RUNNING THE TRIAL

RUNNING THE TRIAL

- Pre-Site selection
- Site Initiation Visit (SIV)
- What kind of questions should you ask
- How you should prepare for this visit
- Delegation logs
- Training logs
- ECRF/CRF

RUNNING THE TRIAL

Checklist prior to recruiting first patient

Item	Document	Requirement	Tick
1.	Pharmacy ‘green light’	Ensure document sent from pharmacy. Save a copy in the study folder	
2.	R&D NHS approval letter	Ensure letter saved in study folder (attach to ‘study live’ email)	
3.	Study folder	Move from in-set-up to open studies	
4.	Study folder	Check all documents (protocols) PIS are the most up-to-date versions and any earlier copies are in the superceded folder	
5.	SLA’s	Check all SLA’s (if applicable) are in place and include the contact details are in the ‘study live’ email	
6.	CRF Manager	Check study has been added to CRF manager	
7.	Edge	If NIHR adopted study is it on EDGE?	
8.	Worksheets	Have the woksheets been completed and approved by relevant parties?	

RUNNING THE TRIAL

- Recruitment issues
- Consent issues
- Screening (contact card)
- Data capture (source worksheets, examples)

Administration of IMP

- Route of administration of IMP
- Things to consider prior to administration
- Pharmacy manual
- IMP prescription-electronic or trial specific
- IVRS
- Pharmacy specific worksheets
- Drug accountability/compliance
- Diary cards

Sampling

- Work sheets
- PK
- PD
- Biopsies
- processing
- Storage
- Shipping

RUNNING THE TRIAL

- Monitoring
- What to expect in a monitoring visit
  - Book a time/space
  - How to book out notes etc
  - Who contacts who
  - Follow-up on monitoring letters

QUALITY & GOVERNANCE

QUALITY & GOVERNANCE

- Source data and documentation
- Audits
- Inspections
- Reports
- CAPA (deadlines)
- Violation
- Deviation
- Delegation /training logs

Documentation in clinical trials: Essential Documents

"Are those documents, which permit evaluation of the conduct of the trial and the quality of data produced.

These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of GCP and with all regulatory requirements"

ICH (8 .1)

Documentation in clinical trials: essential documents

- Are audited by the regulatory authorities or sponsor to confirm the validity and integrity of the data collected
- Are contained in the files established at the beginning of the trial at both sponsor and investigator site
- For the minimum list - see ICH section 8

What needs to be recorded in the patient notes?

- Copy of signed and dated Consent Form and Patient Information Sheet
- Title of the trial including the drug to be received
- Local and trial specific numbers
- Visit dates
- Concomitant medications
- Adverse events
- A letter informing the GP that the patient has been enrolled in the clinical trial

Essential Documents availability

- Essential documents should be retained for 2 yrs following last approval of marketing application in the ICH region (taken to be 15yrs)
  - *ICH (4.9.5)*

- All records must be made available (direct access) for monitors, auditors & regulatory authorities
  - *ICH (4.9.7)*

Subject level documentation requirements: Subject specific documentation

- **Attributable**
  - The author and content should be clear
- **Legible**
  - Capable of being read
  - In a human-readable format
  - Changes don’t obscure original entry
  - Print name if signature is illegible

Subject Specific Documentation

- **Contemporaneous**
  - The notation, signature, and date need to be completed at the same time and as close to the event as possible
- **Original**
  - First recording of the information (paper, electronic)
- **Accurate**
  - Errors have been identified and corrected

Corrections to Documentation

Proper Notation of Corrections:

- One line strike through, write new data, initial, date and explain (if necessary)

Unacceptable:

- Obliteration, correction fluid, write overs
- New information must not obliterate previous information
- Erasing/Recording in pencil
- Exceptions—Do Not “edit” subject’s personal writings

Source Data

- All information in original records and certified copies of original records of clinical findings, observations or other activities in a clinical trial necessary for the reconstruction and evaluation of the study.

Source Data and Documentation

Source Data provides:

- The reconstruction and evaluation of the study
- Confirmation of subject existence and observations
- Substantiation of study data integrity

Source Documents:

"All information in original records and certified copies of original records…" (ICH GCP 1.51)

- Include: Clinical findings, Observations, and Other study activities
- The first time data is captured: paper towel, report, log, database

Examples of Source Documents

A record which contains ORIGINAL data in the **format** and **medium** it was captured:

- Medical records
- Lab reports
- X-rays, ECGs
- Intake/Screening forms
- Telephone contact records, faxes, e-mails
- Subject diaries
- Informed consent forms
- Drug prescription records

Importance of Documentation

- Over the past 5 years, 25-30% of all warning letters from the FDA to Investigators were related to inadequate/inaccurate records

- This is the 2nd most sited deficiency in the country

(Duke Medicine)

Examples of cited issues

- Unscheduled visits not documented
- Phone follow-up not documented
- Lack of medical history files
- Retrospective handwritten annotations without dates
- Discrepancies between clinic notes, clinic visit forms, source document worksheets and CRFs

Source Documentation: In Summary

- If it happened—document it!
- If it was supposed to happen and didn't, document and explain!
- Be thorough and timely in your documentation
- Quality checks periodically during study and before archiving
- If you find documentation errors, be pro-active and file a deviation/file note and activate a corrective action plan