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Short Communication

Maintaining electronic regulatory binder at clinical trials site improves efficiency

Hemlata Sukhija[1]*, Deepika Khanna[2]

[1]City of Hope Comprehensive Cancer Center, Duarte, CA, USA
[2]PRA Health Sciences, Raleigh, NC, USA

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***Correspondence:**
Dr. Hemlata Sukhija,
E-mail: hrsukhija@gmail.com

ABSTRACT

Regulatory binder is one of the essential documents that is required to be maintained by all clinical sites throughout the conduct of clinical trials and post completion of clinical trials. Managing regulatory binders for multiple studies has been challenging due to large volume of documents that needs to be maintained in a paper form especially when the site has 150-200 open studies. To utilize electronic regulatory binders to replace paper based regulatory binders for improve efficiency while maintaining regulatory compliance. Use of document management system effectively allows sites to store regulatory binders electronically. Electronic regulatory binders provide a new way of managing tons of documents in a simplified fashion that helps in redefining the process, tracking documents, reducing physical storage requirements, retention, preparation for monitoring visits, and in prompt audits.

Keywords: Electronic regulatory binder, Clinical trials, Study binder, Investigator's study files

INTRODUCTION

Regulatory binder is also known as Investigator Binder, Study Binder, Administrative Binder, Regulatory Files, or Investigator's Study Files. Per the Federal and state regulations, institutional policy, and good clinical and research practices, investigators are required to maintain regulatory documents related to human subjects research. The regulatory binder is one of the first essential document reviewed by clinical trial auditors, monitors and FDA inspectors. Often it is known in the field of clinical trials that "if it is not documented then it is not done". Proper maintenance of these regulatory documents is required in order to comply with standards of Good Clinical Practice (GCP). In addition, having a standard operating procedure (SOP) is necessary in identifying the required essential documents and successful management of a clinical trials.

CHALLENGES IN MAINTAINING PAPER BASED REGULATORY BINDERS

According to the ICH GCP Guidelines, essential documents are to be maintained throughout the clinical trial and post completion of the clinical trial.[1] Since decades, all these documents have been filed in a paper based forms. As the scientific field progresses, the number of active clinical trials are also increasing, thus providing patients with more treatment options, however increasing the site's burden to effectively maintain large number of paper regulatory binders. It is often observed that a mid to large size research organizations have at least 150-200 active clinical trials especially only in the field of Hematology and oncology, since it is still the field with unmet needs. If the site maintains only paper based regulatory binders then the management and maintenance of these binders becomes challenging as maintenance of such binders is required for at least 2-3

years post marketing approval. However, it takes anywhere between 10-15 years for a new drug to pass from phase I to reach the marketing approval. This means if the site was involved right from Phase 1 of the drug approval process it will need the site to store the documents for those many years. In addition, document management, tracking becomes challenging with increasing staff turnovers, missing documents/ files, lack of storage space, ineffective document retrieval practices.

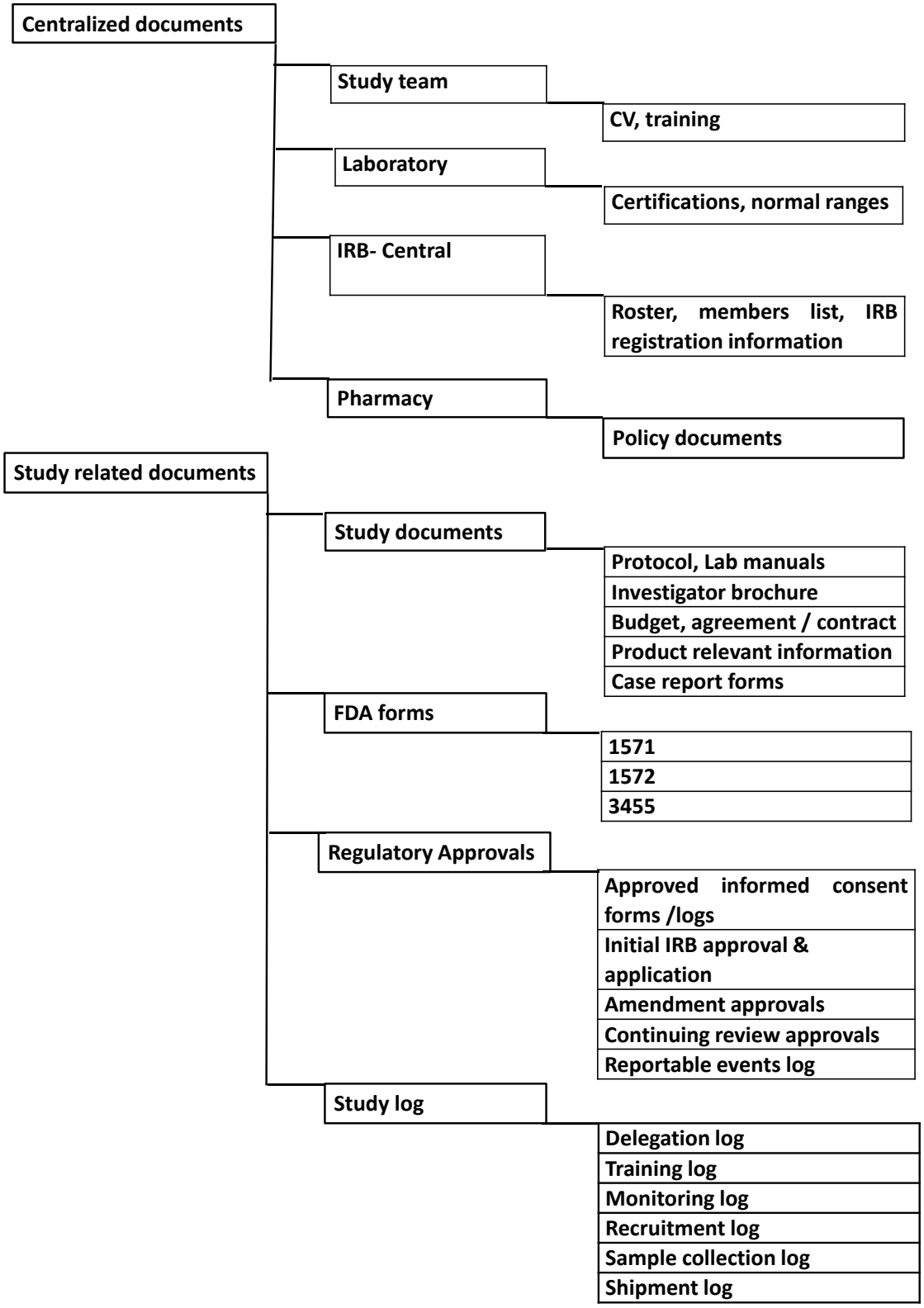

Figure 1: Electronic regulatory folder map.

SOLUTION

It is easier for sites to reduce paper burden and maintain electronic records by establishing a closed system.[3] Often creating an electronic system results in creating multiple spreadsheets, folders, variability in file names that becomes difficult to validate. It is extremely critical that there is a SOP for maintaining regulatory documents especially when there are multiple users. It is difficult for sites to purchase software for maintaining electronic regulatory binders because it requires constant updates, reliance on outside vendors for maintenance of confidential documents. Sometimes sites internal IT support team creates share drives that establish a closed system by providing accessibility to only relevant staff members. However, this system is effective only if a SOP is established and team members are trained on utilizing share drives as the only source to maintain regulatory documents, this will reduce file duplications and confusions in future. For efficient maintenance of electronic binders site needs to perform periodic audits of the electronic regulatory binder by the quality assurance personnel/ team.

Document management system (DMS) is utilized to track, manage and store documents efficiently in a form of electronic regulatory binder. A site can efficiently reduce the paper burden and still maintain compliance with essential documents if they systematically maintain electronic documents. DMS categories essential documents as centralized documents (utilized by all studies) and study specific documents. Frequently sites utilize same study personnel, laboratory services, Institutional review board (IRB) for multiple studies. Therefore keeping study personnel's cv/ biosketch, medical licenses, training (CITI, HIPAA, GCP, IATA, etc.), laboratory certifications (CAP, CLIA), IRB roster/membership List, Federalwide Assurance Confirmation, GCP Compliance Statement under central electronic folder is beneficial for all sites. In addition sites can maintain a centralized tool to oversee all study personnel's certificates validity and can create calendar invites for renewal of training thus remaining in compliance. Study specific documents are set of essential documents that varies from study to study. These include delegation logs, financial disclosure forms, 1571, 1572, study training log. Additional study specific documents includes study manuals, case report forms, protocol, amendments, summary of changes, investigational brochure (IB), Instructions for handling IP/Device, decoding procedures for blinded trials, shipments, drug/device accountability forms, plan for return or destruction of IP/Device safety monitoring plans, screening Log, enrollment log, pharmacodynamics log & reports, serious adverse event Log & Reports, investigational drug safety reports, enrollment Log, shipment Log. In addition, regulatory documents can also be stored electronically, especially if IRB manages documents electronically. This helps in maintaining, tracking and managing regulatory documents efficiently. These documents include approved informed consent forms (ICF) & ICF Log , Initial Institutional Review board (IRB) approval and application, amendment approvals & documentation of approved documents, continuing review approvals, final study report to IRB, certificate of confidentiality (including correspondence), reportable Events Log (DSMB Reports, protocol Violation/Deviation, SAEs, IND safety reports).[2]

Certain documents in clinical trials require maintenance of paper documents if the signatures are done on paper forms. For the purpose of maintenance of these documents, sites often utilize a hybrid system where they sign the paper forms and then scan and save these documents in the electronic regulatory folders. Documents stored in both paper and electronic forms includes delegation logs, financial disclosure forms, 1571, 1572, monitoring logs, protocol receipt and review document, IB review signature document. If the institution utilizes electronic signatures with time stamps, then these documents can be maintained electronically. Often these features are available in Adobe Acrobat pro software, subscribed by institutions.

Identifying the documents that are stored electronically or in form of paper does not completely resolves the problem, as even the electronic storage of documents can soon go out of hand. Therefore a SOP is required to create a structure that will allow all stakeholders to easily access the documents as and when required and to store documents systematically. This architecture can be easily prepared by preparing a prototype electronic regulatory folder with a map that allows the user to store documents in a respective folder as defined in Figure 1.

CONCLUSION

Electronic regulatory binders provide a new way of managing tons of documents in a simplified fashion that helps in redefining the process, tracking documents, reducing physical storage requirements, retention, preparation for monitoring visits, and in prompt audits. Having a defined SOP helps the site personnel to easily cross cover for teammates, switch teams internally if required during personnel turnover crisis thus reducing the re-training internal candidates for new teams within the clinical trials office. In addition, the amount of trial start-up time devoted to regulatory document management has been reduced, since all the documents prototypes are well defined. There is very narrow probability of misplacing a document or a file, since almost all documents are electronically maintained. If correctly implemented and standardized this is extremely beneficial to all clinical trials stakeholders as it efficiently reduces the burden across the study personnel, helps to stay organized, provide faster query turnaround time, keeps the site ready for prompt inspections and helps the study personnel to manage multiple studies simultaneously.

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