GCP in a bioanalytical lab

to ensure the safety and privacy of a subject

4th EBF Open Symposium, 16-18 November 2011, Barcelona

European Regulatory Context

EMA reflection paper **– what is new from a GLP perspective**

MHRA GCP Bioanalytical Lab Inspection – main GCP findings

Quality Assurance Processes

GCP aspects to be considered by GLP labs

Summary

SANOFI

European Regulatory Context

- Directive 2001/20/EC:
  Article 15: Verification of Compliance of investigational medicinal products with good clinical and manufacturing practice - *"to verify compliance with the provisions on GCP & GMP, Member States shall appoint inspectors to inspect sites concerned by any clinical trial conducted, particulary …laboratory used for analyses in the clinical trial…"*
- Directive 2005/28/EC:
  "All clinical trial information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of the records of the trial subjects remains protected"

European Regulatory Context

- MHRA, UK, issue 1. July 2009:
  Guidance on the maintance of regulatory compliance in laboratories that perform the analysis or evaluation of clinical trial samples
- EMA, GCP Inspectors working group, draft, 26 August 2010:
  Reflection paper on guidance for laboratories that perform the analysis or evaluation of clinical trial samples. *The guidance has its basis in the Directive 2001/20/EC and Directive 2005/28/EC and in the Note for guidance on good clinical pratice (CPMP/ICH/135/95)*

  The MHRA Guidance and the EMA reflection paper are more or less identical

EMA reflection paper – what is new from a GLP perspective

- **Informed consent**
  - An informed consent must be obtained from all trial subjets.
    A documented mechanism should be in place that the laboratory is informed in a timely manner if the content is withdrawn to ensure that no further data is generated or collected.

- **Contract and Agreements**
  - A contractual agreement should be signed by the sponsor representative and the laboratory management prior to the initiation of any work.

- **Patient Safety**
  - Lines of communication should be established to ensure that any issues that may impact patient safety are reported without delay (for example anomalous results).

EMA reflection paper – what is new from a GLP perspective

- **Reporting**
  - A documented procedure for reporting should be agreed prior to initiation of the work. For example, a procedure to describe the process for reporting serious breaches (in a non-clinical study the process for reporting contamination)
- **Analysis**
  - Usually, a non-clinical study is not blinded (GLP) versus a clinical study is blinded (GCP).
- **Samples receipt / management and chain of custody**
  - Same process, but subject confidentiality! Information on the Label which may compromise the trial subjects right to privacy should be deleted or masked!
- **Additional test**
  - GLP document the process within a SOP or in an amendment to the study protocol versus GCP the informed consent covers the work that will be undertaken by the laboratory!

MHRA GCP Bioanalytical Lab Inspection – main GCP findings

- **Contracts and Agreements**
  - SOP did not identify what information should be included in a contract or agreement (Terms of content, review period, signatories issue procedures and use).
  - Contract/agreement should be in place prior to the start of any clinical analysis.
  - Contracts reviewed did not ensure that the clinical protocol (or relevant part) was received by the facility. In addition, it was not clear whether or not the facility would routinely receive amendments to the clinical protocol
  - No procedure to confirm the frequency at which master service agreements (MSA) were reviewed.
  - It was not clear how a contract, agreement or MSA would be amended (periodic review)
  - No specification that the facility will work in compliance with GCP

MHRA GCP Bioanalytical Lab Inspection – main GCP findings

- **Subject Confidentiality and Consent**
  - No procedure for dealing with samples received labelled with, for example, the subject's name and date of birth (or any other details which might allow the individual to be identified)
  - No formal mechanism for ensuring that laboratory work conducted at the facility had been consented to by the subjects participating in the clinical trial
  - No procedure dealing with the receipt of unexpected or unscheduled samples

- **Blinding and Randomisation**
  - No procedure which defines lines of communication between the laboratory and the sponsor ensuring that the dissemination of clinical results does not inadvertently compromise blinding

MHRA GCP Bioanalytical Lab Inspection – main GCP findings

- **Subject Safety Consideration**
  - No documented procedure on the expedited reporting of analytical results, information about anomalous results
  - No documented procedure to describe the process for reporting serious breaches
- **Organisation, Personnel and Training**
  - Job descriptions did not state that individuals should work in compliance with the current Clinical Trials Regulations.
  - There was no evidence that the laboratory analysts had received any GCP training.
- **Quality Assurance**
  - for Consultant no contract or Consultant expertise (Training records)
  - Not clear which SOPs the consultant would follow (i.e. their own or company SOPs)
  - SOPs reviewed did not adequately address GCP requirements

Quality Assurance Processes

- **Quality assurance process should be developed to ensure:**
  - Patient safety and confidentiality.
  - Analysis is conducted in accordance with GCP.
  - Analysis is conducted in accordance with the protocol, the contract/agreement, the work instruction (written plan which include the purpose of the analysis and the methodology) and associated methods.
  - The laboratories policies and SOP´s are adhered to.
  - Trial data is recorded, reported accurately and archived.
- **Quality assurance activities include:**
  - Regular facility audit (lab and equipment remain fit for purpose)
  - Periodic review of quality systems (SOP procedure, training records, archiving).
  - Audit of technical procedures, methodologies and routine processes (sample receipt, temperature monitoring, pipette and balance controls)

GCP aspects to be considered by GLP labs

- **What is needed for laboratories that perform the analysis of clinical trials**
  - Relevant personnel (Facility and QA) will receive a GCP training.
  - A Process for routine GCP training refresh should be established.
  - A process (SOP) concerning the content, review and amendment of contractual agreement should be documented.
  - An audit process for bioanalytical reports (all reports or a routine selection of relevant reports)
  - An audit process for inlife audits (study based audits concerning a clinical trial or respective process based audits conducted for GLP activities are sufficient – the audit process need to include the sample receipt for clinical trials!)
  - A facility audit process including quality systems and technical procedures (the relevant facility audits conducted for GLP activities are sufficient, if the audits include the needed GCP aspects)

Summary

- **GCP does not mean a lot of more time and effort, but the GCP aspects need to be considered by the labs.**
- **Both the Laboratory and the Quality Assurance need to adapt their processes and relevant SOP´s.**
- **Both systems – GLP and GCP – does not conflict but complement one another.**
- **GLP and GCP combined audits are possible.**

Finish

Thank you for your attention