Data Fraud and Essence of Data Verifiability

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9.1 History

Incidents of data misconduct and fraud have been periodic in the medical science and biomedical research field history. Sincerity, data integrity, and trustworthiness are the ground principles pertaining to any scientific research [1] toward the progression of science and the public perception of scientific results adhering to the basic principles is a must. Any deviation from the principles described above could be regarded as scientific fraud or misconduct [2].

The history of science and research is crammed with some unusual instances with proven or questionable misconduct in science [3]. A few giants in science have been found vulnerable to suspicion of ambiguous practices, including the great Isaac Newton, who is noted for falsifying a bit of data for making people admit much relatively toward his hypotheses [4]. Claudius Ptolemy, a mathematician, geographer, astronomer, and astrologer, wrote several scientific disquisitions suspected of notifying the work concluded by others as his straight observations [5]. An esteemed scientist regarded as a founder of the modern science of genetics raises doubts about selective notification of some results and even data fabrication [6]. Among those mentioned and even furthermore such examples, there might be no

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straightforward evidence of fraud generally, but just the statistical proof which remarks the perceived observations to be more misaligned to the actual expected theoretical values, whichever could be appropriate, with a probability of affecting the experimental actual data [7].

A researcher, who published a study notifying an association between "measles, mumps and rubella vaccination" with a syndrome comprising bowel disease and autism in 12 children on February 28, 1998, in the Lancet, after which no evidence of this link is established by many epidemiological studies [8]. Nevertheless, retraction of this study happened in the year 2010 after 12 long years, due to the claims against this study stating the children were attributed consecutively, mentioning that the investigations that were accepted by the local ethics committee were proven to be fabricated [9]. Thereby, this researcher's unethical misconduct generated long-standing damage by diminishing the rates of vaccination and distrust in general among healthcare officials, which happened between 1998 and 2010 [10].

A Japanese anesthesiologist and researcher extensively published his clinical trials by involving the agents which are used in the treatment of postoperative nausea and vomiting. In April 2000, attention was caught through an editorial letter to the Journal of Anaesthesia and Analgesia about the atypical results reported through his papers' clinical trials [11]. Such results of the clinical trials were published over the next 12 years. He was penalized for the fabrication of most of his results in 2012, through a *judicial* statistical analysis of data published by him, which showed that the subjects in this study had not been randomly allocated to the different treatment groups as he claimed [12]. With around 190 retracted papers, he holds the current record for the world's most retracted papers [13].

9.2 Types of Scientific Misconduct: Falsification, Fabrication, Plagiarism, and Deception

Scientific misconduct is defined as fabricating, falsifying, plagiarizing, or practicing any fraudulent methods that deviate seriously through the frequently acceptable practices within the scientific group to propose, conduct, or report research that does not comprise differences in interpreting or honest errors or data judgment [14].

Types of scientific misconduct [15]:

1. Fabrication
2. Falsification
3. Plagiarism
4. Deception

Falsification, Fabrication, and Plagiarism are the most frequent kinds of scientific misconduct, among which the most frequent type of misconduct is Plagiarism. Such incidents of scientific misconduct are collectively called the "Unholy trinity of Scientific Writing" [16].

Fabrication means inventing data or information, involving the creation of new documents of results or data. The most frequently fabricated scientific research records are informed consent forms and patient records [17].

For example, a researcher from Berkeley University who is a doctoral graduate with a political degree attempted the replication that gradually advanced to accusation and retraction of another scientist research paper from the *Science* journal. Another researcher is from UCLA, who is a political science doctoral graduate. With his supervising person, another researcher published a paper in "Science," which found that long-term voters' attitude influences gay marriage that can be identified through personal contact by gay canvassers. This researcher had also forwarded a requisition to uSamp, the same surveying firm that another researcher used to collect the data for his study, and discovered that the other researcher has not at all worked together with uSamp. Furthermore, he fabricated the whole mailing communication with a representative of uSamp. Moreover, this another researcher had also made up the uSamp representative himself potentiating the data fabrication leading to scientific misconduct [18].

Falsification means altering the observed result or existing records of a scientific experiment, ranging from fabricating a bit of data to falsifying the entire experiment [19]. Falsification finally leads to omission or distortion of unwanted results or data. Detection of falsification could be challenging, and if identified the retrospective detection of scientific misconduct can even lead to the retraction of several years of published articles [20]. One common example of falsification can be deliberately intensifying sample size for increasing the reputation and credibility of the study for publishing quickly and easily without performing the actual study [21].

For example, "social psychology" Professor from "Tilburg University," the Netherlands in 2010 holds disrepute for his work's misconduct, indicating the study preparation and designs to be created in compliance with his ideas, without administering the questionnaires used for the study to the subjects. Furthermore, Stapel had also fabricated datasets of his own and shared them with his colleagues, intending for authorship on their papers. Later on, Stapel admitted his misconduct for falsifying the studies records and eventually was released from his position at Tilburg University [22].

Plagiarism refers to copying others' work and then projecting the work as their own without proper indexing and citations. The term "plagiarism" comes from a Latin word, "plagiarius," meaning kidnapper or hijacker [23]. From the World Association of Medical Editors' strict definition, an article or paragraph is said to be plagiarized when 7–11 words overlap with a set of 30 letters or 6 consecutive words of a sentence are copied [24]. It is a bit difficult to detect plagiarism, which is hazardous to the well-being of scientific compositions and literature. The availability of free or open access online journals and easy access to the internet could be chief sources of present-day plagiarism amongst the students, researchers, and faculty of every profession [25]. The knowledgeable reviewers suspect plagiarism through notable expertise and excellence in that specific field. Most of the editorial staff of Journals use electronic plagiarism checks (software) to detect plagiarism [26].

The plagiarized words or sentences can be classified into (a) direct (partial/complete copy of files or text including video or audio recordings without properly acknowledging or recognizing the primary source); (b) self-plagiarism (copying or duplicating text of one's own for their other portion of work); (c) mosaic (acquiring the opinions or ideas through actual sources, few phrases and words and improperly quoting those sources) [27].

For example, a person duplicates the other writer's work for their purpose with no effort toward acknowledging the material. The similarity index is *the degree of match or overlap between the author's work compared to the other sources already existing, such as websites, research articles, and books that are available in the similarity checking tool databases.*

Deception refers to deliberately concealing the conflict of inclusion or interests of some ambiguous sentences or statements purposefully within the research protocols or proposals or any other documents related [21]. For example, suppose one of the authors of a research project submits their teamwork to a journal as a primary author without intimating to the coauthors due to some internal conflicts. In that case, this comes under deception through the concealment of conflicts of interest.

9.3 Types of Manipulation

The manipulation of data representation can be:

1. Manipulation by temptation of image

   Each image presented in a scientific article is a precise representation of what is observed actually from the results. Image quality has some implications depending on the care with which it was obtained and processed [28]. It has been assumed that the repetition of an experiment multiple times is required in order to obtain good quality and consistent image for representation [29]. The temptation of image manipulation may look self-convincing to perform, but if such type of misconduct is identified, it will deprive and puts the career and future of that person at stake and even of his/her colleagues [30].

   For example, using a software-based manipulation tool to manipulate an image of research data by applying purposeful changes to those digital images such as double exposure, changing the brightness, etc., can be damaging.
2. Manipulation of graphs

   Graphs are the major constituents of the scientific language and literature due to their ability to condense and summarize large data sets. These graphs are a symbolic representation for displaying the experimental findings of science and research [31]. For example, the use of percentages as labels on a pie chart can be misleading to the readers when the sample size is small. Further, when the percentages are intentionally increased to show more impactful results, they constitute manipulation of graphs.
3. Manipulation of values

   Manipulation of values refers to purposeful control over the data variables, commonly independent variables. The value of an independent variable that a study participant experiences can be manipulated by the researcher for a purposeful outcome, which even helps to control the external variables [32].

For example, when a person working on psychological stress research, *manipulating the participants' stress levels intentionally to depict high impactful results is regarded as manipulating* values.

9.4 Country-Wise Cases of Data Fraud

According to the latest literature, the article retractions from the Journals had increased by ten times in the last decade and the data fraud accounted for around 60% of all those retractions. The retraction numbers increased exponentially in the current times due to the strict and improved editorial practices and encouragement to the editors by the journals to take the retractions seriously [33]. From the PubMed retractions data between 2008 and 2012, when authors belonging to more than 50 countries were noted as having withdrawn papers. USA is the country to retract most papers followed by China to retract "most papers for plagiarism and duplicate publication." Although the unethical publication procedures and practices can differ from one nation to the other, the duplicate publication and plagiarism rates were found to be the most in Finland and Italy [34].

During 1990–2019, a total of 18,603 retractions discovered from 4289 Journals are found to be associated with 753 publishers (or publishing organizations), and China ranked first amongst "top 15" countries, followed by the USA, India, Japan, and Germany [35].

The authors belonging to China, the USA, and India were found accountable for the highest number of retractions in plagiarism and duplicate publications. The global retraction rates differ from country to country, and foremost authors from low-income countries have a greater probability of retraction concerning plagiarism than the foremost authors from high-income countries. Looking into detail about duplicate publications and plagiarism it reflects poorly on the retraction and publishing practices of that country among multiple countries. Duplicate publications and plagiarism together account for approximately 35% of all the retractions. The incidence of fabricated publications is more common than plagiarism, resulting in more papers being withdrawn because of fabricated publication. Besides, many countries are having duplicate publication retractions than plagiarism retractions [36].

In general, the authors working in countries that have developed appropriate policies and offices to handle and enforce rules against scientific misconduct are likely to have fewer retractions. All the countries need to address the issues of plagiarism and duplication of publication in a regulated manner to ensure ethical research practices. Unethical behaviors among scientists manifest as a breach in publishing ethics and vary between different countries [37].

9.5 Misconduct in Clinical Trials

An increased incidence of misconduct in clinical trials is reported in recent years, and there is a chance of additional undetected or unreported cases. Probable fraud of data that is not recognized through routine on-site monitoring measures can be identified by adopting stringent clinical trial monitoring procedures, thereby

improving the overall data quality [38]. Few economic statistical central monitoring procedures must be made as part of the comprehensive data quality assurance programs for early detection of data fraud and other data-related problems and at a correctable point of time during the clinical trial [39].

Most of the Institutions categorize misconduct of research in the clinical trials as a terrible kind of misconduct due to wide-ranging implications and deleterious consequences on the welfare of public and public perception and perspective [40]. Such scientific misconduct requires instant restorative measures. Misconduct in clinical trials is regarded as an offense in contrast to the good practices and ethical principles that are acceptable in the clinical and scientific environment. Procedures and strategies ensuring the data quality in the clinical trials, including the detection and treatment of data fraud are essential and critical to ensuring clinical research integrity [41].

A UK-based scientist in pharmacy practice was condemned to 3-month imprisonment against alteration of the preclinical trial data—procedures formulated in assistance of applications for performing the human trials. He worked on animal preclinical trials to assess the efficiency of recent treatment techniques alongside various bigger multinational drug companies, rather Aptuit has carried out the work. Eaton selectively reported fabricated data during his tenure at Aptuit to assess the working of analytical methods and the concentration of the drug in blood [42]. A General Practitioner from Downpatrick acted as Principal Investigator for an insomnia trial during 2007–2008 by Sanofi. He was jailed for falsifying drug trials in 2016 for conducting the trial deliberately breaching the protocol and conditions of good clinical practices. He is also the UK's first doctor for being condemned for falsifying data deliberately under the regulations of Medicines for Human Use (Clinical Trials) 2004 [43].

9.6 Importance of Data Integrity

Data integrity is an ethical and professional obligation that aims to provide definitive results toward the healthcare system and the governing authorities. This includes validation, accuracy, consistency, and quality of the data involved [44]. Data integrity is the cornerstone of scientific research, which showcases the research process commitment and trustworthiness [45]. Members of a scientific community need to function together, as a team, ensuring better research findings and exchange of research information to innovate and flourish, upholding professional and personal responsibility, acknowledging and respecting the intellectual contributions by the other members of the community [46].

Even if it is not digital, all the research data can be predisposed to misrepresentation and error. The electronic technologies and advancements can bring in some sources of technical error toward the communication, storage systems, or data analysis, making problematic data very difficult to separate from irrelevant information, due to which the methods of research cannot be strongly enacted, and even the asked questions may not be adequately explained [47]. Moreover, the researchers

can get few benefits for structuring gathering data or research to favor a certain outcome, in cases such as the studies related to drugs funded by the pharmaceutical companies that nestle to profit across specific results. The researchers could have some "philosophical, political, or religious convictions" that can influence their work, which can also include the methods to gather and analyze data. Due to numerous data departure methods across the actualities, every individual included in the data collection, preservation, analysis, and dissemination has a discrete responsibility for safeguarding the integrity of the data [48].

Clinical trials that are conducted by the Contract Research Organizations (CRO) complete up to 30% more rapidly than those trials managed internally by the pharma companies. This helps in cost saving to a major extent, better utilization of clinical trials, and likely toward a faster market launch. With on-site monitoring, the overall cost of clinical trials can be compromised up to 25–30%, as monitoring is commonly the costliest facet of clinical trials. Risk-based monitoring, which has emerged over the last decade, is being encouraged by the regulatory authorities to reduce the monitoring expense [49].

Measures for ensuring data integrity are crucial to maintaining the research data in the long-term, including persistent questioning, in what way various organizations ensure the large datasets are to be stored in a relevant manner, indexed and referenced for future. Also, funding for effective data management should be made available to achieve long-term assessment and data conversation. Therefore, scientists and funding organizations or agencies should work on developing tools to manage the metadata, which could help the researchers annotate it and create required software. All these would help track individual pieces of data, which plays a major role for data-processing professionals to attain their scientific enterprise and be well recognized. Therefore, better education, training practices for the scientists pertaining to the data stewardship issues are essential. Training described above practices should include better analytics of data preservation and storage, organization, its annotation, and appreciation of the bioinformatic tools that are currently available [50].

9.7 How to Identify Research Misconduct?

The "Office of Research Integrity (ORI)" under the "Department of Health and Human Services" is the organization authorized to promote and foster research morale and integrity within "U.S. Public Health Service." It supervises the identification and inquiry of allegations related to research misconduct and finally makes resolutions on research misconduct findings accordingly. ORI also provides technical assistance if required to any of the Institutions which are responding to research misconduct allegations through its Rapid Response Technical Assistance Program. A finding of research misconduct under the federal policy requires whether the misconduct be committed knowingly or intentionally or recklessly; a notable departure from the applicable research community's acquired practices happened, and the allegation of research

misconduct is proven by a superiority of evidence. All of these three elements should be presented for a finding of research misconduct through a full-fledged investigation [51].

9.7.1 Software for Data Verifiability

Plagiarism softwares are the critical components in ensuring a scientific research work's quality and data verifiability. Plagiarism detection softwares enable the research personnel to systematically detect and prevent plagiarism, which can reduce the incidence of research misconduct to some extent. This software assesses the similarity of content in the papers with published literature and other information types, comparing the author's text against the citations and abstracts in "PubMed/MEDLINE" with millions of Journal publications, books, and chapters from the leading publishers which may include "Elsevier, Lippincott, Sage, Springer, Ovid and Wiley Blackwell," and many others including conference proceedings and varied databases such as "EBSCOHost, Gale InfoTrac, and ProQuest." Additionally, the software detecting plagiarism also searches the internet for any similar content. A leading software program, 'iThenticate,' has its own web crawler that indexes more than "10 million web pages daily" (iThenticate, 2018). All types of documents, whether it is a manuscript, written assignment for courses, grants, theses and dissertations, other scholarly projects, or other types of reports, can be checked with the plagiarism detection software. "Turnitin," a leading product designed to check the originality of student research papers, was particularly made for classroom use and student work review. It can also be incorporated with the other learning management systems for students to review their papers before submitting them and teachers then to assess those papers during review [52].

9.7.2 Internal Audits (Preclinical and Clinical Research)

Internal audit is defined as an independent and systematic evaluation of the activities and documents related to trial in determining the conduct of trial-related activities evaluation, and the data records, analysis, and accuracy notified in accordance to the protocol, sponsor's Standard Operating Procedures (SOPs), practices and the regulatory requirements applicable. Auditing is a quality assurance function, evaluating the research work's compliance to recognize the standards, i.e., "International Council on Harmonization, FDA's Code of Federal Regulations, International Standards Organization and Standard Operating Procedures" [53].

9.7.3 Electronic Health Record (EHR)

Electronic health records (EHR) are being implemented successfully, where there has been a steeper advance in secondary HER use, particularly for research. EHR is

being redesigned gradually to facilitate future research, and the major barriers toward EHR are adoption costs, acquisition, and maintenance. They provide opportunities for enhancing patient care, embedding the measures of performance in clinical practice, and improving the recognition and enrolment of patients and healthcare providers who are eligible for clinical research. EHRs on a larger scale can aid in the assessment of the new therapies or innovations in the healthcare delivery that can follow the enhanced outcomes or healthcare savings. EHRs can be potentially used in assessing study feasibility, streamline data collection, facilitate patient recruitment, conduct EHR-based observational solely, or comparative effectiveness studies or post-marketing randomized registry studies. The sustainability of using EHRs toward the clinical trials registration is directly dependent on the regulative acceptance of the practices and approach [54].

9.8 How to Prevent Data Misconduct?

Certain guidelines and measures should be adopted and adhered to prevent data misconduct as outlined below.

9.8.1 Guidelines and Measures at the Preclinical Level

9.8.1.1 Universal Code of Ethics for Scientists

The scientists' universal code of ethics is a public declaration of the responsibilities and values to be practiced by scientists. For instance, the universal ethical code of the UK has three main aims: (1) Encouraging ethical research, (2) facilitating scientists to think about the impacts and implications of their work, and (3) assisting the communication between the public and scientists on some of the challenging and complicated issues. Since this code is optional, the Institutions or scientists are instead encouraged to understand and think about how these guidelines can be related to their work [55].

The basic universal code of ethics is the bedrock of science's integrity and credibility, which are referred to as the representatives of all scientific disciplines. Compliance with these principles and values is required by all the scientists and Institutions where the scientific research is being conducted.

A few of the core principles of this Universal ethical code include:

1. **Diligence**—to present the objectives of conducting and intending research, presenting the research methods and procedures, interpreting the findings, information disclosure about possible threats, and potential applications and advantages anticipated in an intentional manner.
2. **Impartiality**—in the approach of the presenting or problem and in sharing the scientific basis and knowledge with the other people.
3. **Courage**—to challenge the views that contradict the scientific practices and knowledge that breach the fundamentals of scientific authenticity.

4. **Objectivity**—to solely interpret and conclude depending on the facts that have acceptable data and reasoning which can be subjected to verification, if required.
5. **Trustworthiness**—to conduct and present research, a condemning approach to the results, apprehension with details and diligence to collect, record, and store the data.
6. **Resistance**—toward any attempts that can exert external influence on the research conducted
7. **Openness**—Regarding the researcher's own scientific work during the discussions or meetings with the fellow scientists, which contributes to the development of knowledge by research findings publication and knowledge sharing with the community.
8. **Transparency**—during the collection, the analysis, and the data interpretation, is decided by the empirical data storage properly and available through the publications.
9. **Concern**—for the future generation of scientists that can be demonstrated by instructing the good ethical standards and norms to the students and the other subordinates involved
10. **Responsibility**—with regard to the participants (subjects) involved in research and the objects that include the cultural and environmental property.
11. **Reliability**—to acknowledge the fellow researchers' scientific achievements by providing adequate referencing to the sources and trustworthy recognition of the other scientist's contributions.

The universities, institutes, or other entities involved in research must be obliged to ensure that the employees of their respective organizations comply with the basic principles and ethics. Those Institutions are also expected to introduce and apply the explicit principles of good scientific practices and promote sensitivity toward ethical issues among their organizations [56]. Most of the countries have their own clinical research regulating authorities, e.g., Food and Drug Administration (FDA) for the United States Health Science Authority (HSA) for Singapore, Central Drug Standards Control Organization (CDSCO) for India, State Food and Drug Administration (SFDA), and Medicines and Healthcare Regulatory Agency (MHRA), etc.

9.8.1.2 Regulations and Measures to Prevent Data Misconduct

The role of Institutional Review Boards (IRBs) or Institutional Ethical Committees (IECs) should be strengthened to safeguard the interests of persons participating or conducting research [57]. There should be some internal regulatory and review procedures to monitor the ongoing studies' ethically acceptable and quality control characteristics. The regulations that are already in existence must be streamlined and made much efficient, ensuring that all the organizations or institutes, whoever associated with clinical research, should have clear policies and procedures for operating and approaching misconduct and fraud in research [58].

The division of roles for dealing with research misconduct allegations differs from one country to the other. The three generic ways for handling the misconduct cases, in general, are:

1. **Ad-hoc committees**—Generally consist of distinguished individuals, established for dealing with specific cases, preferably under the patronage of ethics committees that are already existing as university-based. The major advantage of this approach is the ready existence of ethics committees at various Institutions, as they are chiefly associated with life sciences and handling matters related to human experimental patients and subjects. It is difficult to ascertain if these committees can address all the research misconduct cases while these are very vital and essential. Extension of ethics committee directives to handle research misconduct cases must be seconded by cautious analysis and alterations of already existing procedures and rules if required.
2. **Standing committees**—Constitutes of entities or units (officers, committees, or offices) and procedures corresponding, at the institution level (e.g., bigger laboratory/university) where the misconduct happens in research Institutions. These standing committees can be answerable for accepting allegations, undertaking them (including conduct and necessary investigations), and proposing the outcomes. These entities are generally not autonomous, and there is an interaction measure with government-regulated central national bodies or authorities.
3. "**One or more dedicated committee(s)**"—Selected by the countries where the scientific communities in their regions are small, as it could be difficult for establishing impartial scientist committees, free of conflicts of interest personally at the national level. In such instances, to represent a greater spectrum of applicable expertise, "members of the permanent national committees" can be selected [59].

9.8.1.3 Audit of Data Values

Audit of data compares the contents of the study database to a local document source and noting the irregularities and disparities in the discrete data elements. The available document source could be the clinical records on paper, i.e., medical, pharmacy records, and electronic laboratory reports. Audit findings are expected to be documented on a well-structured audit form paper and entered into the Excel spreadsheets for further analysis. The audit variables could include those that are most relevant to the suggested consortium studies, for example, patient demographic data, risk factors, anthropometric measurements, etc., and all dates associated with each measurement. Audit of data functions as a beneficial control measure for data quality to the data coordinating center (DCC) as well as the participating sites, which allows the DCC for identifying and resolving the weaknesses in the data submitted, thereby preventing incorrect data from affecting the results of the study [60].

9.8.1.4 Good Laboratory Practices for Data Integrity

The Department of the Interior (DOI), USA defines Scientific integrity as the state or condition that applies to a person who adheres to the appropriate scientific community's acceptable standards, practices, and professional values [61]. Adhering to the acceptable standards is suggestive of ensuring clarity, fairness, utility, and authenticity of scholastic and scientific assessments that help in preventing scientific misconduct, licensing, outside interference, and adequate assurance of information and procedural security [62].

GLP was first introduced in the year 1972 in Denmark and New Zealand, and subsequently within the USA during the year 1978 after the scandal of Industrial BioTest Labs, which was then succeeded by the "Organization for Economic Co-operation and Development (OECD) Principles of GLP" in the year 1992—setting up OECD aided in propagating GLP to a large number of countries. Good Laboratory Practices (GLPs) are the formal regulations designed by the "U.S Food and Drug Administration (FDA)" in the year 1978. An "Expert Group on GLP" set up during 1978 built the first "Organisation for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice" for a special program on controlling the use of chemicals [63]. The GLP regulations put together by the US FDA in the year 1976 were undertaken as "international standards" toward the nonclinical laboratory-based studies that are published. Eventually, other countries too started making GLP regulations in their home countries after the USA [64].

Good Laboratory Practices are defined as the principles that provide a framework for planning, performing, recording, monitoring, reporting, and archiving laboratory studies. They offer a set of guidelines that govern the organization, procedures, processes, and conditions under which laboratory studies are conducted and executed, providing an assurance to the regulatory authorities regarding the data submitted, which will be an accurate reflection of the study results [65].

The Good Laboratory Practices (GLP) are centered around four major principles required for achieving good quality data. These also serve as essential functions in accordance to perform and monitor the safety studies. They include:

1. **Management**—has the overall responsibility to implement good organization and science within the Institutions
2. **Quality Assurance**—for assuring the management regarding personnel, facilities, records and practices are strict as per the regulations for maintaining the blueprints of the studies, inspecting every nonclinical study at regular timeframes to make sure about the compliance and reporting the results to management and the study director for reviewing the report finally.
3. **Study Director**—as a unique source of control for the study who must assure that the study protocol is acceptable and followed up accordingly, making sure that entire experimental data is adequately recorded and good GLPs are properly followed, and all the raw data, protocols, documentation, final reports, and specimens are registered effectively.
4. **The National Compliance Monitoring Authority**—an established body within a member country that should be responsible for keeping track of the good laboratory practice receptivity amongst the test facilities of its various areas and discharging other similar purposes associated with good laboratory practices determined nationwide [66].

The major concerns of GLPs for effective implementation are:

Data Records System (DRS) The raw electronic information providing the probability of conducting a complete audit trail can show modifications to the data with-

out concealing the actual data. Associating all data changes by making those changes to the persons through timed and dated (electronic) signatures is required, and retention of the long-term data could be tough if the software and hardware associated with the data are quickly changing. The procedures should be documented well, and the verification of its integrity must be done, wherever the system obsoleteness poses a requirement for transferring the raw electronic data between the two different systems. The raw data should be transferred to the other medium where the migration is not practical, which is subsequently verified as an exact copy earlier to demolition the original electronic records, if any [67].

'Standard Operating Procedures (SOPs)' SOPs are the "written procedures" that are designed for a laboratory program, which are the "approved protocols" indicating the objectives and methods of a test/study. SOPs are intended toward ensuring the integrity and quality of data that is produced by the test facility. SOPs define the ways for carrying out activities specific to the protocols and are frequently written as a sequential listing of the action moves. They also explain the process and procedures for better working principles like calibration, maintenance, general inspection, and testing, actions that need to be taken in cases of failure of equipment, defining the raw data, reporting, keeping the records, data recovery, and storage. Every other test facility area or unit is recommended to possess one currently available manual of Standard Operating Procedures at least that is relevant to the activities which are being conducted therein to assure good clinical practices. Some special Standard Operating Procedures (SOPs) are laid down for the preparation, approval, and control of Standard Operating Procedures (SOPs), together called SOPs of SOPs. These SOPs of SOPs are applicable to prepare and implement all Standard Operating Procedures. Controlled Documents in SOPs constitute copies of mastered documents, distributed in the respective departments, which are stamped as Controlled Copy in Green Colour at the bottom right corner on each page. Uncontrolled documents are distributed to regulatory agencies, customers, or other persons if required, stamped in red ink made from master copies/control copies of filled documents [68].

Peer Review Reviewing the study-specified or non-study-specific data will support recognizing the corresponding findings, which assist in interpreting and influencing the earlier identified microscopic findings [69].

Equipment The equipment that includes the certified computerized systems used for the "generation, storage, data recovery, and controlling the environmental factors" that are relevant and appropriate to the study must be located suitable and must be designed appropriately with an adequate capacity [70].

Records of Chemicals Used Chemicals or reagents of the lab should be labeled properly and appropriately to indicate the compound's identity source concentration and stability. A user must make an entry whenever he/she uses it in a specific log sheet.

It should also include the date of preparation, specific storage instructions, and the earliest expiration date [70]. The specific amount used/spent on chemicals should be entered as well as the remaining balance along with the user signature with date. This activity would help maintain the chemical usage record, which is essential for the tracking of the experiments as well as accountability of the chemicals to avoid deficits in usage and unnecessary purchase. Quality assurance personnel must ensure this practice and proper compliance by the users on a monthly or quarterly basis.

GLP always aims to reduce the mistake occurrences via extensive and more specific labeling prerequisites. As the principles of Good Laboratory Practice (GLP) are developed to promote the validity and quality of test data can be applied for determining the chemicals and the other chemical product's safety. These GLPs also protect the researcher from unfounded allegations that could even benefit the institution or the laboratory. The Food and Drug Administration (FDA) is the organization for validation of the study to report the reflections of conduct of the study accurately, while the GLP regulations, that are framed to promulgate the standards of the laboratory. Eventually, every study is generally compared to the FDA's expectations that progress over time within the regulatory framework. The Quality control and the GLP rules are the process that all the laboratories try to opt for, which is the way forward for the "evidence-based laboratory results" based on trustworthy procedure [71].

9.8.1.5 Preclinical Guidelines (OECDs)

"Organisation for Economic Co-operation and Development (OECD)" is an internationally reputed agency working for framing better policies toward the better and finer lives. Their objective is to outline the policies fostering "prosperity, opportunity, equality, and wellbeing for all." OECD works "together with the governments, policymakers, and citizens to establish evidence-based international standards and find solutions that range around social, economic, and environmental challenges." The OECD dispenses a distinctive knowledge and forum hub toward analyzing data, experiencing exchange, sharing best practices, and guiding international standard-setting and public policies. Mutual Acceptance of Data (MAD) system, a multilateral agreement developed by the OECD, allows countries to participate in public policies and include non-members for sharing their results of various nonclinical investigations done on the chemicals using OECD methods and principles [72].

9.8.1.6 Checklist for Preclinical Studies for Data Verifiability

Data verifiability and irreproducibility of preclinical scientific research are the core principles for ensuring the quality and transparency of research and reporting. Hence, it is suggested for the authors to complete a checklist at the time of the manuscript submission. Data auditing within the preclinical settings and studies is the essential strategy that is extensively used as a significant way forward in identifying errors, monitoring operations of the study, and ensuring superior-quality data. The reliability of quality data assessment can be undermined due to the absence of a precise definition of data quality and error measuring methods [73].

9.8.1.7 Journal Policies

Committee on Publication Ethics (COPE) is a global organization committed to aiding and training the publishers, editors, and the personnel engaged in maintaining the publication ethics with the aim of passing on the publishing culture where ethical procedures and practices turn out to be a normal routine. The approach of COPE is firmly along the direction of influence by educating, providing resources and support to the members, along with the professional debate strengthening the wider community. The journal's policies are framed to maintain the research integrity and the quality published in their journals. This holds the responsibility for the authenticity of scientific observations or findings, precision of statements of fact, scientific expression or other opinions, and any other published material in the journal lies solely with the article author(s). The journal policies are classified as (1). Editorial and Publishing policies, and (2). Peer-review policies. Editorial and publishing policies are related to submitting the manuscript, transferring the manuscript rights from the authors to the journal, responsibilities of the author, and data integrity maintenance. Peer reviewing policies mainly run around the manuscript's peer review process from the initial submission to the final decision on the document. These policies are laid to showcase the quality and transparency of the journal and its procedures [74].

9.8.1.8 Publication Ethics

Scientific research includes a lot of coordinated steps and processes, including the appropriate study design and execution, data collection, processing and analysis, and finally the publication. Every researcher should be aware of the ethical code of conduct that binds them and regulates them. Good ethical standards for the publication of research work exist to ensure superior-quality scientific publications and trust among the public in the scientific findings. The people who conducted the research receive credit for their ideas. An international publisher and editor's forum of peer-reviewed journals, the Committee on Publication Ethics (COPE) provides the "best practice guidelines" and "code of conduct," which defines the publication ethics and advises editors regarding the handling cases of research and publication misconduct. The authors should be aware of publication ethics that can help them consciously avoid scientific misconduct and perform honest and acceptable ethical research [75].

9.8.1.9 Authorship Consent Form

The authors of a manuscript transfers the rights to the publishing company or agency by giving their consent through a form called an Authorship consent form. This also includes the publication rights of nonexclusive, and the authors must assure about the originality of their contribution. All the authors sign the consent form as an acceptance of the responsibility to release the material on behalf of them and publication rights transfer covering the nonexclusive part of the rights for reproducing alongside the research article distribution. The protocols and scientific manuscripts must be seconded by a completed author consent form or cover letter during submission, that include the details such as:

1. A complete affirmation to the editor or relevant authoritative person regarding all the submissions and previous reports, if any.
2. An affirmation on authorship, which can require a letter of submission including a statement about the manuscript, was read and accepted by each author of the article, making sure all the requirements for authorship are clearly understood.
3. An affirmation pertaining to financial or other activities and associations that can direct toward a conflict of interest, when such details are not mentioned within the manuscript or in an authors' form.
4. The author's contact information serves as an interface with the other authors regarding final approval or revision of the proofs when that particular information is not included in the manuscript.

The author consent form must also notify the journal editors if there are any concerns or issues raised or put up (e.g., the Institutional regulatory bodies) concerning the research conduct or any action required [76].

9.8.2 Guidelines and Measures at the Clinical Level

9.8.2.1 Clinical Guidelines: ICH

The "International Council for Harmonisation (ICH) of technical requirements for pharmaceuticals for human use (ICH)" is a global organization, which is unique at its work to bring the regulatory authorities and pharmaceutical industries together for discussing the technical and scientific aspects of registering a drug. It was set up in the year 1990, had its evolution progressively in response to the growing global overlook of drug development. Its goal is to attain harmonization to more considerable extent globally for ensuring effective, safe, and superior-quality medicines being registered and developed in a much resourceful manner. The ICH Guidelines development attains this harmonization through a scientific consensus process with industry and regulatory experts working alongside.

The topics recognized for "harmonization" by the "ICH Steering Committee" are picked out from the quality, safety, multidisciplinary, and efficacy affairs. Quality topics include pharmaceutical and chemical quality assurance (Impurity Testing, Stability Testing, etc.). Effectiveness topics include those associated with the human subject clinical studies (Good Clinical Practices, Dose-Response Studies, etc). Topics of safety include those related to "in vivo and in vitro preclinical studies (Genotoxicity Testing, Carcinogenicity Testing," etc. Interdisciplinary areas or topics include e cross-cutting topics that do not fit individually into any of the above categories.

The ICH guidelines are classified as follows:

Carcinogenicity studies (S1A-S1C):

S1A Guidelines on the need for pharmaceuticals' carcinogenicity studies, guiding studies pertaining to carcinogenicity performed for any pharmaceutical industry.

S1B Testing for pharmaceutical carcinogenicity, providing instructions regarding the need to carry out carcinogenicity studies on both rats and mice.
S1C(R2) Dose selection for pharmaceutical carcinogenicity studies, addressing criteria for selecting high dose to be used in carcinogenicity studies

S2—Genotoxicity:

S2(R1) Guidance on Genotoxicity testing and interpretation of data for the pharmaceuticals intended for human use
S2B A standard battery for Genotoxicity testing for pharmaceuticals, addressing two fundamental areas pertaining to genotoxicity testing: identification and registration of a standard set of assays

S3A-S3B toxicokinetics and pharmacokinetics:

S3A Guidance on Toxicokinetics: systemic exposure assessment in the toxicity studies, giving instructions on developing test strategies in toxicokinetics
S3B Pharmacokinetics: Guidance for repeated dose tissue distribution studies
S4 Chronic toxicity duration testing in animals, rodent and non-rodent toxicity testing
S5 Toxicity detection toward reproduction for medicinal products and toxicity to male fertility
S6 Evaluating the preclinical safety of biotechnology-derived pharmaceuticals, where the preclinical safety evaluation of primary goals is to identify the initial safe and subsequent dose in humans and potential target organs for toxicity and for the study of whether such toxicity is reversible and safety parameters for clinical monitoring.
S7A Safety pharmacological studies for human pharmaceuticals, generated toward protecting participants and patients of clinical trials who receive marketed products from the pharmaceutical's potential adverse effects.
S7B Nonclinical evaluation of the potential by human pharmaceuticals for the delayed ventricular repolarization (Q.T. interval prolongation)
S8 Immunotoxicity Studies for Human Pharmaceuticals, addressing the regulations and recommendations on immunosuppressant nonclinical testing.
S9 Anticancer Pharmaceuticals nonclinical evaluation, providing information for pharmaceuticals that are intended only to treat cancer in patients with advanced disease or later stage regardless of the administration route
S10 Photo safety evaluation of pharmaceuticals, addresses clinical formulation excipients for photodynamic therapy products and dermal applications.
S11 For safety nonclinical testing in support of pediatric medicines development recommend standards for the circumstances under which nonclinical juvenile testing of animals is considered informing

The ICH M3 (R2) guideline states that "conduct of any study related to juvenile animal toxicity must be taken into consideration when human safety and animal data are considered to be sufficient enough for supporting the pediatric studies" [77].

9.8.2.2 Clinical Trial Registry

Clinical Trials Registry by the government is the biggest registry, accepting trials from all over the world, taking steps to detect and avoid probable duplicates whenever identified, keeping only a single version of the trial data active. The clinical trial registration occurs prospectively, which is a scientific and ethical imperative phenomenon whose critical goal is to recognize all the ongoing or already conducted trials appropriate to a given topic. Duplicates of a trial can occur through purposeful or intentional registration of the trial by a person belonging to that trial or uncoordinated enrollment of trial by different people of the same trial. World Health Organization (WHO), through its Mexico statement, addressed the problem of duplicate trial registration, after which it called for "unambiguous identification" of every trial, directed toward the formation of the "International Clinical Trials Registry Platform (ICTRP)" by the WHO. WHO had also created the Universal Trial Number (UTN) scheme to facilitate the explicit recognition of trials by allotment of a distinctive number to that trial related to the trial for its lifetime. An explicit identification of trials essential to prevent double or triple counting of the evidence in systematic reviews and meta-analyses and ensure all the registry records that describe each relevant trial could be identified and retrieved. Hence, the explicit recognition of any trial is a major step to enhance systematic reviews' efficiency and effectiveness using information technology [78].

9.8.2.3 Checklist for Clinical Studies for Data Verifiability

Data verifiability and irreproducibility of clinical scientific research are the core principles for ensuring the quality and transparency of research and reporting. Hence, it is suggested for the authors to complete a checklist at the time of the manuscript submission. Data auditing within clinical settings and studies is the essential strategy that is extensively used as a major strategy in identifying errors, monitoring operations of the study, and ensuring superior-quality data. Nevertheless, the guidelines for clinical trials are not specific to the suggested frequency, nature, and timing of the data audits. The reliability of quality data assessment can be undermined due to the absence of a precise definition of data quality and error measuring methods [73].

9.9 Penalty for Data Fraud or Misconduct

The research institutions or organizations can penalize the researchers, those who are fond of having committed scientific misconduct, through requiring supervision of future research activities or terminating their employment depending on the act. The grantee of a research project should evaluate the impact of the research outcome on that person's ability to continue their work on that research project when the grantee institution or agency finds that person guilty of misconduct in research. "Office of Research Integrity (ORI)," an esteemed international organization, imposes penalties toward research misconduct, where the liability for the misconduct depends on the extremity of misconduct. The aspects that ORI can think about

while picking up a penalty can comprise of the extent of misconduct or committed knowingly, intentionally, or carelessly, any notable influence on the records and subjects of the research, other institutions, researchers, or public well-being. "Office of Research Integrity (ORI)" can even enforce various penalties if the research misconduct is upheld, including Terminating or Suspending the research grant. Suspending or debarred from receiving federal funds in the future, or simply by correcting the research record or letters of reprimand. ORI will promptly refer the issue to an investigating body if it considers that the scientific misconduct might have been associated with criminal or civil fraud [79].

The regulations in India by University Grants Commission (UGC) for scientific misconduct are categorized based on the plagiarism of those scientific materials. Research publications' misconduct is considered a least serious offence when 10% of a manuscript is plagiarized, while the papers containing 60% or more plagiarized material can be considered the most serious offence. There are no penalties levied on the researchers whose papers have 10% or less plagiarized material. A student could be removed from their course, and a researcher would be required to retract their paper if that paper or material is found to be in the most serious plagiarism category. There are also other repercussions for the researchers as they cannot receive a pay raise for 2 years or will not be allowed to supervise a student's dissertation for 3 years [80]. A total of 106 papers problematic papers were retracted from "Council of Scientific and Industrial—Research Indian Institute of Toxicology Research (CSIR-IITR)" in 2019, which were found listed on the Pubpeer website for image manipulation and duplication

9.10 False Allegation of Research Misconduct

As the incidence of scientific misconduct is documented well, the issues about innocence and its establishment in the cases of false allegations are not addressed effectively. Hence, the investigators must be careful enough and need to assimilate the procedures to protect themselves in cases of untrue allegations. Essentiality for proving the innocence from the false allegations by the scientific community's people carries a more comprehensive range of responsibilities that can even exceed the normal legal assumptions. Researchers and Scientists across the world must be well prepared to safeguard their reputation and credibility by proper organization and maintenance of every single original file and the datasheet that is related to their grant proposals and publications, which they should be in a position to put forth all those documents to prove their transparency at any moment when such allegations and concerns are put up [81].

The government regulations for these allegations about the organizational procedures and policies involve two main phases, an inquiry and an investigation. A preliminary evaluation into the allegation with the other details for determining the adequate ground to investigate further into the allegations of misconduct comes under the inquiry phase. At the same time, the investigation involves formal examination and evaluation of relevant information for determining the occurrence of

misconduct. The scientific research procedure can regularly fix the allegations or disagreements that may involve queries against the questionable research practices or scientific judgment can be regularly fixed by the procedure of the scientific research itself questionable research practices or scientific judgment. The proper management of misconduct allegations is long-standing, challenging, and even costly, which can divert faculty and administrative attention from other vital issues. Hence, the false allegations must be carefully dealt with and solved accordingly in a well-structured manner [82].

9.11 Future Directions and Clinical Implications

It is essential to have procedures in place for the early identification of patterns indicating data issues and concerns. The methods and protocols to ensure data quality in clinical trials that include data fraud identification and management must be progressed toward expansion and refinement if required. Central statistical monitoring techniques for ensuring the data integrity of clinical trials could be used heavily for suggesting remedial actions during the trial. Statistical assessments for the data quality can be proved useful during peer review, as journal editors can request access to the source data more often beyond which claims can be made. Open discussions among the researchers worldwide on the data integrity aspect of clinical research and their regular discussions will help reduce the incidence of data fraud.

9.12 Conclusion

Each country should have an official body that investigates and judges clinical or basic research fraud. All the organizations involved in the preclinical and clinical research must have concerning authorities functioning. To carry out transparent policies, strategies, and Standard Operating Procedures (SOPs), that can uplift the misconduct disclosures. Scientific fraud must be regarded as a serious issue without neglecting the actual causes. Transparent communications between the research groups on a crucial feature of clinical research besides discussing the already happening practices and projects can help reduce the fraud and misconduct incidence.

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