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CLINICAL SAMPLE HANDLING – A CRO'S CHALLENGE

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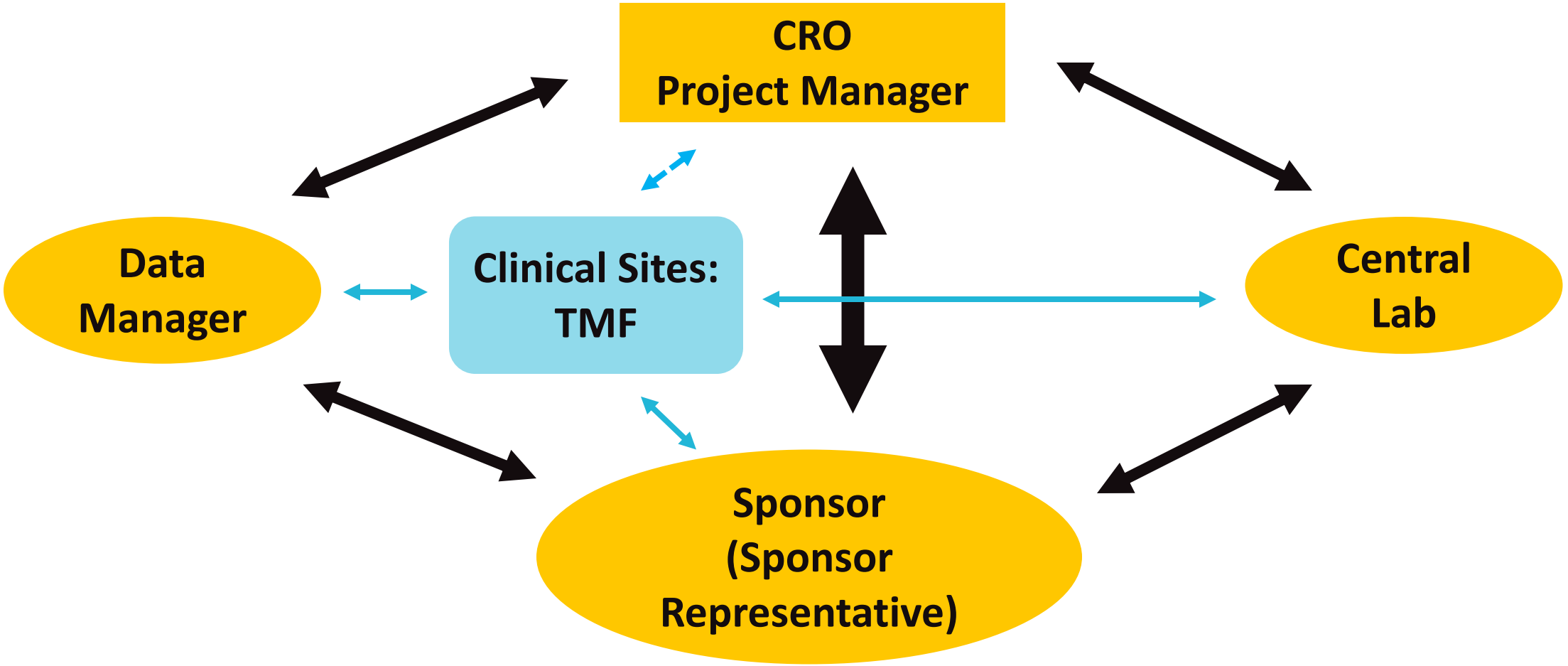
A CRO'S ROLE IN CLINICAL SAMPLE ANALYSIS



SUMMARY OF GCP GUIDELINES

- Declaration of Helsinki
- ICH Guideline for Good Clinical Practice E6 (R2)
- MHRA GCP Guide (UK only)
- The Medicines for Human Use Regulations (clinical Trials) Regulations 2004 and Amendments 2006 (UK only)

International ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

Compliance provides public assurance that the **rights**, **safety** and **well-being** of trial subjects is protected.

Clinical trial data is **credible**.

Objective of ICH GCP Guideline is Mutual Acceptance of Data

WHAT DO GCP GUIDELINES SAY ABOUT BIOANALYSIS?

Not a lot…

Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples
EMA/INS/GCP/532137/2010

What does GCP mean in a CRO setting?

- Rights, integrity and confidentiality of the trial subjects are protected
- Data and Results are credible and accurate

TRIAL SUBJECT'S RIGHTS

Informed Consent

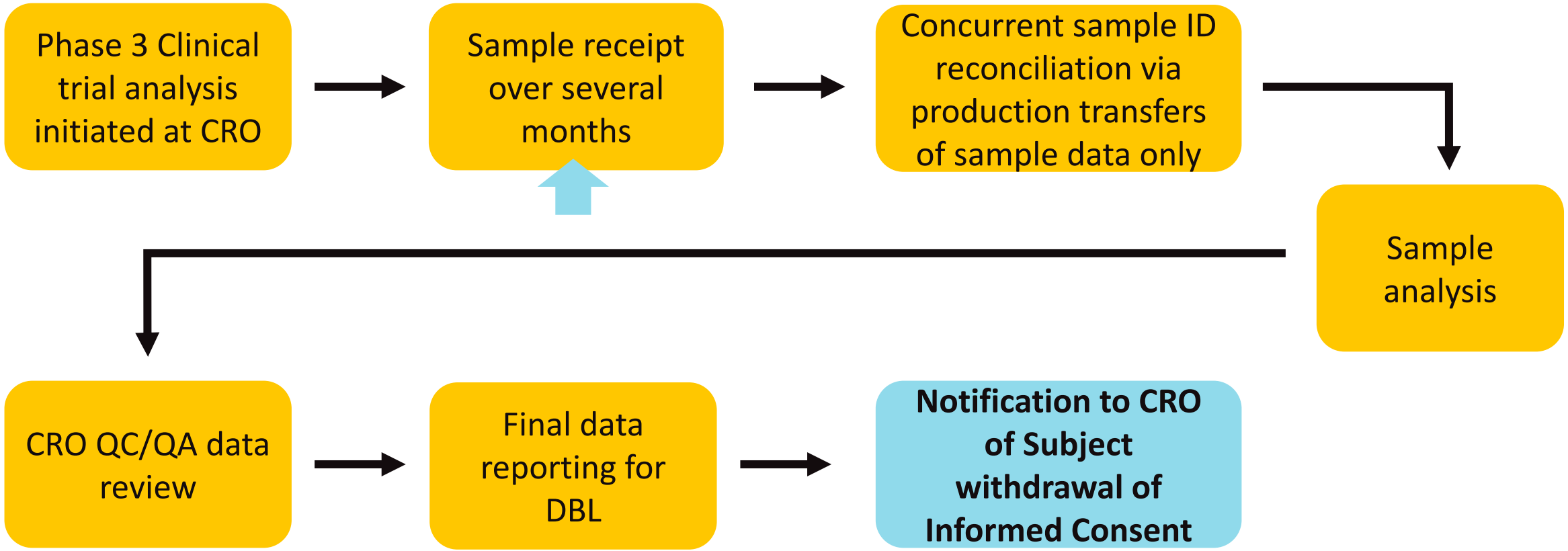
Subject’s legal rights should be documented in the Informed Consent Form

Informed Consent should be given freely and must be in place for all trial subjects prior to taking part in the trial

A trial subject has the right to withdraw their consent to take part in a trial at any point

TRIAL SUBJECT'S RIGHTS – CASE STUDY

Subject withdrawal of Informed Consent:



TRIAL SUBJECT'S CONFIDENTIALITY

Trial Subject's identity

- **Subject initials**
- **Date of Birth**
- **Hospital ID / NHS number**

Examples where this may be recorded and wrongly shared with a CRO:

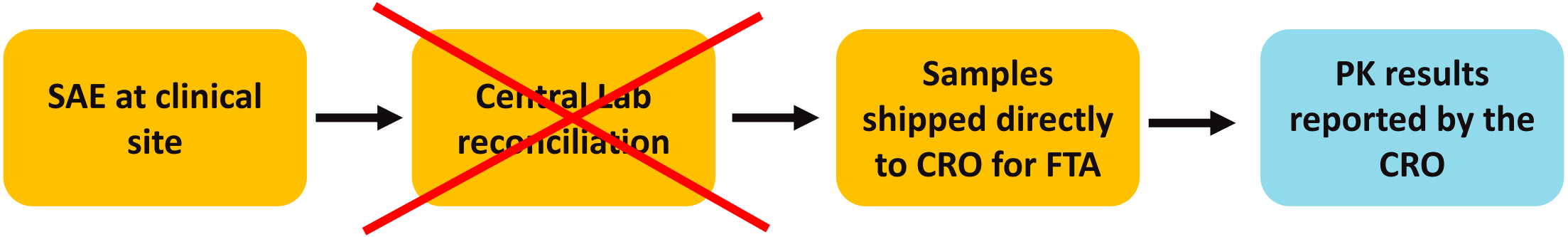
- **Sample manifests**
- **Sample labels**
- **Lab requisition forms**

TRIAL SUBJECT'S INTEGRITY - SAFETY

How does a CRO influence trial subject's safety?

- Decision making in dose escalation studies
- Serious Adverse Events (SAEs)
- Immunogenicity monitoring

TRIAL SUBJECT'S SAFETY – CASE STUDY



- Samples had not been reconciled by central lab
- Clinic provided requisition forms in lieu of a manifest
- CRO created a manifest for reporting by manually combining info from sample label and requisition forms

PK results reported with only sample parameters that could be absolutely confirmed

TRIAL SUBJECT'S SAFETY – CASE STUDY 2

- Scope of the Clinical Objectives?
- Maintaining critical reagents for the validated method
- Maintaining equipment for the validated method

TRIAL SUBJECT'S INTEGRITY - WELL-BEING

Defined as the physical and mental integrity of the subjects participating in a clinical trial

How does that apply to bioanalysis and a CRO?

- **Repeated sample collection**
  - Due to incomplete chain of custody
  - Due to lost samples
- **Invalid analysis results resulting in rejected trial submission**
  - Due to inappropriate method validation
  - Due to fraud

REPRODUCIBILITY OF THE TRIAL DATA

Sample tracking – demonstration of control of;

- **Sample shipping, receipt and chain of custody**
  - Can a CRO be certain of chain of custody outside of their facility?
  - Are method validation parameters sufficient for the life of the trial? (BTS, FTS, LTS)

- **Sample ID reconciliation and changes as a result of data management review**
  - We must be able to clearly demonstrate any updates to sample ID parameters as a result of data management review

REPRODUCIBILITY OF THE TRIAL DATA – SAMPLE RECONCILIATION

For full reproducibility a CRO must be able to demonstrate -

- What was the requested sample ID parameter change?
- Who is requesting the change?
- When did the CRO make the change?

DATA CREDIBILITY

- **Is the reported result valid?**

  - Was the validation appropriate
  - Did analysis meet acceptance criteria
  - Was the data processed appropriately to generate the reported result
  - Were critical materials used appropriately
  - Was repeat analysis performed

- **Who is responsible?**

  - The CRO facility management
  - QA oversight

CONCLUSION

COMMUNICATION

- **When?**
  - Throughout the life-cycle of the trial at the CRO
- **Who?**
  - Sponsor representative and other appropriate individuals
- **How often?**
  - Frequently!
- **Get it in writing**

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