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Article

Keys to Success in Biosimilar Bioanalytical Assay Development and Sample Analysis

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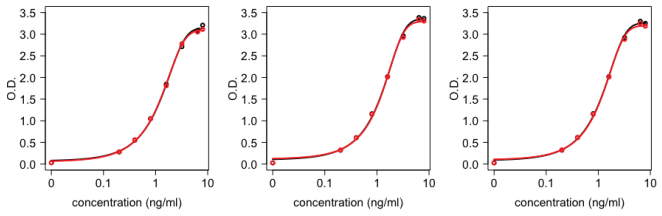
Biosimilars for leading biologics pave their way into the market. Patent expiries attract pharma and biotech companies worldwide to engage in biosimilar drug development.

Celerion supports all requirements for biosimilar drug candidates. Our expertise is in proven large molecule and immunogenicity bioanalytical assays. Leveraging over 30 years' of biologics drug development experience, Celerion discusses critical success factors for your biosimilar drug development program.

The preclinical and clinical development is relatively straightforward. GLP toxicology studies with the biosimilar and the innovator must be performed to assess target organ toxicity and immunogenicity. Clinical studies consist of PK or PK/PD characterization followed by a patient study to establish similarity in drug response, immunogenicity and drug safety with an innovator drug reference.

For PK and immunogenicity testing adequate assays need to be established, requiring a thorough characterization apart from routine. The key to success is the use of assays which similarly detect the biosimilar and the innovator drug levels and anti-drug antibodies.

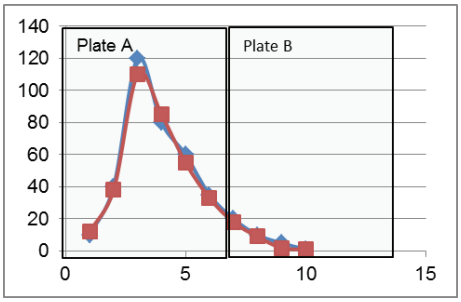
Preferably a **single PK assay** with one calibration curve and one set of quality control samples can be established to evaluate biosimilar and innovator drug concentrations. Several biosimilar and innovator calibration curves are analyzed side-by-side on a 96-well plate and should ideally overlap each other, as shown below for one of our well established biosimilar PK assays (red curves (biosimilar) perfectly superimpose black curves (innovator).



Non-overlapping but parallel curves indicate concentration differences and call for a confirmation and a thorough re-evaluation of drug reference materials supplied and used to prepare the curves.

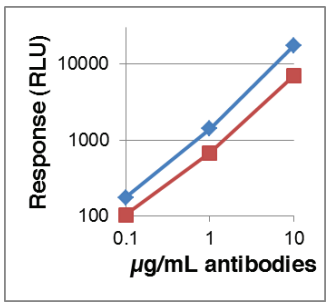
Further, during assay validation similar reactivity of both compounds in the routine validation tests need to be confirmed. Side-by-side robustness testing by performing multiple quality control assessments including multiple dilutions, by multiple operators on several occasions is highly recommended.

The second key to success is a **PK sample analysis** set-up designed to minimize assay variability. The use of liquid handling robotics is a major contributor to push the limits of assay precision. In addition the analytical set-up should mirror the clinical study set-up as close as possible. Samples drawn at same time points from biosimilar and innovator treatment arms should be analyzed side-by-side preferably on the same 96-well plate.



For **immunogenicity** testing essentially the same principals apply. Ideally a one assay approach using the biosimilar as capture reagent in the ligand-binding assay can be established to reliably detect anti-drug antibodies against the biosimilar.

We recommend establishing positive control antibodies against the biosimilar and the innovator generated and purified using the same protocol performed by the same supplier. From both positive controls parallel signal-response curves should be recorded and should show interchangeability.



The one-assay approach, as for the PK assay, has the advantage that blinded study sample analysis is possible and samples only need to be analyzed once, thus enabling tighter study timelines. Confirmation of screening positive samples can be performed either by inhibiting all the samples with biosimilar or innovator drug (if the laboratory is unblinded), or with biosimilar and innovator drug (if the laboratory should stay blinded).

Celerion understands the complexities of biosimilars and what key considerations should be applied for conducting a successful biosimilar drug development program.