Stability Issues In Ligand Binding Assays

Chair: Arjen Companjen

EBF 4th Open Symposium – Less is More
16-18 Dec 2011
Barcelona

Stability test discussion in the validation guidelines

FDA (Bioanalytical Method validation):

- The stability of the analyte (drug and/or metabolite) in the matrix during the collection process and the sample storage period should be assessed, preferably prior to sample analysis.
- For compounds with potentially labile metabolites, the stability of analyte in matrix from dosed subjects (or species) should be confirmed.
- The stability of the analyte in biological matrix at intended storage temperatures should be established. The influence of freeze-thaw cycles (a minimum of three cycles at two concentrations in triplicate) should be studied.
- The stability of the analyte in matrix at ambient temperature should be evaluated over a time period equal to the typical sample preparation, sample handling, and analytical run times.

Stability test discussion in the validation guidelines

EMA (Guideline on bioanalytical method validation) :

Evaluation of stability should be carried out to ensure that every step taken during sample preparation and sample analysis, as well as the storage conditions used do not affect the concentration of the analyte.

Stability should be ensured for every step in the analytical method, meaning that the conditions applied to the stability tests, such as sample matrix, anticoagulant, container materials, storage and analytical conditions should be similar to those used for the actual study samples. Reference to data published in the literature is not considered sufficient.

Stability of the stock and working solutions should be tested with an appropriate dilution, taking into consideration the linearity and measuring range of the detector.

Stability studies should investigate the different storage conditions over time periods that equal or exceed those applied to the actual study samples.

Stability test discussion in the validation guidelines

The validation guidelines discuss stability of drug and reference standard in sample matrix during handling:

- Freeze/thaw stability
- Short/Long term stability
- Stability at room temperature

Stabilty of induced antibodies (ADA) are discussed in the immunogenicity guidelines

Focus of this breakout session

- Stability of drug in matrix
- Stability of induced antibodies (by drug (ADA) or vaccine (AVA))
- Stability of critical reagens
- Issues you might encounter during stability studies

Stability Issues In Ligand Binding Assays
Session agenda

Jenny Hendriks (Crucell)
Binding and activity of anti-vaccine antibodies in short and long term stability studies

Ulrich Kunz (Boehringer-Ingelheim)
Case studies of issues with stability of antibody reagents

Susanne Pihl (on behalf of EBF)
Long term stability investigation of macromolecules in an isochronic study design

Panel Discussion
Moderator: Margarete Brudny-Kloeppel (Bayer Healthcare)