UNIVERSITY OF LEEDS

The Leeds Teaching Hospitals NHS Trust

Laboratory Guidance for Clinical Trials of Investigational Medicinal Products (CTIMPs)

1) MHRA Good Clinical Practice (GCP) Laboratory Inspection Programme

The MHRA now have a programme of inspection focused on laboratories which carry out analysis to support primary and secondary clinical trial objectives, or critical steps such as dose escalation.

This recognises the increased focus on laboratory endpoints within clinical trials.

2) Is this new?

No, the regulations have always allowed for inspection.

2001/20/EC (article 15)

"To verify compliance with the provisions on good clinical and manufacturing practice, Member States shall appoint inspectors to inspect the sites concerned by any clinical trial conducted, particularly the trial site or sites, the manufacturing site of the investigational medicinal product, any laboratory used for analyses in the clinical trial and/or the sponsor's premises."

3) Is this not covered by Good Laboratory Practice (GLP)/ Good Clinical Laboratory Practice (GCLP)?

GLP

The OECD Principles of GLP have been transposed into UK law: UK Regulations SI 3106 as amended by SI 994, 2004.

Compliance with the principles of GLP is a legal requirement for test facilities that undertake health and environmental safety studies that will be submitted to regulatory authorities for the purposes of risk assessment.

This does not include clinical studies… GLP is limited to pre-clinical.

But GLP does provide:

- A useful quality standard.
- Study management.
- Independent quality assurance function.
- Training and documented records of training.

GCP

- Some overlap with GLP requirements.
- GCP is not as prescriptive as GCP.

GCLP

- Commonly used term but **not** a regulatory requirement.

4) What does a MHRA GCP Laboratory Inspection look like?

…Similar to a sponsor GCP inspection visit:

- Notification and data request.
- Inspection visit.
- Report CAPA & Closure.

The inspection visit is a combination of systems and facility reviews, data reviews from exemplar studies and discussions with key staff.

5) Common issues and audit findings

- Records & Reports:
  - Incorrect versions of worksheets being used.
  - Missing sign-off by operator / QC / approver etc.
  - Interim and Final data not clearly identified as such.

- Training:
  - Training not completed / fully documented / performed according to local SOPs.
  - Missing CVs and role profiles.
  - Lack of GCP training.

- SOPs:
  - Not periodically reviewed.
  - Superseded versions not removed from use.
  - Discrepancies / inconsistencies between documents.

- Storage & Archiving of data:
  - Storage is not secure / does not prevent damage to data.
  - Long term storage and retrievability of data (in particular electronic data) not considered.

- Equipment:
  - Calibration and/or maintenance out of date.
  - Validation performed is not adequate to cover the scope of use.

- Contracts / Protocols / Lab Manuals / SOPs.

- Inconsistencies between study documents.

- Relevant GCP aspects not appropriately defined.

6) GCP compliance is not just about doing good science…

Don't forget about:

- Serious breach reporting.
- Informed consent and patient confidentiality.
- Protocols and amendments - control and compliance.
- Data retention and archiving.

Key Resources & Further Reading:

EMA/INS/GCP/532137/2010: '*Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples*'	*European Medicines Agency*	
CPMP/ICH/135/95: '*Note for Guidance on Good Clinical Practice*'		
UK Regulations SI 3106 (as amended by SI 994), 2004	*UK Government*	
2001/20/EC (article 15)	*The European Parliament and the Council of the European Union*	
Good Clinical Practice Guide	*MHRA*	https://www.tsoshop.co.uk/MHRA/Good-Clinical-Practice-Guide/

*** Should you have any queries or concerns, or would like further information regarding the content of this bulletin, * then please do not hesitate to contact the Sponsor Quality Assurance Office on Tel: 0113 30 60465**