GLOBAL BIOANALYSIS CONSORTIUM

Scope and Regulations

Harmonization Team: A1

(Work in Progress)

John Smeraglia on behalf of the HT-A1

A1: Scope and regulations

Team members:

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In scope

- Scope and regulations for bioanalytical method validation and samples analysis
- Extent of validation before analysis of samples
  - ➢ Consider Validation a continuum process
- Glossary

Interdependencies with other teams – if any

- A2 Tiered approach for method validation

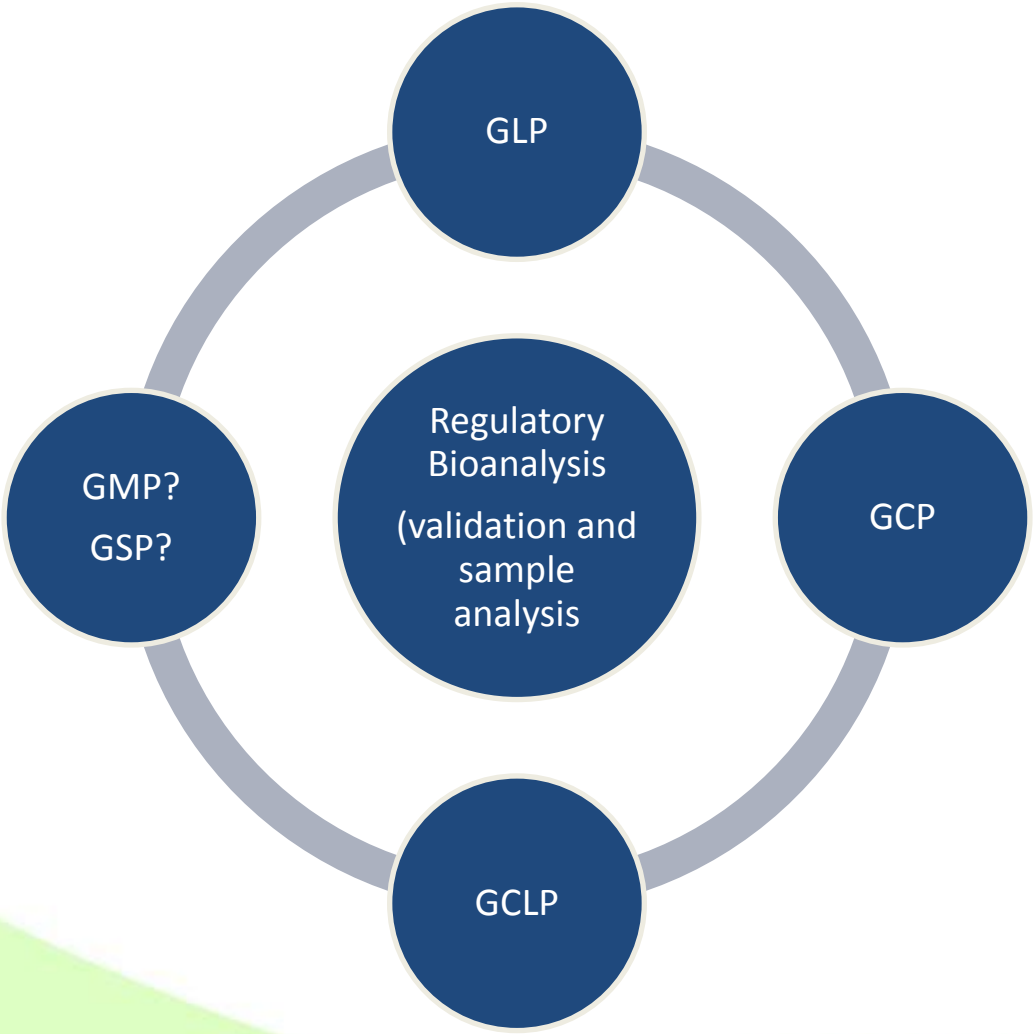
Out of scope

- Biomarkers: Possibly include them as fit for purpose
- Immunogenicity within or out of scope?
  - ➢ Depends if large molecule HT is

Regulations in Bioanalysis

Region	Clinical	Non-clinical	BA guidance
Global		OECD GLP	
US FDA	21 CFR 320.29	GLP 21 CFR Part 58	**Guidance for Industry BMV 2001**
EMA	• Directive 2001/83/EC • Regulation (EC) No. 726/2004 • Guidance for clinical samples analysis • EMA/INS/GCP/532137/2010	• GLP Directive 2004/10/EC • Directive 2004/9/EC	**EMA guidance 2011**
Brazil	GCP from ICH	ISO 17025, GLP	**ANVISA draft guidance 2011**
Japan	Clinical Pharmacokinetic Studies of Pharmaceuticals, June 2001 (Assay should be conducted according to the principles of GLP) GCP	GLP (MHLW Ordinance No. 21, March 1997 and MHLW Ordinance No.114, June 2008)	
China	**China SFDA. Technical guideline on clinical pharmacokinetic studies for chemical drugs. 2005**	**China SFDA. Technical guideline on non-clinical pharmacokinetic studies for chemical drugs. 2005**	**China SFDA. Guideline on human BA and BE studies for chemical drug formulation. 2005**

What does it all mean for Bioanalysis



Regulated Bioanalysis

Regardless of GxP, the regulated bioanalysis is considered to include:

- Adherence to regulatory bioanalytical guidance
- Use validated assays for samples analysis
- Quality Assurance
- Training and qualified personnel
- Instrument qualification (calibration and maintenance included within Performance qualification)
- Certified Reference standards
- Sample tracking, chain of custody
- Full documentation
- SOPs, Study plan, protocol to follow
  - Some mixture of the above
  - A priori documentation of what will be performed
- Reports
- Archiving (documents and data)

Hierarchical structure of Bioanalysis

Validation

- Validation of the method follows Regulated Bioanalysis principles

Samples Analysis :

- Analysis performed according to Regulated Bioanalysis principles
- GLP status is maintained for analysis samples from GLP tox study
- GCP status is maintained for analysis of sample from GCP clinical study

Points to Consider for Scope of Regulated Bioanalysis

Biomarkers:

- EMA guidance: out of the scope
- FDA Current guidance: None
- FDA future guidance: Possibly Fit for purpose

Immunogenicity within or out of scope?

- Depends if large molecule HT is considering them or not.

Extent of validation before analysis of samples

- Consider Validation a continuum process

Validation a Continuum Process

- Drug development is a continuous process from drug discovery to regulated studies for development and marketing
- Bioanalytical method validation is also a continuous process after method development, and also depends on availability of certified reference standards
- We analyze samples within the stream of these two contiguous processes.
- Within scope, we should phrase our validation requirements based on this contiguous processes and consider when
  - Samples are analyzed without validation
  - Samples are analyzed with qualified method
  - Samples are analyzed with full validation
- Stability information may also follow a similar paradigm of continuity.

Scope: a draft

This guideline provides procedures, requirements and specifications for the bioanalytical methods used for measurement of drug and metabolite concentrations in biological matrices obtained from pre-clinical and clinical pharmacokinetic, pharmacology or toxicokinetic studies. The guideline covers validation of methods and analysis of samples for both, chromatographic and ligand binding assays.

Bioanalytical methods are validated to provide evidence for specificity, precision, accuracy, reproducibility, ruggedness and stability of the method. Samples analysis can start after method development and fit for purpose method qualification or full validation has been completed. Bioanalytical method validation is a continuous process after method development. Samples from early discovery studies are generally analyzed using a generic or quickly developed method. As drug development continues, specific methods are developed and qualified and/or validated. Samples from early studies are analyzed using appropriately qualified methods. Validation experiments must be completed before analyzing samples from regulatory studies where pharmacokinetics is a primary endpoint. Furthermore, this guideline describes when partial validation or cross validation should be carried.

Glossary

- Created from existing FDA and EMA documents
- Additional terms will be added from other regulatory documents or from bioanalytical community, as necessary.
- Source of all terms will be identified.
- Glossary will be sent to all HTs for their input
- Hope to create one set of glossary across GBC

We value your feedback and thoughts

Global Bioanalysis Consortium
On harmonization of bioanalytical guidance