Workshop

Towards harmonised implementation of the ICH M10 Guideline

<< Chapter 7, LBA >>

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Themes/questions discussed today

- Joint discussion Chromatography and LBA
  - Endogenous molecules and surrogate matrix

- **Separate discussions in Chromatography and LBA**
  - **Parallelism**
  - **Recovery and microsampling/dried matrix**
  - **New or Alternative Technologies**
  - **Diagnostic kits**

Parallelism

ICH M10: VII. ADDITIONAL CONSIDERATIONS (7)

Parallelism (7.2)

"Parallelism is defined as a **parallel relationship between the calibration curve and serially diluted study samples** to detect any influence of dilution on analyte measurement. "

"Parallelism investigations, or the justification for its absence, should be included in the Bioanalytical Report."

"A study sample with a high concentration (preferably close to Cmax) should be diluted to at least three concentrations with blank matrix."

"when applying the 30% criterion, data should be carefully monitored as results that pass this criterion may still reveal trends of nonparallelism."

EBF proposal for implementation:

- You know your drug program, do what makes sense
- When assessed include sufficient samples to understand any limitations

Recovery, dried matrix methods & microsampling

7.3 Recovery

“Recovery is determined by comparing the analyte response in a biological sample that is spiked with the analyte and processed, with the response in a biological blank sample that is processed and then spiked with the analyte. **Recovery of the analyte does not need to be 100%**, but the extent of recovery of an analyte and of the IS (if used) **should be consistent.”**

EBF proposal for implementation:

- For large molecules recovery needs to be considered for dried matrix methods.

Recovery, dried matrix methods & microsampling

7.6.1 Dried Matrix Methods

"Dried matrix methods (DMM) is a sampling methodology that **offers benefits such as collection of reduced blood sample volumes** as a microsampling technique for drug analysis and ease of collection, storage and transportation."

EBF proposal for implementation:

- It is welcomed that microsampling is supported to allow consideration of 3Rs and reduce patient burden.

New or Alternative Technologies

7.6. New or alternative technologies

”When a new or alternative technology is used as the **sole bioanalytical technology** from the onset of drug development, **cross validation with an existing technology is not required**.”

”The use of new technology in regulated bioanalysis should be supported by **acceptance criteria** established **a priori** based on method development and verified in validation.”

EBF proposal for implementation:

- When technologies not mentioned in the scope of the guideline are used, validation design and acceptance criteria should be science driven.
- Toward decision-based acceptance criteria for Bioanalytical Method Validation: a proposal for discussion from the European Bioanalysis Forum. Philip Timmerman, Michaela Golob, Joanne Goodman, Magnus Knutsson, Robert Nelson, Marianne Scheel Fjording & Steve White. Bioanalysis 2018.

Commercial and Diagnostic kits

7.5 Commercial and Diagnostic Kits

"If an applicant repurposes a kit (instead of developing a new method) or utilises "research use only" kits to measure chemical or biological drug concentrations during the development of a novel drug, the applicant should assess the kit validation to ensure that it conforms to the drug development standards described in this guideline."

EBF proposal for implementation:

- Where commercial kits are used, validation should fulfil expectations in section 4 and relevant parts of section 7.

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