
# Recommendations from EBF Biosimilars Evaluation Group

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Barcelona

http://www.europeanbioanalysisforum.eu

# EBF Biosimilars Evaluation Group - Background

- **Former TT-33 performed a survey on EBF members current approaches for PK and ADA analysis of biosimilars**
- **Results presented at EBF Open Meeting Nov 2012**

- **Preliminary conclusions**
  - Multiple approaches are being used by EBF members for biosimilar PK and ADA bioanalysis
  - Clear need for standardising how Biosimilar PK and ADA bioanalysis is performed
  - A standard approach would ensure a true assessment of comparability between biosimilar and reference
  - Clear requirement for a white paper or regulatory guidelines specifically addressing biosimilar PK and ADA analysis
- **TT-33 closed due to other priorities**

# EBF Biosimilars Evaluation Group – formed Mar 2013

## Aim of the group

*Evaluate the need for a (new) EBF topic team working with the bioanalytical strategy for biosimilar drug development with respect to pharmacokinetic (PK) and immunogenicity (ADA) assays*

- **Evaluate the output from the AAPS Biosimilars Action Program Committee (APC)**
- **Judge if there is need for an EBF initiative in parallel**
- **Give recommendation at EBF open meeting in Barcelona, November 2014**

# PK assay- AAPS Biosimilars APC

## Status

- **The AAPS Biosimilars APC presented their PK assay strategy at the NBC May 2013**
- **White paper published 03 October 2014**

  *Systemic Verification of Bioanalytical Similarity Between a Biosimilar and a Reference Biotherapeutic: Committee Recommendations for the Development and Validation of a Single Ligand-Binding Assay to Support Pharmacokinetic Assessment*

  *JC Marini et al, The AAPS Journal, 03 October 2014*

# PK assay - AAPS Biosimilars APC

## White paper recommendations

- Use one PK assay for comparison of biosimilar and reference

## ➢ Method development

- Evaluate the bioanalytical similarity by *statistical comparison* of calibration curves
- If not similar, investigate cause/resolve or use two assays

## ➢ Method validation

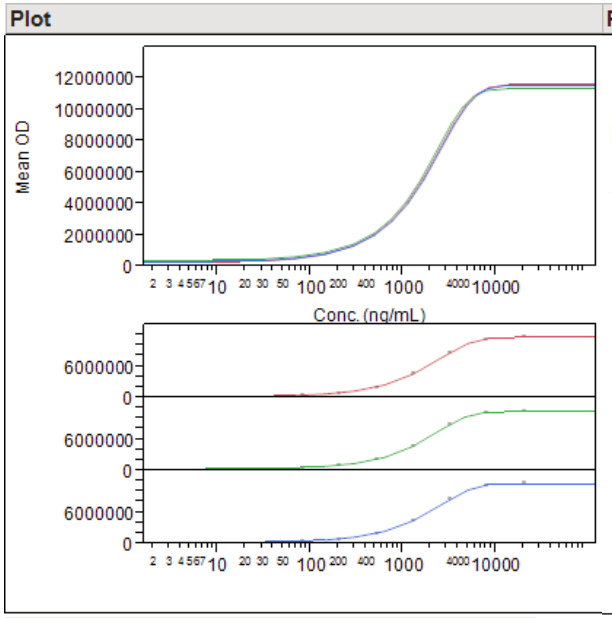
- Confirm comparability *in a single assay* by systematic comparison of QCs
- *Use one calibrator* - typically the biosimilar

## ➢ Study sample analysis

- Use *one validated assay* to assess PK for biosimilar and reference

# PK assay – example
# Calibration curve parallelism assessment

## Day 1 (A1)

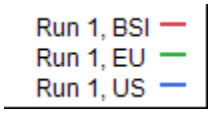



Parallelism Test

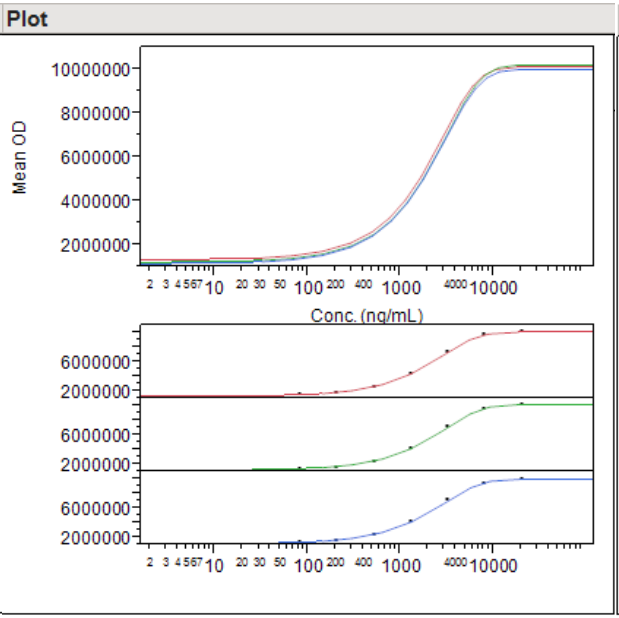
Test Results

Parallelism F Test

| Parallel Fit SSE | Full SSE | NDF | DDF | F Ratio | Prob > F |
|---|---|---|---|---|---|
| 3.715e+11 | 2.5e+11 | 6 | 12 | 0.972 | 0.4836 |




## Day 2 (A2)



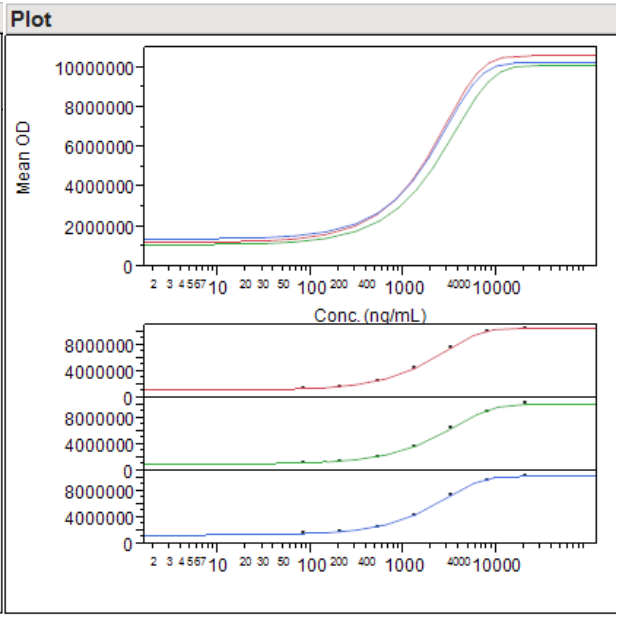

Parallelism Test

Test Results

Parallelism F Test

| Parallel Fit SSE | Full SSE | NDF | DDF | F Ratio | Prob > F |
|---|---|---|---|---|---|
| 1.955e+11 | 1.11e+11 | 6 | 12 | 1.523 | 0.2517 |


## Day 2 (A3)

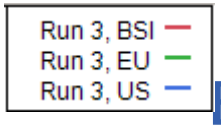



Parallelism Test

Test Results

Parallelism F Test

| Parallel Fit SSE | Full SSE | NDF | DDF | F Ratio | Prob > F |
|---|---|---|---|---|---|
| 1.533e+12 | 2.273e+11 | 6 | 12 | 11.485 | 0.0002* |



# PK assay - EBF Biosimilar Evaluation Group

## Recommendation for PK assays:

- Very well covered by the AAPS Biosimilar APC
- Use of one assay supported by outcome of the EBF 2012 survey
- Clear and feasible statistical approach for establishing bioanalytical similarity (incl. link to software!)
- Follow recommendation for biosimilars but allow for lighter approaches (eg correction factors) for other comparability studies
- No need for further EBF initiative

EBF

# ADA assay - AAPS Biosimilars APC

## Status

- The Biosimilars APC presented on immunogenicity assays at the AAPS Annual meeting in Nov 2013 and NBC 2014
- Going towards a recommendation for **one assay,** where possible
- Working on a recommendation on how to demonstrate comparable response for biosimilar and reference ADA
- The aim is to publish the recommendations in a White Paper early 2015

# ADA assay - EBF Biosimilar Evaluation Group

- **EBF community divided approx. 50:50 in survey from 2012**

**One or two assays?**

- **Two assays:**
  - True ADA response for both, but complex to compare results

- **One assay:**
  - Less inter-assay variability, one analysis only, blinding feasible
  - How to demonstrate that ADAs are detected equally for both drugs
  - One or two positive control ADAs?
  - Drug tolerance one or two drugs?

# ADA assay - EBF Biosimilar Evaluation Group

## Recommendation for ADA assays

- Going towards recommending **one assay**, but criteria needs to be defined
- Maintain biosimilar evaluation group within EBF IGM
- Closely follow initiatives from AAPS Biosimilar APC
- Present final recommendation on ADA assays when AAPS white paper is published