Transfer and cross-validation of a PK assay across 3 different sites (Switzerland, UK and USA)

(Ligand Binding Assay)

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NovImmune – *Company Profile*

- Focused on advancing targeted medicines that address the causes rather than symptoms of disease
- Proprietary next-generation antibody drug platform
- Bench-to-bedside & pilot manufacturing capabilities
- Pipeline of differentiated antibody-based products
- Scientific excellence
  - Ten patent families
  - 60+ peer-review journal publications
  - 30+ collaborations with academic institutes
  - Roche/Genentech Alliance

Presentation Outline

- What drives Biotechs to outsource assays
- Case study: transfer and cross-validation of a PK assay at 3 sites
- Lessons learned & conclusions

What drives Biotechs to outsource assays?

- Expertise
- Limited internal resources
- Regulatory compliance (e.g. GLP)
- Logistical challenges
- Clinical study requirements

Case study: cross- validation of a PK assay at 3 sites

Clinical study requirements

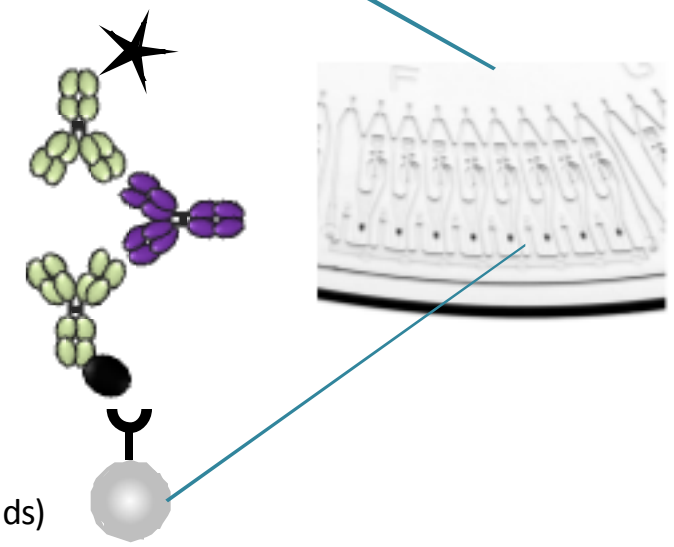
- Challenging patient population
  - Rare and life threatening disease indication
  - Low sample volume
  - Rapid turnaround of data
- Multi-site global clinical trial
  - Sample analysis at the right time, at the right place to satisfy data delivery requirements

Case study: cross-validation of a PK assay at 3 sites

Assay format

- **Gyrolab**
  - **Fast data turnaround capacity**
  - **Suitable with low sample volume**
  - **Microfluids sensitive to sample/reagent quality**

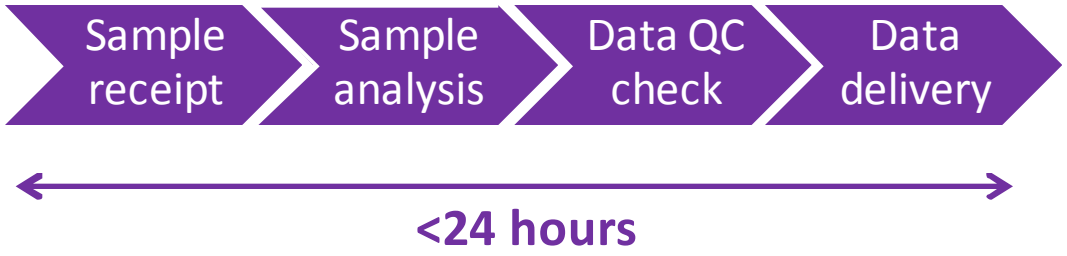
- Bridging assay
- Sequential format



Case study: cross-validation of a PK assay at 3 sites

CRO requirements for the study

- Gyrolab technology availability
- Expertise
- Location (EU + USA)
- Short data delivery turnaround time



Case study: cross-validation of a PK assay at 3 sites

Assay transfer + validation strategy

- Assay developed at NovImmune (CH)
- Transfer + Validation at CRO 1 (UK)
- Validation at NovImmune (CH)
- Transfer + Validation at CRO 2 (USA)
- Cross-Validation at 3 sites (CH, UK, USA)

$\Rightarrow$ Ruggedness assessment

Case study: Transfer of a PK assay to 3 sites

Assay development at NovImmune (CH)

- Critical parameters defined
  - Critical reagents
  - Matrix effect/minimum required dilution
  - Working range & QC levels
  - Selectivity & dilutional linearity assessed
- Transfer to CRO 1 (UK)

Case study: Transfer of a PK assay to 3 sites

Transfer and validation at CRO 1 (UK)

Challenges

- New Gyrolab system
  - Microfluidics present different challenges to ELISA/MSD
  - Time to become familiar with the system and special requirements
- Assay optimisation/troubleshooting required
  - NovImmune analyst visit to CRO 1
  - Technical support from Gyros

Case study: Transfer of a PK assay to 3 sites

Validation summary

Parameter		Validation results
Working range of the method (ng/mL)		From 62.50 to 8000.00
System suitability ✓		Overall Intra- and Inter- accuracy and precision within criteria*
Matrix Effect ✓	Normal matrices	100% of naïve individual <LLOQ Between 80% to 100% of individuals at the LoQC and HiQC levels within criteria*
	Lipaemic and Haemolysed matrices	
Dilutional Linearity ✓		Up to 1 in 2000 (in addition to 1 in 3 MRD)
Hook effect ✓		No hook effect at 500 µg/mL
Short term stability ✓	Room temperature	24 hours
	Freeze/Thaw Cycle	5 cycles
Long Term Stability ✓		18 months stability at both -20°C and -80°C

*** %RE ≤± 20% and %CV ≤ 20%, except for LLOQ and ULOQ for which %RE ≤± 25% and %CV ≤ 25%,**

Case study: Transfer of a PK assay to 3 sites

Validation completed successfully

- Transfer to CRO 2 (USA)

Case study: Transfer of a PK assay to 3 sites

Transfer and validation at CRO 2 (USA)

Challenges

- New Gyrolab system
  - Microfluidics present different challenges to ELISA/MSD
  - Time to become familiar with the system and special requirements
- Assay troubleshooting required
  - NovImmune analyst visit to CRO 2
  - Technical support from Gyros

Case study: Transfer of a PK assay to 3 sites

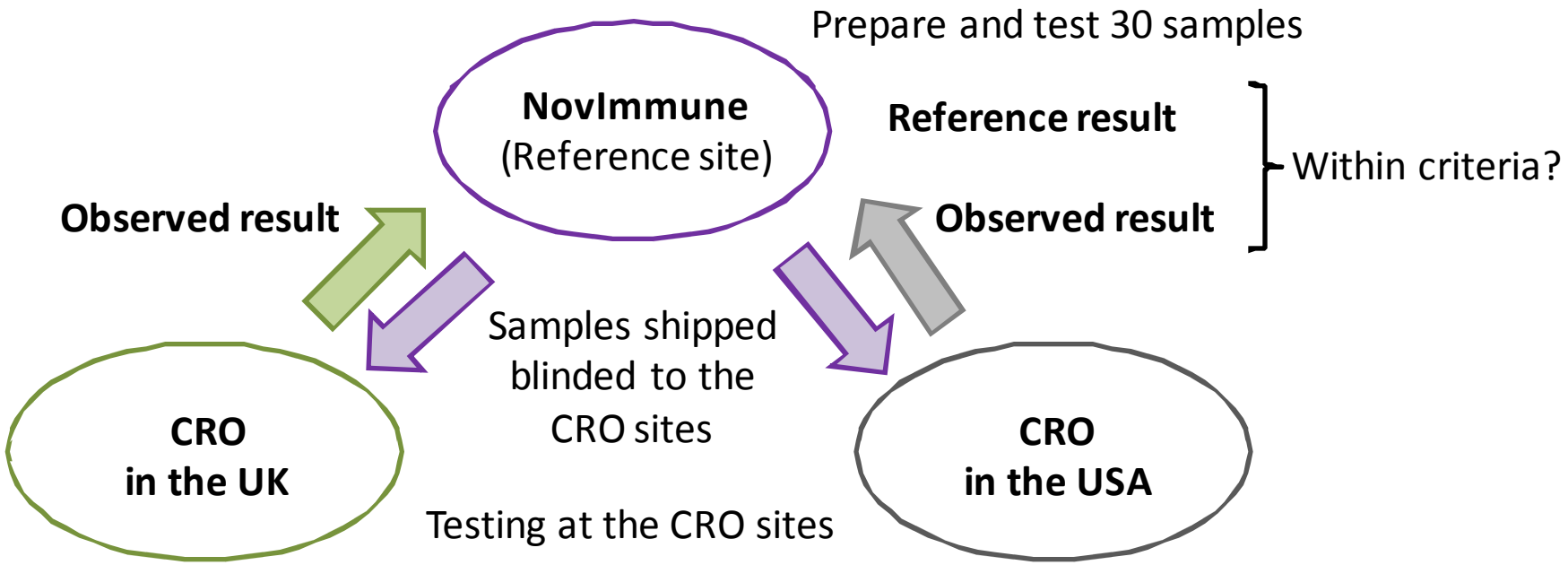
Validation completed successfully

- Cross-validation at 3 sites
  - NovImmune, Switzerland
  - CRO 1,UK
  - CRO 2, USA

Ruggedness assessment

Objective and principle

- Establish inter-laboratory reliability



Ruggedness assessment

Set up of the reference concentration

- Analysis at NovImmune to set the reference concentration
  - 2 assays

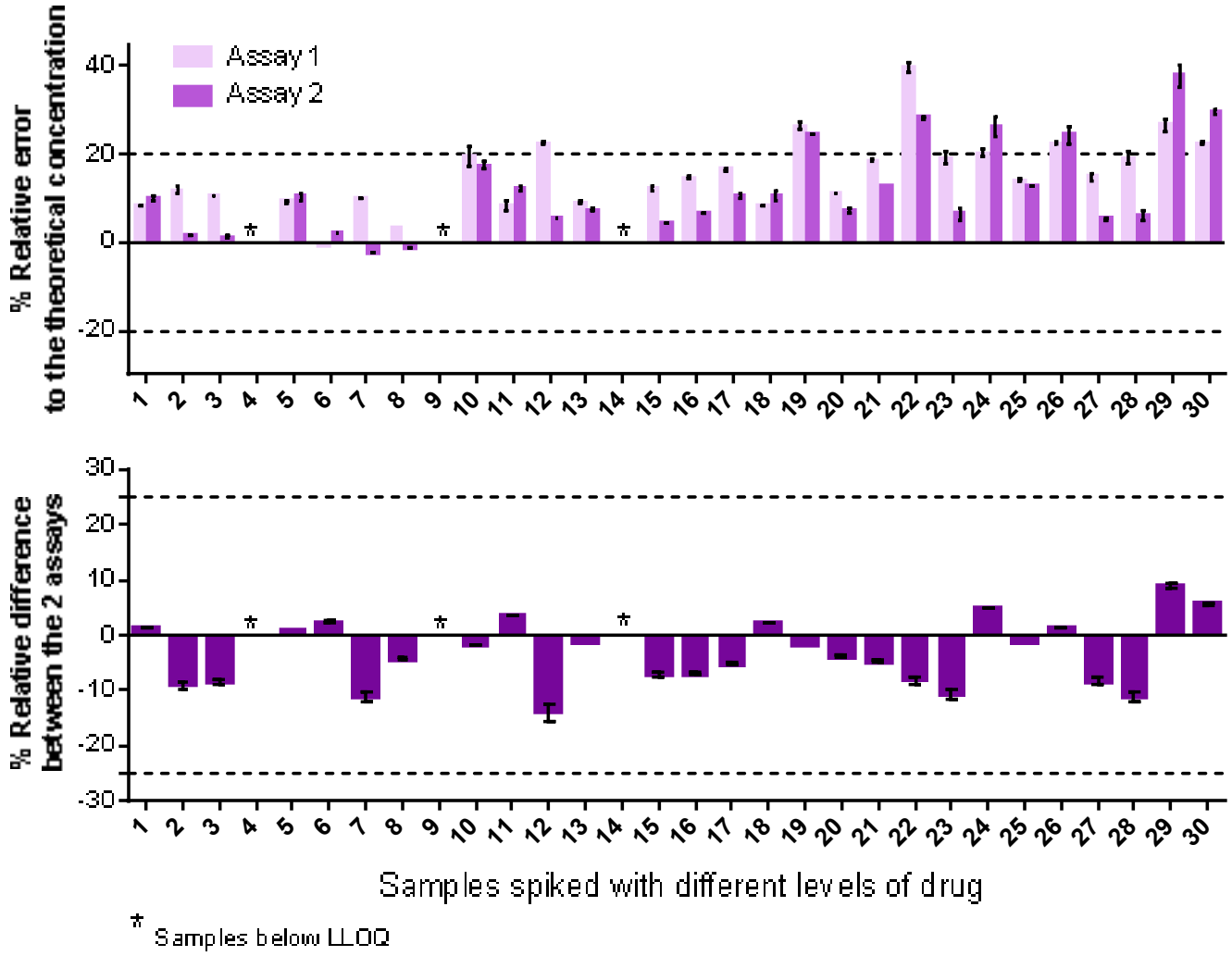
Mean Conc. from the two data sets = Reference concentration for other sites

≠ Theoretical concentration

  - Acceptance criteria:
    - Assay valid (criteria met for calibration curve and QCs)
    - Sample precision ≤ 20%
    - Relative % difference between the 2 assays within ± 25%

Ruggedness assessment

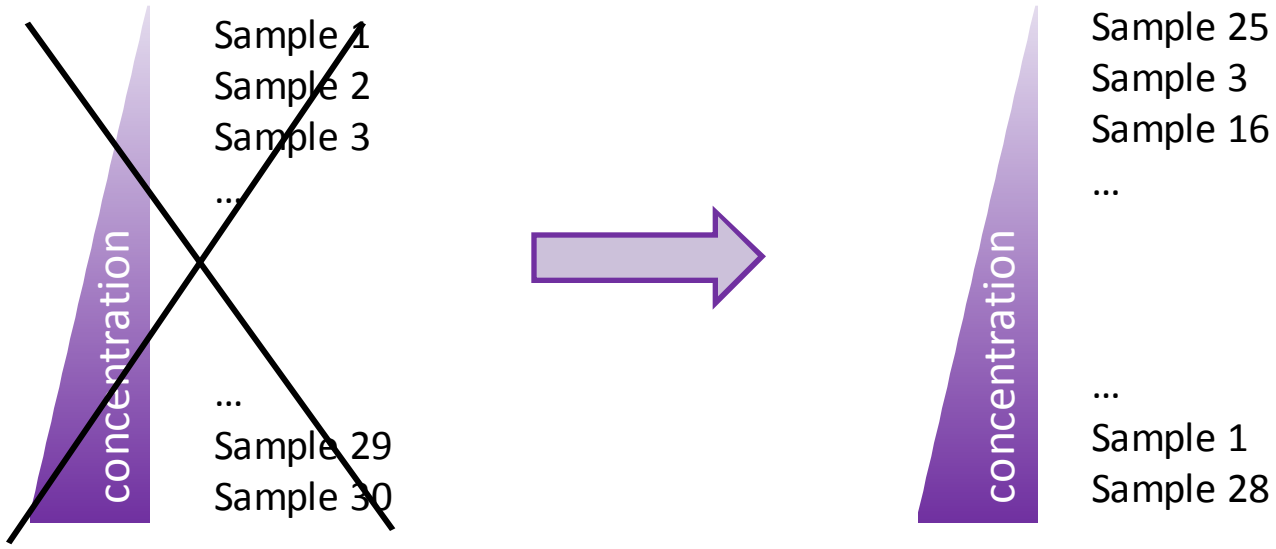
NovImmune data



Ruggedness assessment

Shipment to the CRO sites

- Shipped blinded and analysed at CRO site



Ruggedness assessment

Data analysis

- Results calculated as follows:

Relative Percentage Difference (%) = ((B-A)/A)*100

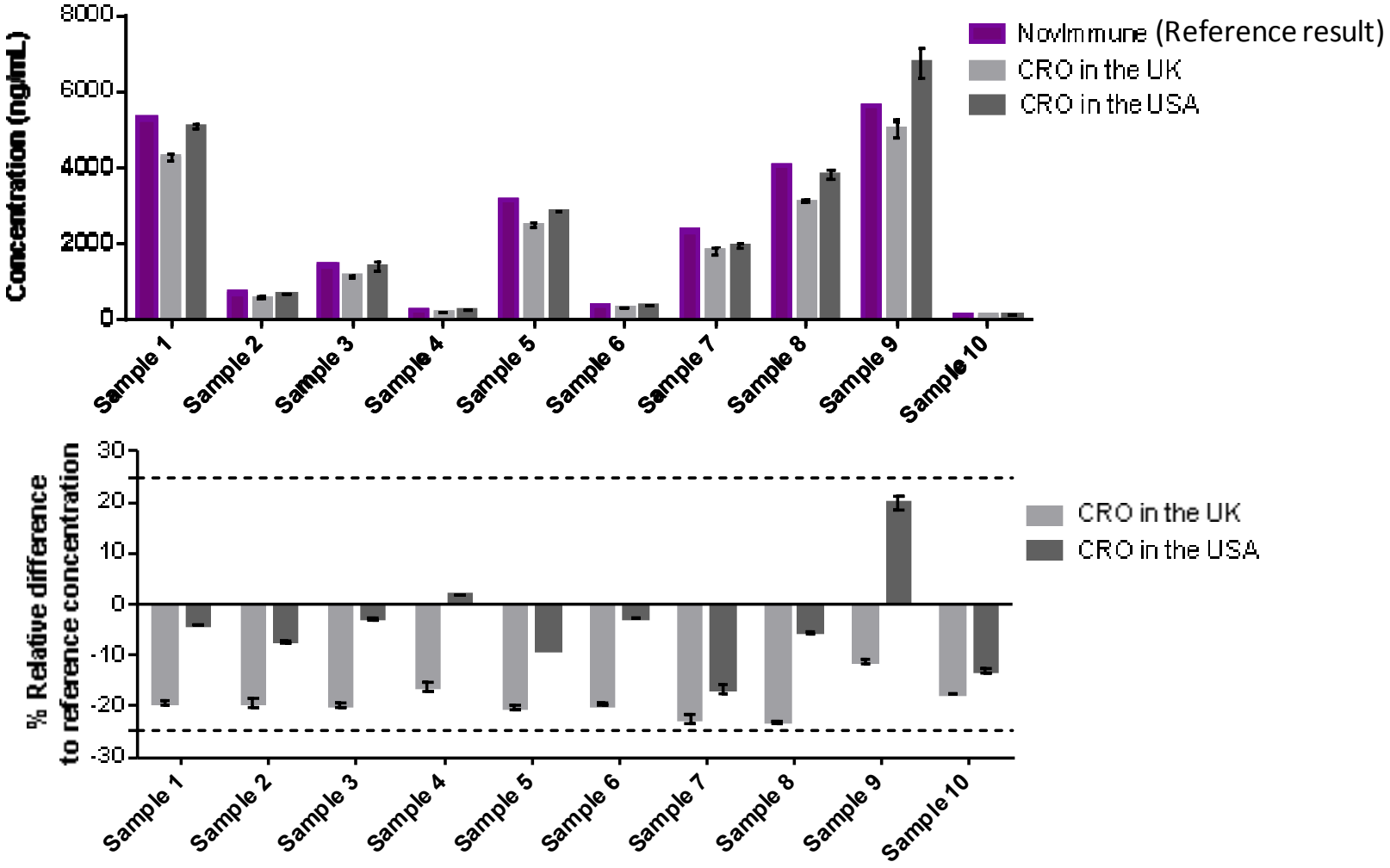
A = Reference result (Mean result from NovImmune)
B = Observed result (at the CRO site)

- Target criteria:

CV ≤ 20% and ***relative percentage difference within ± 25%*** of the reference value for ***at least 80%*** of the samples tested

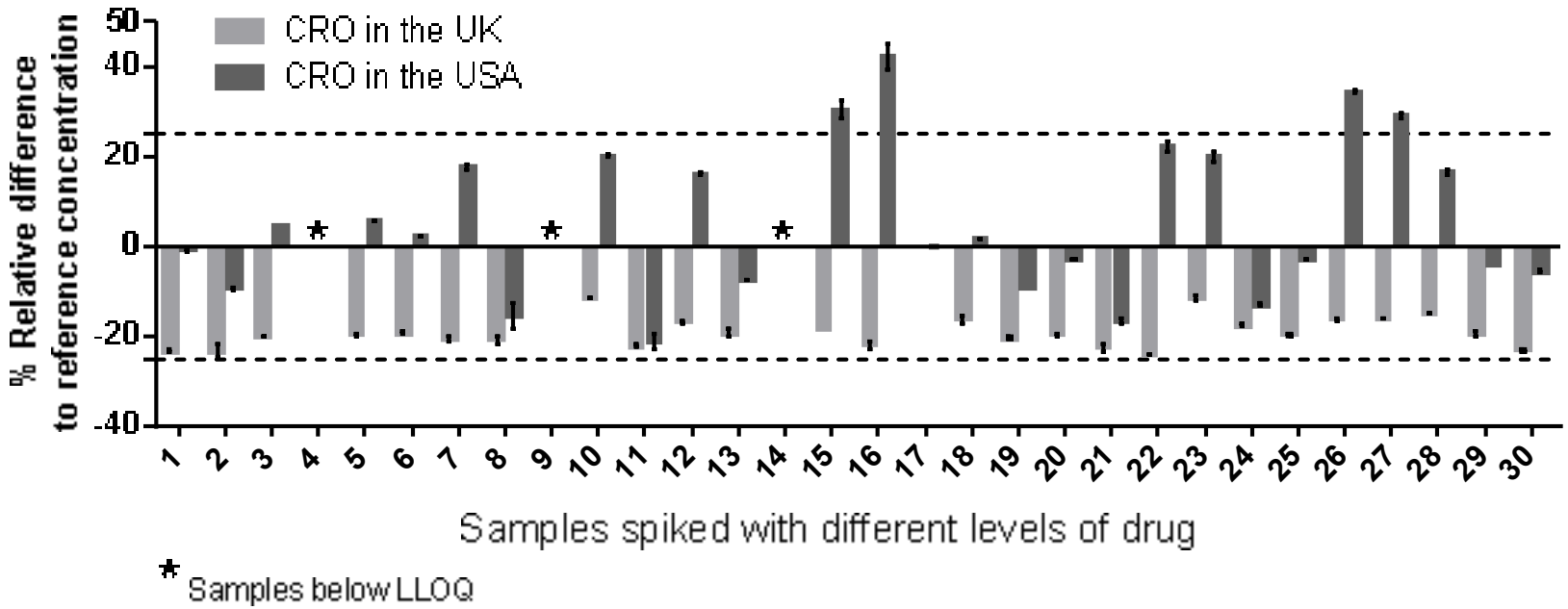
Ruggedness assessment

Data - 10 samples



Ruggedness assessment

Data – Relative percentage difference



⇨ **87% of the samples within criteria** ⇨ **ruggedness assessment successfully passed**

Lessons learned

- State expectations clearly from the start
- Kick off meetings to get to know the teams on both sides
  - Ideally face-to-face meetings
  - Share the background to get buy-in to the project
- Share “know-how” and provide support and advice
  - Let the ***scientists*** talk to each other, share ideas and troubleshoot
  - Be open to client analyst working onsite at CRO

Lessons learned

- ***Good communication*** at all stages of the relationship
  - Expectations and timelines
  - Problems and possible solutions
  - Regular follow-up (TC, email, phone calls)
- Honest feedback from both sides
  - What worked well
  - What could be done better at ***CRO*** and ***Client*** side

Conclusion

- Worked with CRO partners to meet challenging clinical study requirements
- Assay validated at 3 different geographical locations
- Successfully supported data delivery for clinical trial at the different sites

Thank you for your attention!

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