WHITE PAPER

Ensuring Compliance with Drug Accountability with IRT

Lack of accurate accountability logs at the end of a clinical study can set off letters of warning from regulators. Non-conforming sites might face delays or even their trial data might be disregarded and not accepted. The entire product approval process might get delayed due to a lengthy trial completion process. I can say from my past experience, where a crucial trial was held back from completion because of some major inconsistencies between the accountability records on-site and data received for final settlement and destruction by the sponsor's preferred vendor. Moreover, non-compliance with regulatory guidelines might have a severe impact on patient safety. Accountability regulations are intended to ensure that patients received the right dose of the right drug and that investigational drug has been consumed only by trial participants2. Furthermore, accountability can be used to assess a patient's compliance during the trial, and to explain unexpected poor efficacy or side-effects observed for specific patients if their actual dosing varied from that specified in the protocol. Missing information creates hindrance in determining the issues with the results of clinical trials.

The clinical investigator remains accountable for all the happenings at the clinical site. Advanced technology allows IRT systems in maintaining consistency, accountability, and easier tracking, a surprising number of studies still rely on paper-based accountability logs. Also, not all studies employ IRT systems – how can we identify potential discrepancies in these cases, allowing us to start work earlier on resolving potential issues? As the industry moves to a more risk-based, centralized approach to site management with fewer monitor visits this issue is likely to grow in importance.

According to 21 CFR 312.57(a), "a sponsor shall maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug. These records are required to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each such shipment" (2). Additionally, 21 CFR 312.62(a) states, "An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for the disposition of the unused supplies of the drug under 312.59" (3).

Although there is a need to ensure that the entire process of drug approval is compliant and accountable but still there is no definite benchmark to decide on the adequacy. Regulations never make it mandatory to follow a particular method. Still, managerial procedures with investigational product (IP) like management of temperature excursion, the release of an IP or updating date of expiry, drug accountability is necessary to ensure the success of the trial.

To portray accountability of an IMP/IP (Investigational Medicinal Product) it needs to be traceable right from the preliminary release, ordering, allotment, and exemption by returning to the site, reconciling and ending with destruction. If these areas lack accountability then the results of the trials have the risk of being faulty.

Challenges of Paper-based Drug Accountability Management

Paper-based drug accountability systems are inherently complex, making them prone to potential errors and obfuscation. The process begins upon receipt of the investigational drug at the site with staff verifying that shipment records match the contents of the shipping container. With the completion of the verification process, the person in authority needs to put his signature with date and maintain the shipping record in a folder with other regulatory data. He then needs to keep the investigational drug securely abiding the protocol. A staff member must enter shipment information into the drug accountability log. When the trial commences, detailed drug dispensing records must be written and updated across multiple documents promptly.

The drug accountability paperwork does not end at study termination. When the trial is complete, accountability logs must be updated, and discrepancies reconciled. Copies of accountability logs need to be made and returned along with the original drug shipment record; copies are filed on-site, as well. Reconciled log must be included in the shipping container with the returned investigational drug and shipped back to the sponsor.

Drug accountability with IRT

The use of electronic applications for collection and tracking of accountability data may provide considerable benefits over paper records. One prime benefit is when the trial data is centralized; it enhances the visibility as the custody remains with a single accountable system, thus improving the reporting process. In this method achieving regulatory compliance becomes easier and the audit reports related to accountability get easily mitigated. This enables the preparation of end-of-study documents at a faster pace from a single source.

Accountability process and documentation--Typically, the accountability process and documentation involves the following steps:

- Return of dispensed IP to the site (this includes the IP's that have been partially or completely used by the patient and were not administered by any clinician present on-site).
- Accountability of IP carried out by the site and confirmation of returned, lost, or damaged product
- IP reconciliation conducted by the supervisor through the verification of the product held accountable
- On-site destruction or returning the IP to the original facility for final destruction.

The Future

With the advent of several data sources, integration between the different systems involved in the clinical supply chain will give sponsors and regulators increasing visibility of how an investigational drug was produced, stored, shipped, dispensed, consumed and ultimately disposed of. Technologies to address this need should be leveraged that could help companies to further enhance supply chain accountability for both traditional and new-age / complex therapies.

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