GLOBAL BIOANALYSIS CONSORTIUM

Regulated Bioanalysis - A Proposed Global Harmonization Process

General Slides – March 2011

Which teams?
details on scope and deliverables

A1: Scope and regulations

Team members:

Team lead

- Name – region – e-mail

Other members

- Name – region – e-mail
- Name – region – e-mail
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In scope

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis
- Glossary

Interdependencies with other teams – if any

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis
- Glossary

Out of scope

- Scope and regulations (GxPs) for bioanalytical validation and samples analysis
- Glossary

A2: Tiered approaches for method validation

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Definitions of screening, qualification in relation to validation, applicable for
  - Validation/qualification of assays for tissues
  - Tiered approach for metabolites quantification
  - Biomarker assay qualification/validation
- Stability assessment in tiered approach (blood, tissue, urine, metabolites, biomarkers – as applicable..)

Interdependencies with other teams – if any

Out of scope

A3 Method Transfer, partial and cross validation

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Life cycle of a method after first full validation or relation with other validated methods.
  - Partial validation
  - Method transfer
  - Cross validation
- Definitions of method transfer, partial and cross validations
- Recommendation on when to perform method transfer, partial and cross validations
- Recommendations of which experiments are desirable for each proposed steps after full validation

Interdependencies with other teams – if any

- A6

Out of scope

A4: Reference standards and reagents

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Reference standards used for drugs, metabolites and internal standards – Purity certification and COA
- Preparation of stock solutions, calibration standards and QCs

Interdependencies with other teams – if any

- A2

Out of scope

A5: Sample Management

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- All aspects of sample management from collection to disposition - Cold chain management
  - Collection, handling and storage at clinical/ animal lab
  - Storage an shipment from clinical/animal lab to CL or analytical lab
  - Pre analysis storage at analytical lab
  - Post analysis storage or shipment
  - Disposal or archiving/banking

Interdependencies with other teams – if any

- A6

Out of scope

A6: Stability

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Stability in relation to validated methods
- Reference standards and reagent stability
- Process stability established during validation
- Stability in matrix
- Co-formulated drugs, co-administered drugs
- Whole blood and tissue stability for validated methods
- Stability at the sample collection - A6
- Degradation vs. stability *vs*. solubility loss *vs*. absorptive loss

Interdependencies with other teams – if any

- A2
- A3
- A5

Out of scope

- Stability assessment in tiered approach (blood, tissue, urine, metabolites, biomarkers – as applicable..) – A3

A7: Repeat analysis and ISR

Team members:

Team lead

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Other members

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In scope

- Repeats for analytical reasons
- PK repeats
- ISR
- Incl. recommendation onsingle analyte repeat in multi-analyte assay

Interdependencies with other teams – if any

Out of scope

A8: Documentation

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Definitions of different report types
- Documentation of method development
- Method Validation reports
- Study reports
- Failure investigation and documentation
- Documentation at analytical site
- Raw data definitions data (electronic and paper) including notebook records, instrument use and maintenance records
- Archiving

Interdependencies with other teams – if any

- A1

Out of scope

A9: Analytical Instrument Qualification

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Software Validation
- Instrument qualification based on instrument categories
- System suitability
- Instrument decommissioning

Interdependencies with other teams – if any

- A1

Out of scope

A10: New Frontiers

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Understand analogies with established techniques and need for regulatory recommendation *vs.* need fro increased scientific validation prior to recommending regulations, i.e. new techniques already applied in regulatory context (peptide PK/TK with LC-MS/MS)
- Examples are, but not limited to
  - Micro-sampling (includes DBS)
  - Alternate technologies (AMS, ICPMS)
  - Large molecules analysis by new technologies

Interdependencies with other teams – if any

- A1

Out of scope

A10: New Frontiers – biomarkers?

Team members:

Team lead

- Jean Lee – NA – e-mail

Other members

- Name – region – e-mail
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In scope

Interdependencies with other teams – if any

– A1

Out of scope

A10: New Frontiers – others?

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

Interdependencies with other teams – if any

– A1

Out of scope

L1: Large molecule specific run acceptance

Team members:

Team lead

- Marian Kelley – NA – e-mail

Other members

- Name – region – e-mail
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In scope

- Non Linearity of the standard curves
- Assay range (ELISA vs. MSD)
- Accuracy, precision, total error
- Appropriate calibration curve and QC ranges (during validation and for study specific)
- Selection of regression analysis
- Individual runs and overall run acceptance during validation
- Individual runs acceptance during samples analysis

Interdependencies with other teams – if any

- S1

Out of scope

L2: Large molecule specific assay operation

Team members:

Team lead

- Lauren Stevenson – NA – e-mail

Other members

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In scope

- Testing of ruggedness and robustness
- Setting up a balanced validation design
- Dilutional linearity
- Specificity testing
- Selectivity testing
- Parallelism
- Hook effect

Interdependencies with other teams – if any

Out of scope

L3: Assay formats

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Possible assay platforms for LBAs – Gyros, Biacore, ELISA (96, 384 etc), MSD
- Acceptance criteria for these new methods
- How to set up the assays – placement of standards and QCs in these new formats
- Pros and cons of using these formats

Interdependencies with other teams – if any

Out of scope

L4: Reagents and their stability - Link with tiered approach

Team members:

Team lead

- Lindsay King – NA– e-mail

Other members

- Name – region – e-mail
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In scope

- What are the critical reagents
- What to do when you change critical reagents
- Stability of reagents
- Batch to batch variation
- In-house vs. commercial reagents pros and cons
- Specificity testing of the reagents

Interdependencies with other teams – if any

Link with tiered approach

Out of scope

L5: Automation practices in LM bioanalysis

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Choosing automation
- Full automation vs. modular
- How to conduct validation with an automated instrument as an analyst
- Setting acceptance criteria based on the automated assays
- Validating the instrument vs. the method
- Carry over
- Fixed tips vs. disposable tips

Interdependencies with other teams – if any

Link with tiered approach

Out of scope

L6: Immunogenicity (Effect on PK)

Team members:

Team lead

- Jeff Sailstad – NA – e-mail

Other members

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In scope

- How does immunogenicity data affect the pharmacokinetics
- How to assess this parameter during the validation

Interdependencies with other teams – if any

Link with tiered approach

Out of scope

- Immunogenicity Assessment
- Cut point analysis
- Screening assay
- Confirmatory assay
- Nab assay

S1: Small molecule specific run acceptance

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Linearity, Accuracy, Precision
- Appropriate calibration curve and QC ranges (during validation and for study specific)
- Selection of regression analysis (linear vs. best fit)
- Individual runs and overall run acceptance during validation
- Individual runs acceptance during samples analysis

Interdependencies with other teams – if any

- L1

Out of scope

S1: Small molecule specific assay operation

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Carryover and contamination
- Sensitivity
- Specificity - selectivity
- Matrix Effects
- Recovery
- IS evaluation

Interdependencies with other teams – if any

Out of scope

S3: Chromatographic Run Quality Assessment

Team members:

Team lead

- Name – region – e-mail

Other members

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In scope

- Chromatographic resolution and peak shape
- Noise signal
- Peak integration algorithms and manual integrations
- Other quality parameters potentially needed for recommendation, e.g. :
  - Changes in slopes during study

Interdependencies with other teams – if any

Out of scope