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Research article

STUDY OF INTERPRETATION, IMPLEMENTION AND STANDARDIZATION OF CDM PROCEDURES TO SUPPORT DATA OUTPUT AS PER INDIAN GCP REGULATIONS

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ABSTRACT

Clinical Data Management (CDM) plays a pivotal role in ensuring the integrity and regulatory compliance of vaccine trials within the pharmaceutical industry. This abstract presents findings from a survey conducted among 46 participants across 16 organizations in the Indian pharmaceutical sector, focusing on the needs and challenges of CDM specific to vaccine trials. The survey highlights widespread consensus among respondents regarding the complexity and resource limitations faced by in-house CDM units, with a majority advocating for streamlined guidelines to improve data quality and adherence to Indian Good Clinical Practice (GCP) standards. Key concerns identified include procedural heterogeneity across organizations, variability in software usage, and the perceived impact on regulatory compliance. The results underscore the industry's call for structured, systematic approaches to CDM that can support standardized data practices and facilitate regulatory adherence in vaccine development. Addressing these challenges is critical for enhancing the efficiency and reliability of vaccine trials in India's pharmaceutical landscape.

Key Words: - Clinical Data Management, Vaccine Trials, Regulatory Compliance, Indian Pharmaceutical Industry, Survey Results.

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INTRODUCTION

Clinical Data Management (CDM) plays a crucial role in the process of drug development and the outcomes of clinical trials, particularly in biomedical research involving human subjects. These trials are conducted under stringent ethical and regulatory frameworks to ensure the safety and efficacy of investigational products. The data collected from clinical trials serve as essential evidence to support scientific conclusions about the therapeutic or preventive benefits of new treatments. Effective CDM involves maintaining accurate, complete, and reliable databases where clinical information can be securely stored and analyzed. (Gupta S.K., *et al.*, 2007)

Poor management of clinical trial data can significantly impact the validity and reliability of study outcomes, despite substantial investments of time, resources, and effort. Compliance with global standards such as Good Clinical Practice (GCP) guidelines issued by the World Health Organization (WHO), Good Manufacturing Practice (GMP) for pharmaceuticals, and

specific regulations for biological products is essential to ensure the integrity and quality of clinical trial data.

In India, clinical trials are governed by stringent guidelines aimed at upholding ethical standards and scientific integrity. The Central Drugs Standard Control Organization (CDSCO) and the Indian Council of Medical Research (ICMR) provide comprehensive guidelines for the conduct of clinical trials on human subjects. (Decker, C., *et al.,* 2010) These guidelines encompass site management, operational procedures, ethical oversight, and pharmacovigilance to ensure patient safety and regulatory compliance.

Vaccine trials, in particular, are critical for evaluating immunogenicity, safety, and efficacy in healthy subjects, including pediatric populations. They require adherence to high standards of data integrity and regulatory compliance set forth by international bodies like the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and WHO. Compliance with these standards is mandatory for the successful licensing and approval of vaccines.

Given the complex and highly regulated nature of vaccine trials, the role of CDM is indispensable. It ensures that data generated from these trials are handled and processed in a manner that meets regulatory requirements, supports auditability, and facilitates timely decision-making in vaccine development. This study aims to interpret, implement, and standardize CDM procedures aligned with Indian GCP guidelines, thereby enhancing regulatory compliance and supporting efficient vaccine studies.

METHODOLOGY

Indian Pharmaceutical Industry Survey

A survey was conducted to glean in industry perspective of the needs and challenges of CDM practice in India. The survey indicates lack of industry wide common CDM data standard. The ECRIN data management centers survey was used as a reference for the questionnaire. Anonymous input was used and the names of respondents are not disclosed to maintain confidentiality. The 46 respondents, 28 in number having more than 5-year of clinical research experience, representing 16 companies having their offices in India (Ranbaxy Laboratories Ltd., Biological E limited, CliniRx Research Pvt. Ltd., PATH Clinical Research, Kinapse Clinical Research, Novo Nordisk, Parexel International, Cognizant Technology Solutions, INC Research, Quintiles, Apcer Pharma, Panacea Biotec Ltd, Glenmark Pharmaceuticals, Venus Remedies Limited, Theorem Clinical Research and Tata Consultancy Services), responded to the questionnaire. The survey data was considered together with verbal discussion with experts from the CDM field, including representatives of various cross-functional teams involved in CDM and related activities at Panacea Biotec Ltd. The survey was related only to CDM practice in general; it was not connected to a specific clinical trial. No ethical approval for the survey was required because no patient data were collected. (Bajpai N., *et al.,* 2013)

Inferences drawn from Indian GCP in the context of CDM

Compliance with GCP, an ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects, provides public assurance that the rights, safety and well-being of trial subjects are protected. In absence of any guidelines in Indian GCP, in general with respect to specific procedural steps to be adopted in the processing of a clinical trial data, and in specific CDM steps of vaccine as investigational product, inferences were drawn to define CDM procedural steps in the context of Indian GCP. Indian GCP demands that 'raw data processing' from clinical trial should be done in a manner so that the data is credible, reliable and accurate. Of particular note, it is discretion of individual organizations to make a choice of data management steps, based on the inferences drawn as per GCP, and how to conduct the CDM task for a particular intervention (therapeutic or prophylactic or diagnostic), sources of CDM procedural diversity necessitating CDM process standardization. Of further note, no internationally accepted and practiced unified guidelines are available in public domain for GCP related to CDM.

RESULTS AND DISCUSSION

Industry Survey

A survey was carried out to glean in the Indian Pharmaceutical industry CDM perspective (vaccine) of needs and challenges for effective CDM to meet requirements of Indian GCP and thereby regulatory compliance. The survey was responded by 46 participants with relevant CDM experience across 16 organizations. The survey results show that majority of the respondents recognize the need for a structured systematic CDM process in Indian GCP, and thereby ensuring common data standards and regulatory compliance. (Bajpai N., *et al.,* 2014) The survey findings also indicate that CDM practices and thereby regulatory compliance is constrained by both limited human and financial resources for a CDM unit in an Indian Pharmaceutical company.

Although the number of respondents is on the lower side, the data generated is informative considering that the response primarily originated from experienced professionals across the industry. (Bajpai N., *et al.,* 2015)

Figure: 1 Questionnaire: Survey of CDM practice in Indian Pharmaceutical Industry.

Question 1: 'Will you welcome guidelines similar to the following in Indian regulations for CDM (GCDMP by SCDM, CDASH/CDISC by SDTM, US FDA's: Computerized Systems Used in Clinical Trials (05/2007), Electronic Records Electronic Signatures - Part 11, Scope & Application (08/2003), General Principles of Software Validation (01/2002) etc.).'

Question 2: Heterogeneity of CDM procedures exists in India?

Question 3: Heterogeneity of software products for CDM exists in India?

Question 4: Heterogeneity of CDM process/procedures will lead to deficits in quality management?

Question 5: Heterogeneity of CDM procedures will lead to non-compliance to GCP?

Question 6: Existence of limited human and financial resources for CDM for Indian PharmaCompany?

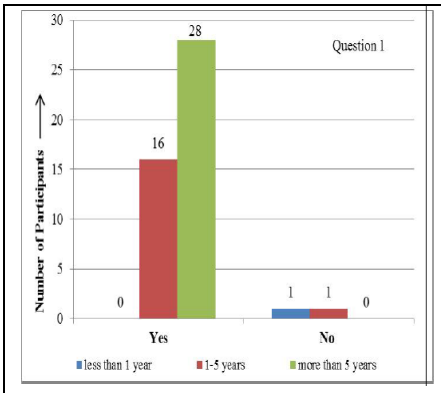
Question 7: In India, for various therapeutic segments, complexity of running an in-house CDM unitexists due to non-standardization of processes and lack of detailed CDM related regulations?

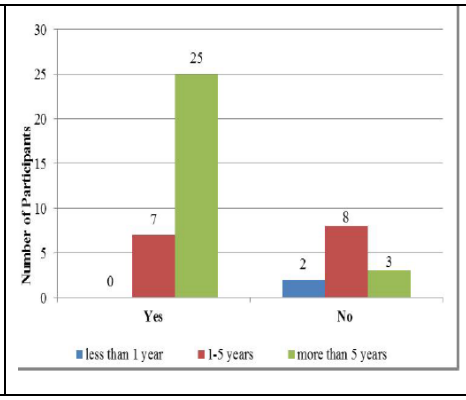
Question 8: In India, no specific, simple, practical, free and open standard explaining the stepwiseprocedures for CDM activities of vaccine trials exists, for GCP-compliance data management?

Question 9: Will you welcome guidelines stating step wise simple procedures for CDM activities fordrug and/or vaccine trials?

Question 10: Please state your total work experience in Clinical Research (CR Operation/CDM/PVG).

Figure 2: Survey Questions 1 to 3, Guidelines are required for common data standard and regulatory compliant CDM.





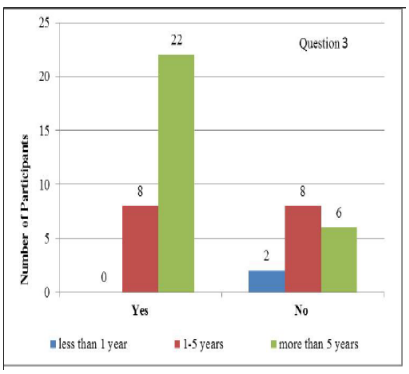
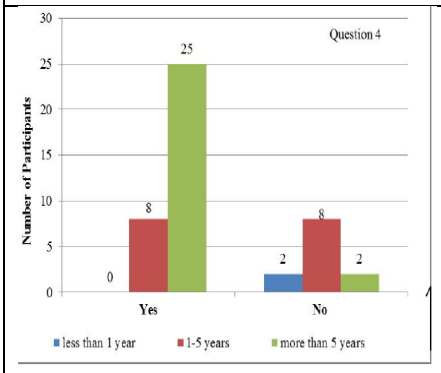
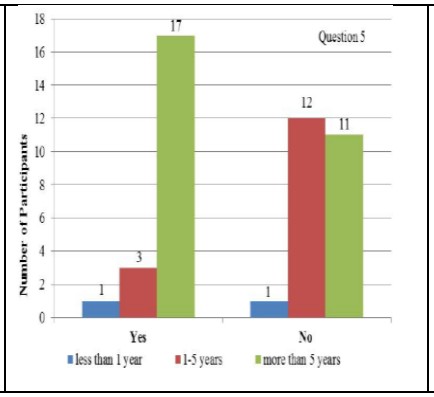


Figure 3: Survey Questions 4 to 6, Guidelines are required for common data standard and regulatory compliant CDM





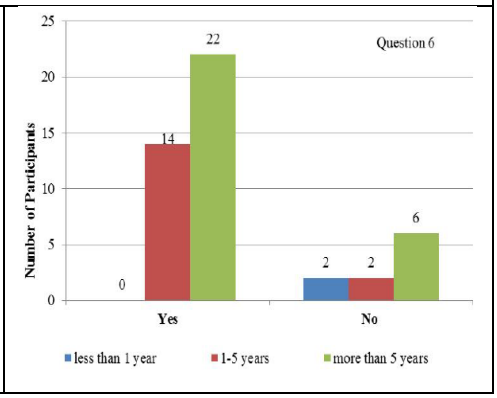
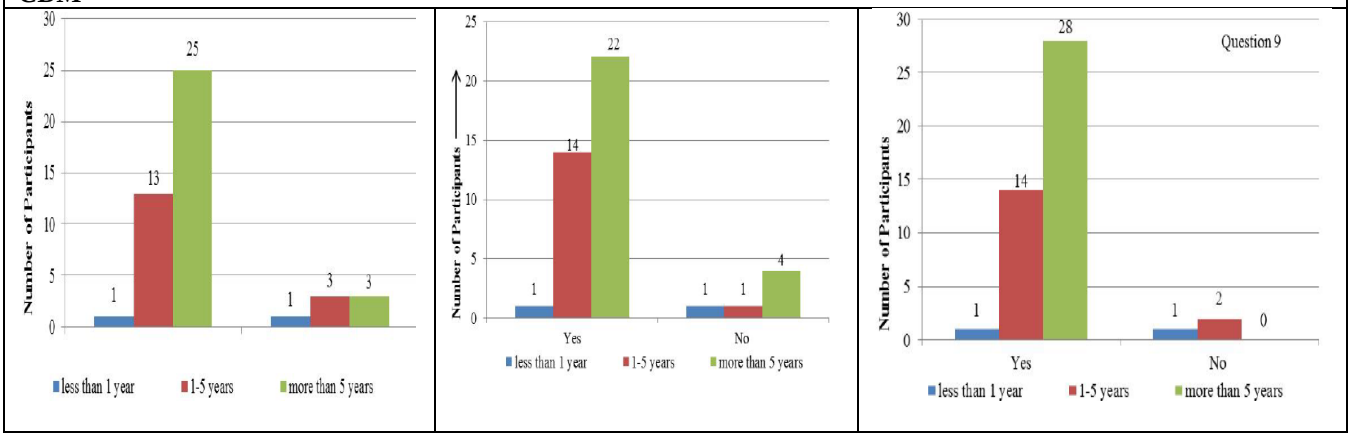


Figure: 4 Survey Questions 7 to 9, Guidelines are required for common data standard and regulatory compliant CDM



More than 95.65% (44 participants) responded 'Yes' indicating that there exist a gap in terms of CDM guidelines and regulations. It is reasonable to conclude that Indian industry expects elaborate guidelines for CDM (Figure 2). It can be seen that more than 71% (32 respondents) agreed that there exist variations in the procedural steps of CDM between various organizations, while 28.89% (13 participants) had marked 'No' (Figure 2). Notable, that maximum number of survey participants (25 in number) who had marked 'Yes' was from the group with work experience 'more than 5 years'. As per the response received from survey participants, 65.22% (30 in number) had the view that there exists variation in the use of software across industry, while 34.84 % (16 participants) had not supported the view. It can be noticed that the maximum number (08) of survey participants who had marked 'No' was from the group with work experience '1 -5 years' while maximum number of survey participants (22) who had marked 'Yes' was from the group with work experience 'more than 5 years'.

73.33% (33 participants) had agreed that there is the need for standardization of CDM procedures to avoid deficits in quality of trial data while 26.67% (12) had disagreed with the statement (Figure 3). The response received for this question is worthy of note. 53.33% (24 participants) had marked 'No' while 46.67% (21 participants) had responded as 'Yes'. A large number of respondents had not supported the fact that non-compliance to GCP will occur due to heterogeneity in CDM procedures. The hung response is an indication that in absence of any specific guidelines stating stepwise procedure for CDM, participants responded to GCP and CDM related tasks as standalone, rather interrelated activities. Due to absence of guidance to specific CDM steps, it was presumed that heterogeneity in CDM procedure will have no impact on GCP compliance. The response has reinforced that there exists a gap in terms of streamlined guidelines stating the stepwise procedures specific to the CDM based on therapeutic area or phase of the trial. It can be noticed that the maximum number of survey participants (17 in number) who had marked 'Yes' were from the group with work experience 'more than 5-year'. This shows participants with maximum experience group support that heterogeneity of CDM procedures will lead to noncompliance to GCP i.e. the requirement of credible, accurate and statistically sound data cannot be met if procedural heterogeneity pervades in CDM. More than 78% (36 participants) had agreed that there exist limited human and financial resources for CDM unit in an Indian Pharmaceutical company.

Due to non-standardization of CDM processes, 84.78% (39 participants) had agreed that for various therapeutic segments it is a tedious and complex task to run an in-house CDM unit. A majority, 86.05% (37 participants), had agreed with the question's statement. When asked from the respondents will they like to have simple recommendations/guidelines with respects to CDM of vaccine trials, more than 93.48 % (43 participants) had responded in positive. 58.70% (27 of the survey participants) had the relevant experience of more than 5 years in the area of clinical research. While, 36.96% (17 in number) was from the group with an experience of '1 -5 years' and 4.35% (2 in number) had the experience of less than 1 year.

Implementation of CDM procedural steps:

CDM Model for MyfiveTM vaccine study was developed considering industry best practices tied with the expectations from regulatory authorities and organizational objectives. The multi-facet mandate of high quality data output, cost effectiveness, and less processing time to reduce the development cycle was primary schema for the interpretation and implement CDM procedural steps within the bracket of Indian GCP guidelines. CDM model was created in OC, one of the leading IT platforms at the time study was initiated, and newer SOPs were developed and existing SOPs were

revised, if needed to address trial conduct business and regulatory demands. Strict compliance was ensured throughout the procedural implementation with relevant internal QCs. All the steps were validated by QA auditors from an independent department, so that the data obtained was not only error-free and statistically analyzable but also legitimate. The procedures implemented were found satisfactory within the scope of QA audit agenda Indian GCP guidelines had left it to the purview of organization to adopt procedures so that the data obtained is reliable, credible and accurate through validated procedures. Thus the study was conducted and data was generated, recorded and reported as per the study protocol, SOPs (updated or developed based on in-house CDM model), and GCP. Hence data recording, data storage, data transfer and data conversion was possible while maintaining full authenticity and integrity of the study database.

CONCLUSION

The survey conducted within the Indian Pharmaceutical industry highlights significant challenges and needs regarding Clinical Data Management (CDM) for vaccine trials. The findings underscore a consensus among participants regarding the complexity and resource constraints associated with in-house CDM units. A clear majority expressed a desire for simplified guidelines to streamline CDM processes, enhance data quality, and ensure regulatory compliance under Indian Good Clinical Practice (GCP) standards. The survey also reveals concerns about procedural variations across organizations, especially regarding software usage and standardization of CDM practices. There is a recognized gap in structured guidelines specific to CDM, reflecting a need for cohesive frameworks that can support consistent data standards and mitigate risks of non-compliance.

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