Successful transfer of ligand binding assays between different laboratories

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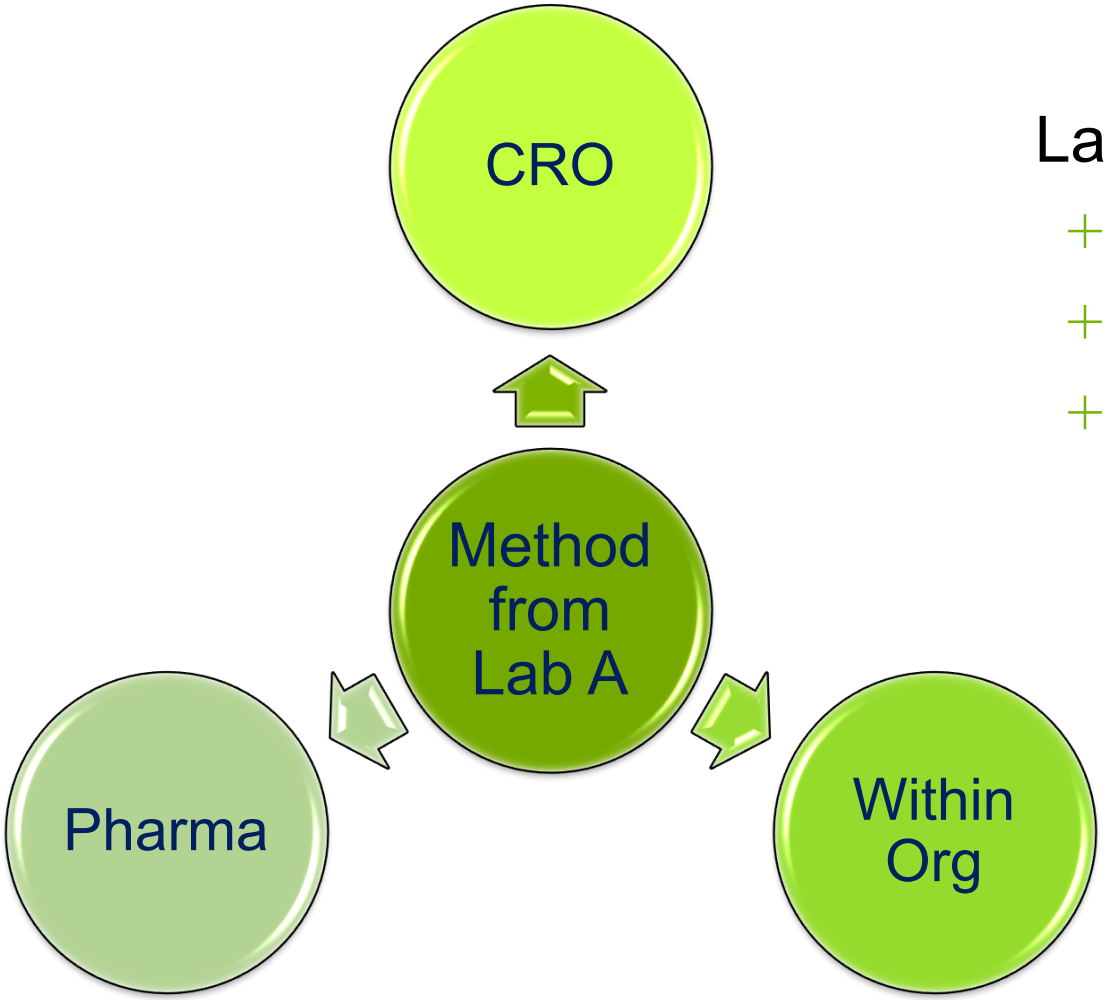
Overview

- Molecular classes and transfers at Envigo
- Method transfer reasons and challenges
- Case studies
- Pre-requisites
- Validation requirements: tiered approach?
- Summary

Range of molecular classes

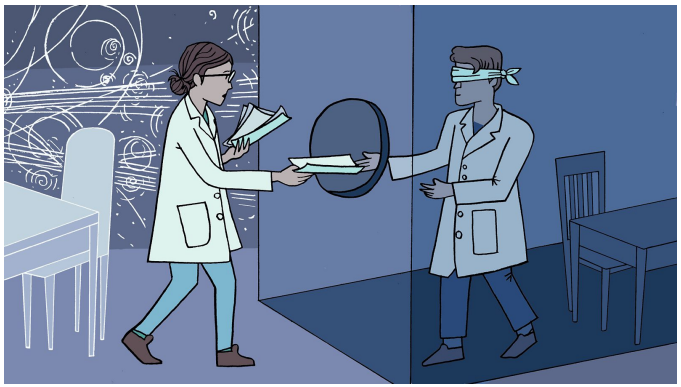
Product Type	Test Materials	Studies
Biopharmaceuticals (Drugs)		
Recombinant Proteins	>150	>550
Monoclonal Antibodies/ADCs	>200	>750
Peptides	>100	>550
Oligonucleotides	>50	>150
Vaccines		
Biotech / Inactive Vaccines	>150	>350
DNA and Live Vaccines	>50	>100
Advanced Therapies		
Gene Therapies	>30	>80
Cell Therapies	>20	>60

What is method transfer?



Lab A:

- Pharmaceutical Company
- CRO
- University (Academia)



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Why is method transfer important?

- Outsourcing trend
- Different laboratories
- Multiple laboratories
- Different regulations
- Different guidelines
- Confidence in assay
- Extent of experiments required?
- Full validation?

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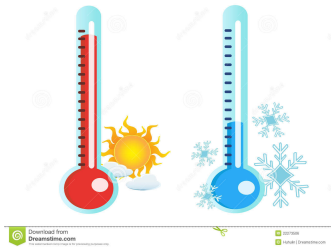
Factors affecting transfer

KEEP
CALM
AND USE THE
SCIENTIFIC
METHOD



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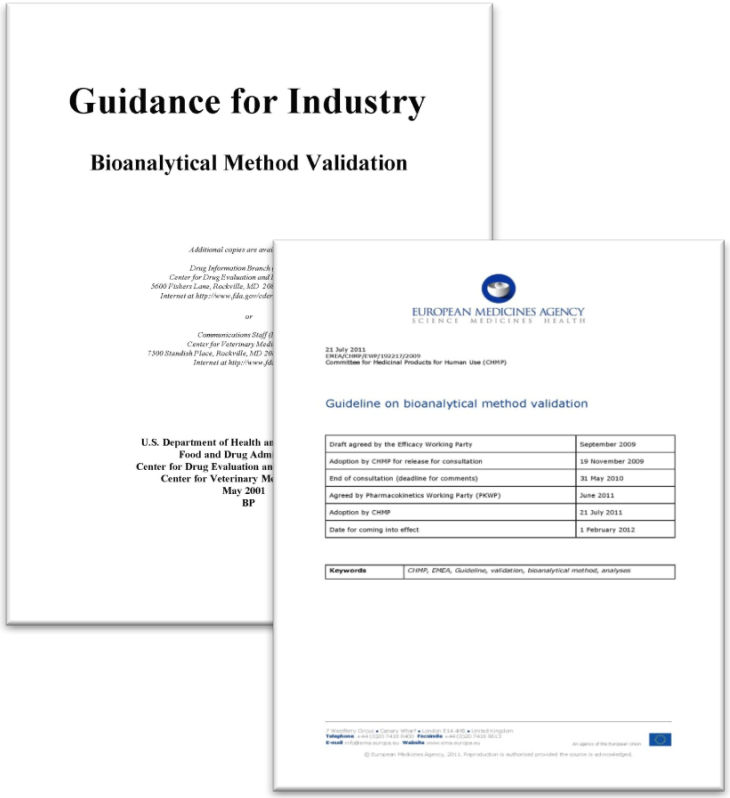
Regulatory

- FDA/EMA guidance - single precision and accuracy assay to almost a full validation

- 2001 FDA Guidance defined different categories of validation:
- Full validation
- Partial validation
- Cross validation



- Method transfers covered in Partial Validation sections – but no details about extent of experiments required

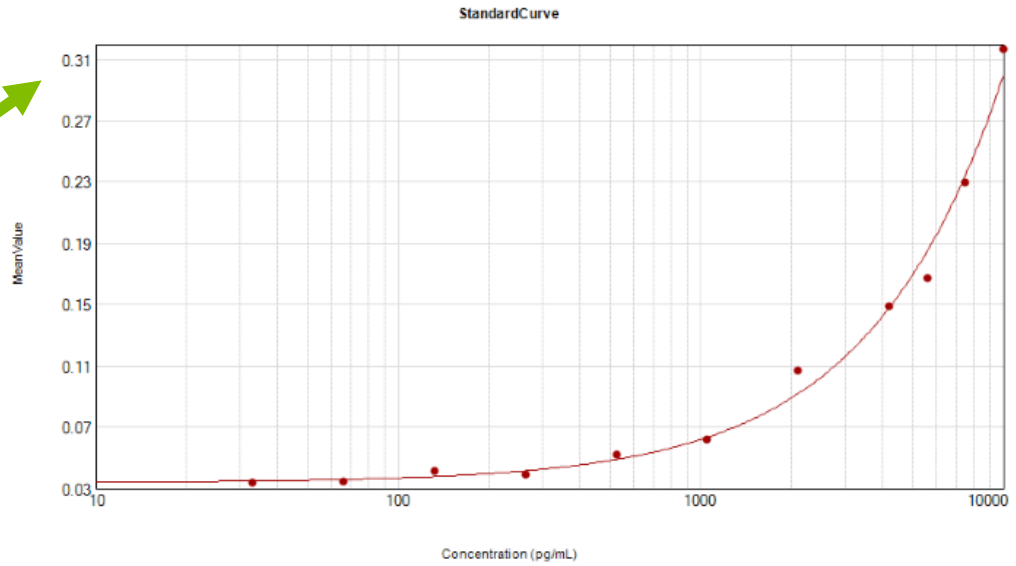
Transfers at Envigo

- Wide range of assay transfers
- Established Sponsor method
- Data comparable between sites
- Suitable for regulatory validation (if required)?
- Three inter/intra runs
- Selectivity/matrix effects
- Biological questionnaire

Case study 1: PK using commercial antibody pair

- Previously developed and validated at another CRO
- ELISA
- Method provided
- Report made available after start of transfer
- EMA/FDA guidelines quoted
- 100 to 5800 pg/mL
- 1 in 20 MRD

Peak absorbance at 0.31
(Wavelength 450-540)



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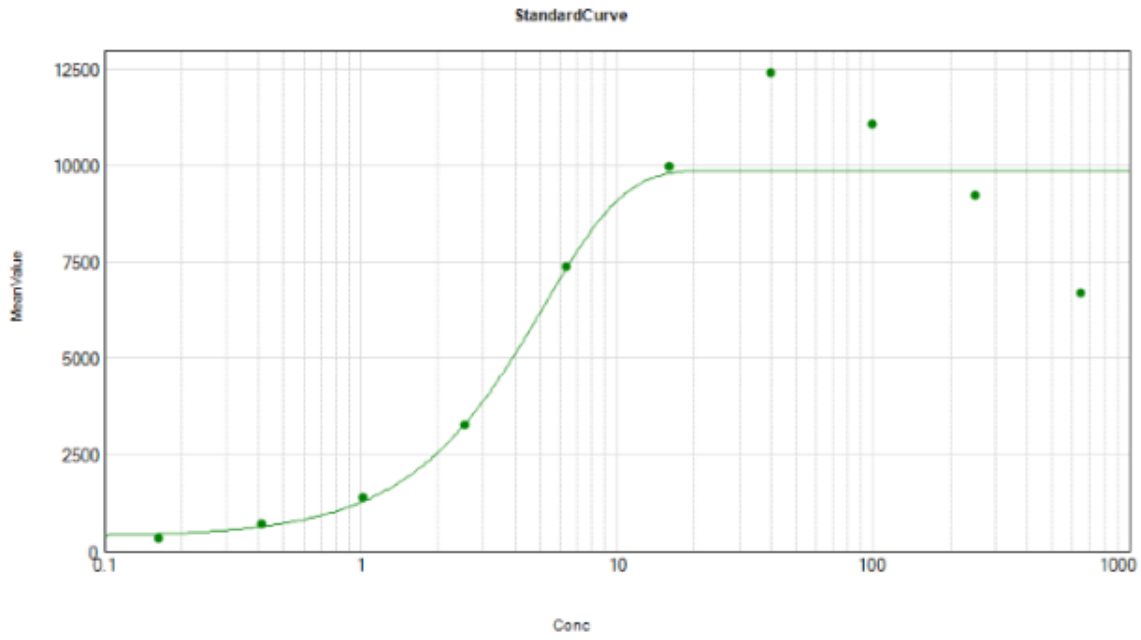
Case study 2: PK developed at Sponsor site

- Method developed and qualified
- MSD
- Used routinely in sample analysis
- Not validated to EMA guidelines
- Change of matrix

- Prozone
- Buffer blanks
- Matrix effects
- Frozen/fresh



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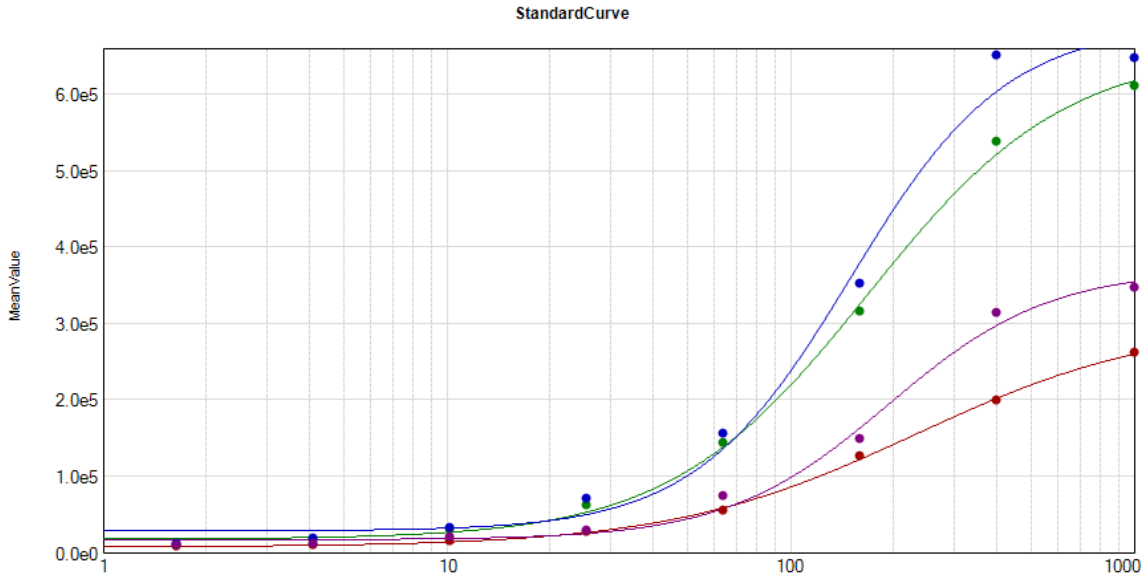
Case study 3: PK developed at alternative CRO

- Developed in buffer
- No buffer monkeys!
- Matrix effects
- Selectivity dependent on cyno strain
- Low sensitivity required
- Transferred to Gyros



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Pre-requisites for successful LBA transfer

- Assay validated to EMA/FDA guidelines
- Clear and concise method
- New reagents fully assessed (e.g. polyclonals)
- ‘Sponsor’ tricks of the trade shared
- Criteria agreed between labs
- Exchange visits?
- In-house QCs (including dilution QCs?)
- Transfer QCs
- ISR agreement
- Considered fit-for-purpose
- Agreement on validation requirements

Validation of transferred LBAs: tiered approach

Tier 1

- Use ‘out of the box’
- May not include QCs
- Assay fit to detect presence of drug

Tier 2

- Pharmacology, comparison of formulations, screening of anti-IDs
- Acceptance criteria within ±30% RE: assay is repeatable (3 QC levels)
- Matrix effects assessed

Tier 3

- Dose Range Finding Studies (internal transfers)
- ‘Scientific Validation’ using 3/5 QC levels
- Selectivity and matrix effects assessed

Tier 4

- GLP tox, GCP
- Full validation according to EMA/FDA guidelines

Summary

- Transfer of assays essential
- Without robust assays, transfers fail
- Transfers become development
- Pre-requisites identified
- Level of validation to be agreed
- Guidelines unclear: case by case basis
- For further discussion at the EBF?

Acknowledgements

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