A Review and Recommendations for Implementing eRegulatory Investigator Site File Systems (eBinder, eISF)

Meghan Blair, MS, CIP , Christine Trani, PhD, CIP, Kathy Tang, Vincent Chan
Abramson Cancer Center (ACC) Clinical Research Unit (CRU)
University of Pennsylvania, Philadelphia, PA

Abstract

Investigators are required to maintain adequate and accurate source documents and records to support the validity/reproducibility of human subjects. These documents are collectively referred to as a 'regulatory binder' or 'investigator site file (ISF).' In a digital world, additional requirements are imposed to ensure the infrastructure managing electronic information is trustworthy, reliable, and generally equivalent to process execution in a paper environment [21CFR11]. The Abramson Cancer Center Clinical Research Unit, Office of Regulatory Affairs (ACC-CRU-ORA) has adopted an e-ISF infrastructure utilizing a commercially available cloud-based document management system.

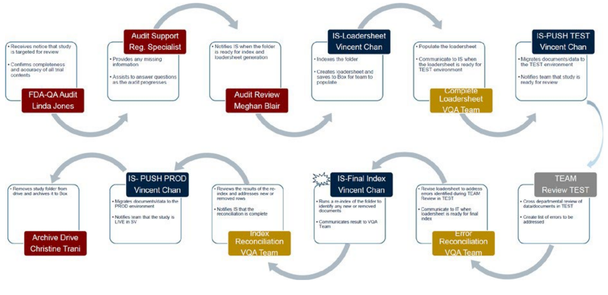
Introduction

This e-ISF contains the administrative regulatory documentation required by law and as associated with the conduct of human subject research. Beginning in 2019, the ACC-CRU-ORA initiated a program to migrate legacy documentation stored on the department shared server to the e-ISF cloud-based application. There was no best practice for how an e-ISF should be created nor maintained; our use of a share departmental drive introduced 21CFR11 vulnerabilities. Implementation of the cloud-based document management system fully addresses the 21CFR11 compliance concerns associated with the shared servers.

Methods

- Performed landscape analysis to make scoping decisions about what trials to migrate, which types of human subjects research to include, and expected timeline for completion.
- Allocated experts and resources in the fields of information systems (IS), institutional policy, and site related regulatory affairs.
- Developed best practices for site based electronic document management leveraging parallels from the TMF DIA reference model.
- Beta-tested team based portfolio migration to inform process and timeline (Figure 1).
- Orchestrated change management control and end-user training to enhance adoption.
- Projected portfolio migration roadmap (Figure 2).
- Consolidated person profile documents comprising credentials and qualifications into the cloud-based application (Figure 3).

Figure 1 Trial Migration Process Map



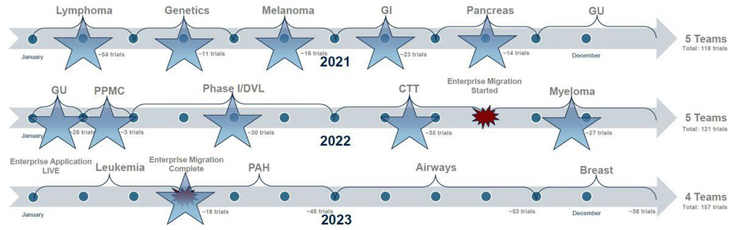
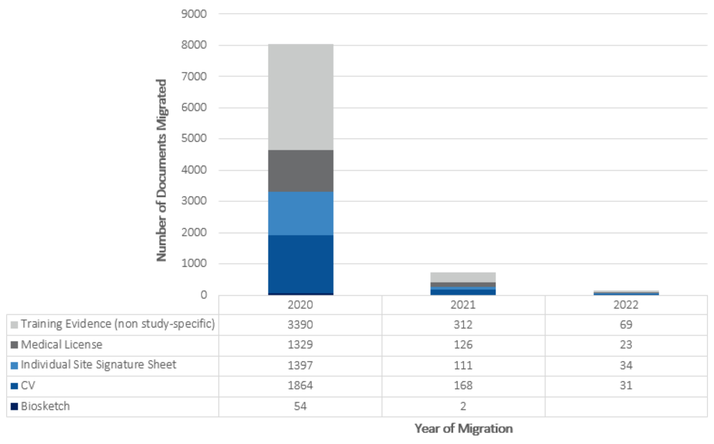


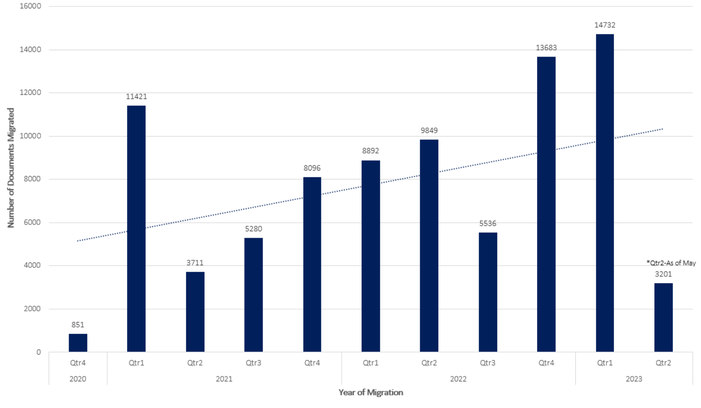
Figure 2: Trial Migration Roadmap:

Figure 3: Number of Migrated Credential Documents 2020-2022



	2020	2021	2022
Training Evidence (non study-specific)	3390	312	69
Medical License	1329	126	23
Individual Site Signature Sheet	1397	111	34
CV	1864	168	31
Biosketch	54	2	

Figure 4: Number of Documents Migrated Per Year



Results

- A central repository of 7000+ person credential and qualification documents was created and immediately leveraged in advance of team based migration events (Figure 3).
- Entirety of ACC-CRU-ORA portfolio will be migrated by end of CY2023 addressing 21CFR11 compliance vulnerabilities. Efficiencies and economies of scale were leveraged to increase number of migrated overtime (Figure 4).
- Implementation enhanced efficiency across both the site and exchanges with external collaborators and forced real-time health authority inspection readiness.
- Improved ability to assess and report out important key performance indicators about the research portfolio including: reports on product utilization, in-patient vs out-patient services, partner organizations, person profile documents, compliance with protocol specific training documentation requirements, time to and outstanding e-signatures documenting investigator oversight, and quality assurance measures for supervisor oversight.

Discussion / Future Directions

A clear vision including scope of documentation for migration and/or decision to begin with only new research projects is essential. Acquiring and implementing an e-ISF regulatory document management system requires a significant upfront investment and translates to increased economies with efficiencies over time, including forced health authority inspection readiness.

Sites must consider future utilization across departments/divisions and ensure unified acceptance of best practices while working within the system. Guard rails should be established for aligned quality control and quality systems management. Centralization of key resources for IS and institutional policy including infrastructure for supporting processes such as account creation and shared document management is essential. Efficiencies demonstrated are offset by the need for resources supporting change control, frontend data entry, and quality assurance maintenance.

Research team portfolios based in the e-ISF cloud-based application can be analyzed for volume and complexity which guides workload management and staffing allocations.

Acknowledgements

Linda Jones, Bethany Ryan, Corliss Moore, Sara Hayes, Adiyam Tikabo,
Arti Patel, Ralph Johnson
Special thanks to Research Team Regulatory Specialists, Program Managers,
and Clinical Team Faculty and Staff.

Penn Medicine | Abramson Cancer Center — Celebrating 50 Years