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PROSPECTIVE FEATURES OF CLINICAL DATA MANAGEMENT

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ABSTRACT

Clinical data management (CDM) involves the collection, validation, and analysis of clinical trial data to ensure its accuracy and integrity. This process is crucial for maintaining high-quality data for regulatory submissions and scientific analysis. Clinical data management (CDM) plays a crucial role in clinical research, ensuring the integrity, accuracy, and confidentiality of data collected during clinical trials. This process involves various steps, including data collection, validation, cleaning, and analysis. CDM employs specialized software and standardized protocols to maintain high-quality data throughout the trial lifecycle. Effective CDM practices are essential for regulatory compliance, maintaining data integrity, and ultimately, ensuring reliable outcomes in clinical research. This abstract provides an overview of the importance and key components of clinical data management in modern healthcare and pharmaceutical industries. Clinical data management (CDM) is a critical component of clinical research, involving the collection, validation, and analysis of data gathered during clinical trials or studies. This process ensures that data integrity, accuracy, and compliance with regulatory standards are maintained throughout the research lifecycle. Effective CDM practices facilitate the generation of reliable and high-quality data, which is essential for making informed decisions regarding the safety and efficacy of investigational treatments or interventions. This abstract provides an overview of the key principles, methodologies, and technologies involved in CDM, emphasizing its significance in advancing medical knowledge and improving patient care. It ensures data accuracy, integrity, and confidentiality throughout the research process. To meet regulatory requirements and stay ahead of the market through quicker product commercialization, there is a greater need to strengthen CDM standards in the current environment. The CDM team canachieve these requirements by implementing regulatory-compliant data management technologies. Additionally, submitting data electronically is becoming required of businesses. Professionals in CDMshould have the drive to keep up with the fast evolving technology, satisfy reasonable requirements for data quality, and fulfil reasonable expectations. crucial stage in clinical research is clinical data management (CDM), which produces high-quality, trustworthy, and statistically sound data from clinical trials. This results in a significantly shorter period of time between drug development and release. From the beginning to the end of a clinical trial, CDM team members are actively involved. They must have sufficient process knowledge to support upholding the CDM processes high levels of quality. At regular intervals throughout a trial, various CDM processes-including Case Report Form (CRF) designing, CRF annotation, database designing, data entry, data validation, inconsistency management, medical coding, data extraction, and database locking are evaluated for quality. A good clinical data management system reduces the duration of the study and cost of drug development. Further a well-designed case report form (CRF) assists data collection and make facilitates data management and statistical analysis. Nowadays, the electronic data capture (EDC) is very beneficial in data collection. EDC helps to speed up the clinical trial process and reduces the duration, errors and make the work easy in the data management system. This article highlights the importance of data management processes involved in the clinical trial and provides an overview of the clinical trial data management tools. The study concluded that data management tools play a key role in the clinical trial and well-designed CRFs reduces the errors and save the time of the clinical trials and facilitates the drug discovery and development. Over the last few decades, most of the pharmaceutical companies and research sponsors are facing a lot of challenges in clinical research for their new drug approval. The sponsor research needs a high-quality data report for

getting new drug approval from Food and Drug Administration for their medical products. Clinical trial data are important for the drug and medical device development processing pharmaceutical companies to examine and evaluate the efficacy and safety of the new medical product in human volunteers. Clinical Data Management (CDM) is a vital phase in clinical research, which leads to establishment of high quality, consistent, and statistically reverberation data from clinical trials. Theyshould have adequate method knowledge that helps maintain the quality standards of Clinical Data Management processes. Various procedures in Clinical Data Management including Case Report Form designing, annotation, database designing, data entry ,data validation, discrepancy management ,medical coding, data extraction, and database locking are assessed for quality at regular intervals during atrial. In the present scenario, there is an increased demand to recover the Clinical Data Management standards to meet the regulatory requirements and stay ahead of the competition by means of faster commercialization of product. With the implementation of regulatory compliant data management tools, CDM team can meet these demands. Clinical Data Management professionals

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should meet appropriate expectations and set standards for data quality and also have a drive to adapt to the rapidly changing technology. This article highlights the processes involved and provides the reader an overview of the tools and standards adopted as well as the roles and responsibilities in Clinical Data Management. CDM and the data management procedures that are being followed up for the proper management of the data so that it is easily accessible by the personnel. Also, the use of various software in the clinical data management process has been discussed depicting how the software perform various functions to keep the data in a managed, secured and an accessible form. As an endpoint, various future challenges and options are considered which give a detailed idea about the growth of clinical data management in the Pharmaceutical Industry. A clinical data management system is a software supporting the data management process in clinical trials. In this system, the effective support of clinical data management dimensions leads to the increased accuracy of results and prevention of diversion in clinical trials. The aim of this review article was to investigate the dimensions of data management in clinical data management systems. Clinical data contains information for developing and sustaining software systems, databases, processes, procedures, training, and protocols. Clinical data management enables organizations to maintain data integrity throughout the duration of a clinical research study. Correct data management ensures that a dataset is accurate, secure, reliable, and ready for analysis.

Keywords: clinical data management, data capture, good clinical data management, validation, clinical research, safety & efficacy, e-CRF, data exchange, analysis of data

1. INTRODUCTION

Clinical data management (CDM) plays a crucial role in healthcare and medical research by ensuring the accuracy, reliability, and integrity of data collected during clinical trials and studies. It involves various processes, including data collection, validation, storage, and analysis, to support informed decision-making by researchers, healthcare professionals, and regulatory authorities. Effective clinical data management practices are essential for ensuring patient safety, regulatory compliance, and the success of clinical research endeavors. Clinical data management (CDM) plays a crucial role in the pharmaceutical and healthcare industries by overseeing the collection, storage, and analysis of data generated from clinical trials and studies. It ensures the accuracy, completeness, and integrity of clinical data, which is vital for making informed decisions about the safety and efficacy of medical treatments. Effective CDM practices are essential for maintaining regulatory compliance, minimizing errors, and facilitating the efficient conduct of clinical research. Clinical data management plays a crucial role in healthcare and medical research by ensuring the accuracy, integrity, and reliability of data collected during clinical trials and studies. It involves a systematic approach to the collection, validation, storage, and analysis of data, ultimately contributing to informed decision-making and the advancement of medical knowledge and patient care. Clinical data management (CDM) plays a crucial role in healthcare and medical research by ensuring the integrity, accuracy, and reliability of data collected during clinical trials and studies. It involves various processes such as data collection, validation, storage, and analysis to support decision-making by healthcare professionals, researchers, and regulatory agencies. Effective CDM practices are essential for maintaining data quality and compliance with regulatory requirements, ultimately contributing to the advancement of medical knowledge and patient care. Clinical data management (CDM) is a vital cross-functional vehicle in clinical trials to ensure high-quality data are captured by sites staff through paper case report form (CRF) or electronic case report form and available for early review. The integrity and quality of data being collected and transferred from study subjects to a clinical data management system (CDMS) must be monitored, maintained, and quantified to ensure a reliable and effective base for not only new drug application (NDA) submission and clinical science reports, but also corporate clinical planning, decision-making, process improvement, and operational optimization.

The gradually increasing use of electronic data-capturing (EDC) technology and electronic CRF to collect data in clinical trials has grown in recent years and has affected the activities of clinical research operations for industry sponsors, contract research organizations (CROs), and clinical sites. This technology must comply with applicable regulatory requirements and offer flexible, configurable, scalable, and auditable system features. Transitioning from paper-based data collection (PDC) to EDC systems has produced many benefits, that is easing the burden associated with organizing paper CRF work and greatly reducing the time, cost, and stress required in bringing a product to market through technology-enabled efficiency improvement, such as the quick and robust interactive voice response system (IVRS) supported and integrated auto casebook creation, early data availability, and fast database lock via Internet-based user interface. Although EDC technologies offer advantages over traditional paper-based systems, collecting, monitoring, coding, reconciling, and analyzing clinical data. Often from multiple sources, can be challenging. High-qualitydata should be absolutely accurate and suitable for statistical analysis. These should meet the

protocol-specified parameters and comply with the protocol requirements. This implies that in case of a deviation, not meeting the protocol-specifications, we may think of excluding the patient from the final database. It should be borne in mind that in some situations, regulatory authorities may be interested in looking at such data. Similarly, missing data is also a matter of concern for clinical researchers. High-quality data should have minimal or no misses. But most importantly, high-quality data should possess only an arbitrarily 'acceptable level of variation' that would not affect the conclusion of the study on statistical analysis. The data should also meet the applicable regulatory requirements specified for data quality. clinical trial conduct, plays an important role in ensuring that clinical trials are conducted according to International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines, applicable regulatory guidance and guidelines, and specific study protocols. A properly developed clinical study protocol is very crucial for ensuring the success of a clinical trial. As such, it is essential that the CDM unit/department, through CDM oversight/lead and team, performs a thorough study protocol review for a new clinical trial. CDM oversight/lead and CDM unit perform effective review of the study protocol to ensure that it is properly designed and appropriate for a specific study from clinical data flow, operation, and analyses perspective. Each section of the study protocol can be very useful to clinical data management functions and activities at study start up, study conduct, andstudy closeout

Tools of CDM:

Many software tools are available for data management, and these are called Clinical Data Management Systems (CDMS). In multi centric trials, a CDMS has become essential to handle the huge amount of data. Most of the CDMS used in pharmaceutical companies are commercial, but a few open source tools are available as well. Commonly used CDM tools are ORACLE CLINICAL, CLINTRIAL, MACRO, RAVE, and e-Clinical Suite. In terms of functionality, these software tools are more or less similar and there is no significant advantage of one system over the other. These software tools are expensive and need sophisticated Information Technology infrastructure to function. Additionally, some multinational pharmaceutical giants use customer made CDMS tools to suit their operational needs and procedures. Among the open source tools, the most prominent ones are Open Clinica, open CDMS, TrialDB, and PhOSCo. These CDM software are available free of cost and are as good as their commercial counterparts in terms of functionality. These open source software can be downloaded from their respective websites.

In regulatory submission studies, maintaining an audit trail of data management activities is of paramount importance. These CDM tools ensure the audit trail and help in the management of discrepancies. According to the roles and responsibilities (explained later), multiple user IDs can be created with access limitation to data entry, medical coding, database designing, or quality check. This ensures that each user can access only the respective functionalities allotted to that user ID and cannot make any other change in the database. For responsibilities where changes are permitted to be made in the data, the software will record the change made, the user ID that made the change and the time and date of change, for audit purposes (audit trail). During a regulatory audit, the auditors can verify the discrepancy management process; the changes made and can confirm that no unauthorized or false changes were made.In regulatory submission studies, maintaining an audit trail of data management activities is of paramount importance. These CDM tools ensure the audit trail and help in the management of discrepancies. According to the roles and responsibilities (explained later), multiple user IDs can be created with access limitation to data entry, medical coding, database designing, or quality check. This ensures that each user can access only the respective functionalities allotted to that user ID and cannot make any other change in the database.For responsibilities where changes are permitted to be made in the data, the software will record the change made, the user ID that made the change and the time and date of change, for audit purposes (audit trail). During a regulatory audit, the auditors can verify the discrepancy managementprocess; the changes made and can confirm that no unauthorized or false changes were made.

CDM Process:-

Like a clinical trial, the CDM procedure starts with the goal in mind. This indicates that the deliverable has been kept in mind throughout the entire process. An error-free, valid, and statistically sound database is what the CDM process is meant to give, much as a clinical trial is madeto provide an answer to the research question.

CDM's Roles and Responsibilities:-

The clinical data coordinator creates all additional CDM-related materials, checklists, and guidelines. The quality control associate performs data audits and verifies the accuracy of data entry. A different quality assurance individual may occasionally audit the data entered. The quality control associate also checks the paperwork related to the protocols being followed. The team responsible for data entry will keep track of when CRF pages are received and enter the information into the database.

Different duties and responsibilities are given to the team members in a CDM team. Graduation in a life science field

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and familiarity with computer applications should be the very minimum educational requirements for team members in CDM. Medical graduates are ideal for the position of medical coder. However, paramedical graduates are also hired in the sector as medical coders. All CDM teams need to fill a few crucial jobs.

The following roles can be regarded as the bare minimum for a CDM team: Medical coder

- Data Entry Associate
- Clinical Data Coordinator
- Quality Control Associate.

Clinical data management team and stages:-

CDM activities start early in the clinical trial process, once the trial protocol, describing the study objectives and methodology, is designed. As a rule, data-related responsibilities are allocated across.

a clinical data manager who supervises the entire CDM process;

a medical coder who translates diagnosis, procedures, adverse events, and other health data into industry-specific codes; and a quality control associate.

a database programmer or designer; data entry associates;

a quality control associate. Now, let's see how data management unfolds and who does what at each stage.

OVERVIEW OF CDM:-

researchers note that automating all dimensions of clinical data management in trials can take them from mere electronic data capture to something that helps with findings in clinical trials. The most helpful strategies for implementing clinical data management systems balance risk reduction and lead time. All trial managers want to have their software deployed rapidly. However, it is best to set up the databases thoroughly before the trial. When staff must make software changes during the

trial, it can be costly and have implications on the trial data's validity. Other strategies that help organizations implement a new system include making sure that, prior to deployment, the intended users give input. These users include entities such as the contract research organization (CRO), the sponsor, staff at the investigator site, and any onsite technical support. Staff should respond well to the graphical user interface (GUI). Additionally, depending on software support, the staff can gradually expand the modules to include more functionality, perform module-based programming, and duplicate the hardware. These actions give the staff the most functionality and the software the best chance at success.

2. CLINICAL DATA MANAGEMENT PROCESS

A. Review and finalization of study documents

During this review, the CDM personnel will identify the data items to be collected and the frequency of collection with respect to the visit schedule. A Case Report Form (CRF) is designed by the CDM team, as this is the first step in translating the protocol specific activities into data being generated. The data fields should be clearly defined and be consistent throughout. The CRF should be concise, self-explanatory and user friendly (unless you are the one entering data into the CRF). Along with the

CRF, the filling instructions (called CRF Completion Guidelines) should also be provided to study investigators for error free data acquisition. CRF annotation is done wherein the variable is named according to the SDTMIG or the conventions followed internally. Annotations are coded terms used in CDM tools to indicate the variables in the study. The type of data to be entered should be evident from the CRF.

B. DATA BASE DESIGNING

Databases are the clinical software applications, which are built to facilitate the CDM tasks to carry out multiple studies. Generally, these tools have built in compliance with regulatory requirements and are easy to use. "System validation" is conducted to ensure data security, during which system specifications, user requirements, and regulatory compliance are evaluated before implementation. Study details like objectives, intervals, visits, investigators, sites, and patients are defined in the database and CRF layouts are designed for data entry. These entry screens are tested with dummy data before moving them to the real data capture.

C. Data collection

Data collection is done using the CRF that may exist in the form of a paper or an electronic version. The traditional method is to employ paper CRFs to collect the data responses, which are translated to the data base by means of data entry done in-house. These paper CRFs are filled up by the investigator according to the completion guidelines. In the eCRF based CDM, the investigator or a designee will be logging into the CDM system and

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entering the data directly at the site. In eCRF method, chances of errors are less, and the resolution of discrepancies happens faster. Since pharmaceutical companies try to reduce the time taken for drug development processes by enhancing the speed of processes involved, many pharmaceutical companies are opting for eCRF options (also called remote data entry).

D. CRF tracking

A CRF is made by for the collection of data from the protocol. A CRF may be paper based or in the form of EDC. There is a proper coding given to the CRF to communicate the collection of data which is to be stored in the database. A CRF should be constructed in such a way that it must be concise and the data must be stored in high quality. The header and the footer given in the CRF must be made in such a way that it should give the details about the study. During the designing of the CRF the discrepancies in the data can be avoided by making a proper layout of the CRF that should be of basically three types that is, time dependent, non-time dependent and cumulative layout [6]. There should be uniform use of layouts, fonts and queries. CRF pages should be orderly arranged according to the unambiguous protocols. Proper organized data will provide simplified data analysis. A proper CRF completion manual should be provided to the personnel for accurate data entry. Thus, there will be reduced query generation and data integrity will be improved. It is suggested that a library of templates for the standard CRF module must be established in order to save time. An example of a CRF is given in the flow chart below.

E. Data entry

Data entry takes place according to the guidelines prepared along with the DMP. This is applicable only in the case of paper CRF retrieved from the sites. Usually, double data entry is performed wherein the data is entered by two operators separately. The second pass entry (entry made by the

second person) helps in verification and reconciliation by identifying the transcription errors and discrepancies caused by illegible data. Moreover, double data entry helps in getting a cleaner database compared to a single data entry. Earlier studies have shown that double data entry ensuresbetter consistency with paper CRF as denoted by a lesser error rate.

3. DATA VALIDATION F

Data validation is the process of testing the validity of data in accordance with the protocol specifications. Edit check programs are written to identify the discrepancies in the entered data, which are embedded in the database, to ensure data validity. These programs are written according to the logic condition mentioned in the DVP. These edit check programs are initially tested with dummy data containing discrepancies. Discrepancy is defined as a data point that fails to pass a validation check. Discrepancy may be due to in consistent data, missing data, range checks, and deviations from the protocol.

In eCRF based studies, data validation process will be run frequently for identifying discrepancies. These discrepancies will be resolved by investigators after logging into the system. Ongoing quality control of data processing is undertaken at regular intervals during the course of CDM. For example, if the inclusion criteria specify that the age of the patient should be between 18 and 65 years (both inclusive), an edit program will be written for two conditions viz. age 18 and >65.

If for any patient, the condition becomes TRUE, a discrepancy will be generated. These discrepancies will be highlighted in the system and Data Clarification Forms (DCFs) can be generated. DCFs are documents containing queries pertaining to the discrepancies identified.

G. Discrepancy management

This is also called query resolution. Discrepancy management includes reviewing discrepancies, investigating the reason, and resolving them with documentary proof or declaring them as irresolvable. Discrepancy management helps in cleaning the data and gathers enough evidence for the deviations observed in data.

Almost all CDMS have a discrepancy database where all discrepancies will be recorded and stored with audit trail. Based on the types identified, discrepancies are either flagged to the investigator for clarification or closed in house by Self EvidentCorrections (SEC) without sending DCF to the site.

The most common SECs are obvious spelling errors. For discrepancies that require clarifications from the investigator, DCFs will be sent to the site. The CDM tools help in the creation and printing of DCFs. Investigators will write the resolutionor explain the circumstances that led to the discrepancy in data. When a resolution is provided by the investigator, the same will be updated in the database. In case of eCRFs, the investigator can access the discrepancies flagged to him and will be able to provide the resolutions online.

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H. Medical coding

Medical coding helps in identifying and properly classifying the medical terminologies associated with the clinical trial. For classification of events, medical dictionaries available online are used. Technically, this activity needs the knowledge of medical understanding of disease entities, drugs used, and a basic knowledge of the pathological processes involved. Functionally, it also requires knowledge about the structure of electronic medical dictionaries and the hierarchy of classifications available in them. Adverse events occurring during the study, prior to and concomitantly administered medications and prior coexisting illnesses are coded using the available medical

dictionaries. Commonly, Medical Dictionary for Regulatory Activities (MedDRA) is used for the coding of adverse events as well as other illnesses and World Health Organization–Drug Dictionary Enhanced (WHODDE) is used for coding the medications. These dictionaries contain the respective classifications of adverse events and drugs in proper classes. Other dictionaries are also available foruse in data management (eg. WHO-ART)is a dictionary that deals with adverse reactions terminology). Some pharmaceutical companies utilize customized dictionaries to suit their needs and meet their standard operating procedure. Medical coding helps in classifying reported medical terms on the CRF to standard dictionary terms in order to achieve data consistency and avoid unnecessary duplication. For example, the investigators may use different terms for the same adverse event, but it is important to code all of them to a single standard code and maintain uniformity in the process. The right coding and classification of adverse events and medication is crucial as an incorrect coding may lead to masking of safety issues or highlight the wrong safety concerns related to the drug.

WHY YOU CLINICAL DATA MANAGEMENT SOFTWARE DEVELOPMENT ENTER:-

Data accuracy and integrity

efficient data collection and entry

enhanced data monitoring and review # streamlined data analysis and reporting# improved regulatory compliance

cost and time saving

FEATURES TO ADD FOR CLINICAL DATA MANAGEMENT SOFTWARE DEVELOPMENT:-

customisable data entry form# role based access controls

data validation rules

automated data cleaning algorithms# query management system

electronic signature capabilities# data export and reporting tools

integration with electronic health record system# real time data monitoring and alerts

audit trail and version control

TRENDS TO INCLUDE TO YOUR CLINICAL DATA MANAGEMENT SOFTWAREDEVELOPMENT:-

cloud based infrastructure# mobile compatibility

predictive analytics and data insights# interoperability and data integration

artificial intelligence and machine learning# real time data monitoring and reporting

block chain technology

ALL ABOUT CLINICAL DATA MANAGEMENT SOFTWARE:-

Clinical data management (CDM) software is smart, organized digital system that keep the track of all the important information gathered during medical research and patient care. It helps healthcare professionals collect, store and analyse data form clinical trials, patient records and research studiesin way that's easy to understand and use.

4. CONCLUSION

The need for medication development to be accelerated by pharmaceutical companies and for regulatory agencies to establish quality systems to guarantee the generation of high-quality data for accurate drug evaluation has resulted in the evolution of CDM. The CDM method and systems have benefited from technology advancements, which have produced encouraging results in terms of data generation speed and quality. Professionals in CDM should simultaneously guarantee that the standards for enhancing data quality are followed. CDM is essential for evaluating one or more interventions aimed at identifying or diagnosing a particular disease or condition. In the drug development process, the value report and data ensures the accurate drug evaluation and full fill the regulatory authorities' expectations for getting NDA approval from FDA. Due to the development of the information technology, data management assessment and evaluation became easy with quality data. Pharmaceutical companies and sponsor research are encouraging EDC tools for high-speed data generation and high-quality reports. Well-designed CRF offers the opportunity to minimize dataprocessing. EDC system is one of the best tools for clinical trial data collection

and data management. It enhances in monitoring and data management, saving time duration, minimal error and query rates, quick assessment, and reliable results. Professionals in CDM should simultaneously guarantee that the standards for enhancing data quality are followed. The establishment of guidelines to specify the processes to be followed and the data standards, as well as the standardisation of the data management process across businesses, would be the biggest regulatory difficulty. The planning and execution of data management systems in a dynamic operating environment where the quick pace of technological advancement outpaces the current infrastructure would present the biggest challenge from the industry's standpoint. Despite these, CDM is developing into a standard-based clinical research entity by balancing the demands placed on existing systems and their limitations with the demands of commercial and technology advancements

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