Compliant and non-compliant devices for mechanical ventilator in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	82.46	87.97	93.29	92.02	97.72	96.30
Non-compliant (%)	17.54	12.03	6.71	7.98	2.28	3.70

Table 9 Compliant and non-compliant devices for anaesthesia machine in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	88.98	94.69	95.35	93.38	97.26	97.01
Non-compliant (%)	11.02	5.31	4.65	6.62	2.74	2.99

Table 10 Compliant and non-compliant devices for incubator in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	76.56	86.15	91.30	85	97.30	87.18
Non-compliant (%)	23.44	13.85	8.70	15	2.70	12.82

if one year is compared to the previous one but that trend ends with the year 2020 when there is an increase in the percentage of non-compliant devices. The smallest percentage of non-compliant devices was in 2021 and the highest percentage was in 2017 (Table 11).

From 2017 up to 2020 the percentage of compliant devices has increased annually. In 2020 the percentage of compliant devices decreased but in 2021 it had a significant growth compared to the previous year as well as for all the years before. For the blood pressure device, the highest value of non-compliant devices was in 2021. Also, the smallest percentage of non-compliant devices was in 2017 (Table 12).

After the devices have been introduced into the legal metrology system from Table 13 it can be seen that not all the devices have increased their accuracy annually. The devices which had increased their accuracy each year (2017–01.09.2022) are: **dialysis machine, therapeutic ultrasound and infant incubator**.

Based on the collected data from Table 13, the average percentage of compliant and non-compliant devices was calculated in order to get the percentage of compliant and non-compliant devices for all the years that had been taken into account for Bosnia

Table 11 Compliant and non-compliant devices for blood pressure device in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	89.01	84.70	88.30	91.44	89.31	91.74
Non-compliant (%)	10.99	15.30	11.70	8.56	10.69	8.26

Table 12 Compliant and non-compliant devices for all medical devices in Bosnia and Herzegovina presented in percentages (01.01.2017–01.09.2022)

Year	2017	2018	2019	2020	2021	2022
Compliant (%)	90.97	92.64	94.27	94.05	95.41	97.18
Non-compliant (%)	9.03	7.36	5.73	5.95	4.59	2.82

Table 13 Compliant and non-compliant devices for the defibrillator in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	91.83	95.33
Non-compliant (%)	8.17	4.67

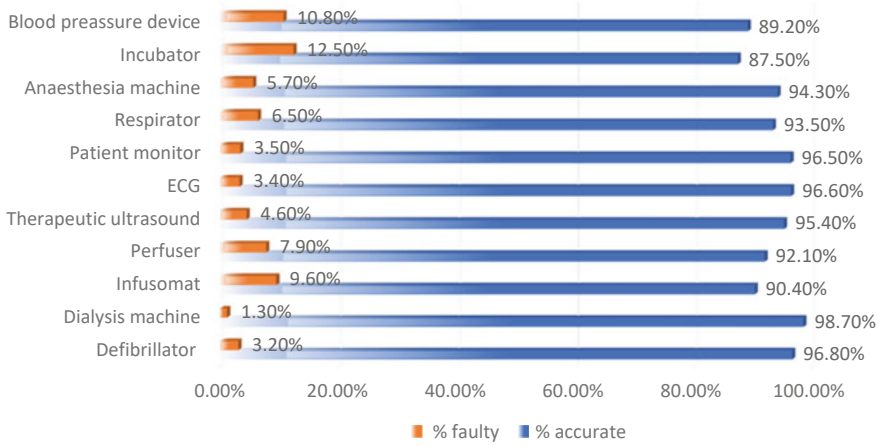

Fig. 1 The average percentages of compliant and non-compliant devices for each medical device in Bosnia and Herzegovina (01.01.2017–01.09.2022)

and Herzegovina. Figure 1. graphically represent the calculated data. For all years (2017–2022) the percentage of total percentage of compliant devices is 94.2% and the total percentage for non-compliant devices is 5.8%. When it comes to the compliant devices the percentage of those devices varies from 87.50% in the incubator and 98.70% in the dialysis machine. On the other side the percentage of non-compliant devices varies from 1.30% in dialysis machines and 12.50% in incubators. Based on the calculated data and graphical chart it can be concluded that there are more compliant devices than non-compliant devices which is of great importance for the health system of Bosnia and Herzegovina and the safety of patients. The percentage of compliant devices is about 16 times greater than the percentage of non-compliant devices. However, the remaining percentage of non-compliant devices poses serious risk of injury for end users of these devices.

1.2 The Data from the Republic of Serbia

The percentage of compliant devices in 2021 was lower than in 2022 so it can be concluded that the percentage of compliant devices did increase in 2022 compared to the previous year. On the other hand, there is a decrease in the percentage of non-compliant devices in 2022 which is positive for the health system in the Republic of Serbia (Table 14).

For this medical device the data show that the percentage of compliant devices is higher in 2021 than it was in 2022. In 2021 there were no non-compliant devices and in 2022 there were only multiple non-compliant devices. This is the only device that has zero non-compliant devices and that is in 2021 (Table 15).

Table 14 Compliant and non-compliant devices for the dialysis machine in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	100	98.44
Non-compliant (%)	0	1.56

Table 15 Compliant and non-compliant devices for the infusion pumps in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	89.13	85.06
Non-compliant (%)	10.87	14.94

Table 16 Compliant and non-compliant devices for the perfusor in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	95.37	94.93
Non-compliant (%)	4.63	5.07

Compliant devices for this category of medical devices show that there are more compliant devices in 2021 compared to 2022. The percentage of non-compliant devices in 2022 increased its value compared to 2021 (Table 16).

In 2021 the percentage of compliant data was higher than in 2022 so it can be concluded that the percentage of compliant devices did not increase in 2022. Also, for the perfusor the data shows a decrease in the percentage of non-compliant devices in 2022 (Table 17).

There were more compliant therapeutic ultrasounds in 2021 compared to 2022 and there is a decrease in the percentage of non-compliant devices in 2022 (Table 18).

In 2021 the value of compliant devices is higher than in 2022. In 2022 there is an increase in the percentage of non-compliant devices compared to the previous year (Table 19).

Table 17 Compliant and non-compliant devices for the therapeutic ultrasound in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	40.68	45.54
Non-compliant (%)	59.32	54.46

Table 18 Compliant and non-compliant devices for the ECG in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	96.13	94.44
Non-compliant (%)	3.87	5.56

Table 19 Compliant and non-compliant devices for the patient monitor in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	92.91	90.83
Non-compliant (%)	7.09	9.17

Table 20 Compliant and non-compliant devices for the mechanical ventilator in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	94.70	85.77
Non-compliant (%)	5.3	14.23

Year 2022 shows a higher percentage of compliant devices in 2021. Also, in 2022 there is an increase in the percentage of non-compliant devices compared to the previous year (Table 20).

The percentage of compliant devices in 2021 was lower than in 2022 so it can be concluded that the percentage of compliant devices did increase in 2022 compared to the previous year. The data for these devices show a high increase in the percentage of non-compliant devices for the year 2022 (Table 21).

The data in 2022 show an increase in the percentage of compliant devices. In 2021 the percentage of non-compliant devices was lower than in 2022 so it can be concluded that the percentage of non-compliant devices had increased in 2022 (Table 22).

For this group of devices, the percentage of compliant devices as well as the percentage of non-compliant devices was higher in 2021 compared to the year 2022 (Table 23).

For the year 2022 there is an increase in the percentage of compliant devices. On the other hand, in 2022 there was a decrease in the percentage of non-compliant devices compared to the previous year (Tables 24 and 25).

Table 21 Compliant and non-compliant devices for the anaesthesia machine in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	98.32	94.52
Non-compliant (%)	1.68	5.48

Table 22 Compliant and non-compliant devices for the manometer (aneroid) in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	94.56	92.44
Non-compliant (%)	5.44	7.56

Table 23 Compliant and non-compliant devices for the manometer (mercury) in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	82.30	95.88
Non-compliant (%)	17.7	4.12

Table 24 Compliant and Non-compliant devices for the high frequency surgical knife in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	95.93	94.33
Non-compliant (%)	4.07	5.67

Table 25 Compliant and non-compliant devices for the incubator in Republic of Serbia presented in percentages (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	83.23	83.84
Non-compliant (%)	16.77	16.16

There is a decrease in the percentage of compliant devices in 2022 so it can be concluded that the percentage of compliant devices did not increase in 2022. In 2022 there was an increase in the percentage of non-compliant devices (Table 26).

Using the data from Table 14 the average percentage of compliant and non-compliant medicine devices was calculated in order to get the percentage of compliant and non-compliant devices for two years that had been taken into account for the Republic of Serbia. Figure 2. is a graphical representation of the calculated data. For this period of time in which data was gathered the percentage of total number of compliant devices is 92.3% and 7.7% for the non-compliant devices. When it comes to the compliant devices the percentage of those devices varies from 42.6% in therapeutic ultrasound and 99.3% in dialysis machines. On the other side the percentage of Non-compliant devices varies from 0.7% in dialysis machines and 57.4% in therapeutic ultrasound. Based on the calculated data and graphical chart it can be concluded that also for the Republic of Serbia as it was the case with Bosnia

Table 26 Compliant and non-compliant devices for the total number of devices in Republic of Serbia (01.01.2021–01.09.2022)

Year	2021	2022
Compliant (%)	93.31	91.25
Non-compliant (%)	6.69	8.75

Note. Because for the Republic of Serbia the data is limited and the data does not cover sufficient periods of the time it is difficult to make deeper analysis and comparison but explanation for each medical device will be based on the same principle as it was done for Bosnia and Herzegovina

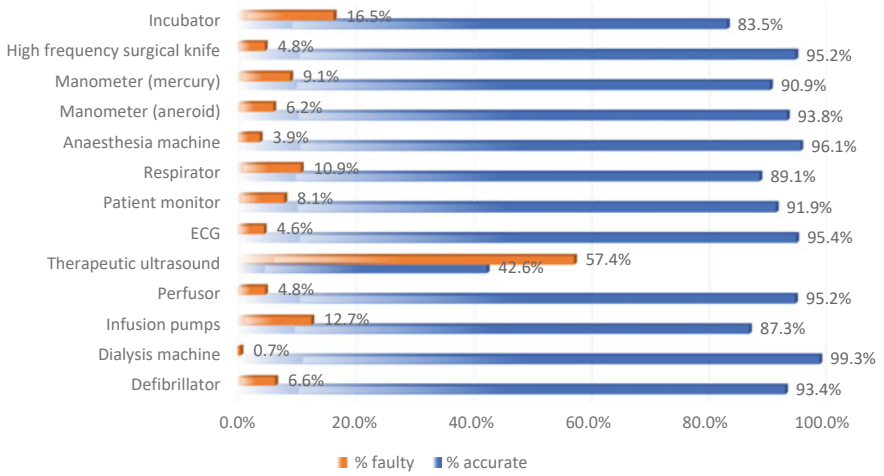

Fig. 2 The average percentage of Compliant and Non-compliant devices for each medical device in Republic Serbia (01.01.2021–01.09.2022)

and Herzegovina there are more compliant devices than non-compliant devices. The number of compliant devices is about 5 times greater than the number of non-compliant devices which also contributes to the health system of the Republic of Serbia. However, the remaining percentage of non-compliant devices poses a great risk to end users and patients.

2 Summary of Data

See Figs. 3 and 4.

3 Regression and Correlation Analysis

For the purpose of this chapter statistical software Stata was used. We assume that the percentage of compliant medical devices and the percentage of non-compliant medical devices are inter-related with respect to certain types of medical devices. This assumption is indicated by Fig. 5.

In this chart the independent variable (X) represents the average annual number of Compliant medical devices. Average annual number of Non-compliant medical devices represent dependent variable (Y).

After the regression and correlation analysis, following results have been obtained:

- Determination coefficient 0.4277

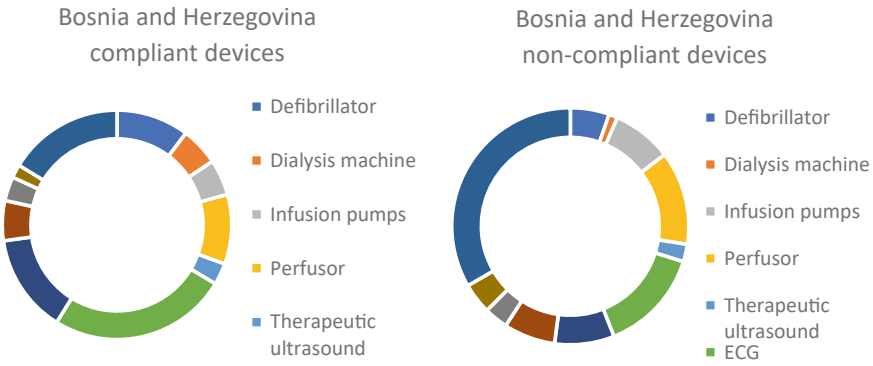

Fig. 3 Total number of devices per device group in Bosnia and Herzegovina

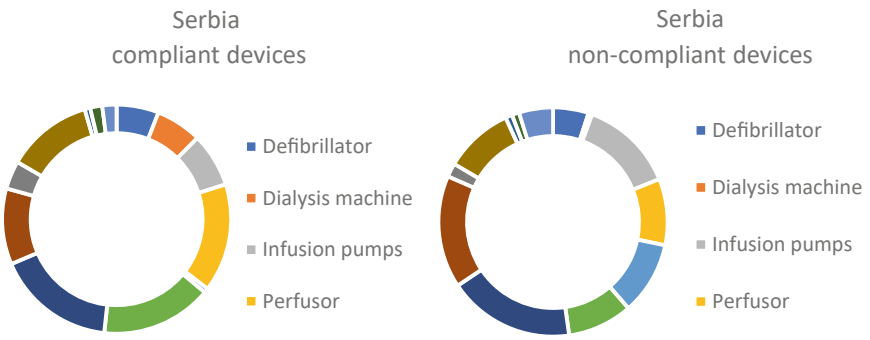

Fig. 4 Total number of devices per device group in Republic of Serbia

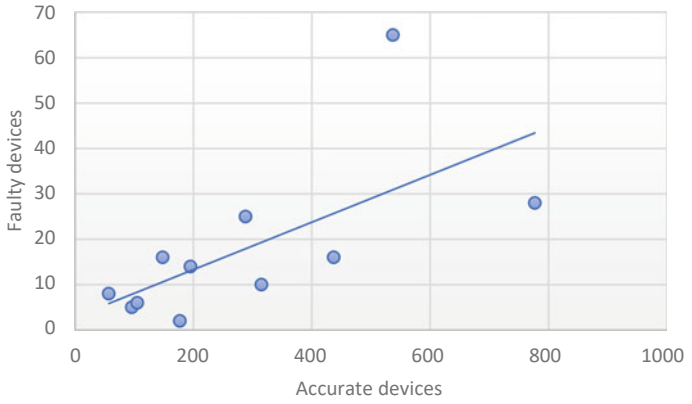

Fig. 5 The correlation between the average annual number of Compliant and the number of Non-compliant medical devices

- Sample size N = 11
- Size in F test F = 6.72, p = 0.0291
- Constant in the Eq. 2.856232 with p = 0.698
- Regression coefficient 0.0522 with p = 0.029

Therefore, the correlation between the average number of Compliant medical devices and the average number of Non-compliant medical devices is positive, strong and statistically significant (p = 0.0291). The connection is positive because the increase in the number of Compliant devices corresponds to an increase in the number of Non-compliant devices. The correlation between these variables explains a total of 42.77% variations. For each increase of 100 Compliant medical devices, the number of Non-compliant devices increases by 5.2% since the equation of the linear regression model is:

$$\hat{Y} = 2.856232 + 0.0522\,X$$

The constant in the equation is not statistically significant which means that the mean effect of all omitted variables may not be important, however, that does not mean that constant should be taken out because it does two other things in the equation.

4 Comparison Analysis Between Bosnia and Herzegovina and Republic of Serbia

Data from the Annual Measurement Reports between the countries Bosnia and Herzegovina and Republic of Serbia were compared. Data was available for the Republic of Serbia only for 2021 and 2022, while the data for Bosnia and Herzegovina were taken for the period 2017- 2022. From the data that was gathered it can be seen from Tables 13 and 14 that each country has a different number of medical devices. Due to the correct implementation of the tests, data were taken for identical medical devices, i.e., for 10 types of devices: *defibrillator, dialysis machine, infusion pumps, perfusor, therapeutic ultrasound, ECG, patient monitor, mechanical ventilator, anaesthesia machine and incubator.* First, the Pearson correlation coefficient was calculated, which is 0.6857 in Bosnia and Herzegovina and 0.6058 in Serbia. The results show that there is a moderately strong positive correlation between the observed average Non-compliant devices and average total devices in each country. For the Pearson correlation coefficient, the closer the correlation value is to 1, the greater is the interconnection between the observed variables. Since the value of the coefficient is positive, it means that with the increase in the number of average total devices, the number of average Non-compliant medical devices also increases.

Considering that it is a small sample of devices in Republic of Serbia and for a short period of time, the Mann–Whitney U test will be used as a non-parametric alternative to the independent t-test in order to test the difference between two groups

in a situation where the assumptions for the application of a parametric test are not met. We presented the original data using ranks with which we circumvented the problem of using data that violates parametric assumptions. The Mann–Whitney U test shows that there is no statistically significant difference between the ratings of the frequency of malfunctioning of medical devices between devices in Bosnia and Herzegovina and Serbia, $z = 0.076$, $p = 0.94$.

> For every used medical device in a healthcare institution which was subject of inspection a standardised record of safety and performance has been entered into the database periodically since inspections are conducted with determined frequency

In general, nowadays data collection has become very common in various industries [10]. Numerous analyses can be made on the basis of the collected data. These analyses are a solid base for forecasts and cost budgeting. Based on this analysis conclusions can be drawn and decisions can be taken. As mentioned in this chapter in Bosnia and Herzegovina and Republic of Serbia data about medical devices were collected and stored in the database for further analysis. By analysing collected data the behaviour of certain types of medical devices could be predicted in the future [11]. The more data is collected the higher is the probability of a correct prediction, but it also complicates collecting itself as well as processing and analysing that data. To speed up and easy the process of analysing the data, machine learning methods using artificial intelligence can be used. By using these methods a lot of data could be analysed in a very short time and conclusions could be made and it could help to better understand device behaviour. Based on that conclusion, maintenance of medical devices could be planned before failure occurs, and the parking time for maintenance of the device can be shortened. It is very important to try to use some machine learning methods to manage the maintenance of medical devices more precisely. Therefore, failures can be predicted and periodic and preventive medical device maintenance can be planned. This could optimise healthcare institutions maintenance programs and reduce total costs. Using good evidence-based management and good predictions could help moving from a reactive toward a proactive approach in medical device maintenance. A significant cost-effectiveness can be achieved in management of maintenance in healthcare institutions because standardised data showed certain patterns for healthcare institutions as described in the previous version of the book "Inspection of Medical Devices" [12].

In the event of crisis situations such as the COVID 19 pandemic, using an evidence-based approach with artificial intelligence, failures could be overlooked earlier, medical devices could be more optimally maintained and could be more efficient and ready for such a situation when devices are heavily needed [13–17].

5 Cost-Effectiveness of Legal Metrology System for Medical Devices

Identify the benefits: Identify the benefits of the legal metrology framework, such as increased accuracy and reliability of medical devices, improved patient safety, reduced risk of malpractice, and increased trust in the healthcare system.

- **Preventing unnecessary healthcare costs**: Framework enables identification of adverse events and safety concerns with medical products, allowing for early detection and prevention of potential harm to patients. This can avoid unnecessary medical costs associated with treating adverse events or complications resulting from unsafe or ineffective medical products.
- **Reducing legal costs**: Framework helps identify potential safety issues with medical products, which reduces the risk of lawsuits and litigation related to the use of unsafe or ineffective medical products. This can result in cost savings associated with legal fees, settlements, and damages.
- **Increasing efficiency**: By identifying safety issues with medical products, the framework leads to more efficient use of healthcare resources, such as reducing the use of ineffective or unsafe products and replacing them with safer and more effective alternatives. This can result in cost savings associated with improved patient outcomes and reduced healthcare utilisation.
- **Increased quality of services provided/ protection of patients**: Providing quality of services in patient treatment which will ensure the best possible protection of the patient with the goal of minimizing medical errors. The framework will ensure more accurate diagnosis and treatment for whom the care is intended which will lead to overall more satisfied patients and therefore increased trust in the healthcare system.

Different stakeholders have cost and benefits which serve as a basisis for cost-effectiveness and include:

For Regulators

- Digital Medical Device post-market surveillance mechanism
- Market insight
- Process standardisation
- Informed policy changes
- Needs assessment & trends

For Healthcare Institutions

- Process according to international standards
- Increased quality of management system
- Reduced costs of medical device maintenance
- Evidence—based management

- Informed decision making
- Gaining precision

For Patients

- Decreased risk of injury
- Increased reliability in diagnosis and treatment
- Increased quality of services/protection of patientsHealth-care institutions use cost-effectiveness analysis to make decisions on allocation of health-care resources. The biggest issue in implementing such type of analysis is reducing costs while maintaining quality. To avoid reducing costs to achieve solely monetary effectiveness the introdcution od legal metrology framework is crucial. Cost-effectiveness analysis in healthcare differs from other industries by introducing metrics like quality-adjusted life-years which combines longevity with health-related quality of life of patients.

Regulators should use cost-effectiveness analysis is a way to examine both the costs and health outcomes.

By comparing the introduction of the legal metrology framework to a situation by not implementing it (or the status quo) it could be estimated how much it costs to gain a unit of a health outcome, like a life year gained or a death prevented.

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Cybersecurity, Data Protection, and Artificial Intelligence in Medical Devices

Luka Jelić

Abstract This chapter gives an overview of the current cybersecurity issues in medical devices, risks concerning the personal data use, and regulatory recommendations for medical devices with artificial intelligence (AI) technologies. First sections describe general cybersecurity principles, cybersecurity pre- and post-market actions, responsibilities among healthcare stakeholders, and the importance of cybersecurity information disclosure. Data protection subsection provides current regulations on the use of personal health data. Subsection on AI-based medical devices explains the current trends in regulatory approvals for software as medical devices (SaMD) that use artificial intelligence and machine learning (ML) methods. Presented are the regulatory proposals concerning the modifications of medical devices to mitigate operating vulnerabilities and potential patient harm.

1 Introduction

Increased use of network communications with medical devices (MDs) has put the focus of both manufacturers and users to the issues of cybersecurity and data protection. Internet, wireless, local, and telemetry connections changed the way users operate with medical devices, and regulatory institutions have provided new regulations to challenge the cybersecurity risks. Manufacturers are required to develop medical systems with increased information security, with minimum recommended pre- and post-market strategies for the cybersecurity risk management. Users of the medical devices, ranging from the healthcare providers to the patients, need to apply increased caution to prevent unauthorised access to the medical data which could pose a health hazard to the patient or to the device safety. Cloud data storage raises the question of ownership of the data, as well as the responsibility for the data integrity and security. Increased use of artificial intelligence (AI) algorithms improves diagnostic and clinical care, but at the same time raises ethical concerns. Regulatory

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mechanisms need to ensure that the clinical decision-making stays at human level, making the AI use explainable and transparent. Software as a medical device, with the AI use, should be inspected in the same if not more rigorous way than the standard diagnostic software.

2 General Cybersecurity Principles

This chapter outlines the basic cybersecurity principles as the focus of the current state-of-the-art regulations relevant to users, manufacturers, healthcare providers, and patients. Operating on these principles should be followed with great care and in turn are expected to provide the users with a safe patient environment and mitigate the risks of device malfunctions and data breach.

2.1 Intended Use and Operational Environment

Manufacturers should design medical devices in accordance with the established quality systems ensuring that the devices meet the required system specifications [1]. These actions should be followed in accordance with the device type and its communication technologies [2], keeping in mind the intended use and operational environment of the medical system. Manufacturers should not rely on the operational environment for security assurance but need to provide a layered protection system to mitigate the security risks and increase the effectiveness of the device. Also, all useful information for the safe operation of the device should be provided, informing the user on the cybersecurity threats in the case of misuses of the device [3]. User and service manuals should contain the guidelines on the intended networking use, as well as recommended cyber environment and user control for which the medical system was specifically designed.

2.2 Information Sharing, Responsibility, and Regulatory Alignment

Sharing the cybersecurity information among all the parties involved in the manufacturing and use of the medical devices increases the safe use of the medical system. Vulnerability disclosure is advocated as the best practice, and cybersecurity organisations promote collaboration and sharing of cybersecurity incidents and threats that can negatively affect the networked healthcare technologies [3]. These actions also promote transparency among the regulators which should align their regulations across all involved stakeholders. These should include standardisation in product

design, risk management, regulatory requirements, information sharing, and after-market activities [3]. Cybersecurity information should be freely available to the medical device user, be it the health service provider or the patient. Having a transparent policy on cybersecurity safety risks helps the end user to mitigate the possible threats. Some examples of the fully disclosed information are [1]:

- Full information on cybersecurity vulnerabilities and on the possibility of the degradation of the device safety and functionality
- Detailed and easily understandable user manuals with information on device upgrades and network protection
- Risks of using a third-party software, whether obtained locally or through the Internet

The manufacturers, healthcare providers, users, and regulators all share cybersecurity responsibility and must work closely to mitigate and respond to cybersecurity threats in the life cycle of the medical device [3]. As a global issue, medical device cybersecurity efforts are necessary to reinforce patients' safety while bringing innovation and effectiveness to medical diagnostics.

3 Pre-Market Actions for Cybersecurity in Medical Devices

Even though medical device cybersecurity is a critical issue throughout the total product life cycle (TPLC), some of the more important safety measures should be taken during the design and development phases of a medical device. Manufacturers should use this period when the medical system has not yet been put to market to apply the cybersecurity actions that will make the medical device robust enough until the end of operation. These pre-market measures include design of the product security features, acceptable risk management strategies, security tests, full disclosure of safety information for user's operation, and planning of post-market activities [3]. Also, as another part of the pre-market actions, manufacturers should consider the intended use and operational environment of the device and predict the possible scenarios of the device misuse. Operational manuals should define the possible risks and give warnings of the possible wrongful operation of the system. All these requirements became particularly pronounced during the COVID-19 pandemic.

3.1 Secure Product Development Framework (SPDF)

To manufacture a safe and long-term functioning medical device, a set of processes called Secure Product Development Framework (SPDF) is recommended [1]. The primary goal of an SPDF protocol is to develop a safe and effective device that will maintain operational with minimum risk through its whole life cycle. An SPDF combines all the aspects of medical device expected operation, from design and

development, market release, after sales support, and end of life disposal. Following this type of developmental process makes the medical system more future proof and requires less re-engineering, which is sometimes needed with software updates and new networking technologies. Devices manufactured in this way also make it easier for health care providers to implement them in their own network and use their own cybersecurity protocols. Large networked medical systems are easily controlled and managed using an SPDF process, ultimately reducing the direct cybersecurity threats.

3.2 Security Design Principles

To predict and avoid potential patient harm and device malfunction, the best recommended practice is to apply the universal cybersecurity design principles. Below are listed some of the main rules of conduct that manufacturers should address during the production phase of the medical devices [3].

- **Secure Communications**
  - Medical device interaction with other devices or networks should be taken into account. Possible interfaces are both wired and wireless, and can include Wi-Fi, Bluetooth, Ethernet, USB, etc.
  - Design features that validate all inputs and take into consideration communication with less secure environments and connected devices (e.g., home network) should be fully implemented
  - The manufacturer should pay attention to data transfer process and ensure safe authentication with encryption protocols
- **Data Protection**
  - The manufacturer should consider if the data stored locally or transferred out of the device should be encrypted and password protected
  - Messages and input fields in communication protocols should be encrypted to ensure confidentiality
- **Device Integrity**
  - A good manufacturer practice is to evaluate if the system-level features should be designed to avoid data repudiation
  - The manufacturer should allow for anti-malware software controls to avoid risks from spyware, ransomware, and virus software to be run on the device
  - Device software should be robust enough to prevent its unauthorised modifications
- **User Authentication**
  - User authentication controls such as passwords, biometrics, or hardware keys should be enabled to prevent unauthorised access to the device functions

  - Different user roles should be defined with specific levels of access, while also allowing for open use of the device in the case of emergency
  - User credentials should be private and are not to be shared inside the network

- **Software Maintenance**
  - Regular device updates should be enabled and communicated to the user
  - The device update process should be automatic, or user defined, keeping in mind the security risks of unauthorised access or malware software
  - Manufacturer should define the response in the case of third-party and open-source software updates which might prevent the normal functioning of the device
  - Code signing digital signatures should be used for connection authentications to carry out the necessary updates

- **Physical Access**
  - Limited physical access to the device should also be considered. Network ports should not be available to unauthorised persons, as well as USB ports and other parts of the system that might be an entrance point for security risk. Locks or physically restricted access should be provided on the device chassis

- **Reliability and Availability**
  - The basic device function and performance should be protected by design features which will allow for the detection and response from cybersecurity attacks

3.3 Security Risk Management

To provide a full account of cybersecurity risks, both the safety and security of a medical device should be considered as a part of a larger system in which the device will be put in function. Security risk management processes are crucial in avoiding cybersecurity hazards since no device can be fully protected and future proof. As such, security risk management should be implemented in the manufacturer's quality system with regulations that will minimise the threats and unwanted access. Technical, operator, and management regulations should include secure design, validated production processes, and preventive actions [1].

The process of managing security risk should be differentiated from the process of managing safety risk, and device manufacturers should conduct both risk assessments to provide a more extensive recognition and management of patient safety risks [1]. The differences between the two risk managements are due to different extent of possible harms, as well as causes that might lead to safety or security risk. The process of security risk management, with SPDF processes, has its aim in providing the details on how vulnerabilities can be exploited by security threats, manifesting in patient harm or other possible risks. Also, while safety risk management targets the

mitigation of physical injury or damage to the goods, the security risk management may also include risks to the manufacturer's reputation and business. The manufacturer should ensure that the measures taken for one risk management don't affect the other risk management processes, meaning that one process should not introduce new risks in the other. To achieve a more complete risk analysis, regulatory institutions' guidelines suggest that device manufacturers provide both risk assessments in such a way that they don't interfere with each other's functionality.

One important aspect of security risk management is that it should be assessed in a non-probabilistic approach, where the likelihood of the occurrence of a certain threat is not modelled on historical data. This means that the security risk processes should prioritise the vulnerabilities within a medical device or within the future operating environment. Given the evolving nature of cybersecurity environments, it is nearly impossible to predict new software or hardware breaches that might occur in the total life cycle of the system. Instead, security risk management should be focused on the susceptibility of the system to known threats and possible hazards. This should be done by the manufacturer as a part of the pre-market strategy with intent to also minimise the post-market vulnerability. The pre- and post-market risk assessments are fundamentally different, and some of the regulations and guidance for premarket activities might not be useful in the post-market environment. For these cases, the best practice would be to speculate the worst-case scenarios and implement suitable risk mitigating measures. For devices that are on the market, one consideration should be the compensatory controls, when the system architecture mitigation is not possible. Also, for devices with vulnerabilities that are not minimised by the design features, risk management should be transferred to the user and operator of the medical system, and sometimes, when necessary, to the patient. However, this risk transfer should be conducted only with all information provided and communicated to the user. This should include supply chain risks as well as information on how the risk management should be processed at the end of support and end of the system's life cycle. Regulatory institutions recommend that manufacturers provide these instructions in the pre-market submissions of the medical device.

3.3.1 Basic Risk Management Principles

Risk management principles for the security and safety of the medical system should be implemented for the total product life cycle (TPLC). Cybersecurity threats which alter device performance and decrease device safety can have negative consequences on the diagnostic and therapeutic functions of the system. This could result in wrong interpretation of the medical finding or in serious patient harm. Risk and cybersecurity risk managements should be incorporated by manufacturers using the following or similar steps [3]:

- **Security risk analysis**
  - Intended use and security factors
  - Cybersecurity vulnerability and threats identification

  - Risk estimation according to threats and vulnerabilities

- **Evaluation of security risk**
- **Control of security risk**
  - Risk control analysis
  - Application of control methods
  - Analysis of control methods
- **Evaluation of residual risk**
  - Analysis of residual risks
  - Benefit analysis
  - Acceptability decisions
- **Providing production information and risk management report**

The first part of the process, risk analysis, should be focused on risks and severity of patient harm in case of the abuse of the cybersecurity vulnerabilities, while also incorporating risk compensation controls and threat mitigation. Risk assessment part should relate to the design phase of the system to provide threat modelling, risk mitigation, and evaluation of potential patient harm. Establishing a safe design architecture with processes such as security risk assessment, threat modelling, and vulnerability scoring [4], enables the complete risk management process [3]:

- **Security risk assessment**

  Manufacturing phase with analysis of cybersecurity risks, threats, and controls through total product life cycle (TPLC). Cybersecurity guidelines should be referenced to specific cybersecurity threats and vulnerabilities in case the requirements can be used to avoid the recognized hazards.

- **Threat modelling**

  A process of recognizing, specifying, and mitigating risks in the medical system, such as risks regarding the device components, risks in system production, design, and installation in the user environment, and risks in connection to device maintenance. As an aid in threat modelling, sufficient information should be provided by the manufacturer, such as system diagrams and installation manuals. When doing threat modelling, manufacturers should assume the worst-case scenarios of unintended software and hardware breaches and try to determine how the system architecture might facilitate these unwanted actions.

- **Vulnerability scoring**

  A scoring methodology which should be implemented to specify the exploitability and severity of all cybersecurity exposures. Common vulnerabilities identified in the design and development phases should be tested and assessed using a standardised vulnerability scoring system [4].

3.3.2 Security Testing

A process of security testing should be carried out during the design and development phase to determine that there are no significant vulnerabilities left in the code and that security controls have been properly applied. As mentioned in the previous sections, while doing the pre-market testing for vulnerabilities, future network and intended use of the device should be considered. Following are some of the most important factors that medical device manufacturers should take into account [3]:

- Manufacturers should conduct searches on software modules and components aimed for known flaws or weaknesses. Static code analysis, dynamic analysis, robustness testing, vulnerability scanning, and software composition analysis are some examples of security testing techniques that should be done periodically.
- Technical security analyses, fuzz testing, and search of different entry points by reading hidden files, configuration, data streams, or hardware registers are additional testing techniques.
- Vulnerability assessment which includes analysis of the impact of the vulnerability on other manufacturer's products (variant analysis), identification of corrective procedures, and the correction or minimization of vulnerability.

3.3.3 Cybersecurity Management Plan

Since the technologies of cybersecurity threats constantly change and evolve, manufacturers should devise a cybersecurity management plan for the total product life cycle (TPLC). This plan should be employed as a part of product development and focus on [3]:

- Anticipatory monitoring and recognition of new cybersecurity vulnerabilities, their threat assessment, and proper responses
- Formal disclosure of all known vulnerabilities with suggested mitigation strategies, shared with all parties involved in medical device use
- Defined and shared software update plan, requested by demand or done periodically
- Recovery plan for restoration of normal device functionality following a cybersecurity incident
- Information sharing about security risks

3.3.4 Security Documentation

Manufacturers should provide all important documentation regarding the security of the medical system. This can include labelling, customer, regulatory, design, risk management, and security testing documentation in form of user manuals, guidelines, or recommendations.

Labelling

Labelling has a purpose of informing the end user on the important security information and the relative cybersecurity risks, with the following aspects included [3]:

- Product manuals and specifications related to cybersecurity controls for the intended operating environment: anti-malware software, network connectivity configurations, firewall
- Backup and restore procedures to recover configurations
- Listed network and other interfaces used to send and receive data, with a description of each interface functionality (unused ports should be disabled)
- Detailed system diagrams

Customer Security Documentation

Operating instructions, installation and configuration instructions, and specification sheets with minimal requirements for the operating environment are the documents that should be provided to the customer for the safe and secure use of the medical system. All of them should include [3]:

- Infrastructure and operating environment requirements
- Description of secure configurations with protection solutions such as anti-malware software and firewall configurations
- Methods for restoring device configuration by an authenticated user
- Information on systematic processes for authorised users to install manufacturer updates
- Technical instructions to allow connected secure network servicing
- Instruction on device supporting systems for user notifications of risk anomalies
- Information on cybersecurity end of support
- A Software Bill of Materials (SBOM) to inform users about the cybersecurity of commercial or open-source software which is delivered with the medical device

Regulatory Documentation

Manufacturers of medical devices should document all their cybersecurity actions for regulatory purposes, as this documentation might be requested by the regulator

before the market entrance of the device, or in the post-market phase [3]. When required for pre-market approval, documentation about the design characteristic, risk management, testing, labelling, and monitoring and response plan, should be presented by the manufacturer.

- **Design documentation**

  Design documentation for regulatory purposes should include description on hardware and software components, device interfaces, communication protocols, and all other features used to avoid or minimise cybersecurity risks (e.g., encryption, updates, user authentication).

- **Risk management documentation**

  This documentation should provide information on:

  – cybersecurity threats and vulnerabilities
  – estimation of the cybersecurity risks
  – proposed cybersecurity controls
  – evidence of tested and applicable controls
  – risk management report with threat modelling
  – information about correlation between security risk management and minimising other risks

  Cybersecurity risk management documents should use cybersecurity standards for guidance. Risk controls should maximise device cybersecurity while at the same time preserving its safety controls.

- **Security testing documentation**

  Security testing documentation should include:

  – test reports with technicalities on specific testing
  – descriptions of used methods, results, and conclusions
  – traceability matrix on security risks, security controls, and testing
  – references to used standards and internal documentation

4 Post-Market Actions for Cybersecurity in Medical Devices

Even though the post-market cybersecurity approach shares many of the same guidelines with the pre-market security activities, there are some specifics that need to be applied after the medical system has reached the market. Post-market surveillance

(PMS) processes specify the procedures needed to keep the integrity, functionality, and safety of the medical device during its entire lifecycle. These actions are intended for all medical device stakeholders and should be followed with proper reporting to ensure the appropriate response in case of patient harm or device malfunction incidents. The importance of PMS activities has led the International Medical Device Regulators Forum (IMDRF) [5], European Union Parliament and Council [6], United States Food and Drug Administration [7], and other [8] regulatory bodies to define global and local regulations concerning the PMS implementation. The regulatory authorities have recognized the PMS standards and incorporated them into national laws as part of a worldwide medical device legislation [9]. According to these laws, all parties involved in the development and use of medical devices must regularly evaluate the usability, efficiency, and safety of their products and, when necessary, take proper corrective or preventive action which is especially highlighter during crisis situations such as COVID-10 pandemics [10]. Also, manufacturers, clinicians, and patients should utilise PMS to report all problems with medical devices. These reports are then used to assess the status and condition of the device and to determine whether any additional action is necessary. Modern digitalization and artificial intelligence (AI) technologies provide good ground for making these PMS strategies more feasible, with the goal of making an evidence-based PMS approach [11], which could help in specific and correct preventive or corrective actions taken by the medical device user or manufacturer. Harmonious information sharing among all stakeholders is crucial to make sure that the PMS scenarios are applied in a proper and timely manner.

Since cybersecurity threats evolve and are becoming more sophisticated, some of the pre-market controls might not be suitable in the post-market environment. Also, pre-market actions are done mainly by the manufacturer of the medical system, while the cybersecurity of the post-market use is a responsibility of multiple users: healthcare providers, patients, or technical staff. The following sections give an overview of post-market activities and concepts intended for all users throughout the total product life cycle (TPLC).

4.1 Operating Environment

Healthcare providers are responsible for providing the optimal operating environment in which the medical system will be used. Regarding the cybersecurity point, this means that the healthcare provider should adjust its network infrastructure to maximise risk avoidance, while maintaining normal diagnostic and therapeutic capabilities of the medical device. Some of the more important steps that should be applied are [3]:

- Prepared IT infrastructure
- Integration of a new medical device with the IT network

- Adjustments of the operating system and IT network (software and firmware) with updates or modifications

Other than a more specific risk management system, healthcare providers should also employ some of the general cybersecurity principles, namely:

- Prevention of unauthorised physical access to medical device and its network access points, stored information, services, and applications
- Configuration management to identify all current assets and track future configuration changes
- Application of the recommended configuration and protection protocols
- Establish a control over the network access to a medical system
- Up-to-date security updates
- Malware protection
- Introduction of session timeouts for prevention of unwanted activities and access

These principles should be adjusted according to the clinical environment. Some of the limitations needed for cybersecurity purposes might not be applicable in other use scenarios, e.g., emergency departments. The healthcare providers should choose the best practices responsibly.

Important part in keeping the operating environment safe is proper training to all the personnel that will be using the medical system. Physicians, nurses, medical technicians, biomedical engineers, IT service technicians, and manufacturer representatives should be educated on how to operate the medical device in a most cyber secure manner. Also, if the medical device is intended for home use, patients should receive the exact same training and adhere to the same cybersecurity principles. Human factor is often the weakest link in the cybersecurity risk management, and user training should be of the highest priority to any stakeholder.

4.2 Information Sharing

No cybersecurity strategy is complete or valid if there is no proper information sharing among all stakeholders: manufacturers, healthcare providers, patients, and regulators [4]. Sectors outside of healthcare have implemented information exchange standards for cybersecurity threats and vulnerabilities mitigation, so medical device stakeholders should do the same with proper adjustments. These efforts will help in creating a true global medical device ecosystem where all the participants will know how to best prevent and respond to a cybersecurity risk, independent of the source of the risk itself [3].

This following is a list of key principles that should be followed to achieve a satisfying level of information sharing but is by no means a total list of all the valid approaches [3]. Each participant in the use of the medical devices should adhere to its specific environment and in coordination with adopted regulations.

- Cybersecurity information should be shared with all participants in the total life cycle of the medical device: manufacturers, manufacturers of other components or devices inside the network, distributors, healthcare providers, users, patients, and the public
- Shared information should be balanced: meaningful and actionable for different participants, as not all information is useful to all the participants
- Information should be shared irrespective of commercial interests, with the end goal of improving patient safety
- Information should be globally consistent, exchanged synchronous across administrations to enable participants in various administrations to respond appropriately

4.2.1 Key Types of Information

Medical device stakeholders are encouraged to share some of the main information about the system cybersecurity [3]:

- What products are, and how, affected by a cybersecurity vulnerability
- What components have what vulnerabilities
- Which IT equipment might impact the security of the medical device
- Is there any availability of code exploitation and what type of attacks are possible
- Confirmation of the cybersecurity incident
- Which security controls are available
- Instructions on the temporary measures of use and integration of medical device
- What is the optimal IT configuration for minimising the cybersecurity risks

4.2.2 Key Participants

The sector of medical devices reaches far beyond the borders of local manufacturers. Administrative recommendations of one country or area might not be applicable to the global market, so medical device users should develop global networks. Therefore, cybersecurity information sharing should also be international, and include all the stakeholders listed below [3].

- **Regulators**
  - Key receivers of security information of the medical devices, involved in information promulgation
  - Should build processes that encourage up-to-date cybersecurity information disclosure, which also includes shared information between the regulators to establish a globally uniform response
- **Medical Device Manufacturers**
  - Responsible for sharing vulnerability information which will help regulators provide regulatory requirements

  - Should synchronously inform regulators in all markets
  - Shared information should be written in simple terms and language
- **Healthcare Providers**
  - Responsible for acting or enabling and action. Should be provided with all information needed to follow cybersecurity standards and guidelines
  - Key source of information from the user perspective, should provide feedback regarding the cybersecurity breaches and share the information on applied solutions
- **Users (clinicians, patients, caregivers)**
  - Usually, the last ones who decide if the cybersecurity update is implemented
- **Other stakeholders, including administrative bodies responsible for information disclosure**
  - Government agencies like law enforcement and national security
  - Government or private organisations that provide security advice or expertise

4.3 Vulnerability Disclosure and Vulnerability Countermeasures

4.3.1 Vulnerability Disclosure

To further improve transparency about cybersecurity vulnerabilities, there should be an arrangement of a more formal process of information sharing.

One such proposed mechanism is a coordinated vulnerability disclosure (CVD) [3]. CVD is a formalised process of gathering and assessing cybersecurity vulnerability information, constructing mitigation, proposing solution controls, and sharing this information to all medical device stakeholders. This proactive approach enables end users to make more informed cybersecurity actions to help protect the device, network, and, ultimately, patient. Adopting CVD policies is common across different industry sectors and is seen as a sign of manufacturer's maturity and responsible behavior. Medical device stakeholders are endorsed to enquire about manufacturers' CVD policies to further bolster CVD adoption as a standard norm, and not an exception.

One way through which manufacturers can distribute information in a timely fashion is using bulletins and notifications, while being aware of administrative requirements in the respective market. Proactive approach which manufacturers could adapt is not about the number of disclosed vulnerabilities but the consistency and timely response to cybersecurity risk. Below are some of the steps that can guide manufacturers to proper CVD strategies [3]:

- Sources of cybersecurity information should be monitored to ensure proper detection of vulnerabilities and risks
- Adopt an existent CVD policy
- Develop and share procedures for identifying and managing vulnerabilities
- Analyse stated vulnerabilities according to incorporated security (e.g., common vulnerability scoring system) and clinical risk management techniques
- Develop a solution if possible, or, if not, create suitable controls with defined procedures for informing about deployment errors and undoing changes
- Keep constant communication with regulators to raise their awareness of upcoming vulnerability disclosures

To reduce the danger of an exploit, regulators can facilitate the coordination of the vulnerability assessment/evaluation, performance measurement, and mitigation/remediation activities between both the manufacturer and the vulnerability finder [3]. Since CVD is accepted as a best practise, this communication often involves concurrent worldwide communications as necessary.

When vulnerabilities are detected, they should be promptly disclosed to the relevant manufacturer or to a coordinating third party, such as the authorised government agency. Having followed that, the manufacturer organises and collaborates with the vulnerability finder throughout the vulnerability investigation and repair. Finally, the manufacturer and vulnerability finder should cooperate to disclose the vulnerability to the public.

4.3.2 Vulnerability Countermeasures

Vulnerability countermeasures are crucial to mitigate the risk of harm for the patient. Broad range of measures can be applied, and main stakeholder groups with their roles are described in more detail below [3, 4].

Medical Device Manufacturers

- **Risk management**

  Risk assessment should be the first step in any risk management in medical device. Existing risk management practices are well-established [3, 4] and should be adhered to when evaluating the cybersecurity risk. Cybersecurity risk management process should be aligned with the risk management processes to establish the impact of the cybersecurity vulnerability to the risk of patient harm. A mitigation approach that is centred on patient safety should then be created and consolidated. As mentioned in previous chapters, information sharing is a crucial part of this process, especially concerning the justification of a countermeasure as appropriate solutions to cybersecurity vulnerability. Priorities of risk management are timely decisions on solution so manufacturers and regulators should have a common

goal of shared risk perception. This risk perception should also be noted with other users, who may have different views and suggestions on risk management. These different positions can produce different expectations on how, and how fast, should the manufacturer resolve the cybersecurity risk. Misunderstanding among different stakeholders might lead to inaccurate information being given to the patients, who in turn could have a negative view on healthcare providers, manufacturers, or medical technologies in general. As already mentioned, golden rule of cybersecurity risk management is to approach it with that earnestness that is required for the gravity of potential patient harm.

- **Third-party components**

As a standard part of the medical device, whether it is a software or a hardware, third-party components are important regarding the overall cybersecurity. These components pose a risk on their own and should be managed in similar ways through risk mitigation, quality management, and design decisions. Post-market operation of the medical device, and its third-party is expected by the end user to be a responsibility of the manufacturer, who should be aware of the compatibility and the risks of the components used in their medical systems. In the same way as with the original in-house components, manufacturer should share information about the cybersecurity vulnerabilities associated with third-party software and hardware. Even though manufacturers might not have control over vulnerability countermeasures of a third-party component (e.g., availability of an update), they should still take precautions to minimize the risk to patients and users.

- **Communication**

  Clear and concise communication is crucial to those the users of medical system, i.e., those who manage security risks. Key information that should be provided is: timeline for vulnerability solution, mechanism for resolution, vulnerability score, exploitability index and method, as well as temporary risk mitigating measures.

- **Corrective actions**

  Actions for resolving the cybersecurity vulnerabilities depend on numerous factors, such as user safety, type of the device, local regulations, operating environment, and intended use. However, some general principles should be followed independent on type of vulnerability countermeasures [3]:

  - Compliance with local regulatory requirements
  - Following the safety and essential performance principles
  - Information sharing with stakeholders
  - Cooperation of stakeholders to achieve risk mitigation

- Timely solutions, risk dependant

If the medical device lacks basic protective measures, and updates are not available, risk-mitigating alternatives should be applied in a form of compensating controls [4], such as installing a firewall between the medical system and the IT network, or completely removing the medical system from the local network. Using the data provided by the manufacturer, the healthcare provider typically implements these compensating controls. Some regulatory guidelines [2] even propose having an incident response time as a higher level of preparedness. Manufacturers should have in mind that the regulators are bound by the laws of their respective jurisdictions, and thus may impose conditions before vulnerability countermeasures can be implemented to medical devices in the post-market scenarios. To avoid delaying the cybersecurity countermeasures, manufacturers should inform regulators in a timely manner, which will provide regulators with enough time to initiate regulatory processes or required actions, while at the same time assisting the stakeholders in risk mitigation. Also, vulnerability information must be shared. When a vulnerability is resolved in one area, but users from other jurisdictions are not informed, it gives an open space to unwanted breaches and misuse of medical systems, leading to potential patient safety risks. Manufacturers should have coordinated information sharing with all the regulators in the markets where the manufacturer's system is being distributed and used. Some vulnerability countermeasures can be only applied temporarily, or they can be taken only by some users (e.g., IT technicians), so effective information sharing is crucial. For example, some actions can only be taken by a hospital IT department. When vulnerability resolutions are not possible, compensating controls should be exercised.

Healthcare Providers and Patients

- **Updates**

Manufacturers should inform users on how to acquire and install software changes needed during the software life cycle. If a manufacturer intends to name certain personnel responsible for installing the updates, and if this is approved by the local regulatory authority, these users are expected to apply manufacturer-provided updates in accordance with related installation guidelines. If the required update cannot be installed in the desired timeframe, the manufacturer might suggest compensating controls or changes of the settings of the medical system. Local regulatory authority can direct the manufacturer to limit or totally disable certain features of the medical device or a supporting network (for example, updates from cloud servers could be temporarily prohibited), if these actions might reduce the risk of patient harm.

- **Operating environment in the healthcare facility**

  In the environment of the healthcare facility, risk management is applied by the "responsible organisation" [3], which can be different from the healthcare provider. This organisation can be approved by the manufacturer and have the educated personnel trained by the manufacturer. Even more, all changes to medical devices which are taken without the formal consent of the manufacturer, or without the organisation authorised by the manufacturer, should be avoided. Responsibility agreements might be signed to ensure that all users involved in medical systems operation understand each responsibility in risk management. If there is a need for manufacturers to disable certain functions of the medical system, a healthcare provider should adjust their clinical workflow to maintain patient safety.

- **Home operating environment**

  Home healthcare environment is radically different from the one in a healthcare facility, as a medical system is exposed to a wide range of potential users which are not healthcare professionals. Also, patients as users of medical devices can have certain disabilities which can pose a difficulty in operating the device in a way which will be safe and secure from cybersecurity attacks. Some of the vulnerability countermeasures might not be applicable in home environments, such as software updates where internet connection is not present. If remote updates are not possible, a service visit might be needed to keep the device up to date with cybersecurity risk management. As with all users in all environments, patients operating the medical devices at home or in other personal environments, should follow healthcare provider's and manufacturer's instructions to keep the device operating and to avoid potential harm to patients.

Regulators

- **Post-market updates**

  Software maintenance and updates are usually required to strengthen the medical device's cybersecurity resilience. However, not all these actions require regulatory review, as too many regulatory requests would make regulators inefficient and not able to provide their full service. The regulatory organisations should review the potential modifications of the medical system software only if those changes might negatively impact the patient safety or performance of the device. In coordination with the manufacturer who proposes the updates and modifications, regulators can decide if a pre-deployment review is necessary.

4.4 Medical Devices with Outdated Cybersecurity Technologies

There is a substantial number of medical devices in today's markets that cannot be reasonably protected against the current cybersecurity threats, as their technologies are outdated or obsolete [3]. Many of those devices were designed without cybersecurity in mind, which today poses a great cybersecurity and usability challenge. More often, technologies for diagnostic and therapeutic applications in such medical systems outlast the security technologies which can be beneficial for the owners of the system, but in the end makes the device less and less usable as new cybersecurity threats emerge almost daily. A medical device that cannot be reasonably protected against the current cybersecurity threats is not necessarily an old device, since some devices of more recent production date (in the last five years) might have outdated cybersecurity technologies, while devices older than ten years can still be safeguarded if the deployment technology is still up to date.

To prevent more cybersecurity outdated devices from entering the market, the first step is for the manufacturers to implement reasonable protection technologies during the design and development phase of the medical device. This should be done to maintain a reasonable cybersecurity level throughout the total product life cycle (TPLC). Manufacturers should disclose the End of Life (EOL) and End of Service (EOS) dates, so the customers can expect the timelines for limited support and end of support for their systems. When approaching the EOS date, the manufacturer should communicate that the medical device will be considered as that it cannot be reasonably protected against the current cybersecurity threats, and that it should be disposed of. Should the device be used after the EOS date, the customer accepts the sole responsibility for maintaining the device cybersecurity as well as the risk of potential patient harm as a result.

To help healthcare providers in replacing the cybersecurity obsolete devices, regulatory authorities might encourage manufacturers to use compensating controls for cybersecurity vulnerabilities mitigation. This would be applied after the EOL date so the consumers might have enough time to prepare the replacement of the system after the end of support. As with all threats and threat mitigation processes, communication and information sharing among the stakeholders is crucial to overcome the cybersecurity challenges.

5 Medical Data Protection

New networking and communication technologies have brought up one more important aspect in maintaining the integrity of medical devices, and that is medical data protection. Diagnostic algorithms, remote storage sites, telemetry data sharing, and medical devices for home use, are all specific features and use scenarios where personal medical data might fall under unwanted access. Biomedical big data consists

of both health and non-health data which can be obtained through multiple sources. Inspection of a medical device now gets an additional task in view of keeping the patient and diagnostic data secure and safely stored. Under risk of purposeful or accidental disclosure are patient data such as name, address, phone number, social security and tax number, medical history records, and prescriptions, and as such are being regulated globally.

The European Union has protected personal health data under the General Data Protection Regulation (GDPR) [12]. Apart from regulating the processing and right of access to health data, GDPR introduces the right to be forgotten, which means that all medical systems must provide the option to erase all patient data upon request. Another GDPR specific requirement is the regulation to anonymize the personal data [2], which has a goal of disabling the connection of personal identifiers to personal information. Furthermore, GDPR regulations define mandatory impact assessments which are to be designed to assess risk and vulnerabilities countermeasures in case of data breach. Every data breach should be reported by the trained data controller or data protection officer (DPO), two roles also defined by the EU regulations. Additionally, medical device users should be in constant communication and cooperation with cloud service providers for support of the remotely stored health data.

In the USA, health data protection is regulated by the Health Insurance Portability and Accountability Act (HIPAA) [13]. According to HIPAA regulations, medical device manufacturers must design a device that enables protection of sensitive information. Healthcare providers and other stakeholders should adopt measures to protect patient data, restrict data access, and meet the HIPAA security standards. To enable and assist their own compliance practices, healthcare providers should request that manufacturers of medical devices adhere to HIPAA requirements, so that the protection of healthcare data against data breaches and cyber-attacks is integrated in medical devices.

6 Artificial Intelligence in Medical Devices

Artificial intelligence (AI) technologies are becoming a standard part of medical devices. At the intersection of computer science, statistics, and engineering, AI models and algorithms mimic human capabilities, such as problem-solving and learning, with the results in the form of decision and prediction making. Healthcare organisations are using AI for an expanding range of clinical, research, and administrative purposes to improve clinical diagnosis, monitoring of patient's health, or maintaining patient records and scheduling visits. Image analysis, wearable sensor data analysis, risk prediction, disease progression and readmissions, are just some of the examples in which AI methodologies have been proven usable and valuable. A growing number of medical device manufacturers are developing their own strategies to include AI into their systems as a result of technological advancements and new regulatory policies that have made AI more accessible. This section will provide

a brief overview of the fundamental AI techniques and the most recent regulatory requirements for the use of AI in medical devices.

6.1 General Overview of Artificial Intelligence

Artificial intelligence algorithms are being used to perform tasks such as visual perception, speech recognition, decision-making, and language translation, with the varying level of autonomy in the AI-based systems. Operating in the real or virtual environments, AI systems can analyse large amounts of data, giving outputs in form of predictions, decisions, or recommendations.

As a subset of AI techniques, machine learning (ML) algorithms are based on statistical and mathematical modelling methods to describe and analyse data for applications such as pattern recognition, natural language processing, signal processing and expert systems. According to how it learns from data, machine learning can be divided into three categories:

- Supervised learning
  - Training data is labelled, and the output variables are known
  - Model derives a function between the input and output
  - Can be used to make output predictions when given new input data
- Unsupervised learning
  - Unlabelled training data
  - Machine identifies patterns and connections between the input and output data
- Reinforcement learning
  - Machine learns by trial-and-error process
  - Machine is "rewarded" or "penalised", depending on how well it reaches the desired objective

Deep learning is another subset of machine learning which can be supervised, unsupervised, or semi-supervised. It is based on multiple layers used for progressive feature extraction from very large amounts of the input data ("big data"). "Big data" refers to complex data in large volumes, and, other than its large size, is characteristic for fast generation of new data, variety in the data, and data inconsistency. All these characteristics make "big data" difficult to handle by conventional methods, which is why machine learning techniques have proven valuable for its analysis.

Bayesian networks, neural networks (e.g., feedforward neural networks, recurrent neural networks, convolutional neural networks), support vector machines, and decision trees, are some of additional examples of the multiple types of machine learning methods.

In the context of artificial intelligence and machine learning methods used in medical devices, International Medical Device Regulators Forum (IMDRF) [14]

uses the term *ML training algorithm* to describe a software process that defines a machine learning model's parameters from data analysis. Accordingly, the term *ML model* is used by IMDRF as a mathematical construct that produces predictions based on new input data, as a result of ML training algorithm.

6.2 Artificial Intelligence in Healthcare Applications

Artificial intelligence for health applications has been used for clinical care, drug research and development, management of health systems [15–17], and public health surveillance.

According to the FDA reports [18], a total of 521 medical systems which have AI/ML technologies have been approved in a span of seventeen years, from 1995 to 2022. Figure 1 shows the trend of the number of FDA approved AI/ML-enabled medical devices in the last ten years, from 2012 to 2022.

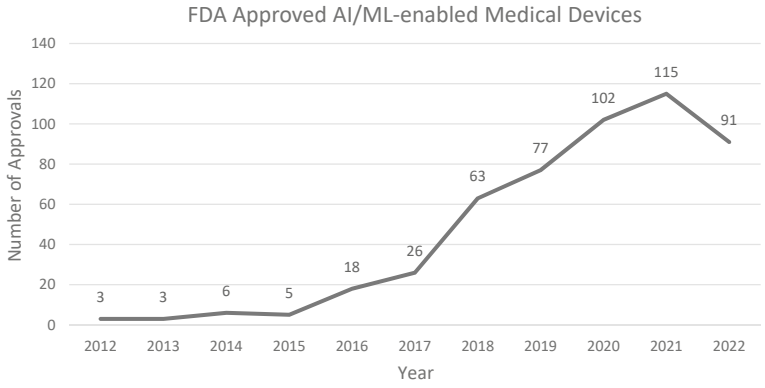

Fig. 1 FDA Approved AI/ML-enabled Medical Devices, 2012–2022. Data gathered from [18]

As it can be seen, there is a steep rise in the number of approvals emerging in 2016. Another big rise, more than double, is again in the year 2018, after which the trend keeps rising until reaching 115 approved systems in 2021. Year 2022 has 91 devices approved, but with the notion that this is the info with the date of October 5, 2022, which means that by the end of 2022 this number can be bigger.

Figure 2 shows the share of each clinical application in the total number of FDA approved AI/ML-enabled medical devices in the period from 1995 to 2022.

As shown, radiology systems make for 75% of the total number of approved systems. Cardiovascular devices have a share of 11%, while haematology and neurology systems make for 3% each of the total number of approved systems [18].

AI-enabled systems continue to increase each year, and regulators have a task to define policies for the use of each one of them. A large share of radiology systems

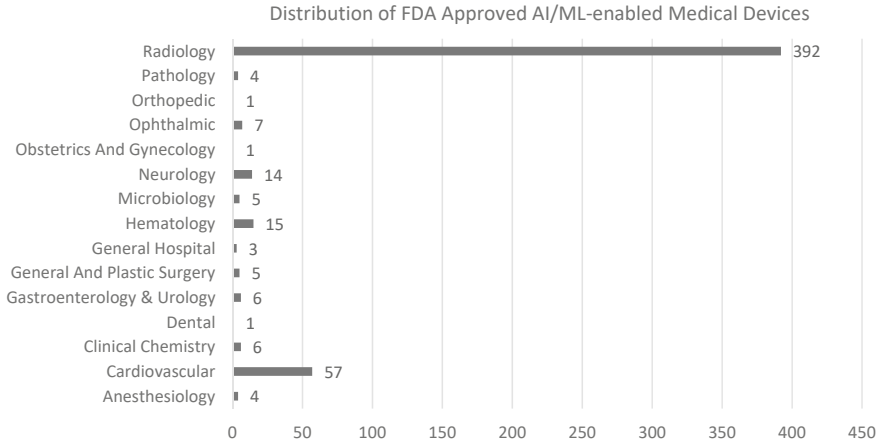

Fig. 2 Number of FDA Approved AI/ML-enabled medical devices in clinical applications, 1995–2022. Data gathered from [18]

among all approved and cleared devices can be explained by the fact that radiology diagnostics have been digitised earlier than other systems. This makes it easier for ML algorithms to learn on data that is relatively standard, although not without challenges.

6.2.1 Software as a Medical Device and Artificial Intelligence

According to IMDRF [19], software as a medical device (SaMD) is a software intended for medical use as a standalone feature, without being part of a hardware medical device [19]:

- SaMD can run on general purpose (non-medical purpose) computing platforms
- The software is not necessary for a hardware device's medical purpose
- Software is not a SaMD if its intended purpose is to drive a hardware medical device
- SaMD can be used in combination with other products, including medical devices, other SaMD software, and general-purpose software
- Mobile apps and in-vitro diagnostic (IVD) medical device can be considered SaMD if they meet the above conditions

As a medical device, this means that SaMD can be used for [19]:

- "Diagnosis, prevention, monitoring, treatment, or alleviation of disease"
- "Diagnosis, monitoring, treatment, alleviation of or compensation for an injury"
- "Investigation, replacement, modification, or support of the anatomy or of a physiological process"
- "Supporting or sustaining life"

- "Control of conception"

SaMD can also have changes through its total product life cycle (TPLC), such as security updates and performance improvements. The preventive, corrective, and perfective maintenance of SaMD is the responsibility of the SaMD manufacturer, along with standard regulated obligations defined for hardware medical devices, which are also applicable for SaMD [19]:

- Compliance with regulatory requirements in local jurisdictions
- Meeting pre- and post-market requirements
- Design and manufacture of the device
- Any person who constructs or modifies a medical device already supplied by another person is not the manufacturer if the construction or modification does not change the intended use of the medical device
- A person should be regarded as the manufacturer of a modified medical device if they change or modify a device's intended purpose without doing so on authority of the original manufacturer and provide it for use in their own name
- The person in charge of the design and/or manufacture of the medical device accessory is regarded as a manufacturer if the accessory is subject to the regulatory requirements

One of the biggest advantages of AI/ML techniques is in their ability to learn from real-world use on a large daily generated health data, while also having the capability of improving its performance [19], which makes artificial intelligence techniques superior as an SaMD. However, traditional regulations for medical devices are not sufficient for constantly changing AI/ML technologies, which require a new total product life cycle (TPLC) regulatory approach. A regulatory framework specifically designed for AI/ML-based SaMDs should allow for rapid changes in the improvement of algorithms and methods, making the new regulations more adaptive to these highly iterative and autonomous processes.

6.2.2 Regulatory Approach for AI/ML-Based SaMD

When used to treat, diagnose, cure, alleviate, or prevent disease, AI/ML-based software is considered a medical device, and is labelled as a Software as a Medical Device (SaMD) [20]. Similar to other SaMDs, the intended use of AI/ML-based SaMD can have different impact on patients, according to potential risk categorised by IMDRF SaMD risk categorization framework [21]. This framework has a risk-based approach for SaMD categorization based on the intended use, which is similar to traditional risk-based approaches.

Two major factors are used to provide a description of the intended use of the SaMD:

- Significance of information provided by the SaMD to the healthcare decision—used as identification of the intended use of the SaMD provided information:

  - To treat or diagnose
  - To drive clinical management
  - To inform clinical management
- State of healthcare situation or condition—used to identify the intended user, disease or condition, and the population for the SaMD:
  - Critical
  - Serious
  - Non-serious

Used together, these factors define the intended use for the AI/ML-based SaMD into one of four risk categories: lowest (I) to highest risk (IV), as shown in the Table 1.

Table 1 IMDRF SaMD risk categorization

State of healthcare situation or condition	Significance of information provided by SaMD to healthcare decision		
	Treat or diagnose	Drive clinical management	Inform clinical management
Critical	IV	III	II
Serious	III	II	I
Non-serious	II	I	I

Adapted from [21]

Other than risk categorization, AI/ML-based SaMD can be categorised according to the level of adaptation of the algorithm [20]:

- Locked algorithm
  - Fixed function (e.g., a static look-up table, decision tree, or complex classifier)
  - Same output for the same input
  - Manual updates and validation procedures
- Adaptive algorithm
  - Continuous learning algorithm
  - Different output after applying changes to the same input
  - Automated updates and validation

For both locked and adaptive types of algorithms, the same data and training considerations can be applied, as well as evaluation of the algorithm's performance.

As mentioned in the previous section, a total product life cycle (TPLC) approach is particularly important for the regulation of AI/ML-based SaMD, as AI/ML-based SaMD may change and improve based on actual use. A proposed FDA approach [20] is to evaluate a company's operational effectiveness and quality culture, and to have reasonable certainty that the software they develop, test, and produce is of the highest

class. To give patients, caregivers, health professionals, and other users confidence in the safety and quality of those products, this strategy would provide reasonable assurance of safety and efficacy all throughout the lifecycle of both the company and the products. With the use of this TPLC strategy, a software product's performance can be evaluated and documented from its pre- to post-market development, while also continuously showcasing the company's quality.

Additionally, FDA proposes a TLPC approach based on the following general principles to fully accomplish the AI/ML learning algorithms potential, while keeping the continuous improvement of their performance and at the same time limiting their failures [20]:

- **Clear expectations on quality systems and good ML practices (GMLP) should be established**

  Quality systems and good ML practices means that the medical device manufacturer should have a system oriented at creating, delivering, and maintaining high-quality products that conform to the necessary standards and laws throughout their total life cycle. Similarly, SaMD developers who use AI/ML should adhere to the excellence principles of organisational success and a quality mindset [20]. For the devices based on AI/ML, analytical and clinical validation is expected to be demonstrated, as it is for the "standard" SaMDs. Depending on the risk of the SaMD and its intended use, different data (e.g., pre-market review, study design) should be provided to assure of the safety and effectiveness of the SaMD. Examples of GMLP considerations that should be applied for SaMD are:

  – Applicability of the available data to the clinical issue and current clinical practice
  – Consistent and clinically relevant acquired data aligned with the intended use of the SaMD and modification plans
  – Adequate separation between training, tuning, and test datasets
  – Appropriate level of transparency of the output and user-oriented algorithm

- **Pre-market review for SaMDs that require pre-market submission**

  This is a proposed framework to give manufacturers the option to provide a modification plan for the initial pre-market review of an AI/ML-based SaMD. Based on these plans, FDA would provide reasonable assurance of safety and effectiveness and give a review of the manufacturer's ability to manage and control risks resulting from modifications [20]. The proposed change control plan would include:

  – SaMD Pre-Specifications (SPS)
  – Manufacturer's predicted modifications related to the intended use of the AI/ML-based SaMD
  – Algorithm Change Protocol (ACP)
  – Manufacturer's proposed solutions for risk control resulting from the changes made to the intended use of the SaMD

- **Modifications approach after an established SPS and ACP**
  Learning, adaptation, and optimization are basic capabilities of AI/ML-based SaMD and could be considered modifications to SaMD intended use and vulnerability to risk after the market authorization [20]. Manufacturers should do an evaluation of the modifications and perform a risk assessment to evaluate if the risks are mitigated in a reasonable manner. According to the type of the modification, the present software modifications guidelines propose either a submission of a new pre-market review, or documentation of the modification with new risk management analysis:
  - If the modifications are within the defined SPS and the ACP, manufacturers should document the change and file it for reference
  - If the modifications are outside of the intended SaMD approved use, manufacturers should submit a new pre-market submission
  - According to this proposed FDA framework, manufacturers should benefit from engaging in transparent and timely communication with the FDA to ensure all modifications are in the bounds of the current SPS and ACP, so no time is wasted on idle regulatory processes.
- **Full transparency to users and FDA with post-market performance reporting**
  Manufacturer implemented transparency and real-world performance monitoring through the TPLC of the AI/ML-based SaMD, will help in assuring the safety and effectiveness of their products [20]. This is a crucial component of medical devices' safety and is particularly important for devices that incorporate AI/ML and evolve over time, like SaMD. Transparency about these modifications to AI/ML-based SaMD can be leveraged by collecting and monitoring real-world performance data, as it can help manufacturers in understanding the use of their products, identifying improvement opportunities, and planning proactive responses to SaMD safety or usability concerns. Also, manufacturers should routinely report to the FDA on changes made as a result of the approved SPS and ACP, as well as SaMD performance indicators. All labelling and specifications should be changed accordingly, with the complete description of the modifications in the SPS and ACP. It's also important to report on the compatibility of any impacted accessories, non-device components, or supporting devices. Manufacturers can set up communication procedures to notify users via letters, email, software notifications while disclosing important information about the modifications.

7 Summary

New technologies bring new benefits but also new challenges. The increasing reliance on technology and interconnected devices in healthcare has highlighted the importance of cybersecurity in medical device inspection for regulatory purposes. Medical

devices that are connected to the internet or other networks can be vulnerable to cybersecurity threats such as hacking and data breaches. When doing an inspection of a medical device for regulatory purposes, medical device users should have in mind the cybersecurity threats as well as potential patient harm and device malfunction that come with data usage and AI technologies in modern medical devices.

Following the local and international regulatory guidelines, all healthcare stakeholders (authorities, independent/inspection bodies, manufacturers, distributors, healthcare providers, patients) must work on mitigating risks and vulnerabilities that keep growing in today's fast technology advancement. Full disclosure among all participants during the total product life cycle of a medical device ensures that all parties are notified of possible changes in the intended use of the system. This, in turn, helps identify threats that might cause device misuse and, in worst cases, patient injury. Fast growing technological advancements mandate that all healthcare participants approach the safety and risk management with great concern and responsibility to bring the most out of the designated function of the medical systems.

Medical device cybersecurity is crucial for protecting patient safety and maintaining the trust of healthcare providers and patients. The regulatory inspection process plays an important role in ensuring that medical device manufacturers are following best practices and taking appropriate steps to protect against cybersecurity threats.

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