



DECODING THE ROLE OF MEDICAL WRITER: EXPLORING THE KEY COMPONENTS IN RESEARCH AND REGULATORY DOCUMENTS

Author: Sampreethi Harikeerthi

Designation: Clinical Research Coordinator

Organization: AIG Hospitals, Hyderabad, India

ABSTRACT

A medical writer involves in writing/preparing various types of documents which includes educational and promotional literature, drug or disease related documents, healthcare websites, health related magazines and articles, regulatory and research related documents. Although they majorly work pharmaceutical and research organisations, there are various streams where a medical writer plays a vital role. This article majorly focuses on the design and components of Protocol, Investigator's Brochure (IB), Informed consent form (ICF), clinical study reports (CSR), common technical document (CTD) and Case report form (CRF) which are the most prominent documents in the field of medical writing and to provide a basic idea to the aspiring medical writers. A protocol is a document that forms the basis of any research or study. Investigator's Brochure provides overall information about the investigational medical product its dose, frequency, handling, administration etc. Informed consent form is a voluntary consent/permission given by the subjects to participate in the study. The CTD is a format, that is internationally accepted for the submission of new drug application to the regulatory authority. A CRF is used to collect data from subjects who are involved in the trial. There are also many other documents like IMPDs, research proposals, subject narratives etc. which are beyond the scope of this article. In conclusion, for a medical writer apart from having sound knowledge in medical science and writing skills it is consequential to have thorough knowledge of specific requirements of documents, and being well informed with the relevant guidelines.

Keywords: Medical writing, clinical trial, regulatory documents, drug development.

INTRODUCTION

A Medical writing professional majorly works with pharmaceutical industries and research organisations. However, there are various streams where a medical writer is necessary. A competent medical writer requires sound knowledge in medical and therapeutic area, medical terminology, drug development process, good understanding of language and grammar, literature and reference searching and ability to write without grammatical errors.

Medical writer involves in writing various types of documents for different purposes which include educational and promotional literature, drug or disease related documents, healthcare websites, health related magazines and articles, regulatory and research related documents.

Clinical trial protocols, Investigator's brochure (IB), Informed consent documents, research proposals etc. come under research document.

Clinical study reports, common technical document (CTD) Patient information leaflet, subject narratives come under regulatory documents. (S 2010)

This article aims to focus on the contents and design of the Protocol, IB, CRF, CSR, ICF and CTD which are the major documents in the field of medical writing to provide a basic idea to the aspiring medical writers. There are also many other documents like IMPDs, research proposals, subject narratives etc. which are beyond the scope of this article.

PROTOCOL:

Protocol explains each and every aspect of a particular clinical study. It is one of the most important documents that forms the basis of any research or a clinical trial. It helps in keeping track of the progression of the study.

Once the protocol is designed, finalised and study is launched, it should not be changed. If under any circumstances it has to be changed, that part of the study must be omitted. (A1-JunDi 2016)

COMPONENTS OF A PROTOCOL:

The protocol typically contains Signature page (which is signed by the senior member of the research as confirmation of their approval), Synopsis (overall summary of the study protocol), Abbreviations, Introduction (background and study purpose), Study aims and objectives, Study population/patient selection (inclusion and exclusion criteria), Statistical considerations (methods and analysis), Trial committee, Ethical considerations, References, Appendices and others which includes Data collection, management and analysis, Project management and Annexure. (Guideline 2015)

INVESTIGATOR'S BROCHURE:

Another prime document in the conduction of clinical study is an Investigator's Brochure. It is used to understand complete information about the investigational product, handling, dosage, frequency, route of administration and safety monitoring methods.

IB is study specific. A new IB must be designed if the marketed drug is studied once again for a new indication

Depending upon the phase of the study and new information, frequent revision of an IB may be appropriate.

It is the sole responsibility of the sponsor to provide an up to date IB to the investigator(s) and the investigators in turn are responsible for providing the up-to-date IB to the IRBs/IECs. (G.E. 1993)

Investigators Brochure contains the following sections:

Introduction, which contains information about the investigational product, pharmacological classification and its rationale.

Pre-clinical studies include pharmacology, ADME in animals and information on toxicology.

Pharmacokinetic and pharmacodynamics in humans, safety and effectiveness of the investigational product, summary of the data and guidance. (Guideline 2015)

INFORMED CONSENT FORM:

ICF is used to obtain consent from the trial subjects who are willing to take part in the study. This consent is given by the subjects after understanding all the advantages and disadvantages.

Its motive is to safeguard the wellbeing of the trial participants. The consent process is continuous, as long as the subject is involved in the study.

The subjects who have signed the form and are part of the study, must be provided with the physical copy of the ICF.

Elements of an Informed Consent Form:

Title of the study, Patient information, purpose of the trial, its duration, about the trial product, rights and responsibilities of trial participants, advantages and disadvantages, participation & withdrawal details, details about end of the study, compensation and other expenses, confidentiality of subject information, point of contact if there are any questions or problems, details of the authorities that approved the study, subject consent, details of the investigator who conducted the consent discussion. (Guideline 2015)

CLINICAL STUDY REPORTS:

This document provides information about the structure, conduction and result of a clinical trial and also analyzes the safety and efficacy of the new treatment.

Structure of CSR

Based on the prerequisite of ICH E3 the structure and contents of CSR are as follows:

- Synopsis
- Introduction
- Methods
- Results
- Discussion
- Conclusion
- Appendices

Synopsis (contains over view of main findings and conclusion), Introduction (Background of the investigational product, uses and rationale), Methods (Study design, objectives, end points, patient population, interventions, outcomes, information about ethical

considerations and any statistical analysis that are performed), Results (Both numerical and descriptive information along with tables and figures that illustrate the results) Discussion (Clinical implications and limitations of the study) Conclusion, Appendices (Additional information and information about documents like protocol, ICF, data tables and patient narratives).

Submission of CSR

Submission process depends on requirements of particular regulatory authority.

Medical writers use the templates like TransCelerate template, ICH E3 template and CORE (clarity and openness in reporting) templates to create CSRs that compliant with regulatory guidelines as references. (Taranum 2023)

COMMON TECHNICAL DOCUMENT (CTD):

The CTD is a format, that is internationally accepted for the submission of new drug application to the regulatory authority.

According to the guidance of ICH M4, the font style should be Times New Roman, size should be 12 for a narrative text. Short forms or acronyms must be explained at first and literature references at last. The Common technical document dossier has 5 modules. (Jordan 2014)

Module 1: General information (Administration and Prescribing information) (Guidance for Industry on preparation of common technical document for the import, manufacture and marketing approval of new drug 2010)

Module 1 is not the same for all the regulatory authorities. Module 1 is specific to a respective regulatory body.

Module 1 in CDSCO, contains administrative information that includes applicant's introduction, treasury challan, Form 44, legal documents. Product information: composition, dosage form, ROA, storage conditions etc. and prescribing information. (Guidance for Industry on preparation of common technical document for the import, manufacture and marketing approval of new drug 2010)

Module 2: Summaries & Overviews

Overview of the documents with summaries are included in this Module. There are seven sections in this module. They are:

1. Table of contents
2. General introduction of the IMP
3. Chemical and Pharmaceutical data of the product (Summary)
4. Non clinical overview
5. Clinical overview
6. Nonclinical written and tabulated summaries
7. Clinical summary

Module 3: Quality

This Module constitutes information on quality, manufacturing, chemistry and control reports.

Sections under module 3 includes

- Table of contents
- Body of data (Drug substance & Drug product)
- Literature references used in this module

Drug substance is an active molecule within the drug product that provides the intended therapeutic effect.

Drug product is the final form of the drug that is ready for consumption by patient.

Module 4: Non clinical study reports

Sections that come under this module are Pharmacology (1^o 2^o Pharmacology, safety pharmacology), toxicology and Pharmacokinetics (Absorption, Distribution, Metabolism, Excretion) and References.

Module 5: Clinical study reports

Module 5 consists of studies relevant to human pharmacokinetics and pharmacodynamics, biopharmaceutical studies, safety and effectiveness, CRFs and individual patient listings. (Jordan 2014)

CASE REPORT FORM:

A CRF is used to collect the data in clinical research, from the subjects who are have signed the Informed consent form.

A CRF must be in compliance with protocol and fulfil the requirements of the regulatory authorities, in such a way that it answers the research related questions. A CRF is written in compliance with protocol, therefore, it's better to design it after the protocol if finalised.

The design of CRF defines the quality of data collected.

There are two types of case report forms. They are 1. Paper case report forms, 2. Electronic case report forms.

Paper CRFs are the traditional way of data capture. But now a days eCRFs preferred over paper CRFs because it is less time consuming, zero to minimal error, faster regulatory submission etc.

Apart from all the data entry points, header and footer are the most important ones in the CRF. Header contains protocol ID, site ID and subject details (Initials, ID no). Footer consists of signature column along with date, version and page number.

The following points must be considered while preparing a CRF.

- Format, font style and font size shall be maintained the same throughout the CRF.
- Page numbering should also be maintained consistently.
- Standard data format must be followed (E.g.: dd/mm/yyyy)
- Pre coded answers such as YES/NO, MALE/FEMALE, MILD/MODERATE/SEVERE in case of Adverse event, must be used in order to minimise text /written responses.
- Use Bold wherever important instructions have to be given.
- In case of adverse event, the details of AE must be entered in AE module.

Designing a Case Report Form:

A well designed CRF, not only helps in reducing the data entry errors, but also helps the site personnel/Investigator to enter the data without any confusion.

Design of CRFs will be different for different studies depending upon the specifications of the protocol. But it is important to maintain library of standard templates by sponsor/CRO/Pharmaceutical organisations, to maintain consistency and to save time.

If the same parameters have to be recorded at different visits, then same CRF module can be used in order to reduce the number of query generation.

Use the indicator questions wherever necessary, in connection to the set of other questions. For example, in case of Medical/ surgical history, an indicator question would be, “Any medical or surgical history?” If the answer is “yes” then other set of questions (Diabetes, hypertension, obesity etc., if not specified then blank space has to be provided where it can be typed or written depending upon the type of CRF used) need to be answered. If the answer is “no” then this step can be omitted.

In order to obtain error free data entry and data capture, providing CRF completion guidelines is necessary. A CRF completion guideline is a document which provides clear, step by step details on data entry. It must be designed in such a way that it enables Investigator/his team members to complete the CRF with ease and decipherable. (Bellary 2014)

In certain cases, wrong data may be entered. Therefore, instructions must be provided to strike off the wrong data with a line and put the initials of the person who entered or corrected the data and enter the correct data beside the margin. This is applicable in case of paper CRFs.

CONCLUSION:

Medical writing is not only an integral part in the fields of research and regulatory but also in the fields of marketing healthcare products, medical journalism, medical education (patient education material) and publications. Medical writers facilitate communication of complex information to general audience as well as healthcare professionals. It is important to have good understanding of medical terminology and better writing skills. In addition to this, a thorough knowledge of specific requirements of documents, and being well informed with the relevant guidelines is essential. (S 2010)

REFERENCES

1. Sharma, S. (2010). How to become a competent medical writer?. *Perspectives in clinical research*, 1(1), 33.
2. Al-JunDi, A., & SAKKA, S. (2016). Protocol writing in clinical research. *Journal of clinical and diagnostic research: JCDR*, 10(11), ZE10.
3. Pakes, G. E. (1993). Writing Clinical Investigator’s Brochures on Drugs for a Pharmaceutical Company. *Journal of Technical Writing and Communication*, 23(2), 181-189. <https://doi.org/10.2190/63P5-WMTD-4644-60MD>
4. Taranum, S. (2023). Clinical study reports: A snapshot for aspiring medical writers. *Medical Writing*, 32, 70-74.
5. Jordan, D. (2014). An overview of the Common Technical Document (CTD) regulatory dossier. *Medical Writing*, 23(2), 101-105.

6. Bellary, S., Krishnankutty, B., & Latha, M. S. (2014). Basics of case report form designing in clinical research. *Perspectives in clinical research*, 5(4), 159
7. Guideline, I. H. (2015). Integrated addendum to ICH E6 (R1): guideline for good clinical practice E6 (R2). *Current Step*, 2, 1-60.

