How To Implement The EMA Guideline On Bioanalytical Method Validation

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Dates and Places

- **18-Dec-2008**
  Concept paper/recommendations on the need for a (CHMP) guideline on the validation of bioanalytical methods
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002964.pdf

- **19-Nov-2009**
  Draft. Guideline on the validation of bioanalytical methods
  http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/12/WC500018062.pdf

- **21-Jul-2011**
  Guideline on the validation of bioanalytical methods
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/08/WC500109686.pdf

- **21-Jul-2011**
  Overview of comments received on 'Guideline on the validation of bioanalytical methods'
  http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/08/WC500109687.pdf

- **21-Feb-2012**
  'Guideline on the validation of bioanalytical methods' coming into effect
  http://www.ourplace.com/

Points of Attention

- Clinical: validation and sample analysis according to GCP
- Non-clinical: GLP validation for GLP studies
- Full validation for each species (pg 4) ↔ Partial validation species change (pg 10)
- Runs ≠ batches
- Cross-validation: different methods. How different can different be before it is different?
- Report overall statistics of QCs
- Overall accuracy & precision < 15%
  … and for LBA?
- Statistics: proper calculation of between-run accuracy & between-run precision
- Matrix effect: 6 individual samples, two concentrations, haemolysed and hyperlipidaemic

Points of Attention

- QC levels: Lo 3x LLOQ, Me at 50% of cal curve range, Hi at 75%
- Recovery: not requested by EMA (but in FDA 2001)
- Deviating IS response: sample reanalysis
- ISR: 10% for first 1000, 5% of the rest
- IS: CoA not mandatory
- Reporting: 20% Chromatograms in BE studies, representative in other cases.
- Selectivity: co-medication normally used in the subject population
- Stability during sampling/before storage (blood)
- Multi analytes: stability in matrix containing all analytes
- LTS results must be available before issuing the study report

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- EMA
  for stimulating us to continuously improve our work