GLOBAL BIOANALYSIS CONSORTIUM

S1: Small molecule specific run acceptance

Summary Presentation

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S-1 Team Members

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Scope: Presentation Today

- We have covered many topics for both validation and sample analysis
- Some of those topics are shared with other HTs
- I will present three topics that are common to the Small Molecule and the Analytical Instrumentation Qualification HTs
- We welcome your feedback and input on these topics to any of the four HTs

Scope: Validation Run Acceptance

1. Calibration curve and range
   - Selection of regression model
2. QC placement
3. Criteria for individual runs and overall
4. Multiple analyte validations
5. Validation of plasma blank samples
6. Change of anticoagulant or counterion

Anti-coagulant, Counterion Change

- For a validated assay (species-matrix-anti-coagulant combination), a change of counterion does not require re-validation
  - Examples: Na_2EDTA to K_2EDTA; Na to Li Heparin; K_2 to K_3EDTA
  - Matrices are considered equivalent, no validation action required
- For a validated assay and species-matrix combination, change of anti-coagulant type requires re-validation
  - Examples: K_2EDTA to Na Heparin; K_3EDTA to NaF/KOx
  - Partial validation may be sufficient to cover inadvertent use of wrong anti-coagulant at sample collection in a limited instance
  - Full validation is recommended for a fundamental change in anti-coagulant for the development program

Scope: Sample Analysis Run Acceptance

1. System conditioning
2. System suitability testing
3. Individual run acceptance
4. Internal Standard criteria
5. Observed results and effect on run acceptance
   - Carryover
   - Positive control or predose sample results
   - Anomalous sample results
6. Sample and run reinjection

System Suitability

- Prior to the submission of an analytical batch it is recommended that the performance of the analytical system be verified by means of a System Suitability Test.
  - This test should be described in a standard/laboratory operating procedure and documented in study records.
- The test should be capable of demonstrating that the system has sufficient:
  - Sensitivity
  - Specificity
  - Chromatographic reproducibility

  to enable accurate analysis of the sample batch.
- System suitability test results do not replace or substitute for the documented run acceptance criteria.

Run Performance: Anomalous Result I

- When an anomalous result is observed, an investigation must be conducted
  - Study samples analysis runs only
  - Analytically valid result and only the concentration value is questionable
- An SOP should describe evaluation, investigation, and documentation of any anomalous results for bioanalytical studies
- Investigations should be thorough, timely, unbiased, well-documented, and scientifically defensible
  - Documentation may be in bioanalytical report or separate investigation report
  - The impact of the cause on previous analytical results should be evaluated.

Run Performance: Anomalous Result II

- Investigation and remediation system can also be a useful tool in managing anomalous results.
- Examples of anomalous results may include but are not limited to:
  - Single ISR failure, predefined by SOP
  - Positive pre-dose or control
  - Differences in IS response
  - Chromatographic anomalies
  - Other major systemic problem

S-1: Conclusions

- Approximately 25 teleconferences held so far
  - Several more anticipated to complete topic list
- Broad agreement on topics is common
  - Large number of distinct topics identified under Run Acceptance
  - Establishing the specific language of the details for recommendations is challenging
- Excellent participation and contributions from all members
- Expect final recommendations, taking into account comments and input from HT Leader meetings, to be completed by mid-June
- Will start drafting recommendation text end June