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Scientific, Strategic and Medical Writing in Clinical Trial Development

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ABSTRACT:
Clinical protocols are designed to improve the standards for patient care quality and healthcare overall in all clinical and medical environments. It establishes the essential components that make it easier to deliver individuals with superior care and minimize the risk of participant harm.Medical writers (medical writing) are important for the process that explains to participants, sites, sponsors, and regulatory authorities the objectives, tactics, analyses, and medical knowledge of a clinical trial or program. Our staff of writers that are inclined towards science has a lot of expertise in putting up clinical papers including protocols, clinical study reports (CSRs), and investigator's brochures. The protocol is a document that details the objectives, design, technique, statistical considerations, and organizational structure of a clinical study. It also assures the safety of trial participants and the accuracy of the data obtained.
Keywords: Medical writing, Clinical trial Protocols, clinical study reports (CSRs), Investigator Brochures.

INTRODUCTION:

Clinical trial protocols are comprehensive documents that describe the ethical, moral, and legal justifications for research evaluating pharmaceutical products. Medical writers work with teams of subject matter experts (such as pharmacokinetics, statisticians, regulatory experts, operational experts, medical experts, etc.,) to develop concise protocols that address the suggested medical issues and protect the rights and safety of participants. To do this, authors must understand and be able to articulate the occasionally complex concepts of clinical trial design. In addition, although efforts have been made to harmonize the structure of trial protocols and the International Council for Harmonisation (ICH) Good Clinical Practise (GCP) offers recommendations on what a trial protocol should include, a standard akin to ICH E3 for trial reports, defining what information to present, has not yet been established[1].

MEDICAL WRITING

Technical writing also referred to as "Medical writing" transmits scientific information to other scientists via written communication in the form of a report, book, or presentation. The possibility of grant requests, peer reviews, and a summary of the results need careful research and exact writing [2].

Roles Of Medical Writer

Writing manuscripts for documents, various nonclinical, clinical, and marketing materials, as well as the legal documents needed for marketing novel medications are all essential responsibilities for medical writers. Medical writers should know the fundamentals of clinical research and provide scientific or medical information in a manner that is simple and clear.

They ought to have both technical and non-writing abilities (knowledge of therapy and statistics). They should create the highest-quality scientific documentation that adheres to all applicable regulatory criteria [3].

They prepare documents such as,

1. Research proposals
2. Investigator brochures
3. Informed consent documents

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4. Clinical study reports
5. Clinical study protocols
6. Patient information leaflet
7. Patient safety narratives

Ensuring that all deliverables adhere to standards, regulations, and guidelines is an essential responsibility of the medical writer. The medical writer's regulatory documentation must adhere to ICH, GLP, GCP, and the regulatory authority's submission requirements for clinical studies. Medical writers must stay up-to-date on current literature, developing research, technology advancements, and medical trends as well as industry practices and regulatory needs.

1. Research proposal:

A research proposal is a written statement by a researcher illustrating in complete detail their proposed field of study. It gives a reader a summary of the information involved in a project, exactly comparable to an assessment of the full research process. The proposal comprises a flowchart outlining the researcher's steps, from developing the hypothesis and considering its practical applications to doing the final data analysis [3,4].

2. The Investigator's Brochure (IB)

The investigator's brochure (IB), which is kept up to date by a drug developer or investigator, is a thorough compilation of clinical and nonclinical data on the investigational product (drug, supplement, device, or other products) amassed both before and after a drug trial. An IB facilitates understanding of the rationale for, and their compliance with, many key features of the proposal, such as dose (of the study drug), dose frequency and dosing interval, methods of administration, and safety monitoring procedures.

Information in the IB should be given in concise, objective, balanced, and non-promotional language so that a physician or potential investigator can understand it and figure out if the proposed trial is suitable based on risk and benefit [5].

3. Informed consent documents

A document known as an Informed Consent Document/Informed Consent document (ICD/ICF) is required whenever you propose doing research with human subjects. This form's purpose is to demonstrate that the research subject has freely chosen to participate in the study.

Any biomedical and health study involving human participants must first receive the prospective participant's free, written informed permission. Three key steps make up the ongoing process of informed consent: presenting pertinent information to potential participants, confirming the person's competency, ensuring the information is understandable by the participants, and confirming the voluntariness of the participation. The protection of a person's autonomy and freedom of choice is ensured through informed voluntary consent [6].

4. Clinical study reports

The clinical study report is the cornerstone of a pharmacological product's case for use in people since it summarises the findings of single human research. A medicine or biologics business is required to report the findings of all human trials it has done, albeit the reporting format might vary. In close cooperation with a diverse team that at a minimum possesses medical, statistical, and regulatory skills, the structure and content of clinical study reports are created [7].

5. Clinical study protocols

A document that outlines a trial's goals, methods, design, statistical concerns, and organizational structure. The context and justification for the trial are typically also stated in the protocol, although they may also be found in other papers that the protocol refers to. The term "protocol" refers to both a protocol and a protocol modification throughout the ICH GCP Guideline [8].

6. Patient information leaflet (PIL)

All patients should consult the Patient Information Leaflet (PIL) as a valuable resource for information. The PIL that comes with the drug is valued more highly by patients than any other information source outside physicians and chemists, and they desire more information than they now receive [9].

7. Patient safety narratives

Patient accounts are a crucial component of clinical study reporting. It gives a chronological record of every circumstance a subject faced throughout or soon after a clinical study. Narratives would be required for occurrences leading to death or study termination in addition to significant adverse events (SAEs) in the regulatory filings. Patient accounts are included in the safety data

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throughout all stages of clinical trials that are reported to the regulatory authorities [10].

STEPS TO WRITE A PROTOCOL:

The protocol also specifies how to safeguard participants and get reliable data. Before a Sponsor is permitted to conduct research, protocols are submitted to both an Institutional Assessment Board (IRB) and regulatory authorities (e.g., the U.S. FDA) for a thorough assessment to verify compliance with subject protection standards and legal requirements.

Guidelines

Submitting a protocol that is missing important information, or even entire sections, is not unusual, yet it is entirely preventable. To compile a list of requirements for a clinical trial protocol, consult the pertinent ICH guidelines (ICH E6 [R2]) and FDA guidances.

Methodology

The most crucial portion of the protocol is the methodology section. The interventions to be performed, the methods to be followed, the measurements to be made, the observations to be made, the laboratory tests to be conducted, etc. should all be covered in full. When several sites participate in a given protocol, the procedure should be regulated and made clear.

The medicine, gadget, or vaccination being studied should be explained in full along with the interventions. Interventions may also be made in the field of social sciences, for as through educating or educating groups of people.

Standardized and/or documented procedures/techniques should be described and bibliographic references, if not provided earlier should be provided. Instruments that are to be used to collect information (questionnaires, FGD guides, observation recording forms, case report forms, etc.) must also be provided [11,12].

Develop the Synopsis and Schedule of Events Early in the Process

A summary or overview of the protocol is provided in the synopsis. The calendar of events is a table-formatted summary of all study-related activities, including subject selection and enrolment, safety evaluations, effectiveness assessments, pharmacokinetics sampling, etc. Before the entire protocol is written, these parts provide the ideal chance to finalize the research design with all parties involved, including the sample and evaluation time points. Before writing the entire body of the protocol, it is advisable to finalize a summary and a schedule of evaluations to remove any inconsistencies and avoid any misunderstandings or deviations that could call for a protocol change.

Provide Clear Objectives and Associated Endpoints

The Sponsor, regulatory bodies, and the IRB will be able to critically assess whether the proposed research design is likely to yield the necessary information if the study's objectives are written in clear, unambiguous terms. Additionally, it might be useful to the Sponsor as they start to consider potential outcomes and how the research's design would assist both the development program as a whole and the findings from this particular study. It is strongly advised that scientists and medical professionals assess the research design's validity, considering the objectives, endpoints, and other components as a whole.

Describing Assessments with Operational Feasibility

Each study assessment description should have enough information for people to carry out the steps without needing any extra guidance, and it should be written such that all steps are carried out consistently even if they are carried out by different people. Consider typical inquiries that could come up throughout the research while writing the protocol. For vital signs, as an illustration: Should the seriousness of adverse events be categorized using a quantitative scale, such as the Common Terminology Criteria for Adverse Events (CTCAE), or using phrases like mild, moderate, or life-threatening? It is important to keep in mind that thorough protocols are necessary to achieve a seamless clinical study. It might be essential to be a little more lenient with the terminology to permit the gathering of crucial data without causing a protocol deviation.

Arrange the Protocol to Promote Ease of Reference

While it will be the responsibility of each Investigator and staff person engaged in the study to familiarise themselves with the protocol, the protocol's structure should make it easy to access specific information quickly. So that material may be found easily using the Table of Contents, provide useful sub-headers. This will make it easier to access crucial information quickly during

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protocol review for the trial personnel as well as IRB/regulatory officials.

Practice Judicious Redundancy

When using redundant language in the document, caution should be used to avoid introducing discrepancies because modifications made to one area may accidentally go unnoticed in others.

Regulatory:

A medicines regulatory authority (MRA) must provide its permission for clinical studies utilizing research pharmaceutical products to proceed. The MRA is in charge of ensuring that the requisite standards for safety, quality, and efficacy are met in all clinical studies for both newly approved uses of already-registered medications as well as those using unregistered medications.

FDA (Food and Drug Administration) is the regulatory organization in the US, whereas EMEA (European Agency for the Evaluation of Medicinal Products) is the equivalent organization in Europe. The Medicines Control Council (MCC) is the legally mandated authority in South Africa that oversees the conduct of clinical studies and the registration of pharmaceuticals and medical devices for use in treating particular conditions [10]. Before conducting a clinical study, an institutional review board (IRB) or ethics board approval is required. They play a crucial part in ensuring the trial is moral, that the welfare and human rights of the participants are protected under GCP guidelines, the protection of personal information, and that the trial is inspected for medical safety and the protection of the trial participants before approval [13].

PROTOCOL AMENDMENT

A written description of a change(s) to or formal clarification of a protocol.For every clinical trial, the study protocol is important and the study protocol dictates how the study should be conducted, what data will be collected, and how the data will be analysed.

Usually, after the IND (Investigational New Drug) including the study protocol is filed and FDA does not provide any comments (or put it on clinical hold) within 30 days, the sponsor will consider the study protocol approved to proceed. However, it is very common that during the study conduct, some aspects of the study protocol need to be changed or amended [14].

REASONS FOR PROTOCOL AMENDMENT

The protocol amendment is done because of the following reasons – eventually the protocol may go through several rounds of amendments before the first patient is enrolled in the study.

- Protocol amendment after FDA pre-IND meeting
- Protocol amendment per external committees' requests – such as Data Monitoring Committee (DMC), Steering Committee
- Protocol amendment after the investigator meeting
- Protocol amendment after FDA's IND comments
- Protocol amendment due to the difficulties in patient enrolment
- Protocol amendment after the blinded interim analysis
- Protocol amendment due to expansion in the number of countries[15]

IND Application Reporting: Protocol Amendments

The sponsor of the application may make changes to the IND application as necessary after it has been approved to ensure that the clinical studies are carried out following the procedures specified in the IND application. Before putting new protocols into effect or making modifications to existing ones, sponsors are required to submit protocol revisions. When the sponsor has submitted the amendment to the FDA for evaluation and the new protocol, or changes to the current protocol, have been approved by the Institutional Assessment Board (IRB), which is in charge of reviewing and approving the research, new trials can begin. If the sponsor of an IND application wants FDA to comment on a submission, they must submit a request for such comments along with the particular queries that the FDA response should address [16].

Any particular technical material that has been previously submitted to the FDA as part of an IND application modification is anticipated to be cited in the amendment with its name, reference number, volume, page number, and date of submission. The following list contains protocol amendments' general categories [17].

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