Autumn Focus Workshop
Managing GCP in Regulated Bioanalysis

GCP and MHRA – Setting the Bar

Stuart McDougall, on behalf of the EBF

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A little history…..

- In **2006**, **WHO/TDR** convened a meeting of organizations engaged in clinical trials in disease endemic countries to discuss the applicability of GCLP guidelines to their work. It was agreed that GCLP would be a valuable tool for improving quality laboratory practice. In line with that agreement, TDR/WHO recently acquired copyright to GCLP guidelines that were originally published in **2003** by a working party of the **Clinical Committee of the British Association of Research Quality Assurance** (BARQA), with the aim of disseminating them widely in developing countries and developing related training materials. These GCLP guidelines are presented here. Compliance with them will allow clinical laboratories to ensure that safety and efficacy data is **repeatable**, **reliable**, **auditable** and **easily reconstructed** in a research setting. GCLP guidelines set a standard for compliance by laboratories involved in the analysis of samples from supported clinical trials.*

* www.gov.uk

A little deeper…

GCP / GCLP Regulatory Landscape

- Regulatory focus on requiring more rigorous control within the organisations performing clinical trials in order to ensure patient safety and the reliability of data produced.
- Global acceptance of the ICH Guideline for Good Clinical Practice (GCP) and the implementation of the European Union Clinical Trials Directive (2001/20/EC).
- EU Clinical Trials Directive and ICH GCP Guideline clearly specify roles (e.g. Ethics Committee and Investigator), but only vaguely defined the standards to be applied in the analysis of samples from a clinical trial.
- ICH indicated the standards required for the analysis of samples
  - Section 2.13 “Systems with procedures that assure the quality of every aspect of the trial should be implemented”
  - Section 8 “Essential Documents” parts 8.2.12 and 8.3.7.

WHO GCLP ISBN 978 92 4 159785 2

GCLP Scope

- Applied equally to different types of laboratory analysis i.e;
  - haematology/biochemistry
  - pharmacokinetics (bioanalysis)
  - ECG trace analysis.
- Facilities analysing clinical samples may include;
  - pharmaceutical company laboratories
  - contract research organisations (CROs)
  - central laboratories
  - pharmacogenetic laboratories
  - hospital laboratories
  - clinics
  - specialized analytical services.

MHRA GCLP Guidance High Level Details

- Organisation
- Personnel
- Serious breaches
- Contracts and agreements
- Study conduct
- Requests for additional work
- Subcontracting laboratory analysis
- Patient safety
- Informed consent
- Sample receipt and chain of custody
- Method validation
- Repeat analysis
- Data recording
- Reporting
- Facilities
- Equipment maintenance
- Computerised systems
- Quality assurance (QA) process
- Quality control (QC) process
- SOP and facility policies
- Blinding/unblinding
- Retention of data
- Preparation and distribution of clinical kits

MHRA GCLP Impact in UK for bioanalytical labs

- Quality emphasis was very similar to GLP, so little impact for those labs already within MHRA GLP compliance program;
  - Organisation; responsibilities, laboratory management, master schedule, etc
  - Personnel; education, training, training records, etc
  - Study conduct; control, documentation, communication plan, chain of custody
  - Method validation as per existing BMV guidances
  - Defined processes for sample analysis and repeat analysis
  - Data recording (ALCOA+) and reporting
  - Laboratory facilities of suitable size, design and construction
  - Equipment fit for intended use, validated, calibrated and maintained
  - Computerised systems for capture, processing, reporting and storage of data are developed, validated and maintained to ensure validity, integrity & security of data
  - Quality Control (QC) and independent Quality Assurance (QA) oversight to ensure quality and compliance
  - Laboratory has written procedures (SOPs and Policies) to underpin quality and integrity of data
  - Archiving and secure retention of data

MHRA GCLP Impact in UK for bioanalytical labs

- Additional requirements for GCLP covering;
  - Formal GCP training & periodic refresher training
  - Impact of ‘Serious Breach’, including process for direct communication to MHRA if necessary
  - Contracts and agreements are approved in advance of analysis and don’t contradict Clinical Protocol or approved Analytical Plan (work instruction)
  - Clinical analysis is conducted in accordance with Clinical Trials Regulation, EU Directives, applicable Commission guidance and the Declaration of Helsinki
  - Analytical lab has, or can verify that, they have approved Clinical Protocol (and any Amendments)
  - The Analytical Plan is approved / controlled and does not conflict with Clinical Protocol and/or Informed Consent
  - Safety of trial subjects takes precedence over any other aspect of trial (i.e. documented communication plan)
  - Compliance with Informed Consent and documented process if IC withdrawn.
  - Maintain integrity of blinding process (compromised blinding is likely to constitute a serious breach)

Setting the bar?

*“to set the bar is set some kind if **standard**”*

“to set the bar means *to establish a level of quality for **others** to meet”*

Setting the bar

“Set the bar at the right level!”

Acknowledgements

- T.R. Stiles, V. Grant & N. Mawbey. A quality system for laboratories which undertake the analysis of samples from clinical trial. British Association of Research Quality Assurance (BARQA), 2002.
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- World Health Organization (WHO). Good clinical laboratory practice (GCLP), ISBN 978 92 4 159785 2 (2009)
- T.R. Stiles & V. Grant. An international quality system for laboratories which undertake the analysis of samples from clinical trials. Research Quality Assurance (RQA), ISBN 978-1-904610-21-2 (2012).
- European Medicines Agency. Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples. EMA/INS/GCP/532137/2010 (2012)

Contact Information

Questions: info@e-b-f.eu

European Bioanalysis Forum vzw

www.e-b-f.eu