Why Duplicate's in PK Ligand Binding Assays

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on behalf of the EBF

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10 – A New Journey Begins

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Historical reasons for duplicate analysis

- Scientific
  - Limitations in the technology
  - Quality of reagents

Is this still the case?

Technology has advanced – LBA and automation
Reagent's are of higher quality

Regulations

- FDA – calibration curve can use single or replicate. For all assays the key factor is the accuracy of the reported results. This accuracy can be improved by the use of replicate samples

- EMA - It is recommended to assay a study sample in replicate

What is this based on?
These are recommendation's?
Are these recommendations still valid?

Current practice in industry

- Three approaches
  - Those that always do duplicate
  - Those that scale towards both
  - Those that do singlet

EBF

- Identified this subject as an important topic for the industry

- Ongoing and future direction
  - Discussed in March 2017 and EBF surveyed
  - Re-surveyed October 2017
  - At this meeting:
    - Today's Session
    - Tomorrow's Workshop

We are not alone

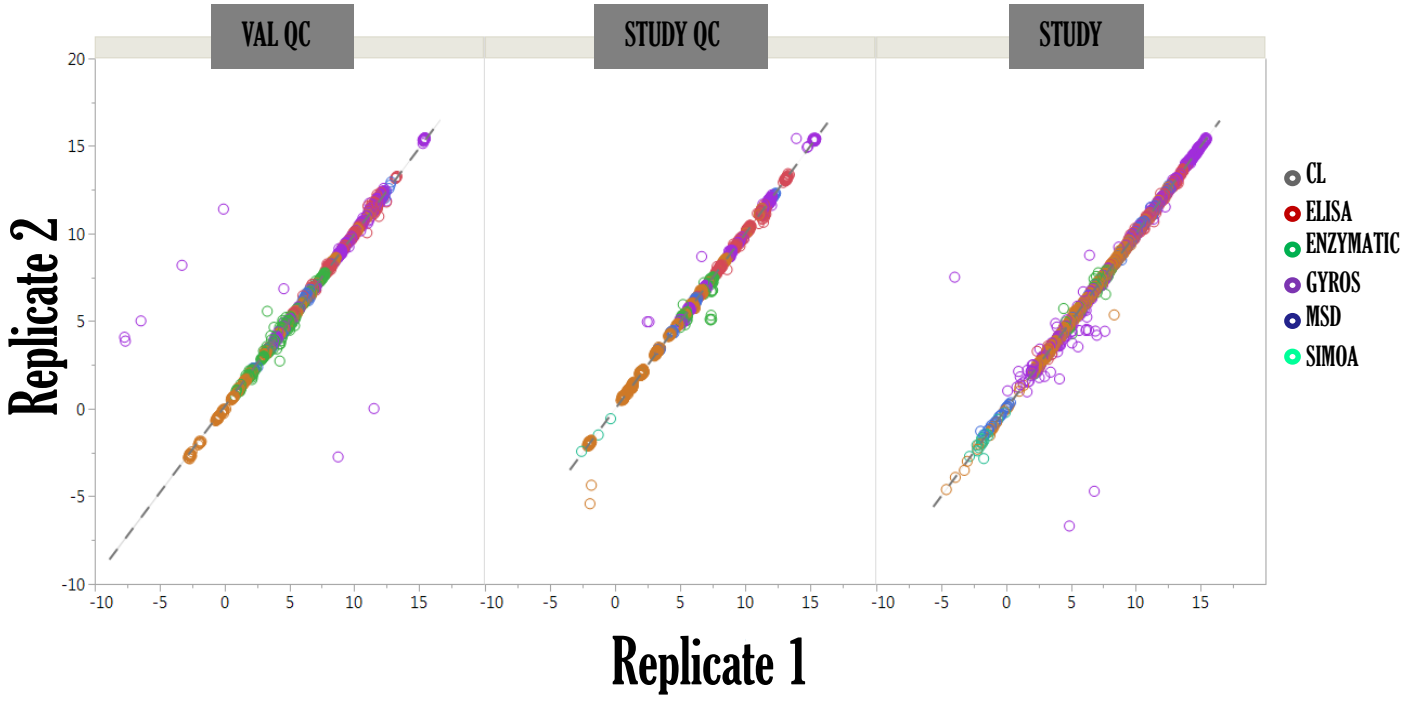
- Discussions at other conferences
- EBF and IQ engaged in a synergistic initiative
  - IQ data presented @ EBF/AAPS/JBF sister meetings

IQ progress

Blinded' data from validated assays across 5 companies, looking at validations and study runs across multiple platforms

Draft data

Presented at both sister meetings, (September 2017, Lisbon and Weehawken)



IQ progress

- Conclusions from ongoing initiative
  - Preliminary results are very encouraging and support the continued investigation into use of singlets in ligand-binding assays for bioanalysis
  - We will continue to gather additional data for a more inclusive dataset that will allow comprehensive statistical analysis for quantitative assessment
  - Based on our preliminary results, other data in literature, and in anticipation of future improvements in technology, we recommend that the ICH M10 guideline provide language that allows flexibility for the use of singlets in LBAs when appropriate

Why challenge duplicate analysis?

- The driver for what we do, should be data driven, not based on historical reasons and the fear to change

  - Sound scientific data
  - Quality, no impact to safety
  - Speed of deliverables
  - Ethical – cost

Discussion's in this session

- Engage scientific (EBF) community to put their shoulders under one of the game changers for LBA
  - 'Do more with less', or at least 'do the same with less'
- Use data to drive process change across the industry
  - Share with the industry who are not experienced
  - Share with industry who are reluctant to change
  - Share with industry fearing '483'
- Aim at influencing current and future guidelines to acknowledge singlet data as valid
  - ICH M10

Next steps in EBF

- Continued discussion
  - Data sharing to ensure data driven recommendations
  - Workshop tomorrow
  - Further collaboration with other industry groups

- Value of EBF in this
  - Open sharing of pre-competitive (non-IP) data in a Pharma/CRO non profit organization

Acknowledgment

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