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FDA U.S. FOOD & DRUG ADMINISTRATION

Quality and Control of Clinical Trial Data

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Data Integrity and Data Life Cycle in Data Management

- Data Capture (CRFs and Electronic Data Transfer)
- Investigator control of the data
- Management of investigator source and transcribed data including eSource worksheets & health records
- Validation of eSystems (e.g. eCRF)
- Management of data changes
- Prevention of unauthorised changes/deletion (database lock)
- Assessment of impact of non-compliance on data quality/reliability
- Traceability of data during analysis
- Data retention

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Learning Objectives

- Understand how application of GCP and data integrity principles apply to data management processes

- Identification of risks to compliance with increasing use of electronic systems in clinical trials

- How to avoid pitfalls - hear about some data management EMA/UK GCP inspection findings.

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1.11 Case Report Form

A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

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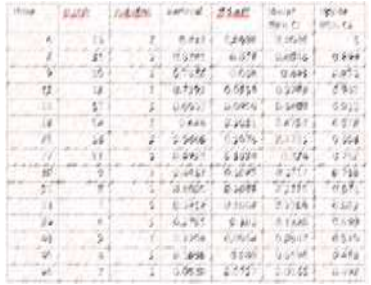
Data Base and eCRF

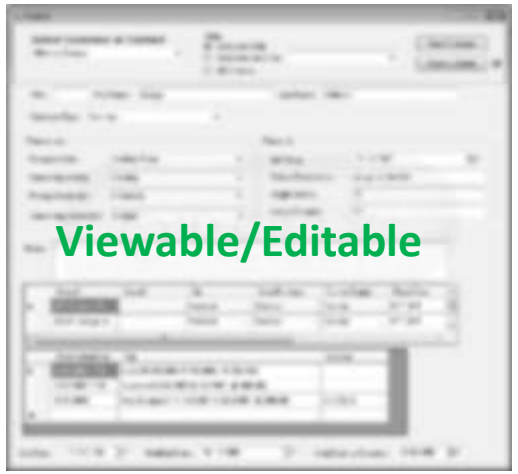
Relational Database

Paper Data Query Forms

Held in Database



Data Entry Screen – Human Interaction



Viewable/Editable

Manual Entry

Paper CRFs

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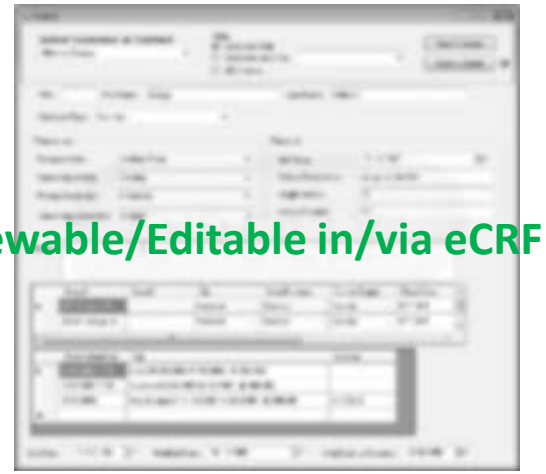
Data Base and eCRF

Relational Database

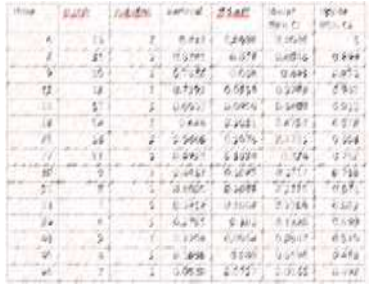
Paper Data Query Forms

eCRF Data Entry Screen – Human Interaction



Viewable/Editable in/via eCRF

Held in Database



Manual Entry

Source Data at Site

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4.1.5	The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
4.2.5	The investigator is responsible for supervising any individual or party to whom the investigator delegates study tasks conducted at the trial site.
4.9.3	Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections (see 5.18.4 (n)). Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
8.3.24	SIGNATURE SHEET To document signatures and initials of all persons authorised to make entries and/or corrections on CRFs

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Using Electronic Case Report Form

Sponsor use of an eCRF

- SAE processing
- Protocol and GCP Deviation Capture
- Data Management Workflow (queries/coding etc.)
- Central Monitoring (CRF completion rates etc.)

Use of Interactive Response Technology (IRT) to collect clinical data

- Stratified Randomisation (baseline medical history)
- Dosage calculations/titration (e.g. patient height/weight/BSA etc.)

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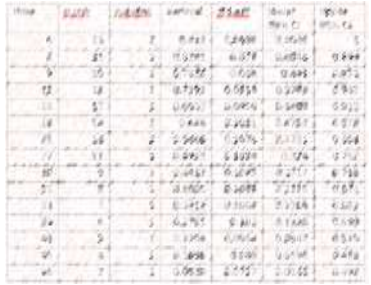
Data Base and eCRF

Relational Database

Audit Trail

Paper Data Query Forms

Held in Database



eCRF Data Entry Screen – Human Interaction

Viable/Editable in/via eCRF

Manual Entry

Source Data at Site

Entry/Viewable Restrictions by User Type

Sponsor entering data into eCRF?

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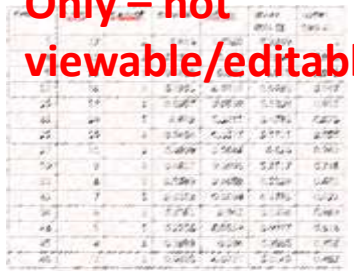
Database and eCRF

Relational Database

Held in Database Only – not viewable/editable

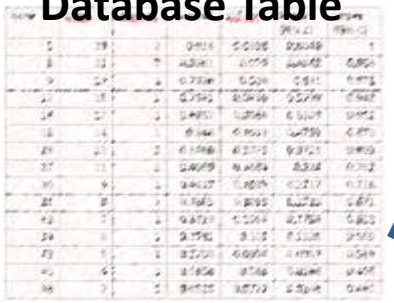


2

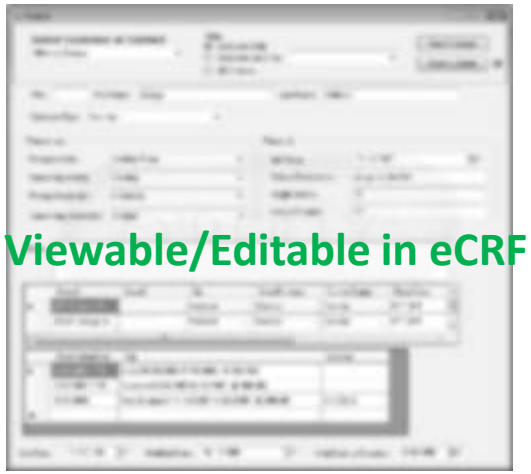
Electronic Transfer (e.g. lab data)

1

Database Table



eCRF Data Entry Screen – Human Interaction



Viewable/Editable in eCRF

Electronic Transfer (e.g. from IRT system integration)

IRT system is fulfilling role of CRF

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Transfers of Data

- Any transfer of electronic data into the database requires mapping of data fields and characteristics between original and transferred dataset – data transfer specification agreed between parties
- Electronic transfer methodology requires validation
- Hybrid paper/eCRF systems
- Data provided will form part of data validation checks (e.g. CRF says blood sample taken, imported data should have result – ID – Bar Codes)
- Data query processes with third parties should be documented to allow reconstruction

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Example Findings

- IRT acting as an eCRF – functionality for GCP compliance not addressed
- eCRF used by sponsor (edit rights etc.) not authorised by investigator
- Mapping errors – data fields in the database were numerical and alphanumerical data was being transferred resulting in errors.
- Data extraction tool selecting/pointing to the wrong dataset
- No documented validation of electronic transfer process.
- Failure to demonstrate QC or an audit trail (query detection and resolution) on non-CRF (third party) data (labs, ECG etc.).
- Laboratory values from local hospital laboratory in the D/B, but no fields for this data in CRF - no formal process or any reconstructable process for how data was transferred from site (sponsor had some pdf scans but not consistent with documentation at site).

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5.5.3

c) Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. maintain an audit trail, data trail, edit trail).

d) Maintain a security system that prevents unauthorized access to the data.

e) Maintain a list of the individuals who are authorized to make data changes (see 4.1.5 and 4.9.3).

6.4.9 The identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data

8.1 The investigator/institution should have control of all essential documents and records generated by the investigator/institution before, during and after the trial.

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.

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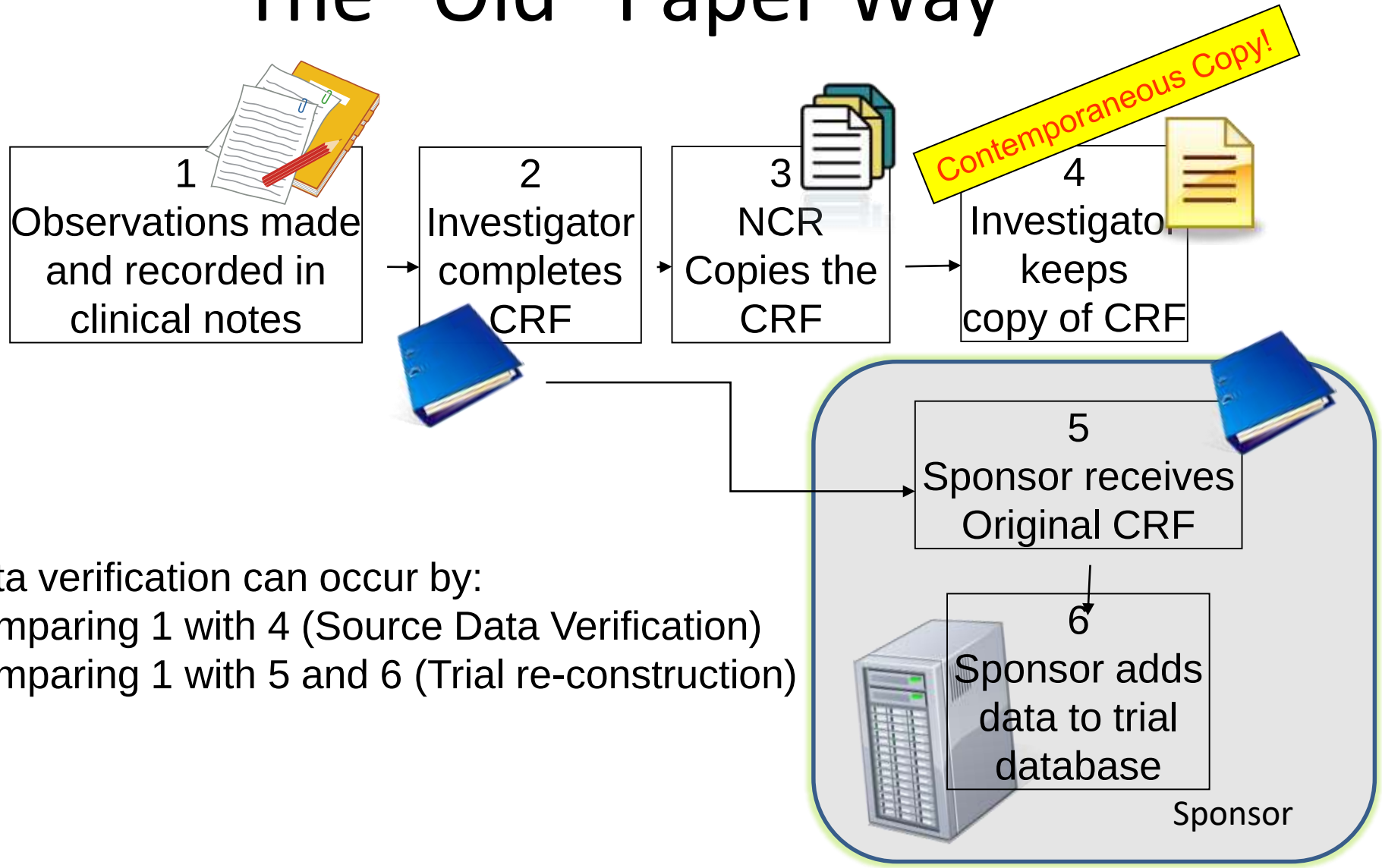
The "Old" Paper Way



Data verification can occur by:
Comparing 1 with 4 (Source Data Verification)
Comparing 1 with 5 and 6 (Trial re-construction)

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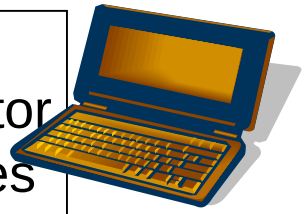
Electronic Capture of Transcribed Data

1
Observations made and recorded in clinical notes/work books

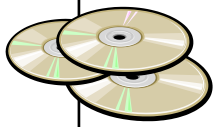
2
Investigator completes e-CRF



3
e-CRF data Storage

Sponsor

4
Sponsor copies data



5
Investigator given a copy of their data & access to eCRF by PI revoked

Non- Contemporaneous Copy!

Data verification can occur by: Comparing 1 with 3 and/or 5

Investigator lost control of transcribed data

DVD/CD could be replaced by access to portal?

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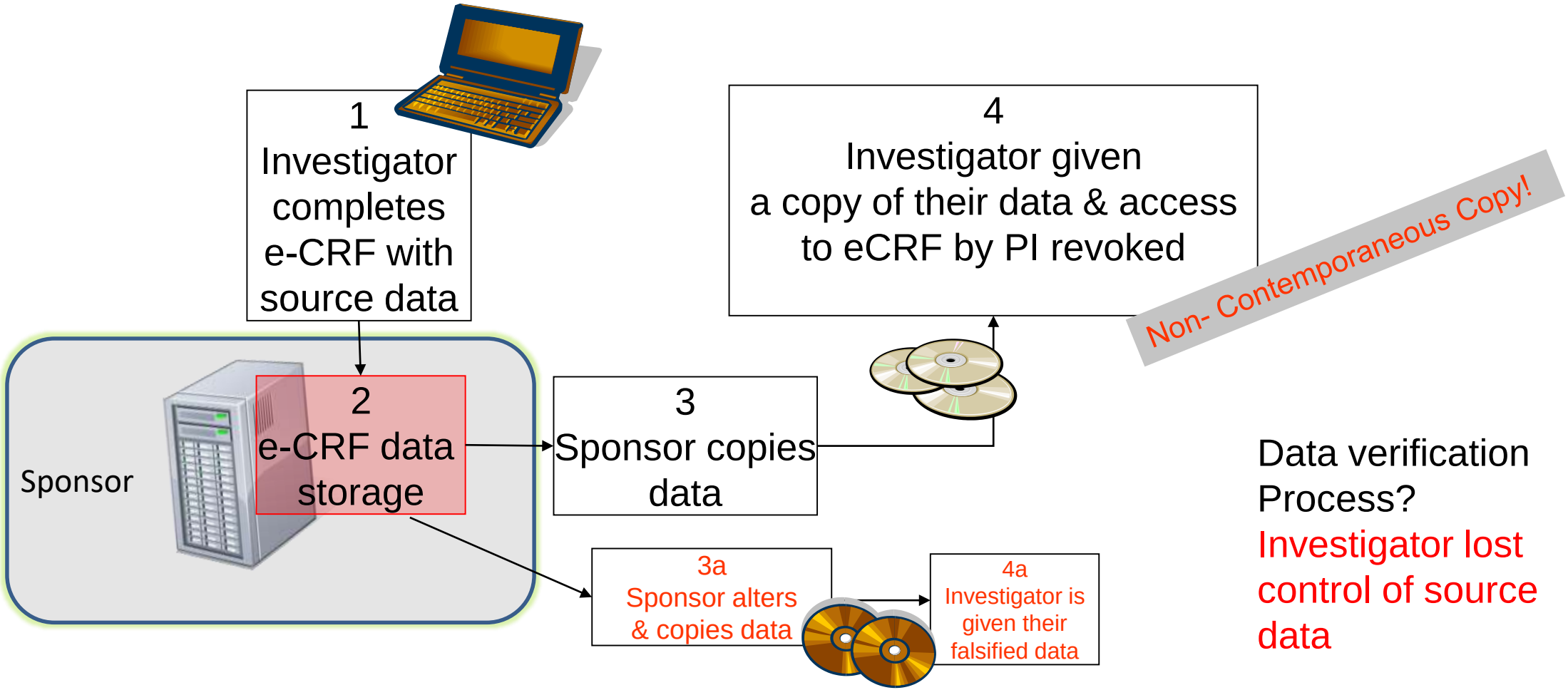
Electronic Capture of Source Data



Data verification Process?

Investigator lost control of source data

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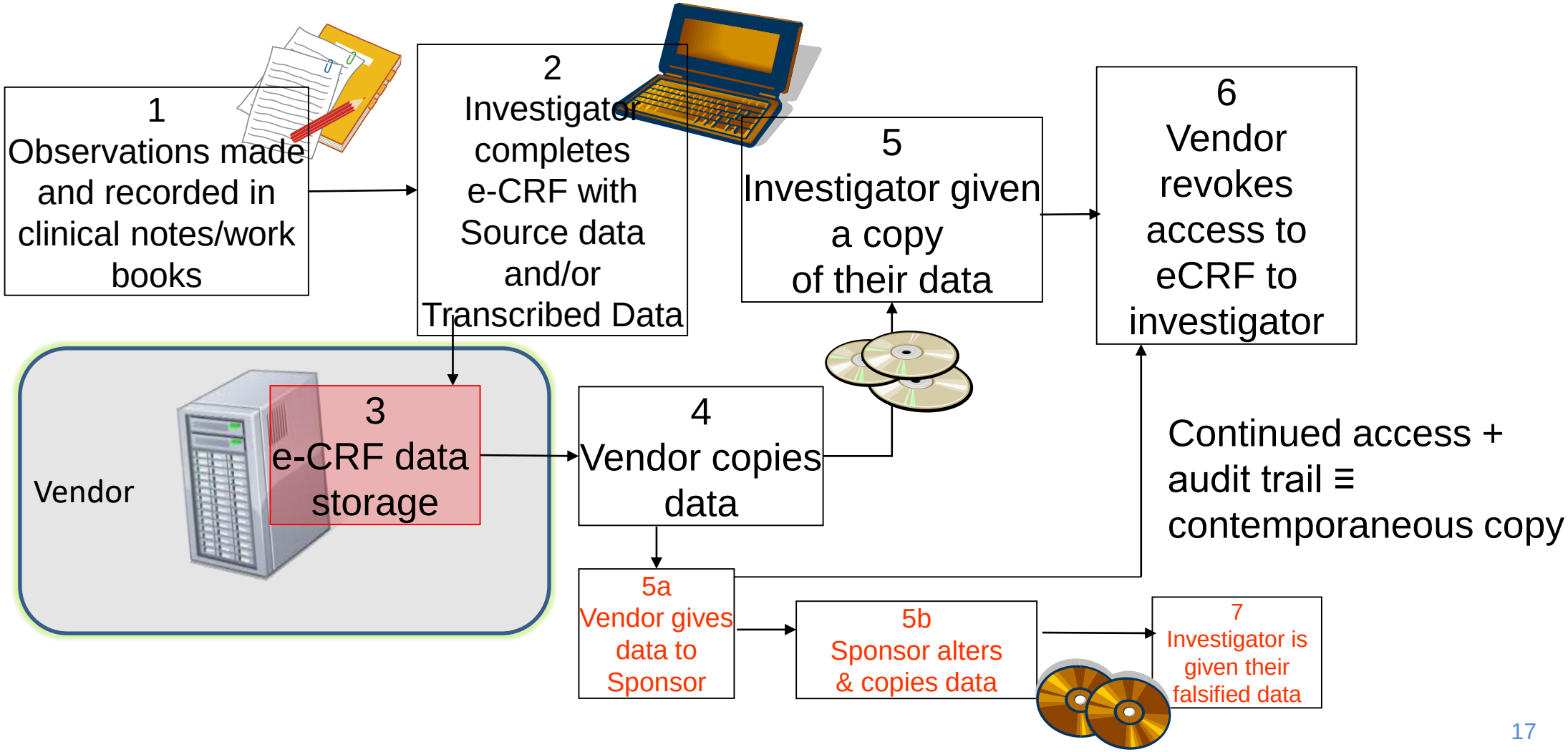
Electronic Capture of Data using eVendor



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Contemporaneous Copy of CRF

The eCRF system is often not designed to reflect paper process it is replacing

e-CRF data storage

Without contemporaneous copying at site, data storage should be **independent and outside of control of sponsor** (or a CRO full service?) i.e. a specific Vendor for eCRF/data storage

Sponsor alters & copies data

Detection and risk mitigation

- –Audit trails - robustness and review (system design)
- –Access and system owner controls
- –Back end change control established
- –Security on DVD copies

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Example Findings

- eCRF data returned to investigator via sponsor and/or Sponsor holds eCRF database
- Incomplete eCRF data returned to investigator site (lack of audit trails)
- Access to eCRF by investigator site staff revoked prior to provision of data on CD/DVD
- Investigator signs to confirm returned data is accurate, but has not undertaken or there is no evidence of a review
- Account Administrator rights to eCRF given to sponsor by eVendor to set up investigator site accounts (could easily set up account using an email address) – no oversight by investigator of who has access to eCRF

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Example Findings

Control of Data Changes

- Not always having Investigator authorisation of changes for site entered data (including pre-authorisation of self-evident corrections)
- Lack of controls to changes made to data by staff at eCRF vendor by back end (non audit trailed) and lack of investigator authorisation
- eCRF not signed by PI, signature does not invalidate if the data changes
- Sponsor staff have edit rights to all eCRF clinical data without investigator authorisation
- Sponsor can dictate user permissions, eCRF vendor accepts this, even if inappropriate (e.g. sponsor staff have edit rights)
- Lack of documentation of process for data changes to non-CRF data (queries to laboratories, ePRO vendors etc.)

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1.11.1	Certified Copy A paper of 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.
2.10	All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
2.11	The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

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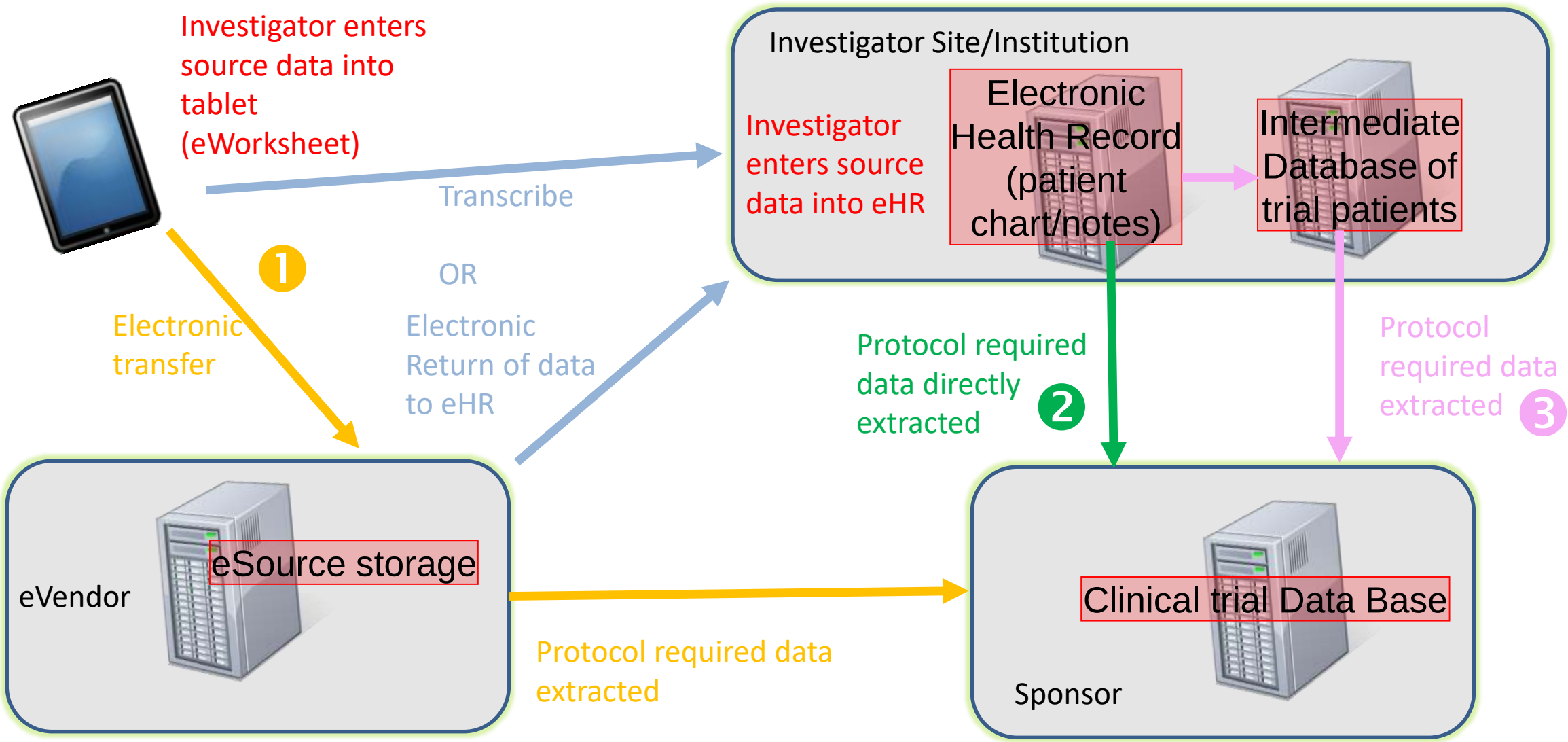
4.2.6	If the investigator/institution retains the service of any party to perform study tasks they should ensure this party is qualified to perform those study tasks and should implement procedures to ensure the integrity of the study tasks performed and any data generated.
4.9.0	The investigator should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. 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* and audit trail).
4.9.2	Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
8.1	When a copy is used to replace an original document, the copy should fulfil the requirements for certified copies.


Investigator enters source data into tablet (eWorksheet)
Transcribe
Investigator Site/Institution
Investigator enters source data into eHR
Electronic Health Record (patient chart/notes)
Intermediate Database of trial patients
1
OR
Electronic transfer
Electronic Return of data to eHR
Protocol required data directly extracted
2
Protocol required data extracted
3
eVendor
eSource storage
Protocol required data extracted
Clinical trial Data Base
Sponsor

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Key GCP Compliance Issues for consideration

- What constitutes the CRF?
- Method of source data verification – reliant on validation instead?
- Management of data changes to maintain data integrity and investigator control/authorisation
- Computer Systems Validation.

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Key GCP Compliance Issues for consideration

1

- What data is recorded in the eWorksheet (protocol specific vs. all for visit)
- Maintaining contemporaneous data in the eHR
- Ensuring copies of source documents in the eHR are certified copies
- The format of the eSource returned to the eHR.
- Can the data be placed in eHR or would an additional database be required (interim)
- Anonymisation of data at vendor being assigned to correct patient when returned to eHR.
- Access and control by the investigator of their source data during/after trial

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Key GCP Compliance Issues for consideration

❷ ❸

- Maintenance of subject confidentiality (extraction of anonymised data)
- Ensuring access to data for trial patients only
- Control of data extract format– can this be changed outside of the system?.
- Validation of system to manage the myriad of eHR systems
- Synchronisation frequency
- Management of changes required in eHR to capture appropriate data
- Sponsor remote access to eHR is strongly discouraged in EU MS

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5.18 Monitor's responsibilities

b) Verifying that the investigator has adequate qualifications and resources (see 4.1, 4.2, 5.6) and remain adequate throughout the trial period, that facilities, including laboratories, equipment, and staff, are adequate to safely and properly conduct the trial and remain adequate throughout the trial period.

k) Verifying that source documents and other trial records are accurate, complete, kept up-to-date and maintained.

m) Checking the accuracy and completeness of the CRF entries, source documents and other trial-related records against each other. The monitor specifically should verify that:

(i) The data required by the protocol are reported accurately on the CRFs and are consistent with the source documents

n) Informing the investigator of any CRF entry error, omission, or illegibility. The monitor should ensure that appropriate corrections, additions, or deletions are made, dated, explained (if necessary), and initialled by the investigator or by a member of the investigator's trial staff who is authorized to initial CRF changes for the investigator. This authorization should be documented.

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Data at the Investigator Site

Not just the monitor's responsibility

- eHR and source data – need to define the source documentation – recommend "Source Data Agreement"
- Data Management must be aware if the CRF contains source data and it should be stated in the protocol
- Management of data from vendors for ePRO, ECG etc.: - data and metadata should be at the investigator site
- Data query processes for ePRO etc. should be GCP compliant (subject involvement)

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Example Findings

- Failure to clearly specify source documentation
- Failure to verify all source (printouts from electronic notes not complete or inconsistent with eHR), monitor unaware of or no access to electronic source data, no QC of printouts to ensure certified copies
- eHR not available for direct access, eHR not been assessed for GCP compliance (e.g. no audit trail)
- Inconsistencies between source data and CRF, even where 100% SDV undertaken
- eCRF being used, unknowingly by sponsor, for source data (SAE reporting)

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Example Findings

- Entry/sign-off of eCRF pages by staff not delegated these activities by investigator
- eCRF Password sharing occurring at investigator site
- Sponsor required to “validate” changes made to subject’s eDIARY data requested by site or forbid any changes
- All data and meta data from third party vendor not at the site (e.g. printout reports present, but not audit trails from system & raw data)
- Failure to understand true source e.g. audio recording by transcribed by secretary into eHR and approval by physician, report/numeric data from scans uses, but images with measurements not reviewed/retained

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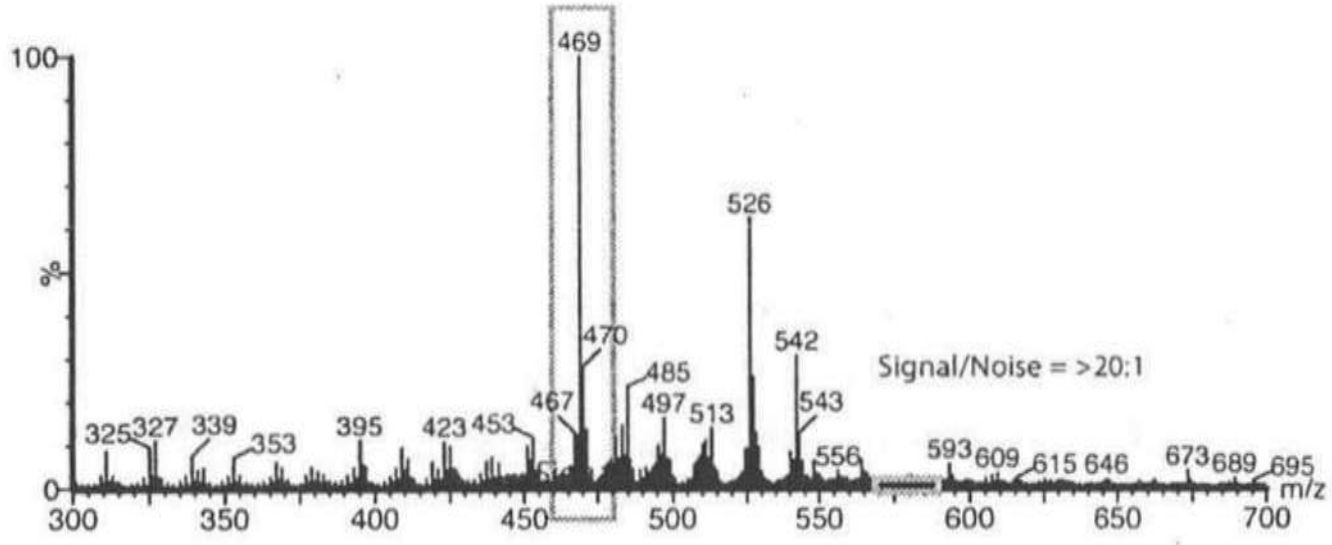
Verification of Clinical Trial Endpoint

Mass Spectrometry of Urine Bile Acids



The mass spectrum was evaluated to determine the level of abnormal bile acid metabolites and scores of 0 (normal), 1 (slight), 2 (significant) and 3 (marked) were assigned by the investigator and this outcome measure was the primary endpoint of the trial to assess efficacy.

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Verification of Clinical Trial Endpoint

- The qualitative methodology for assigning scores to the spectra had not been documented and validated to determine the variability, consistency and reproducibility of the interpretation of the output into the assigned scores prior to activity and not included in the marketing application dossier or as an appendix to the CSR

- The assignment of the scores to the urine spectra had not been done in a blinded manner. Possibility of bias.

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Verification of Clinical Trial Endpoint

Blindly graded selected spectra by the investigator (who had previously done this activity for the CRF) during the inspection resulted in numerous [60%] inconsistencies (*)

This suggests a high degree of variability within the efficacy data, it was not reproducible nor verifiable from source documents/data and their reliability was dubious.

Subject Number	Sample Number	Urine Bile Acid Score (Clinical Study Report)	Urine Bile Acid Score Blinded Assessment During Inspection
1	1311	2	1*
1	1190A	1	0*
1	773A	3	2*
9	3016	3	3
9	4662	2	2
9	2363	2	1*
9	2293	1	1
159	9963	3	0*
159	10091	1	2*
159	9154	2	2

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1.60.1 Validation of computerized systems

A process of establishing and documenting that the specified requirements of a computerized system can be consistently fulfilled. Validation should ensure accuracy, reliability and consistent intended performance, from design until decommissioning of the system or transition to a new system.

5.5.3 When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:

a) Ensure and document that the electronic data processing system(s) conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e. validation).

b) Maintains SOPs for using these systems.
The SOPs should cover system set up, installation and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data back up, recovery, contingency planning and decommissioning. The responsibilities of the sponsor, investigator and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in the use of the systems.

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Validation

- Records pertaining to the validation of the software are essential documents and sponsor access to these should be maintained (even if at an eCRF vendor)
- Various models of validation process are acceptable (waterfall, agile etc.)
- Validation records for **trial specific configuration must be available as part of the TMF**. Typical records include:

  - SOPs, Plans etc., completed quality records
  - eCRF specifications (annotated CRF, dynamic screen flows, on-entry and batch data validation etc.)
  - Testing (unit/UAT) documentation: scripts, annotated scripts/screen shots, test outcomes, re-tests etc
  - Communications/Meeting minutes from following processes
  - Reports to confirm completion of validation and acceptable release of system to production
  - Change control records, Help desk tickets/bug fixes etc.

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Example Findings

Documentation inadequate to demonstrate software or the trial specific eCRF was in a validated state

- Inability to link eCRF to version of protocol and version specification documents
- Lack of or incomplete evidence of testing (e.g. for edit check UAT)
- Lack of traceability (e.g. an edit check and its testing)
- Document version control issues
- Lack of contemporaneous records – cumulative logs only (e.g. Edit Checks Specification, Data/Base Tables Specification)
- Lack of detailed risk assessment
- No/Poor documentation to demonstrate move from test to production environments
- Key areas of functionality not tested – e.g. calculation of eligibility calculated scores
- **eCRF inconsistent with protocol requirements**

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Design Issue (consistency with protocol)

- Patients recorded pain/sleep scores in paper diary daily for 35 days as per protocol. Site staff entered into eCRF. eCRF had only sufficient fields to capture the diary pain/sleep scores for 34 days.

- Result: Day 35 data had not been entered into the eCRF. The mean of the last 7 diary pain scores was used in the efficacy primary endpoint analysis and there was potential that the results of the trial could be affected.

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Example Findings

- Release of eCRF: against a draft specification/ prior to approval (Installation into a production environment prior to confirmation of validated) / after trial start / incomplete eCRF or edit checks not released in a timely manner
- Deferring “critical” test failures for future release with no documented rationale
- User manuals not produced in timely manner

- No documentation of detailed data integrity risk assessment as part of change control
- No change control process or Change control record not completed in a timely manner or adequately (not documented the issue and resolution)
- Change control process not applied for all changes, change control and ticket backlogs
- Lack of awareness by the sponsor of bug fixes/updates
- **Amended eCRF not released in relation to protocol amendment approvals**

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Change Control - Protocol Amendment

Initial eCRF and amendments (change control) should only be released when protocol (amendment) upon which it is based has been approved by CA and REC/IRB in each country. **All eSystem vendors inspected by MHRA failed to have adequate controls in place**

(1) Release of an eCRF implements amendment that never gained approval
(2) Amendment implemented at site, but updated eCRF not released in timely manner

Impact – non-compliance with approved protocol or potential data integrity/patient safety issue

EXAMPLE: Protocol amendment changed age range for eligibility from 18-65 to 18-70 years old. eCRF requires age input and confirms eligibility met.

(1) New eCRF used, patient aged 67 recruited – ineligible with current approved protocol.
(2) Investigator uncertain what to enter into old eCRF, as 67 old is recorded as ineligible and eCRF completion cannot continue

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Example Findings

Contractual issues when using eSYSTEM (eCRF) vendor

- Vendor does not confirm that they will comply with regulations/GCP.
- Lack of due diligence (e.g. ensuring have approved protocols & amendments (Specification) to maintain compliance).
- Lack of detail on TMF arrangements (do they know they have part of the TMF – trial specific builds, software validation records assumed to be held etc.) and long term access to records
- Lack of detail on archival of data (and metadata) and re-commissioning in future if needed & timely manner (some say vendor will delete data, sponsor may not have all of it)
- Vendor does not assert to inform sponsor of non-compliance/errors/issues
- Location and security of cloud storage

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2.13 Systems with procedures that assure the quality of every aspect of the trial should be implemented.

5.0 Sponsors should focus on trial activities essential to ensuring human subject protection and the reliability of trial results. Quality management includes the efficient design of clinical trial protocols, data collection tools and procedures, and the collection of information that is essential to decision making.

5.0.1 During protocol development, the sponsor should identify those processes and data that are critical to assure human subject protection and the reliability of study results.

5.1 Quality Assurance and Quality Control

5.1.1 The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).

5.1.3 Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

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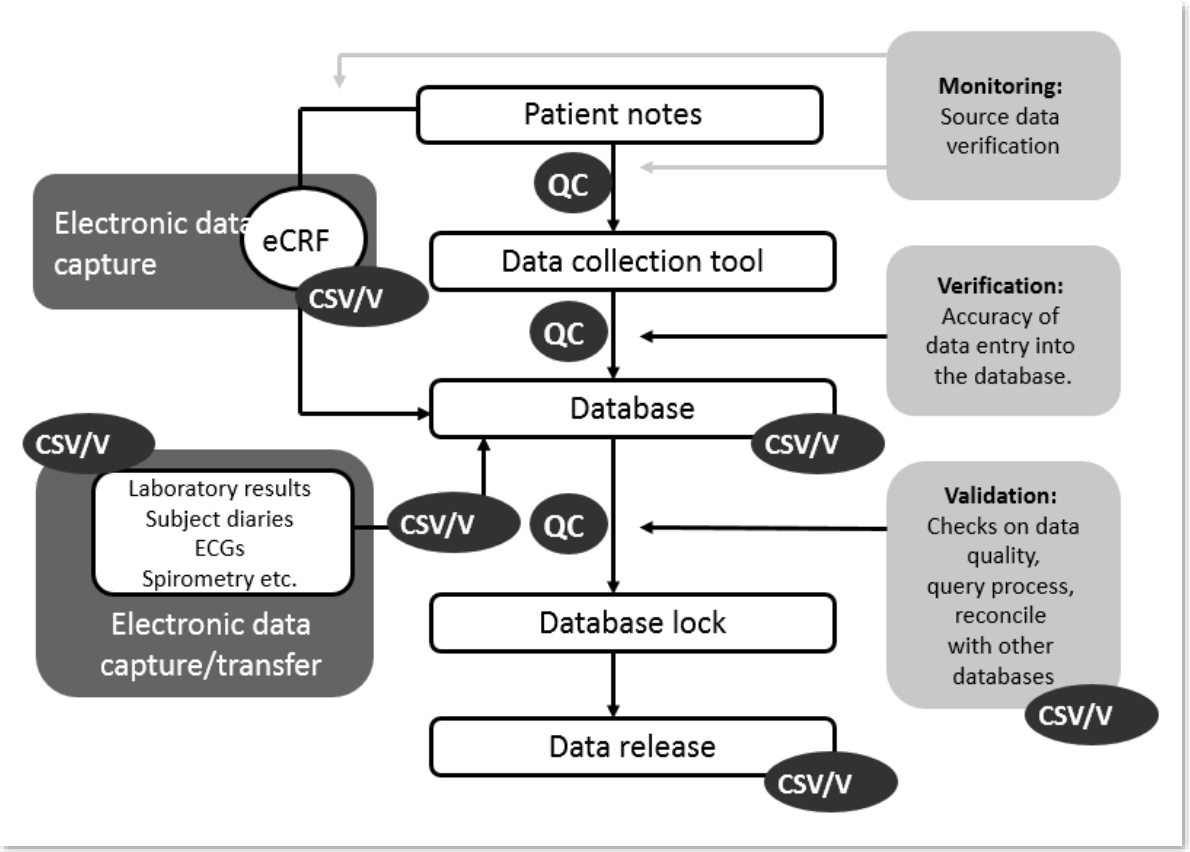

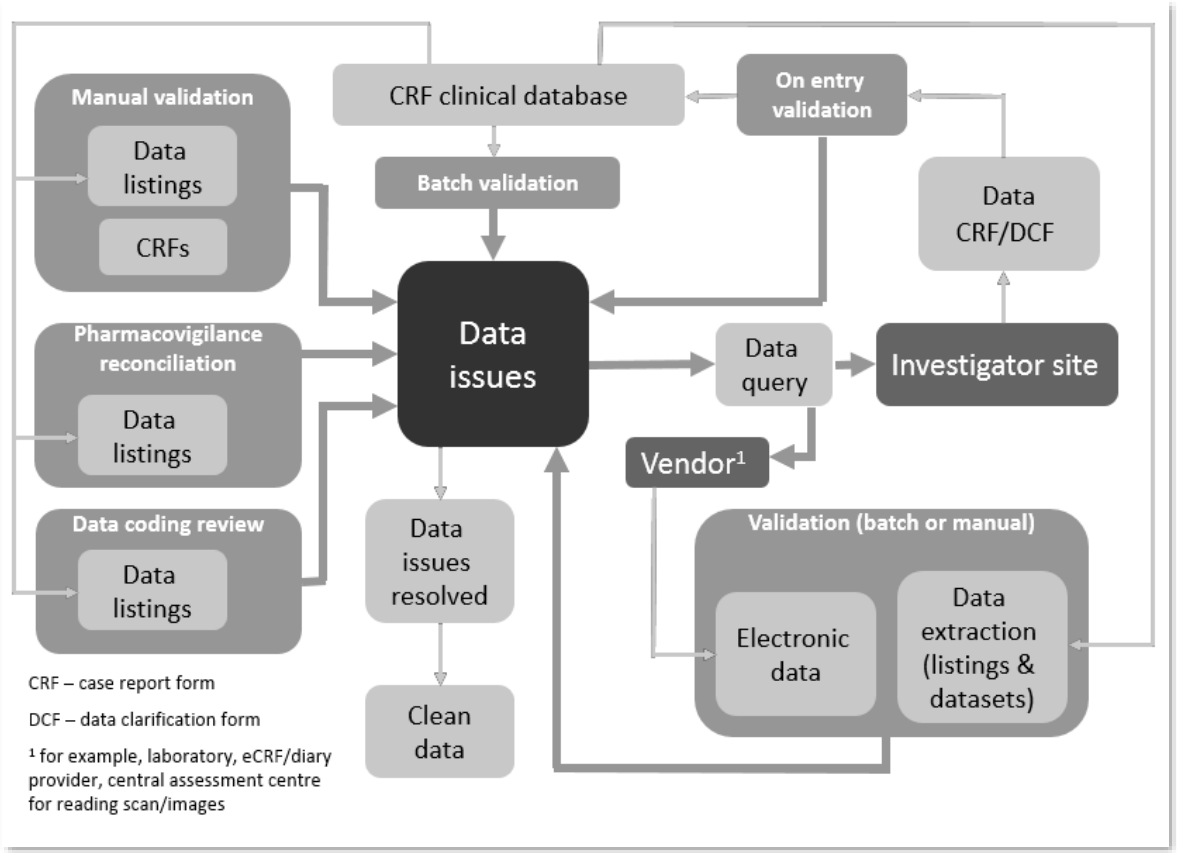

CSV/V Computer System Validation/Validation of configuration or programming

QC Quality Control process

From MHRA GCP Guide

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Database Quality

- The quality and accuracy of data extracts used for decision making must be appropriate to support the decision making, based in its importance/risk
  - Dose escalation decisions
  - Interim analysis (for regulatory submission and data monitoring committees, publications)
  - Final analysis (for same purposes)
  - Data review for other purposes may apply different quality level (e.g. ongoing adverse event review)
- Which data, how is quality level assessed and defined? - Pre-planned and adaptable – Risk Assessment, Monitoring Plan, Data Management Plan, Data Validation Plan, Protocol

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Data Cleaning

- Focus data validation of critical data rather than supplemental data using risk assessment to identify data that impacts on reliability of trial results
- Clinical operations input into review of data validation checks specification
- Escalation/expansion of cleaning activities if issues identified
- Compliance with risk/statistically based SDV risk based monitoring
- Documentation of manual medical coding and changes following medical review

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Lack of Data Validation

In a trial, the DAS28 (measure of disease activity in rheumatoid arthritis) score eligibility requirement of >5.1 had not been checked as part of data validation for the trial despite the fact that the CRF contained all the necessary data to calculate this.

A trial was examining the impact on the treatment plan of an IMP used in a scanning diagnostic procedure. The primary endpoint of the trial was whether there was a change in the post scan treatment plan compared to the pre-scan treatment plan. The trial was non-comparative and open label. There had been no check on whether there were any data changes in the eCRF to the pre-scan plan undertaken after the scan had been performed (i.e. bias by amending the initial plan). On examination approx. half the patients, the initial plan data had been entered into the eCRF after the scan and/or changes to the data had been made. It required checks that contemporaneous source documents at site supported the initial plan, but several circumstances arose where source was not available despite 100% SDV required as part of the monitoring plan.

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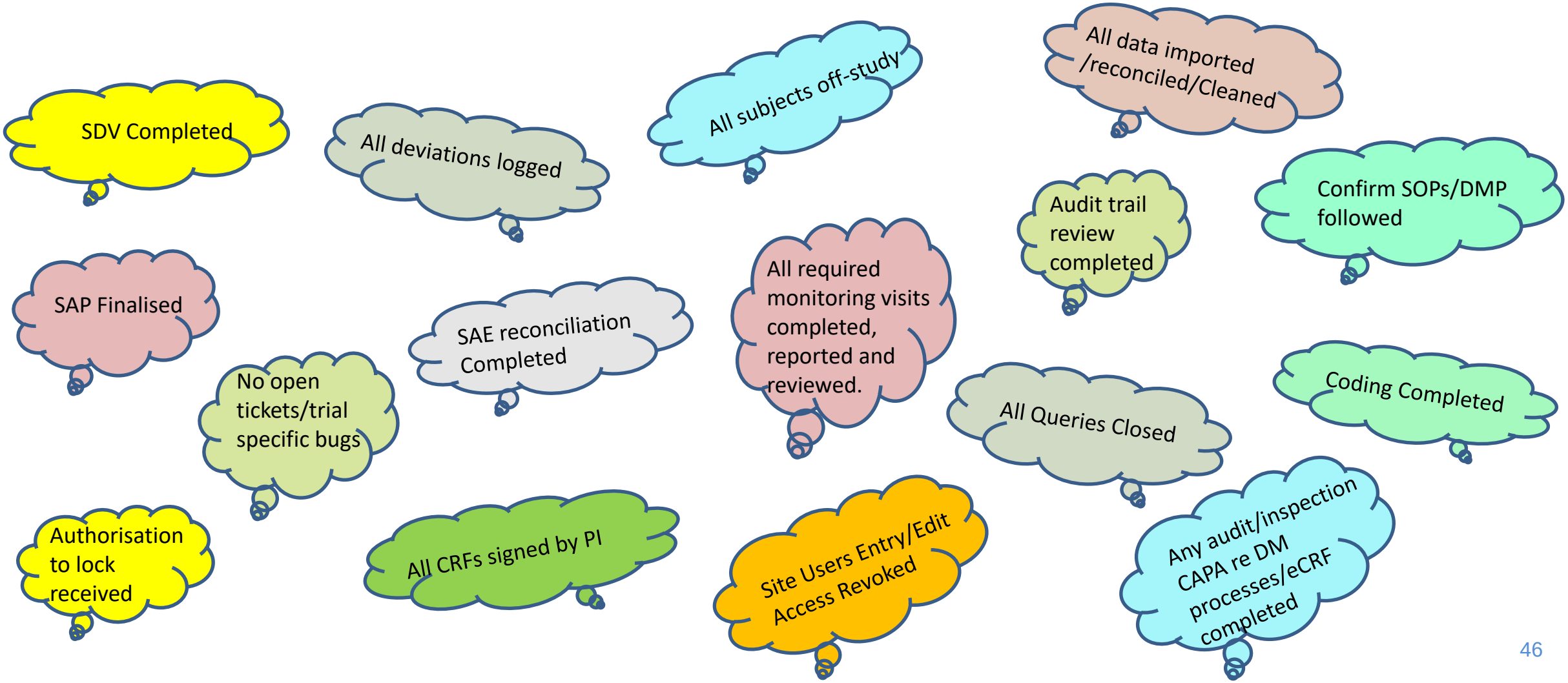
Activities prior to Database/eCRF Finalisation



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Database/eCRF Finalisation

- Evidence of decision to lock (Checklist/Authorisation Forms, Emails) and demonstrate activities required to lock database have been completed
- Evidence from system of lock (users/ access/permissions)
- Data Extraction – validation of process, location of data and protection
- Procedures required for unlocking database (particularly after unblinding)
- SAP finalisation and unblinding timings critical around Data Base lock
- Investigator sign off for data used in regulatory submissions

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Example Findings

- Failure to have a robust process or not following own SOPs for database lock/unlock
  - Pre-lock activities incomplete, e.g., reconciliation of database with SAE database, outstanding queries with no documented rationale
  - No lock performed, restrictions following database lock insufficient, eCRF lock only stopped sites modifying data, not entering new data
- Data Extraction
  - No validation of data extraction programming (from database to SAS® datasets), system update overwrote extracted data, release of data not controlled, data extractions not undertaken post lock, partial data extractions

Ineffective Lock and additional data changes made to data other than those described in the approved unlock request

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Database Lock Finding Example

- Evidence was seen of a database release undertaken in December (database release form approved) upon which a data extraction (SAS datasets) had taken place in December and which the results in the CSR (coincidently submitted to the EMA as MAA) were based.

- Form also showed that pharmacovigilance database reconciliation was completed in the following January and the database was then locked.

- The reconciliation resulted in numerous changes to the database after the data had been extracted for statistical analysis.

- There was the potential that the safety data reported to the EMA in the CSR were unreliable. Required sponsor to review, new data extraction and update to CSR was submitted.

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5.20.1 Noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirement(s) by an investigator/institution, or by member(s) of the sponsor's staff should lead to prompt action by the sponsor to secure compliance.

When significant noncompliance is discovered, the sponsor should perform a root cause analysis and implement appropriate corrective and preventative actions. If required by applicable law or regulation the sponsor should inform the regulatory authority(ies) when the noncompliance is a serious breach of the trial protocol or GCP.

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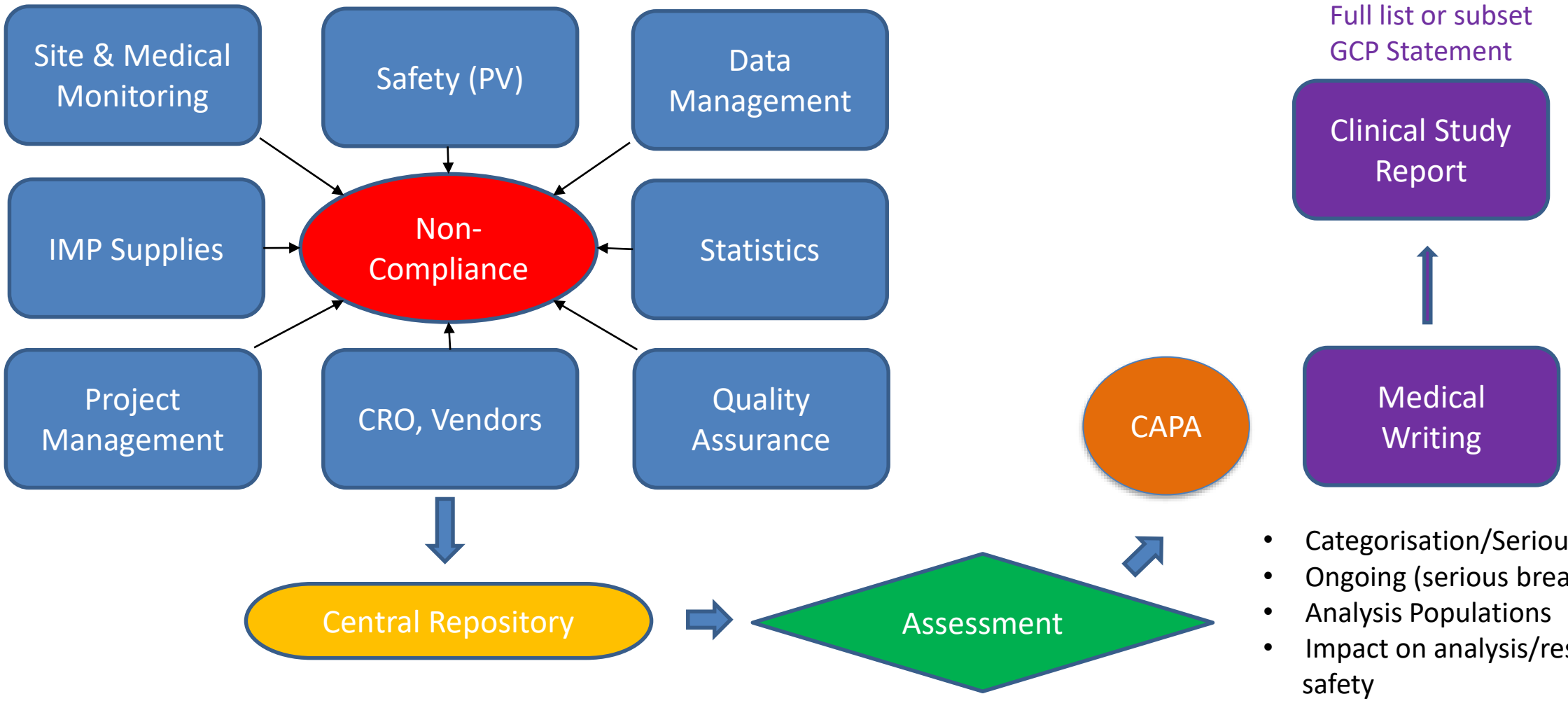
Protocol and GCP Non-Compliance



- Categorisation/Seriousness
- Ongoing (serious breaches)
- Analysis Populations
- Impact on analysis/results/Patient safety

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5.5.4 If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data.

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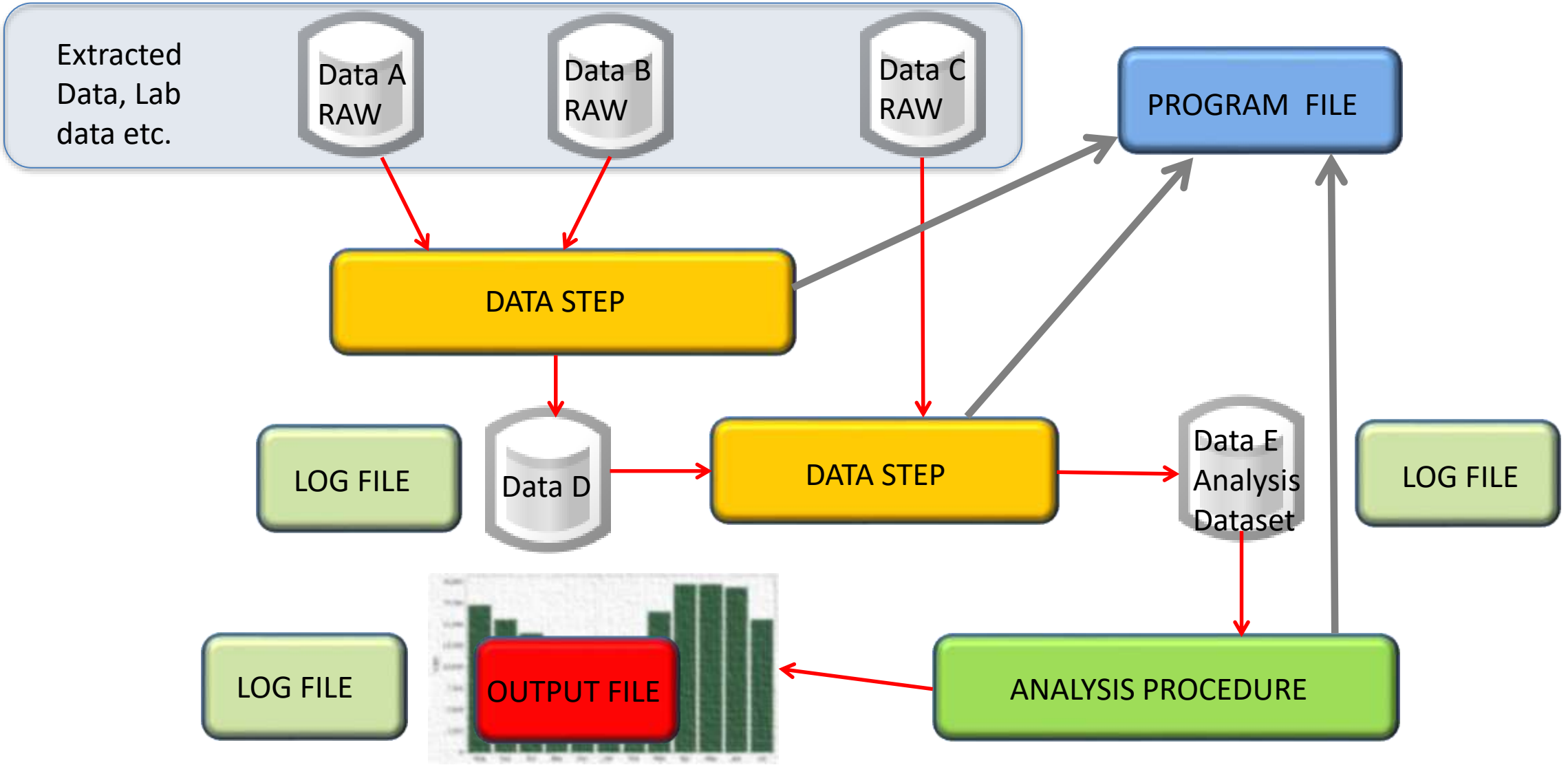
Analysis



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5.5.3 (h) Ensure the integrity of the data including any data that describe the context, content and structure of the data. This is particularly important when making changes to computerized systems, such as software upgrades or migration of data.

5.5.6 The sponsor, or other owners of the data, should retain all of the sponsor-specific essential documents pertaining to the trial (see 8. Essential Documents for the Conduct of a Clinical Trial).

5.5.7 The sponsor should retain all sponsor-specific essential documents in conformance with the applicable regulatory requirement(s) of the country(ies) where the product is approved, and/or where the sponsor intends to apply for approval(s).

5.5.11 The sponsor specific essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirement(s) or if needed by the sponsor.

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5.5.10	Any transfer of ownership of the data should be reported to the appropriate authority(ies), as required by the applicable regulatory requirement(s).
8.1	Essential Documents are those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements. 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. 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
8.3.13	SOURCE DOCUMENTS To document the existence of the subject and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment, and history of subject
8.3.14	SIGNED, DATED AND COMPLETED CASE REPORT FORMS (CRF) To document that the investigator or authorised member of the investigator's staff confirms the observations recorded
8.3.15	DOCUMENTATION OF CRF CORRECTIONS To document all changes/additions or corrections made to CRF after initial data were recorded

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Data/Document Retention

- All data, documents, computer systems files etc. generated from data management/statistics from following procedures are essential and should be retained in the TMF

- Retention should be in a system suitable for the type of file and that it satisfies the requirements for an archival system

- Process should be in place for “Managed Archiving” of electronic files?

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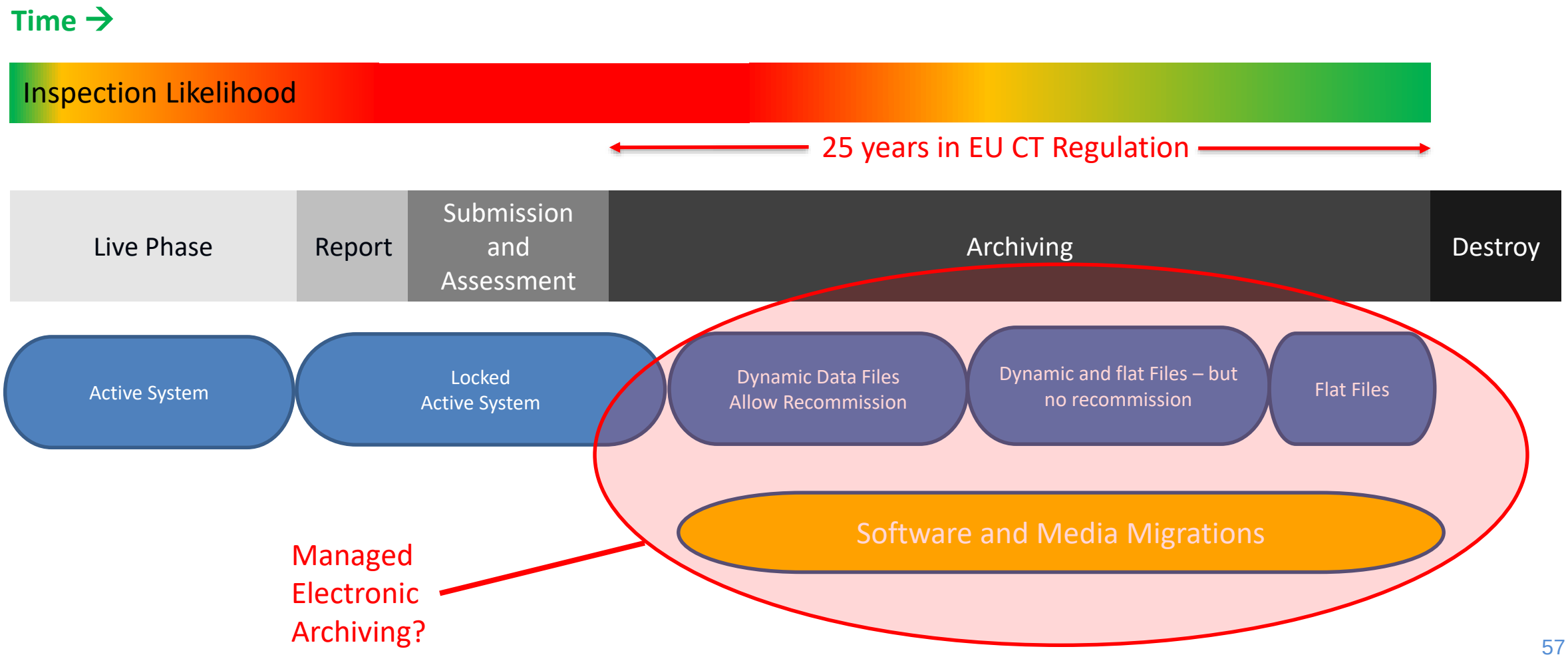
eCRF Retention by Sponsor



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Example Findings

eCRF CD/DVD at investigator site:

- Did not contain or has incomplete clinical data audit trail (e.g. did not contain the information about initial data entry, user ID not present, last data change only, queries and resolutions, ivestigator sign off)
- Not readable by human because of poor formatted display or not provided with the software to decrypt the data

Sponsor:

- Have only flat pdf only – long delay to get datasets from vendor as system decommissioned and not contractual arrangement with vendor
- Unable to recommission the eCRF to see all meta-data (e.g. clinical data audit trial, user access changes, queries, workflow etc.). Retained files not sufficient.

- Data Management and Statistics documents not in TMF (not considered essential)
- Lack of comprehensive procedures for electronic archiving at the sponsor site

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Challenge Questions

- Can you describe 2 situations where the lack of investigator oversight and control of clinical trial data could potentially risk data integrity?

- How are processes for computer system validation of eCRF trial specific configurations important for ensuring protocol compliance?

- How can poor clinical trial data quality impact on the safety of patients taking medicines?

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