EU 1907/2006 – Registration, Evaluation, Authorisation and Restriction of Chemicals

Indumathy Jagadeeswaran and Harini Sriram

1 Introduction

1.1 Regulation EC 1907/2006

Regulation (EC) no 1907/2006 of the European Parliament and the Council of the European Union, concerning the registration, evaluation, authorization, and restriction of chemicals (REACH), in regard to the treaty establishing the European Community, particularly Article 95, in regard to the Commission's proposal, in regard to the European Economic and Social Committee's opinion, execution in accordance with the procedure laid down in Article 251 of the Treaty, European Commission (EC), comprises of regulations which work to ensure the safety of the patient and efficacy of the device [1]. This regulation ensures a high level of protection of human health and environment as well as the free movement of substances, with the goal of achieving sustainable development. The European Union, in pursuant to the implantation plan adopted on 4 September 2002 at Johannesburg World Summit, is aiming to achieve sustainable development where chemicals are produced and used with minimal adverse effects on human health and the environment [1].

I. Jagadeeswaran (✉)
Department of Biological Sciences, Southern Methodist University, Dallas, TX, USA

H. Sriram
National Dental Centre Singapore, Singapore, Singapore

© The Author(s), under exclusive license to Springer Nature Switzerland AG 2022

P. S. Timiri Shanmugam et al. (eds.), *Medical Device Guidelines and Regulations Handbook*, https://doi.org/10.1007/978-3-030-91855-2_13

1.2 Establishment of Compliance with REACH Regulation

An important objective for establishing REACH is to encourage and ensure that substances of high concern are eventually replaced by less dangerous substances or economical technologies where viable alternatives are available. This regulation does not affect the application of directives on worker protection and the environment, and employers are required to eliminate or substitute the dangerous substances, wherever possible to protect the health and safety of their workers. The key components of REACH are [1, 2]:

- Registration.
- Evaluation.
- Authorization.
- Restriction.
- REACH safety datasheet.

This regulation requires manufacturers and importers to generate information on substances, to assess their risks, and to develop and recommend appropriate risk management measures. The European Chemical Agency (Agency) requires manufactures and importers to submit this information for registration, and only registered substance is allowed to circulate on internal market. The Agency and member states shall evaluate whether the registration is in compliance with the requirements of this regulation. Such information submitted for registration can also be used by the Agency to initiate authorization or restriction procedures under this regulation. Authorization provisions ensure good functioning of internal market and assure that the very high-risk substances are properly controlled. The EC will provide authorization for a substance to be placed in market and usage. Restriction provisions allow manufacturing, placing on market, and use of substance with subject to total or partial ban or other restrictions [1, 2].

1.3 Purpose and Scope [1]

The primary strategy of the regulation is to ensure safety of human health and environment, including promotion of alternative methods for hazard assessment and free circulation of substances, as specified in Article 3. This regulation is based on principle that it is for manufacturers, importers, and downstream users to ensure that they manufacture, place on market, or use such substances that do not adversely affect human health or environment.

1. This regulation does not apply to the following:

   (a) Radioactive substances and mixtures that are in the scope of Council Directive 96/29/Euratom of 13 May 1996 which has laid down the primary safety standards for the protection of workers' health. It also takes public

health into account ensuring against the danger arising from ionizing radiation.

(b) Substances, on their own, in a preparation or in an article, which are in subject to customs supervision which do not undergo any treatment or processing, which are in temporary storage or in a free zone or free warehouse with a re-exportation or in transit view.
(c) Non-isolated intermediates.
(d) Dangerous substances and dangerous substance in preparations by air, road, sea, rail, or inland waterways transportation.
(e) Waste as defined in Directive 2006/12/EC of the European Parliament and Council of 5 April 2006, which is not a substance, mixture or article within the meaning of Article 3 of this Regulation.
(f) In specific cases where, the substances on their own or in a preparation or in an article are interest of to defense, the member states may allow for exemptions from this regulation.

2. This regulation shall apply without prejudice to:

(a) Community workplace and environmental legislation, including Council Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work [3]; Council Directive 96/61/EC of 24 September 1996 concerning integrated pollution prevention and control [4]; Directive 98/24/EC and Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy [5]; and Directive 2004/37/EC.
(b) Directive 76/768/EEC testing involving vertebrate animals.

3. The provisions of Title II, V, VI, and VII of this regulation shall not apply to the extent that a substance is used:

(a) In medicinal products for human or veterinary use within the scope of Regulation (EC) No 726/2004, Directive 2001/82/EC on the Community code relating to veterinary medicinal products [6] and Directive 2001/83/EC on the Community code relating to medicinal products for human use [7].
(b) Food or feeding stuffs as defined in Regulation (EC) No 178/2002 including when they are used as a food additive (89/107/EEC), flavoring (Directive 88/388/EEC and Decision 1999/217/EC), additive (Regulation (EC) No 1831/2003), or animal nutrition (Directive 82/471/EEC) in foodstuffs or feeding stuffs within the scope of these Directives.

4. The provisions of VI of this regulation shall not apply to the following preparations in the finished state intended for final user:

(a) Medicinal products for human or veterinary use, within the scope of Regulation (EC) No 726/2004 and Directive 2001/82/EC and as defined in Directive 2001/83/EC.
(b) Cosmetic products as defined in Directive 76/768/EEC.

(c) Medical devices which are invasive or used in direct physical contact with the human body in so far as Community measures lay down provisions for the classification and labelling of dangerous substances and preparations which ensure the same level of information provision and protection as Directive 1999/45/EC.
(d) Food or feeding stuffs as defined in Regulation (EC) No 178/2002 including when they are used as a food additive (89/107/EEC) [8], flavoring (Directive 88/388/EEC [9] and Decision 1999/217/EC [10]), additive (Regulation (EC) No 1831/2003 [11], or animal nutrition (Directive 82/471/EEC) [12] in foodstuffs or feeding stuffs within the scope of these Directives.

2 Registration of Substances [1]

2.1 General Obligation to Register and Information Requirements

The stakeholders (manufacturers or importers) of a substance on its own, in articles or in preparations, shall submit a registration to the Agency, if they meet any of the following conditions:

(a) In quantities of 1 ton or more per year.
(b) If the polymer consists of 2% weight by weight (w/w) or 0.1% weight by weight (w/w) for the substance present in articles.

These substances shall not be manufactured or placed on market unless they have been registered subject to articles 6, 7, 21, and 23 of this regulation. Registration of article is exempted if the substance in the article has already been registered for that use. Submission for registration shall be accompanied by the fee required by Title IX of this regulation.

2.2 Exemption to Register for Product and Process-Oriented Research or Development (PPORD)

This general obligation to register is exempted for a period of 5 years for the substances manufactured or imported for the purpose of product and process-oriented research or development (PPORD). However, the manufacturer or importer or producer of articles shall notify the agency regarding their identity, identity of substance, its classification and labelling, estimated quantity, and list of customers. This notification shall be accompanied by the fee required in accordance with Title IX. The agency will check the completeness of the information submitted and shall assign a notification number and date, which shall be the receipt of notification.

They agency might ask for additional information from the notifier or shall impose some conditions to ensure safe handling of the substance or the preparation or article. The agency shall also communicate this information to the concerned member state(s) authority. The 5-year period shall begin at receipt of notification at the Agency. The manufacturer or importer or producer of articles shall request for extension for the substance justifying their exclusive use in research and development of medicinal products for human and veterinary programmed. The Agency shall make decision on extending the exemption period considering the comments from Member state(s) authorities, for any 5 years or further up to 10 years for the substance that are not placed on the market.

2.3 Information to Be Submitted for General Registration Purposes (Article 10)

For the purpose of registration required by article 6 or 7(1) or 5, the manufacturer or importer or producer of articles shall notify the following information to the Agency:

A. **A technical dossier including:**

(i) The identity and contact details of the manufacturer or importer or producer of articles as specified in section 1 of Annex VI.
(ii) Registration number in article 20(1).
(iii) Identity of the substance (section 2 Annex VI) and classification of substance (section 4 Annex VI).
(iv) Estimated quantity as specified in section 3.1 of Annex VI.
(v) Brief description on the safe use of the substance or substance in the article specified in section 5 of Annex VI and use(s) of the article(s).
(vi) Study summaries of the information derived from the application of Annexes VII and XI.
(vii) Robust study summaries of the information derived from the application of Annexes VII to XI, if required under Annex I.
(viii) An indication of information which has been reviewed by an assessor with appropriate experience.
(ix) Proposals for testing where listed in Annexes IX and X.
(x) For substances in quantities of 1 to 10 tons, exposure information as specified in section 6 of Annex VI.
(xi) A request by the manufacturer or importer with justification, if any information shall not be made available on the Internet in accordance with article 77(2)(e), given his or other party's commercial interest.

B. **A chemical safety report required under Article 14, with relevant use and exposure categories**

When a substance is intended to be manufactured by one or more manufacturers and/or imported by one or more importers and/or is subject to registration under Article 7 of this regulation, the following shall apply:

(i) One registrant shall submit the information in Article 10(a)(iv), (vi), (vii), and (ix) and any relevant indication under Article 10(a)(viii) to the Agency (hereinafter referred to as "the lead registrant") acting with the agreement of the other assenting registrant(s).
(ii) Each registrant shall subsequently submit separately the information specified in Article 10(a)(i), (ii), (iii), and (x) and any relevant indication under Article 10(a)(viii).
(iii) The registrants may decide themselves whether to submit the information specified in Article 10(a)(v) and (b) and any relevant indication under Article 10(a)(viii) separately or whether one registrant is to submit this information on behalf of the others.

But the information specified in Article 10(a)(iv), (vi), (vii), and (ix) for the purposes of registration shall be submitted by each registrant within his tonnage band. The physicochemical, toxicological, and ecotoxicological information that is relevant and available to the registrant shall be specified in Article 10 under points (vi) and (vii). As soon as the quantity of a substance per manufacturer or importer reaches the next tonnage threshold, the Agency must immediately be informed with necessary information as required by this regulation.

A registrant may also submit the information specified in Article 10(a)(iv), (vi), (vii), and (ix) separately, along with dossier if:

(i) He disagrees with the selection of this information with the lead registrant.
(ii) Filling jointly would be disproportionately costly for him.
(iii) Joint filling would lead to disclosure of commercially sensitive information.

2.4 General Requirements for Generating Information on Intrinsic Property of Substances

The intrinsic properties of substances can be produced with other test methods as per the conditions set out in Annex XI. The information on human toxicity should be generated through the alternative methods such as in vitro methods or qualitative or quantitative structure-activity relationship models, whenever possible to avoid the use of vertebrate animals for testing. The test methods in vertebrate animals shall be regularly reviewed and improved to reduce the testing and the number of animals involved. Commission Regulation shall be adopted in accordance with the procedure referred to in Article 133(4), and the Annexes of this Regulation, so as to

replace, reduce, or refine animal testing. Ecotoxicological and toxicological tests and analyses shall comply with the principles of good laboratory practice provided for in Directive 2004/10/EC or other international standards recognized as being equivalent by the Commission or the Agency and with the provisions of Directive 86/609/EEC, if applicable.

2.5 Chemical Safety Report and Recommended Risk Reduction Measures

A chemical safety assessment shall be performed, and a chemical safety report shall be completed for all substance (in quantities of 10 tons or more per year per registrant) subject to registration, without prejudice to Article 4 of Directive 98/24/EC. A chemical safety assessment shall be conducted for either each substance on its own or in a preparation or in an article in accordance with Annex I of this regulation.

A chemical safety assessment shall be exempted if the concentration of substance is less than the lowest of any of the following:

(i) Concentration defined in Article 3(3) of Directive 1999/45/EC.
(ii) Concentration limits in Annex I to Directive 67/548/EEC.
(iii) Concentration limits in Part B of Annex II and Annex III to Directive 1999/45/EC.
(iv) Concentration limits in the classification and labelling inventory established under Title XI of this Regulation.
(v) 0,1% weight by weight (w/w), if the criteria in Annex XIII of this Regulation is met.

A chemical safety assessment of a substance shall include the following steps:

(i) Human health hazard assessment.
(ii) Physicochemical hazard assessment.
(iii) Environmental hazard assessment.
(iv) Persistent, bioaccumulative, and toxic (PBT) and very persistent and very bioaccumulative (vPvB) assessment.

Based on the results from the chemical assessment steps, the registrant concludes that the substance meets the criteria for classification as dangerous in accordance with Directive 67/548/EEC or is assessed to be as a PBT or vPvB. The exposure scenarios (where appropriate the use and exposure categories), exposure assessment, and risk characterization for all identified uses of the registrant shall also be addressed and included in the chemical safety assessment. Any registrant shall identify and apply the appropriate measures to adequately control the risks identified in the chemical safety assessment and, where suitable, recommend them in the safety data sheets which he supplies in accordance with Article 31. Any registrant required to conduct a chemical safety assessment shall keep his chemical safety report

available and up to date. The chemical safety report need not include consideration of the risks to human health from the end uses (a) in food contact materials within the scope of Regulation (EC) No 1935/2004**1** and (b) in cosmetic products within the scope of Directive 76/768/EEC.

2.6 Data Sharing and Avoidance of Unnecessary Testing

This regulation tries to avoid animal testing and limits the duplication of other tests. The sharing and joint submission for the purposes of this regulation enables the registrants to refrain from exchanging concern technical data and their market behaviors (such as production or sales volume, production capacity, import volume, or market shares). If a substance has already been registered at least 12 years (in accordance to Article 26(3)) previously, a new registrant shall be entitled to refer to the study summaries or robust study summaries under this regulation, provided that he can show that the substance that he is now registering is the same as the one previously registered, including the degree of purity and the nature of impurities. In this case, if the substance has previously been registered for less than 12 years, the new registrant might request the previous registrant for information specified in Article 10 under points (vi) and (vii) in order to register. In such situations, the previous registrant and the potential registrant shall share the costs of data generation in accordance with Article 77(2)(g) of this regulation. The new registrant shall access the full study reports, given that the previous registrant(s) have given permission to refer for the purpose of registration. However, a new registrant shall not refer to such studies to provide the required information on substance identity (section 2 of Annex VI).

2.7 Registration Process

- On submission of notification for registration of a substance on its own or in a preparation or in an article to the Agency, the Agency shall assign a submission number and submission date (date of receipt) to each registration.
- The Agency shall check the completeness of each registration in order to ascertain that all elements required under this regulation and the appropriate registration fee referred in this regulation have been provided. But this completeness check does not include assessment of quality or adequacy of any data or justifications submitted.
- The Agency shall undertake the completeness check within 3 weeks or within 3 months (for in-phase substances in accordance with Article 23).
- If the registration is incomplete, the Agency shall inform the registrant, regarding further information required to be submitted for the registration to be complete within the stipulated time window.

- The registrant shall complete his registration and submit it to the Agency within the deadline. Failure to complete the registration within the deadline set shall pose rejection of the registration. The registration fee shall not be reimbursed in such instances.
- On the registrant completing his registration, the Agency shall perform further completeness check along the information provided. On completion of registration, the Agency without delay shall communicate the registration number and date to the registrant, which shall be used for all subsequent correspondence.
- The registrant may start the manufacture or import of a substance or production or import of an article if there is no indication to the contrary from the Agency within 3 weeks after receipt by the Agency, without prejudice to Article 27(8).
- The Agency shall also notify the competent authority of relevant Member State(s) within 30 days of the submission date, regarding the registration relevant information available in the Agency database.
- Following registration, it is the responsibility of the registrant to update his registration without undue delay with the relevant new information regarding the substance along the relevant part fee in accordance with this regulation. The Agency shall intimate relevant competent Member state authority regarding the update available in the database.

3 Evaluation [1]

3.1 Dossier Evaluation

The agency shall examine testing proposal submitted in a registration or a downstream user report for substance-relevant information specified in Annexes IX and X. Substances which have or may have PBT, vPvB, sensitizing and/or carcinogenic, mutagenic, or toxic for reproduction (CMR) properties or substances classified as dangerous according to Directive 67/548/EEC above 100 tons per year with uses resulting in widespread and diffuse exposure shall be given priority for evaluation.

The name of the substance, hazard end-point of the proposed vertebrate testing (testing proposal), and the set deadline (usually 45 days) for third party to submit scientifically valid information shall be published by the Agency on its website. Such scientifically valid information and studies that address relevant substance and hazard end-point, submitted by the third party, shall be considered by the Agency in preparing its decision in accordance to this regulation. In accordance to the procedures laid down in Articles 50 and 51, the Agency shall draft one of the following decisions:

(a) A decision requiring the concerned registrant(s) or downstream user(s) to perform the proposed test and submit the study summary (or the robust study summary if required by Annex I) within a set deadline.

(b) A decision in accordance with point (a), but modifying the conditions under which the test is to be carried out.
(c) A decision in accordance with points (a), (b), or (d) but requiring registrant(s) or downstream user(s) to carry out one or more additional tests in cases of non-compliance of the testing proposal with Annexes IX, X, and XI.
(d) A decision rejecting the testing proposal.
(e) A decision in accordance with points (a), (b), or (c), if several registrants or downstream users of the same substance have submitted proposals for the same test, giving them the opportunity to reach an agreement on who will perform the test on behalf of all of them and to inform the Agency accordingly within 90 days. If the Agency is not informed of such agreement within such 90 days, it shall designate one of the registrants or downstream users, as appropriate, to perform the test on behalf of all of them.

Compliance Check of Registrations

To verify its compliance with the regulation, the Agency may examine any registration for:

(a) That the requirements of Articles 10, 12, and 13 and with Annexes III and VI to X are submitted in the technical dossier (in pursuant to Article 10).
(b) That the adaptations of the standard information requirements and the related justifications submitted in the technical dossier(s) are in compliance with the rules governing such adaptations set out in Annexes VII to X and with the general rules set out in Annex XI.
(c) That any required chemical safety assessment and chemical safety report comply with the requirements of Annex I and that the proposed risk management measures are adequate.
(d) That any explanation(s) submitted in accordance with Article 11(3) or Article 19(2) have an objective basis.

In accordance to Article 50 and 51 of this regulation, within 12 months of the start of compliance check, the Agency may prepare a draft decision requiring the registrants to submit any further information within a stipulated deadline, required to bring the registration into compliance. To ensure the dossier compliance with this regulation, the Agency will select no lower than 5% of the total dossier received for each tonnage band. The list of dossiers checked by the Agency for compliance with this regulation shall be made available to the Member States competent authorities. The Agency shall examine any information submitted in consequence of decision taken under Article 40 or 41. On completion of dossier information, the agency shall notify the Commission and the competent authorities of the Member States of the information obtained and any conclusions made.

3.2 Substance Evaluation

To ensure harmonized approach, the Agency in cooperation with the Member states develops criteria for prioritizing substances grounded on risk-based approach. The criteria shall consider:

(a) Hazard information, for instance, structural similarity of the substance with known substances of concern or with substances which are persistent and liable to bio-accumulate, suggesting that the substance or one or more of its transformation products has properties of concern or is persistent and liable to bio-accumulate.
(b) Exposure information.
(c) Tonnage, including aggregated tonnage from the registrations submitted by several registrants.

Based on these criteria, the Agency shall compile a draft community rolling plan which shall cover a period of 3 years and shall specify the substances (based on their risks to human health or environment) to be evaluated each year. A draft annual update to the rolling plan will be submitted by the Agency to the Member States by 28 February each year. Based on the opinion from the Member State Committee (set up under Article 76(1)(e)), the Agency shall adopt the final Community rolling action plan and publish the plan on its website, identifying the Member State who will carry out the evaluation of the substances listed therein as determined according to Article 45.

Competent Authority

The Agency shall be responsible for coordinating the substance evaluation process and ensuring that substances on the Community rolling action plan are evaluated. In doing so, the Agency shall rely on the competent authorities of Member States. The competent authorities may appoint another body to act on their behalf to carry out an evaluation of a substance. A Member State may notify the Agency at any time, if a substance has priority for evaluation, not on the Community rolling action plan. The Agency shall decide whether to add this substance to the Community rolling action plan on the basis of an opinion from the Member State Committee. If the substance is added to the Community rolling action plan, the proposing Member State, or another Member State who agrees, shall evaluate that substance.

If the competent authority considers that further information is required, it shall prepare a draft decision, stating reasons, requiring the registrant(s) to submit the further information within a set deadline for its submission. A draft decision shall be prepared within 12 months of the publication of the Community rolling action plan on the Agency's website for substances to be evaluated that year. The decision shall be taken in accordance with the procedure laid down in Articles 50 and 52. The competent authority shall finish its evaluation activities within 12 months of the

start of the evaluation of the substance or within 12 months of the information being submitted under paragraph 2 and notify the Agency accordingly. If this deadline is exceeded, the evaluation shall be deemed finished.

Follow-up to Substance Evaluation

Once the substance evaluation has been completed, the competent authority shall consider how to use the information obtained from this evaluation for the purposes of Article 59(3), Article 69(4), and Article 115(1). The competent authority shall inform the Agency of its conclusions as to whether or how to use the information obtained. The Agency shall in turn inform the Commission, the registrant, and the competent authorities of the other Member States.

Adoption of Decisions

- The Agency shall notify its draft decision in accordance with Article 40 or 41, together with the comments of the registrant, to the competent authorities of the Member States.
- Within 30 days of circulation, the Member States may propose amendments to the draft decision to the Agency.
- If the Agency does not receive any proposals, it shall take the decision in the version notified under paragraph 1.
- If the Agency receives a proposal for amendment, it may modify the draft decision.
- The Agency shall refer a draft decision, together with any amendments proposed, to the Member State Committee within 15 days of the end of the 30-day period referred to in paragraph 2.
- The Agency shall forthwith communicate any proposal for amendment to any registrants or downstream users concerned and allow them to comment within 30 days.
- The Member State Committee shall take any comments received into account.
- If within 60 days of the referral, the Member State Committee reaches a unanimous agreement on the draft decision, the Agency shall take the decision accordingly.
- If the Member State Committee fails to reach unanimous agreement, the Commission shall prepare a draft decision to be taken in accordance with the procedure referred to in Article 133(3).
- In accordance with Articles 91, 92, and 93, an appeal may be brought against Agency decisions.

Publication of Information on Evaluation

The Agency by 28 February of each year shall publish on its website a report on the progress made over the previous calendar year toward discharging the obligations incumbent upon it in relation to evaluation. This report shall include, in particular, recommendations to potential registrants in order to improve the quality of future registrations.

4 Authorization [1]

4.1 Requirement and Considerations for Substitution

The purpose of authorization is to properly maintain dangerous substances in the market with risk controls and finding lesser dangerous substances/technologies to replace them while considering the economic and technical feasibility and viability. This responsibility lies for the manufacturers, importers, and downstream users that apply for and claim authorization.

Article 56 talks about the general provisions for the requirement of authorization procedure. A substance included under Annex XIV of this regulation is not to be placed on the market or used by the manufactures, importer, or downstream user without authorization. The exemptions are made when the substance/mixture's use has been authorized, or it has been exempted from authorization considering the community legislation governs the use of the substance and the risk control measures. The exemption also holds if the date until which the substance can be placed and used in the market has not been reached and 18 months from this date once the extension for the authorization has been submitted. The immediate downstream user can be authorized to use the regulated substance. This use has to be the same as given in the authorization application submitted. These exemptions do not apply for the use of the substance in scientific research and development, and for the product and process-oriented research, the maximum quantity exempted has to be provided by Annex XIV. Substances used as plant protection products [13], biocidal products [14], motor fuels [15], and fuel in mobile or fixed combustion plants of mineral oil products and use as fuels in closed systems do not follow the exemptions mentioned above. The substances are to be authorized when classified under Article 57 as hazardous to human health, and the exemptions provided do not apply for their use in cosmetic products [16] and food contact materials [17]. Persistent, bio-accumulative, and toxic substances used in preparations containing concentration below 0.1% weight/weight and along with substances with lowest concentration limits [18, 19] classified as dangerous are subject to authorization without exemptions.

Article 57 specifies the substances to be included in Annex XIV following the procedures in Article 58. The substances included are carcinogenic category 1 or 2 [20], mutagenic category 1 or 2 [20], and toxic for reproduction category 1 or 2 [20].

The substances classified under Annex XIII of this regulation as persistent based on the half-life in marine water (higher than 60 days), fresh- or estuarine water (higher than 40 days), marine sediment (higher than 180 days), fresh- or estuarine water sediment (higher than 120 days), or in soil (higher than 120 days) are to be included in this Annex. The substances bioaccumulating with bioaccumulation factor greater than 2000 and toxic substances are included as well. A substance with observed toxicity of long term no-observed effect concentration (Noec) for marine and freshwater organisms is less than 0.01 mg/ml and showing chronic toxicity is identified as T, R48, or Xn and R48 [20]. A substance classified as very persistent when the half-life of the substance in marine/fresh/estuarine water or in marine/fresh/estuarine water sediment or in soil is higher than 60 days, 180 days and 180 days respectively. The very bioaccumulative substances with bioaccumulation factor more than 5000 are included in Annex XIV. Annex XIV also includes substances that have endocrine-disrupting properties and are persistent, bioaccumulative, and toxic in nature and do not follow the criteria laid out above but are scientifically proven to have adverse effects on human health and environment.

The inclusion of a substance in Annex XIV (Article 58) shall follow the regulatory procedure laid out by the Commission along with the Scrutiny Committee formed by the representatives of the Member States chaired by representative of the Commission [21]. Annex XIV must contain the identity of the substance such as name or other identifier, molecular and structural information, composition, degree of purity, impurities, additives, etc. [22]. The intrinsic property of the substance given by Article 57 has to be included in the Annex. The date (sunset date) from which the substance is placed on the market and its use is authorized. The date or dates before the sunset date by which the authorization application must be received for the continued use of the substance in the market after the sunset date is reached. The review period for the use of the substance wherever appropriate also has to be included. The exemptions from authorization for use/category of use for the substance also have to be mentioned with the basis of these exemptions. The substances to be included are prioritized by the Agency along with the Member State Committee based on their persistent, bioaccumulative, and toxic properties, wide dispersive use, or high volume. The number of substances and the dates mentioned above have to account for the Agency's ability to handle the applications. The first set of priority substances to be included in the Annex recommended by the Agency was included by 1 June 2009, and further inclusions are done every second year. The Agency has to publish the substances to be included in the Annex with public access at free of cost over the Internet with comments enabled before recommending to the Committee. With the comments received from interested parties within 3 months of the publication, the Agency can update its recommendation. The substances included in the Annex shall not be subjected to new restrictions under Title VIII when used on its own or in a preparation can possess risk to human health and environment. The substances can be subjected to new restrictions when its presence in an article proves as risk. The substances prohibited from all uses as per Title VII or by Community legislation shall not be included in the Annex or shall be removed.

The substances which do not fulfill the criteria mentioned in Article 57 resulting from a new information are to be removed.

The procedure for identification of substances referred to in Article 57 is laid out under Article 59 together with the candidate list for inclusion in Annex XIV. The Committee can ask the Agency to prepare dossier with the information on harmonized classification, identification, and restrictions (Annex XV) and make it available to the Member States. Any Member State can prepare and forward the dossier to the Agency, and the Agency has to make it available within 30 days of receipt. The Agency has to communicate the preparation of the dossier and invite other Member States and all other interested parties to comment within a deadline which is ideally within 60 days. If no comment is received, the Agency can recommend the inclusion of the substance in the list. When comments are received, the Agency has to refer the dossier to the Member State Committee within 15 days before the 60-day deadline. The Member State Committee reaches a unanimous agreement within 30 days, and the Agency shall include the substance in its recommendation list. When a unanimous agreement is not arrived, the Commission shall prepare a draft proposal on identification of substance to be submitted to the European Parliament and the Council for review. If no opposition is offered within 3 months of the draft submission, then the draft shall be adopted by the Commission and published on its website without delay.

4.2 Granting of Authorizations

Article 60 advices on granting of authorizations. The Commission is held responsible for taking decisions on applications and authorizations. The authorization is granted to the use of substance possessing risk to human health or environment in Annex XIV provided these risks are controlled and documented in chemical safety report with the opinion of the Committee of Risk Assessment [23]. It shall note the discharges, emissions, and losses, including risks arising from diffusion and dispersive uses while granting authorization. The risks to human health from use of a substance in medical device, active implantable medical devices, or in vitro diagnostic medical devices shall not be considered by the Commission [24–26]. This lenience is not given for substances listed in Article 57 for which the threshold exposure levels and likelihood and severity of the event occurring due to the physicochemical properties of the substance cannot be determined. The persistent, very persistent, bioaccumulative, very bioaccumulative, endocrine disrupting, and toxic substances cannot be given any exceptions with respect to controlled risk measures stated above. In this case, an authorization can only be granted if the socioeconomic benefits of the use of the substance are greater than the risk to human health or environment and no alternative substance or technologies are available. The decision is made considering the opinions of the Committee for Risk Assessment and Socioeconomic Analysis along with the appropriateness and effectiveness of the risk management measures proposed, socioeconomic benefits, socioeconomic

implications arising from refusal of authorization, analysis of alternatives or substitution plans submitted, and information on the risks to human health or environment from alternative substances or technologies. The Commission shall look into all relevant aspects of the suitable alternative substances or technologies including whether this transfer could reduce overall risks given the appropriateness and effectiveness of risk management measures and technical and economic feasibility of these alternatives. The use of the substance shall not be authorized if it involves relaxation of restriction set in Annex XVII. The grant of authorization is only possible when the application is confirming with the application requirement set in Article 62 of this regulation. The authorizations can be dependent on time-limited review with monitoring with the duration determined on a case-by-case basis. The authorization shall include the person to whom the authorization is granted, identity of the substance, the use for which the authorization is granted, any conditions under which authorization is granted, time-limited review period, and monitoring arrangement. The holder of authorization shall always ensure the exposure is reduced to as low technically and practically as possible.

Review of Authorizations

The review process for these authorizations is done according to Article 61 of this regulation.

- The validity of the authorization is granted until the Commission decides to amend or withdraw it for review unless the holder of authorization submits a review report 18 months before the expiry of time-limited review period.
- The holder shall submit an update of alternatives analysis, relevant research, and development activities done by the applicant and substitution plan.
- A substitution plan shall be submitted when a suitable alternative is available with timetable for proposed actions.
- When the holder can control the risk, then a chemical safety report is needed, and when risks cannot be controlled, an update to the socioeconomic analysis in the original application shall be given.
- Any updates to the elements of the original application have to be communicated in this review. The authorizations can be reviewed whenever the circumstances of the original authorization have changed affecting the risk to human health or environment or socioeconomic impact and suitable substitutes are available.
- The Commission sets a deadline by which the holder can submit further information required for review. The Commission can amend or withdraw the authorization under the changed circumstances with all the necessary information about these changes submitted by the holder of authorization.
- The Commission can decide to suspend the authorization pending review when there is serious and immediate risk for human health or environment.
- When the environmental quality standards and environmental objectives [27, 28] are not met, the authorization for the use of the substance can be reviewed, and

also if use of a substance is subsequently restricted/prohibited as persistent organic pollutant, then the authorization can be withdrawn by the committee [29].

Applications for Authorizations

The information regarding the application of authorization is given under Article 62 of this regulation. The application shall be submitted to the Agency. The application can be submitted by the manufacturer(s), importer(s), and/or downstream user(s) of the substance. An application can be submitted by more than one person. The application can include one or a group of substance with similar physicochemical, toxicological, and ecotoxicological properties for one or more uses. The applicant can submit application for own use and for uses for which the substance is placed on the market. The application shall include the identity of the substance(s), the name and contact detail of the person(s) submitting the application, a request for authorization for the specific use of the substance and use of preparation in which the substance is incorporated, a chemical safety report (unless submitted before as part of registration) mentioning the risks to human health or environment arising due to the intrinsic properties of the substance, analysis for the alternative substance or technology with information on research and development activities by the applicant, and a substitution plan with timetable when suitable alternatives are available for the substance in question. Additionally, the substance can include socioeconomic analysis and a justification for not considering risks to human health and environment through emissions of substance from a permitted installation [15] and discharges of the substance from point source [30]. The application shall not include risks to human health arising from use of the substance in medical device [24–26]. The application shall include the appropriate fee required as given under Title IX of this regulation. The subsequent applications are submitted as per Article 63. A subsequent application is filed for parts of the existing application such as chemical safety report, analysis of alternative to the applied substance, and substitution plan for the suitable alternatives proposed and socioeconomic analysis. This subsequent applications provision applies for already granted authorization. The subsequent application shall also update the information in the original application.

Procedure for Authorization Decisions

The procedure for decisions on authorization is listed in Article 64. Firstly, the Agency shall acknowledge the receipt of application with date. The Agency's Committees for Risk Assessment and Socioeconomic analysis shall give their opinions on the draft within 10 months of receipt of application. The Agency shall make information on use of the substance publicly accessible at free of cost as soon as the application is received with the deadline for alternative substances or technologies submissions. The Committees shall check that the application shall include all

information asked for as per Article 62. The Committees shall consult with each other and request for additional information from the applicant and consider all information submitted by third parties. The Socioeconomic Analysis Committee requires for the applicant or third parties to submit additional information on possible alternative substance or technologies within a specified time period. The draft opinions shall contain Committee for Risk Assessment and Committer for Socioeconomic Analysis. The Agency shall communicate the draft opinions to the applicant by end of deadline and considered to be received by the applicant within 7 days of sending. The applicant shall give in writing if he/she wishes to comment within 1 month of receipt of draft opinion. When no comment is made, the Agency shall send the opinions to the Commission, the Member States, and the applicant within 15 days of end of period for applicant's comment or within 15 days of receipt of notice of "no comment" from applicant. The applicant shall send his written arguments/comments to the Agency within 2 months of receipt of draft opinion, and the Committee shall consider the comments and make their final opinions within 2 months of receipt of applicant's arguments. The Agency shall send the opinions with written argumentations to the Commission, the Member States, and applicant in further 15 days. The Agency decides which part of opinions and attachments to be published for public access on its website. When subsequent applications are submitted to the original application, the Agency can consider the application together within the deadlines for the original application. The Commission shall decide on the draft authorization within 3 months after receiving the Agency's opinion. The final decision on granting or refusal of the authorization is within a time limit determined by urgency by the advice of the Commission or sometimes by voting. The Commission decisions with the authorization number and reason for the decision shall be published in the Official Journal of the European Union and made available publicly database which is kept up to date by the Agency. For subsequent application, the deadline is shortened by 5 months.

4.3 Obligation of Holders of Authorizations

The obligations of holders of authorization are described in Article 65. The holders of authorization and the downstream users shall include the authorization number of the substance on the label before placing the substance or preparation including the substance on the market for its authorized use as soon as the authorization number is published. The downstream users shall notify the Agency within 3 months of start of the supply of the substance. The Agency shall document the downstream users through a register and maintain it up to date. This register has to be accessible for competent authorities of the Member States.

5 Restrictions on the Manufacturing, Placing on the Market, and Use of Certain Dangerous Substances, Preparations, and Articles [1]

5.1 General Provisions for Introducing New and Amending Current Restrictions

The provisions for the restrictions for the substances to be placed on the market and be used are given under Article 67 of this regulation. Annex XVII specifies the restrictions and conditions under which the restrictions can be relaxed for product and process-related research and development along with the maximum exemption quantity. The substance or the preparation of the substance included in the Annex XVII with a restriction shall not be placed on the market or used beyond the conditions mentioned in the Annex. For example, chloroform shall not be used in concentrations equal to 0.1% or more by weight for public sale and/or in diffusive purposes such as surface cleaners or fabric cleaners. This restriction does not be considered for use of the substance in scientific research and development. The restrictions do not cover the use of the substances in cosmetic products as it is already defined by a different directive [16]. The Commission is responsible for compiling and publishing the inventory of the restrictions by 1 June 2009. A Member State shall maintain record of existing and stringent restrictions in Annex XVII after having notified till 1 June 2013.

The restriction process is detailed under Article 68. An unacceptable risk to human health or environment occurs from manufacture, placing on the market, or use of a substance. Annex XVII has to be amended with new restrictions altering the current restrictions [21]. These restrictions shall be made considering socioeconomic impact and availability of alternatives. The use of substance as onsite isolated intermediate can be exempted from the amendment. For substances or preparations classified as carcinogenic, mutagenic, or toxic to reproduction category 1 or 2 and used by consumers, the Commission proposes the restrictions and amended by the regulatory procedure laid out by Commission along with the Scrutiny Committee formed by the representatives of the Member States chaired by representative of the Commission [21], and the following Article does not apply.

5.2 Restriction Process

Preparation of Restriction Proposal

- When the manufacture, placing on the market, or use of a substance or its preparation proves as risk to human health or environment and these risks are not adequately controlled, then the Commission and the Member States can request the Agency to prepare Dossier with restriction proposal, information on

alternatives, justification for the restriction, and socioeconomic assessment following Annex XV of this regulation.
- The Agency can also prepare the dossier after the sunset date when it considers the use of substance or its preparation generates risk which is not adequately controlled. The Agency has to suggest restrictions to initiate the restriction process if the dossier proves more actions are needed within 12 months of the Commission's request.
- The Member State is responsible for preparing and submitting the dossier for restrictions when the substance is not included in the list maintained by the Agency within 12 months after notifying the Agency to initiate the restrictions. The Agency or Member States can refer to any dossiers, chemical safety reports, and risk assessments submitted for other purposes and also can request other agencies under the Community law for this information.

Agency Opinion: Committee for Risk Assessment and Socioeconomic Analysis

- The Committee for Risk Assessment and Socioeconomic Analysis shall oversee if the dossiers submitted by the Agency or the Member State conform with the requirements within 30 days of submission. Any conform problems shall be communicated to the Agency or the Member States within 45 days of receipt of the dossier with reasons and corrected within 60 days of receiving the reasons from the Committee.
- The Agency shall publish the opinion of the Commission of Member State to initiate the restriction procedure and inform the registrant of the same. The Agency is responsible for maintaining the list of substances for which dossiers are planned or underway. A substance included in this list shall not have any other dossier.
- If an existing restriction has to be re-examined, it has to be decided by the Commission assisted by an advisory committee composed of the representatives of the Member States and chaired by the representative of the Commission. This representative has to submit a draft of measures to be taken to the Committee, and the decision has to be taken within a time limit based on the urgency based on the evidence presented and may be through a voting system [21].
- The Agency shall make the dossiers publicly accessible on its website with the restrictions suggested and the date of publication.
- The interested parties can submit their comments on the dossiers and suggested restriction together with socioeconomic analysis or any other information studying the advantages and drawback of these restrictions within 6 months of the date of publication.
- The Committee for Risk Assessment shall check and render its opinion if the suggested restrictions are necessary to reduce the risk to human health or environment within 9 months considering the Member State dossier, the dossier prepared by the Agency, and the views of the interested parties (Article 70).

- The Committee for Socioeconomic Analysis shall come to an opinion on the suggested restrictions after studying the dossier and the socioeconomic impact within 12 months of publication. This opinion has to be published on the website by the Agency and invite comments from interested parties within 60 days of the opinion publication.
- The Committee shall adopt its opinion considering comments received. If the opinion of the Committee for Risk Assessment deviates from the restrictions suggested, the deadline for delivering opinion of the Socioeconomic Analysis Committee can be postponed by 90 days (Article 71).

Submission of an Opinion to the Commission

- The submission of an opinion to the Commission is as per Article 72 of this regulation. The opinions of the Committees of Risk Assessment and Socioeconomic Analysis shall be submitted to the Commission by the Agency on the restriction suggestions with documents and evidence submitted upon request. If either of the Committee is not able to come to an opinion by the deadline, then the Agency shall inform the Commission with proper reasons. The opinions of the Committees shall be published on the website by the Agency without delay.

Commission Decision

- Article 73 covers the decision made by the Commission. The Commission shall prepare a draft amendment to Annex XVII once Article 68 conditions. It shall be fulfilled either 3 months after obtaining the opinion or before the deadline set in Article 71 if the Committee has not come to an opinion.
- The Commission shall provide a detailed report with explanation for the difference when the amendment differs from the original proposal or the opinion of the Agency is boycotted. The Commission is assisted by an advisory committee composed of the representatives of the Member States and chaired by the representative of the Commission. This representative has to submit a draft of measures to be taken to the Committee, and the decision has to be taken within a time limit based on the urgency based on the evidence presented and may be through a voting system [21]. The draft amendment shall be submitted to the Member States by the Commission 45 days before the voting.

6 Reach Safety Data Sheet [1]

The supplier of a substance or a preparation shall provide the recipient of the substance or preparation with a safety data sheet complied in accordance with Annex II where (i) a substance or preparation meets the criteria for classification as

dangerous (Directives 67/548/EEC or 1999/45/EC) or (ii) substance is persistent, bioaccumulative, and toxic or very persistent and very bioaccumulative in accordance with the criteria set out in Annex XIII or (c) a substance is included in the list established in accordance with Article 59(1) for other reasons. The safety data sheet might not be supplied for dangerous substances or preparations sold to general public if sufficient information and measures necessary for protection of human health, safety, and environment are available to users. However, the supplier shall provide the safety data sheet (electronic copy or free of cost) at request by the recipient in accordance with Annex II.

The safety data sheet shall be supplied in an official language of the Member State(s), where the substance or preparation is placed on market, and shall contain the following information:

(i) Identification of the substance/preparation and of the company/undertaking.
(ii) Hazards identification.
(iii) Composition/information on ingredients.
(iv) First-aid measures.
(v) Fire-fighting measures.
(vi) Accidental release measures.
(vii) Handling and storage.
(viii) Exposure controls/personal protection.
(ix) Physical and chemical properties.
(x) Stability and reactivity.
(xi) Toxicological information.
(xii) Ecological information.
(xiii) Disposal considerations.
(xiv) Transport information.
(xv) Regulatory information.
(xvi) Other information.

Any downstream user shall include relevant exposure scenarios and use other relevant information, from the safety data sheet supplied to him when compiling his own safety data sheet for identified uses. The suppliers shall update the safety data sheet without delay if:

(i) New information which may affect the risk management measures or new information on hazards becomes available.
(ii) Once an authorization has been granted or refused.
(iii) Once a restriction has been imposed.

The new, dated version of the information, identified as “Revision: (date),” shall be provided by the supplier to all former recipients, who have been supplied with the substance or preparations within the preceding 12 months.

Bibliography

1. legislation.gov.uk - Regulation (EC) No 1907/2006 of the European Parliament and of the Council. 18 Dec. 2006, https://eur-lex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:32006R1907&from=EN. Accessed 12 Apr. 2020
2. Chemsafetypro, https://www.chemsafetypro.com/Topics/EU/REACH_Regulation_EC_No_1907_2006.html. Accessed 4 Jun. 2020
3. OJ L 183, 29.6.1989, p. 1. Directive as amended by Regulation (EC) No 1882/2003.
4. OJ L 257, 10.10.1996, p. 26. Directive as last amended by Regulation (EC) No 166/2006 of the European Parliament and of the Council (OJ L 33, 4.2.2006, p. 1).
5. OJ L 327, 22.12.2000, p. 1. Directive as amended by Decision No 2455/2001/EC of the European Parliament and of the Council (OJ L 331, 15.12.2001, p. 1).
6. OJ L 311, 28.11.2001, p. 1. Directive as last amended by Directive 2004/28/EC of the European Parliament and of the Council (OJ L 136, 30.4.2004, p. 58).
7. OJ L 311, 28.11.2001, p. 67. Directive as last amended by Directive 2004/27/EC of the European Parliament and of the Council (OJ L 136, 30.4.2004, p. 34).
8. OJ L 40, 11.2.1989, p. 27. Directive as last amended by Regulation (EC) No 1882/2003.
9. OJ L 184, 15.7.1988, p. 61. Directive as last amended by Regulation (EC) No 1882/2003.
10. OJ L 84, 27.3.1999, p. 1. Decision as last amended by Decision 2004/357/EC (OJ L 113, 20.4.2004, p. 28).
11. OJ L 268, 18.10.2003, p. 29. Regulation as amended by Commission Regulation (EC) No 378/2005 (OJ L 59, 5.3.2005, p. 8).
12. OJ L 213, 21.7.1982, p. 8. Directive as last amended by Commission Directive 2004/116/EC (OJ L 379, 24.12.2004, p. 81)
13. Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market.
14. Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market.
15. Directive 98/70/EC of the European Parliament and of the Council of 13 October 1998 relating to the quality of petrol and diesel fuels.
16. Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products.
17. Regulation (EC) No 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC.
18. Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations.
19. Annex I to Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.
20. Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.
21. Article 133(4) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC and COUNCIL DECISION laying down the procedures for the exercise of implementing powers conferred on the Commission (1999/468/EC).

22. Section 2 of Annex VI of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC.
23. Section 6.4 of Annex I, of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC.
24. Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices.
25. Council Directive 93/42/EEC of 14 June 1993 concerning medical devices.
26. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.
27. Council Directive 96/61/EC of 24 September 1996 concerning integrated pollution prevention and control
28. Article 4(1) of Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy.
29. Regulation (EC) No 850/2004 of the European Parliament and of the Council of 29 April 2004 on persistent organic pollutants.
30. Article 11(3)(g) of Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy and legislation adopted under Article 16 of the same Directive.