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REVIEW

Fraud and misconduct in clinical research

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Abstract: The clinical research industry is one of the most heavily regulated industries that exists. One cannot function in this industry in a compliant manner without knowing the regulations and the responsibilities they are expected to maintain. Good Clinical Practice (GCP) is a set of guidelines for the design, performance, monitoring, recording, analysis, and reporting of clinical trials. Only by maintaining such policy can fraud and misconduct in biomedical research be minimised, and it is manifestly in the interest of patients and healthy volunteers who participate in research projects. These guidelines are recognized as overall standard operating procedures in conducting clinical research. Compliance with GCP standards ensures the proper and ethical conduct of trials while preventing, or at least reducing, the chances of misconduct and fraud. This is why it is crucial for all research professionals to understand and to be familiar with GCP. In essence, GCP can be viewed as a system of shared responsibilities between sponsors, clinical investigators, Institutional Review Boards, and the Food and Drug Administration (FDA), all working together to preserve the integrity of clinical research. When questionable accuracy or fraud infects a trial, the affects become contagious.

Key words: clinical research, misconduct; fraud

INTRODUCTION

Good Clinical Practise (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Helsinki Declaration, and that the clinical trial data are credible. The objective of International Conference on Harmonisation (ICH/WHO) Good Clinical Practise (GCP) Guideline is to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions. This guideline should be followed when generating clinical trial data intended for submission to the regulatory authorities. However, the principles established in this guideline may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects [1].

All clinical trials should be conducted in accordance with the ethical principles that have their origin in the Helsinki Declaration, and are consistent with GCP and the applicable regulatory requirement(s) [1]. On the other hand, organisations conducting research should have a framework of good practice guidance, research general HR policies, and a framework of research monitoring and auditing. These policies, guidelines and research monitoring and auditing will help act as a deterrent to research misconduct and fraud, and importantly help identify inadequate research practices before they become cases of research misconduct [1, 2].

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WHAT IS MISCONDUCT AND FRAUD IN CLINICAL TRIALS?

Clinical research makes a significant contribution to medical practice and it is therefore expected that all clinical research is conducted maintaining the highest standards of research practice. Therefore, it is expected that the research staff fully comply with local regulations and guidelines, and with the principles of the ICH – GCP Guideline.

Scientific misconduct/fraud is a violation of the standard codes of scholarly conduct and ethical behaviour in scientific research. Fraud is an intentional deception made for personal gain or to damage another individual, for instance, intentionally falsifying and/or fabricating research data, and misleading reporting of the results [3]. Misconduct may not be an intentional action, rather an act of poor management, but the effects may be very much the same as that caused by fraud. Misconduct can occur at any stage of the research process, and often results when researchers seek to avoid negative consequences, gain prestige, or receive further funding based on their data. Research misconduct can be defined as: fabrication, falsification, plagiarism or deception in proposing, carrying out or reporting results of research, or deliberate, dangerous or negligent deviations from accepted practices in carrying out research [4]. It also includes failure to follow established protocols if this failure results in unreasonable risk or harm to humans, other vertebrates, or the environment, and facilitating misconduct in research by collusion in, or concealment of, such actions by others [4, 5]. Intentional, unauthorised use, disclosure or removal of, or damage to, research-related property of another, including apparatus, materials, writings or devices used in or produced by the conduct of research can also be considered as misconduct [5]. It does not include honest error or honest differences in the design, execution, interpretation or judgement in evaluating research methods or results, or misconduct unrelated to the research process. Similarly, it

does not include poor research unless this encompasses the intention to deceive [2, 6].

It is normal to have errors in trials and most are unintentional as they are usually caused by misunderstanding or inattention to detail. The impacts of errors on study results are not as significant since they are traceable and easily corrected once they are caught. Errors can be eliminated, or at least reduced, through various means of monitoring, reviewing, and analysis of statistical data.

Misconduct most often occurs when researchers report data, publish results, or write grant applications and progress reports .In many cases of misconduct, data are falsified to align more closely with the researcher's predicted results. Data falsification could involve substituting one subject's record for that of another subject, altering dates and results on subject records to fit research protocol, altering the results of blood sample tests, or claiming to have performed a procedure on a subject who had not undergone that procedure [7].

In more serious cases of clinical research misconduct, data are completely fabricated. In these incidents, a researcher might create records of interviews or subject visits that never occurred, insert falsified notes into medical records or report progress data for a subject who had died. Fabricating data involves creating entirely new records of data, whereas data falsification involves altering existing records [3].

The most common types of misconduct/fraud in clinical research are: failure to follow an investigational plan; inadequate and inaccurate records; inadequate drug accountability; inadequate completion of informed consent forms; failure to report adverse drug reactions; failure to obtain and/or document subject consent; failure to notify an Institutional Review Board (IRB)/Ethics Committee (EC) of changes/progress reports; failure to obtain or document IRB approval [9].

Cases of intentional falsification and/or fabrication of research data and misleading reporting of the results are less common than poor quality related to poor management or education. The reasons for such unacceptable behaviour can be financial, promotional, or contract retention. But probably more significant is the ambition to be famous [7, 10].

Clinical trial auditors occasionally discover very serious patterns of deviations from the study protocol or Good Clinical Practice (GCP) regulations. In some instances, the deviations appear to go beyond innocent error and may constitute fraud, misconduct, or gross negligence. In at least some cases, sponsors do not report them to the institutional review board (IRB) and/or the EC [11].

On the basis of audit's reports it became possible to recognize data identifiers of fraud. The most important identifiers include implausible trends, e.g. 100% drug compliance, identical lab on Electrocardiogram (ECG) results, no Serious Adverse Events (SAE) reported, subjects adhering perfectly to a visit schedule [4].

Therefore, the most important identifiers to perform site audit are: immaculate CRFs, difficulty in arranging meetings, differences from other sites, faster recruitment, fewer adverse events, fewer withdrawals, add hours worked, add days of week/month worked, separate pages made for hospital notes, separate folders for GP notes, cannot find things 'will send later', or one pen used throughout [4, 6, 12].

CAN RESEARCH FRAUD BE PREVENTED?

Audit and control. Government agencies treat research misconduct very seriously. A researcher who has been found guilty of research misconduct may be prevented from applying for federal funding, removed from advisory committees, and prevented from serving on peer review boards. Articles published by a researcher guilty of misconduct may be corrected or retracted, if necessary. In most cases, research misconduct is the end of a person's research career. Many cases result in job termination [3, 8, 13].

All research institutions are required to have internal control routines in order to carry out their activities in a responsible manner. In addition, a number of public agencies have auditing and supervisory functions with respect to research. Advance audits are the most comprehensive. Audits of ongoing research and of completed research projects are likely to be more fragmentary, both at the level of research institution and levels above. The Data Inspectorate has passed advance audits prior to approval of processing of sensitive personal information in research projects to a locally nominated Data Protection Inspector, for example, while they themselves now undertake a greater number of audits of ongoing projects. Many research institutions also have their own bodies and routines for monitoring the ethical and quality aspects of ongoing research projects [8, 14].

Publishing results. Once a research project has been completed, publishing mechanisms become an important factor in revealing errors or deficiencies. Preliminary findings are presented often as lectures or posters, and manuscripts revised according to the feedback received before submission to an academic journal. Methodological, ethical and presentational aspects of the study are evaluated through the peer review system of academic journals and, as a rule, articles have to be revised a number of times before they are published. The underlying assumption is that peer review improves the academic quality of published work, but there is general agreement that the system cannot guarantee exposure of fraudulent research. Peer reviewers are not close enough to data sources to be able to check the validity of results, although they do sometimes discover irregularities which may lead to suspicions of fraud. Editors may then request further information. It is a matter of some debate among editors of leading medical journals how the peer review process may be improved, and also the degree of responsibility editors have for articles they publish. It has become increasingly common for journals to require authors to declare the exact nature of the contribution they have made to the study and the publication [8, 15, 16].

On the other hand, presentation of research data and methodology not only provides opportunities for improving the scientific quality of projects, but also ensures openness in the research environment which, in turn, makes fraud more difficult. Fraud would soon be discovered if large amounts of data appeared after only a brief period of time, since other researchers in the group are fully aware that data collection can take several years. The opinion is that supervisors, as a rule, should be well acquainted with all aspects of a project, including quality control of data collection, electronic data processing and statistical analyses, in addition to contributing to the publication process itself [8, 16, 17].

The 'culture' of research. The opinion of the authors is that more bureaucracy and control could easily lead to research being paralyzed by over-regulation, and may result in many researchers giving up their careers. On the other hand, the culture of research must be based on a fundamental ethos of integrity, openness and honest work of high quality in all parts of the research process, as well as an awareness on the part of research institutions of their responsibility for the system. In practice, the integrity of researchers themselves and internal social control are probably more significant than external control, which is chiefly designed to expose the most serious cases of fraud. The opinion of the authors is that research institutions must continue to be the cornerstone of initiatives promoting sound research ethics and prevention of misconduct. Internal and external control systems must be improved and existing rules and regulations must be clarified, simplified, and made more effective. Continued promotion of sound principles in research environments and an increased awareness of the moral, professional and legal responsibilities of researchers are also important. Open communication in research groups about ongoing research projects, in addition to discussions on sound research practice and research ethics, should contribute to the promotion of sound research and help prevent misconduct and fraud [16, 17].

CONCLUSIONS

Complex issues demand complex solutions. Addressing research fraud and dishonesty requires comprehensive focus on informing researchers and staff personnel on reporting and dealing with unethical research practices. Considering the competitive environment between researchers within the scientific community, there should be a greater focus on the quality of research rather than quantity.

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