Facilitating Compliance with ICH GCP E6(R2)

How Complion helps clinical research sites meet new changes.

When the original ICH E6(R1) was released in 1996, clinical trials were performed in a paper environment. At the time, AOL was the largest Internet Service Provider and YouTube, Facebook and DVDs did not exist.

Over 20 years of technological advances have reshaped the way we work. The proliferate use of scanners, email, shared drives and specialized research systems points to the fact that clinical trial organizations no longer operate in a purely paper-based world. Sites are now operating in a 'hybrid environment' consisting of both paper and electronic processes.

Recognizing that adoption of technology offers "new opportunities to increase efficiency," ICH E6 guidelines have been revised to reflect two decades of technological changes. Among these changes, include updated standards regarding electronic records and essential documents.

Here's how Complion helps clinical research sites meet compliance with ICH GCP E6(R2).

Essential Document Location

Typically, sites store essential documents across many different systems and even locations. CVs, medical licenses, and protocols are often stored in a paper binder, as well as a shared drive. Furthermore, they are often duplicated across the site as copies are faxed, emailed, or uploaded to separate research systems for others to access.

> ***"The sponsor and investigator/institution should maintain a record of the location(s) of their respective essential documents. The storage system (irrespective of the media used) should provide for document identification, search and retrieval." -- 8.1***

Complion supports this by providing a central location to manage, access and archive essential documents pertaining to a trial, thereby eliminating the need to redundantly store, route and update essential documents. Furthermore, standardization and search capabilities facilitate efficient retrieval for site staff and auditors. Without a centralized system, sites will need to implement cumbersome tracking sheets and SOPs to meet this requirement, which only adds an additional layer of burden to staff.

Document Control & Ownership

Sites often rely on sponsor-provided systems, such as electronic Trial Master Files (eTMFs) or Investigator Site Files (ISFs) to store, manage and access site records.

> ***"The investigator/institution should have control of all essential documents and records generated by the investigator/institution before, during and after the trial." -- 8.1***
>
> ***"The sponsor should ensure that the investigator has control of and continuous access to the CRF data reported to the sponsor. The sponsor should not have exclusive control of those data." -- 8.1***

Here, the guidance indicates that sites should maintain control and have continuous access to essential documentation. Complion enables sites to retain control of their documentation by providing a site-owned system that allows for secure monitor access. This also streamlines monitoring by eliminating the need for a double upload into a portal. Sites maintain control of their documents, allowing monitors to view them in a "self-serve" manner with restricted, read-only access settings, thereby eliminating the need to email or redundantly upload documentation into a sponsor portal. Sites can also control the monitor's window of entry, enabling or restricting access for a period of time. Lastly, built-in archival further enables compliance and eliminates the need to send documents to storage upon study close-out.

Certified Copies

A paper or electronic copy of the original record that has been verified (e.g., by a dated signature) or has been generated through a validated process to produce an exact copy having all of the same attributes and information as the original. -- 1.11.1

In E6(R1), there's a clear reference to making a copy, and it's clearly a paper reference. The changes in E6(R2) identify how to verify a copy electronically through a 'validated process'. This is the next generation of a certified copy. If you can verify that the content is the same through a validated process, you have a certified copy.

A validated process simply means that sites need to have a process to ensure that each page has been reviewed and accounted for. Essentially, a systematic check must be performed to ensure that the scanned copy is an exact replica of the original paper document. If the certified copy is an essential document, additional controls must be in place.

Considerations for Storing an Electronic Copy:

- Any system for housing and managing certified copies must meet compliance with 21 CFR Part 11
- The system must be validated (to confirm that it does what it was designed to do)
- Adequate back-up or disaster recovery measures must be in place
- Training must be provided, and training should be documented
- Tracking should include the date, time and identification of any changes including initial save (or upload), approvals, views or downloads
- Tracking information should remain attached to the copy
- Each copy should also be assigned a unique ID and naming convention
- Access should also be considered, especially if the document contains financial or Personally Identifiable Information (PII)

Complion's 21 CFR Part 11 compliant eRegulatory solution supports all of the requirements to to properly control essential documents and certified copies. A certified copy process is supported with built-in audit trails and the ability to assign a unique ID and naming convention to each control copy. This provides a consistent way to search for documents and know what it is without opening the document or looking any further. Robust access controls enable sites to control who can see certified documents that contain PII or financial information that must be restricted. Lastly, our Customer Success teams partners with you to facilitate validation and training.

ALCOA & Audit Trails

> ***"Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry and should be explained if necessary (e.g. via an audit trail). -- 4.9.0***

While ALCOA (Attributable, Legible, Contemporaneous, Original, Accurate) has been a standard in the clinical research industry for a while, the ICH update has officially adopted it into its guidance. This update indicates that storage and archival systems must provide clear document identification, version history, reporting, and search and retrieval capabilities.

Many research sites currently rely on shared drives or electronic systems that don't offer this functionality - at least without considerable customization, maintenance or workarounds.

Complion ensures that every record, once filed to a binder, meets this requirement without additional cost or effort. Site staff can quickly file documents as work is completed, rather than waiting hours or days. Furthermore, Complion maintains an audit trails for every filed document, allowing sites and auditors to quickly identify when a document has been uploaded, changed, signed or reviewed, and by whom.

Documentation of Oversight

> ***"All clinical trial information should be recorded, handled, and stored in a way that allows it's accurate reporting, interpretation and verification [ADDED " This principle applies to all records referenced in this guideline, irrespective of the type of media used"] -- 2.10***

This addendum points to advances in technology as data is being collected and stored in a variety of sources. Emails, calls, texts and other records may be used to document oversight, and therefore may be subject to review. The ability to centrally store and manage records, in a way that facilitates accurate reporting and review, presents a challenge without a quality, purpose-build system.

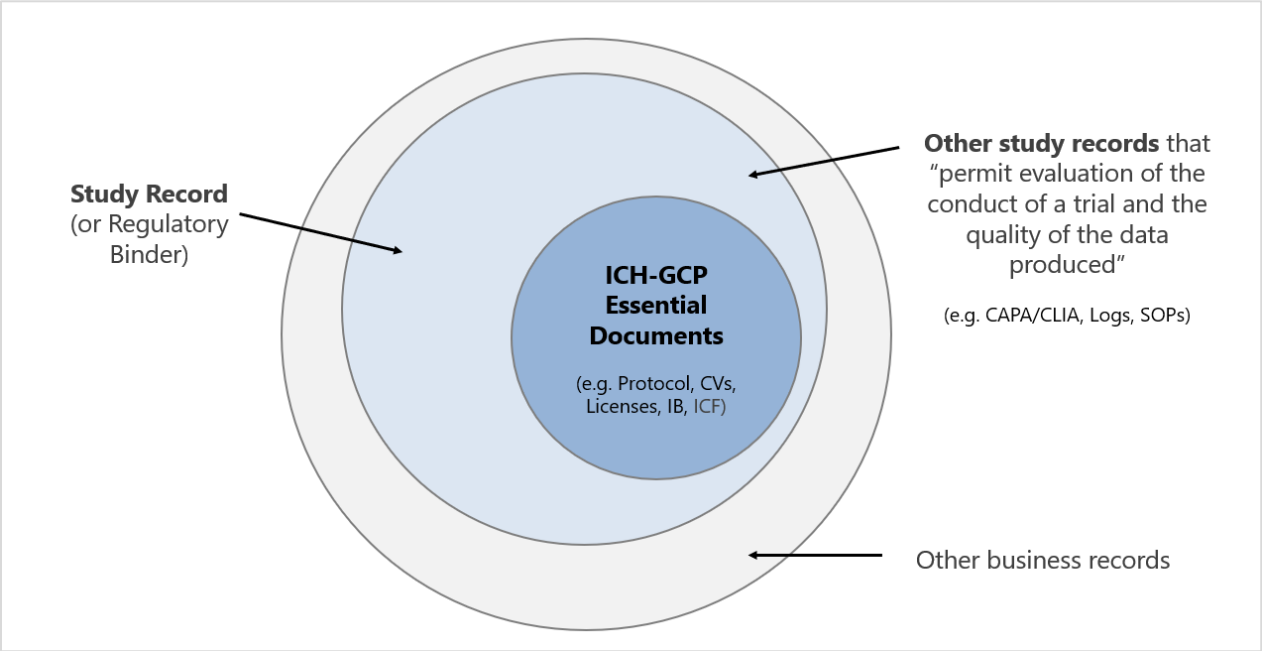
Not only does Complion provide a central location to store electronic documents, including certified copies, emails, and other records, but our unique filing process creates data on every document that can be used for reporting and insights for improved visibility and decision making. For example, sites can review all CVs set to expire in the next month or safety reports related to a specific drug or trial.

Additional Documents Provided to Sponsor

Around 50 types documents are listed by ICH GCP as "essential." However, when you take into consideration the additional documentation that sites create and maintain during the conduct of a trial, we've found the number to be much higher.

"Depending on the activities being carried out, individual trials may require additional documents not specifically mentioned in the essential document list. The sponsor and/or investigator/institution should include these as part of the trial master file." -- 8.1

By partnering with over 60 research sites, health systems, Academic Medical Centers and NCI designated cancer centers, Complion has identified 200+ different types of document that sites commonly store as part of their auditable record. These may include additional logs, checklists, policies and procedures, and signature pages.



Additional documentation should be managed and controlled in the same way as essential documents considerations taken for location tracking, monitor access, and audit trails. Complion enables sites to manage additional documentation that is pertinent to a trial in a highly controlled manner to ensure staff and auditors only have access to the documents they need.

Managing clinical trials in a digital world will be resource efficient, cost efficient, and will ultimately benefit sites and participants. Patients will be better managed and have a better experience when the documentation is available digitally and available sooner for an assessment.

The journey towards efficiency and standarddization in clinical trials may not be easy, but it is worthwhile. This is the way our industry and our landscape is moving, and it's better to be onboard rather than be surprised by it. A knowledgeable and experienced partner will take time to understand your processes and implement a solution that will grow with your organization. To learn more about Complion can support your research, call 800-615-9077 or visit www.complion.com.

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