Unilabs
York Bioanalytical Solutions

Qualifying the measurement of endogenous and synthetic spiked pharmacodynamic biomarker in matrix, in the presence of drug

Tessa McDonald – Unilabs York Bioanalytical Solutions

Pharmacodynamic biomarker; What, Why and Context

Unilabs
York Bioanalytical Solutions

"a molecular indicator of drug effect on the target in an organism"

Routinely assessed as exploratory endpoints, increasingly used as proof of concept

Increased scrutiny and regulatory guidance;

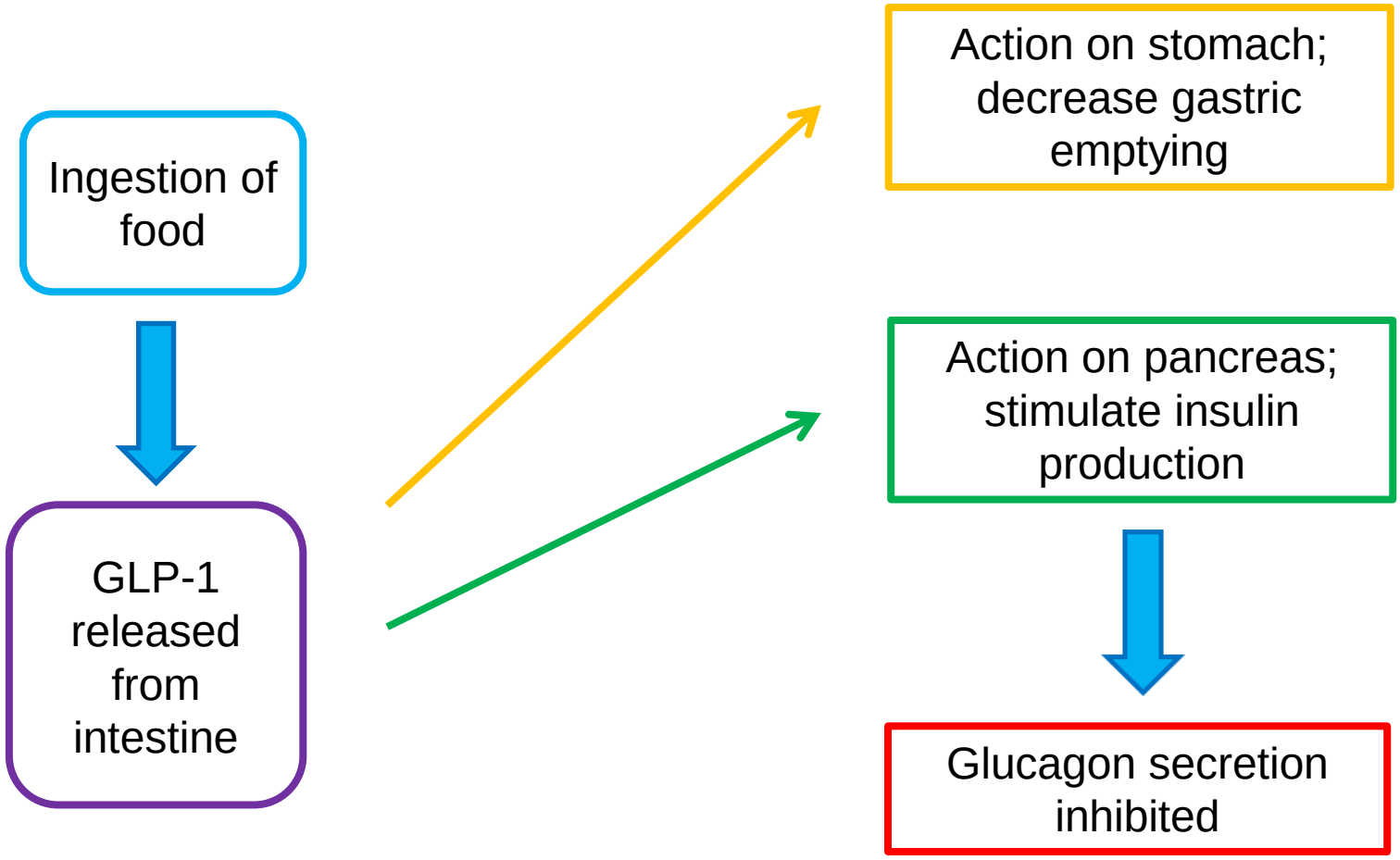
This biomarker method development and validation was conducted in accordance with

The FDA Bioanalytical Method Validation

Guidance for Industry 2018

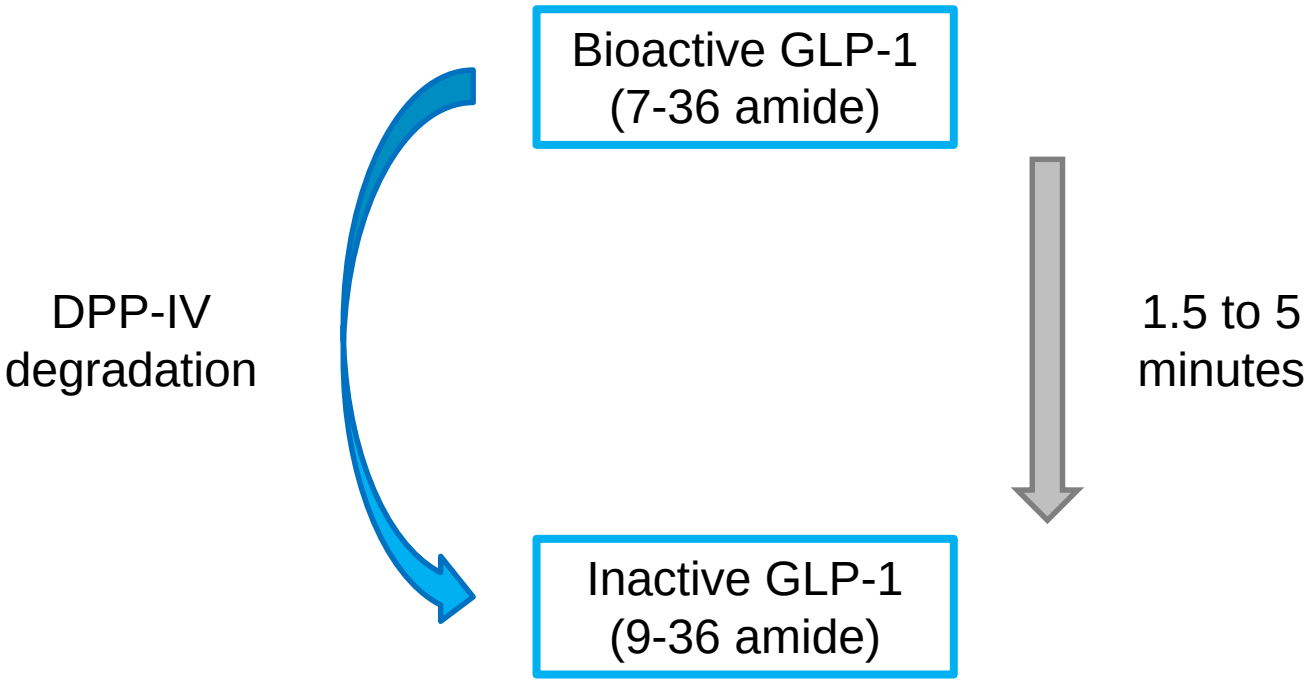
Context of measurement at a CRO – what might the data be used for?

Glucagon-Like Peptide-1 (GLP-1)

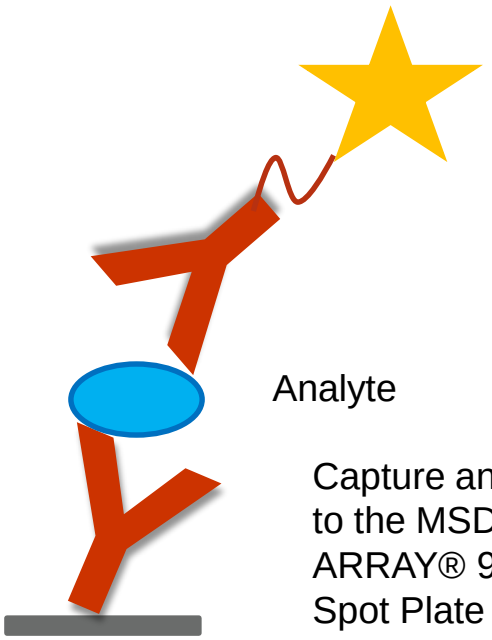


Glucagon-Like Peptide-1 (GLP-1)

Incretin released from intestinal cells in response to food



MSD V-Plex assay



Electrical current applied to the electrode causes the SULFO-TAG to luminesce; Electrochemiluminescence (ECL)

Calibration Standards; made with kit supplied Calibrator and buffer

Quality Controls made with matrix and spiked with external standard

- Low QC – endogenous GLP-1 diluted with buffer
- Medium QC – endogenous GLP-1 only
- High QC – endogenous GLP-1 spiked with externally sourced calibrator

Two-fold MRD

Fit for purpose

MRD = 2 fold ⟶ Target ULOQ QC conc. = 1110 pg/mL

Limitations of assay – highly concentrated standard not available

ULOQ QC level not *quite* achieved in development or validation
(986 pg/mL achieved)

Rules out dilutional linearity – assessment not done

Selectivity data not meaningful – assessment not done

Method was not fully validated but instead was qualified as fit-for-purpose

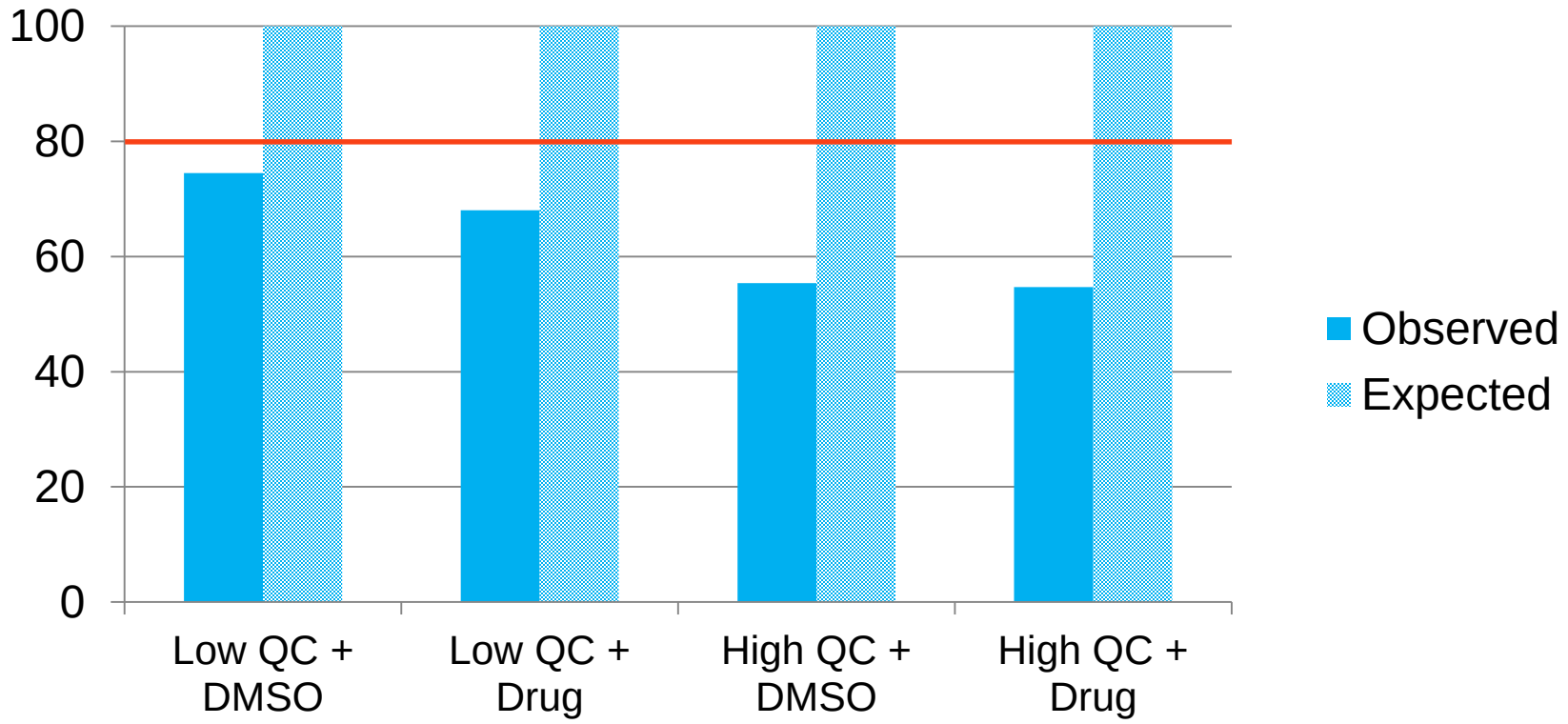
Validation parameters achieved

LLOQ QC – 0.336 pg/mL (target 0.272 pg/mL)
ULOQ QC – 986 pg/mL (target 1110 pg/mL)

Storage at -80°C – one month (further assessments on-going)
Storage at RT – 8 hours
Freeze/thaw cycles – 5
Measurement of GLP-1 in lipaemic sample – acceptable
Measurement of GLP-1 in haemolysed sample – acceptable

Specificity in the presence of Drug

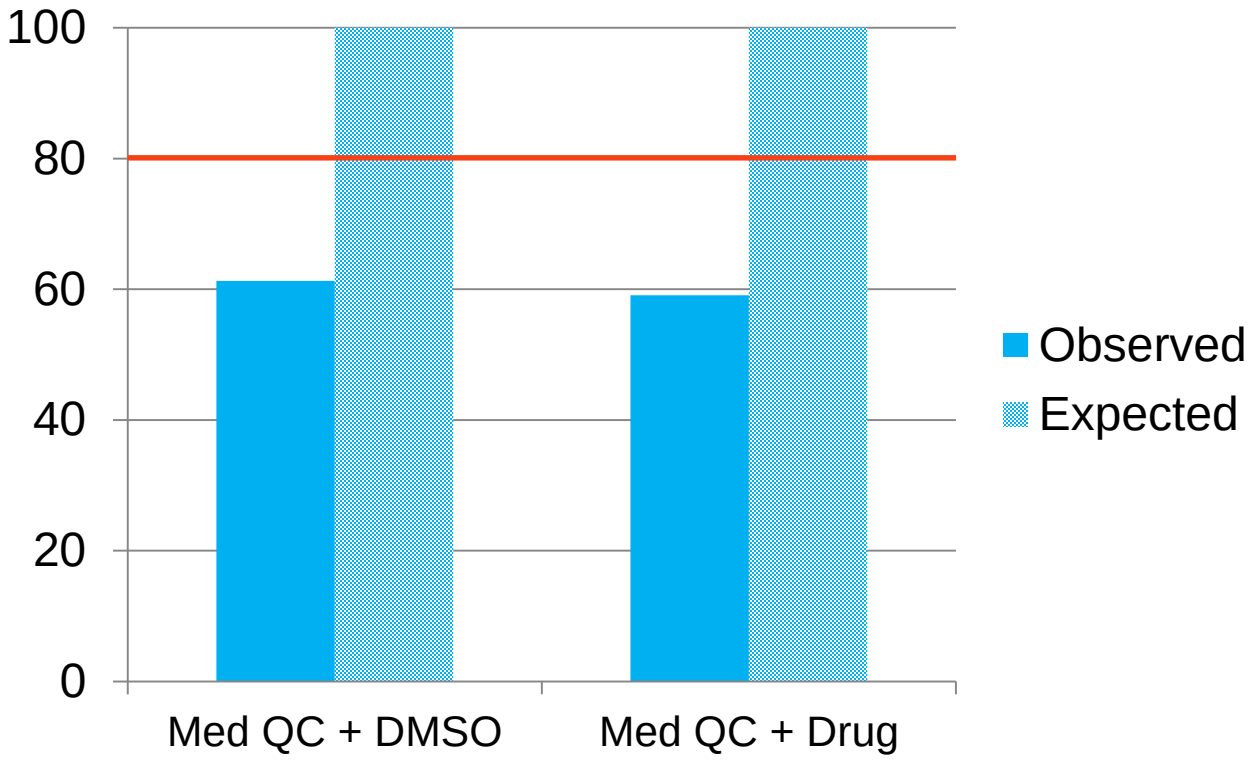
1. Low QCs and High QCs spiked with Drug in DMSO or DMSO alone at 5% spike volume
Accuracy (%) from nominal



Specificity in the presence of Drug - continued

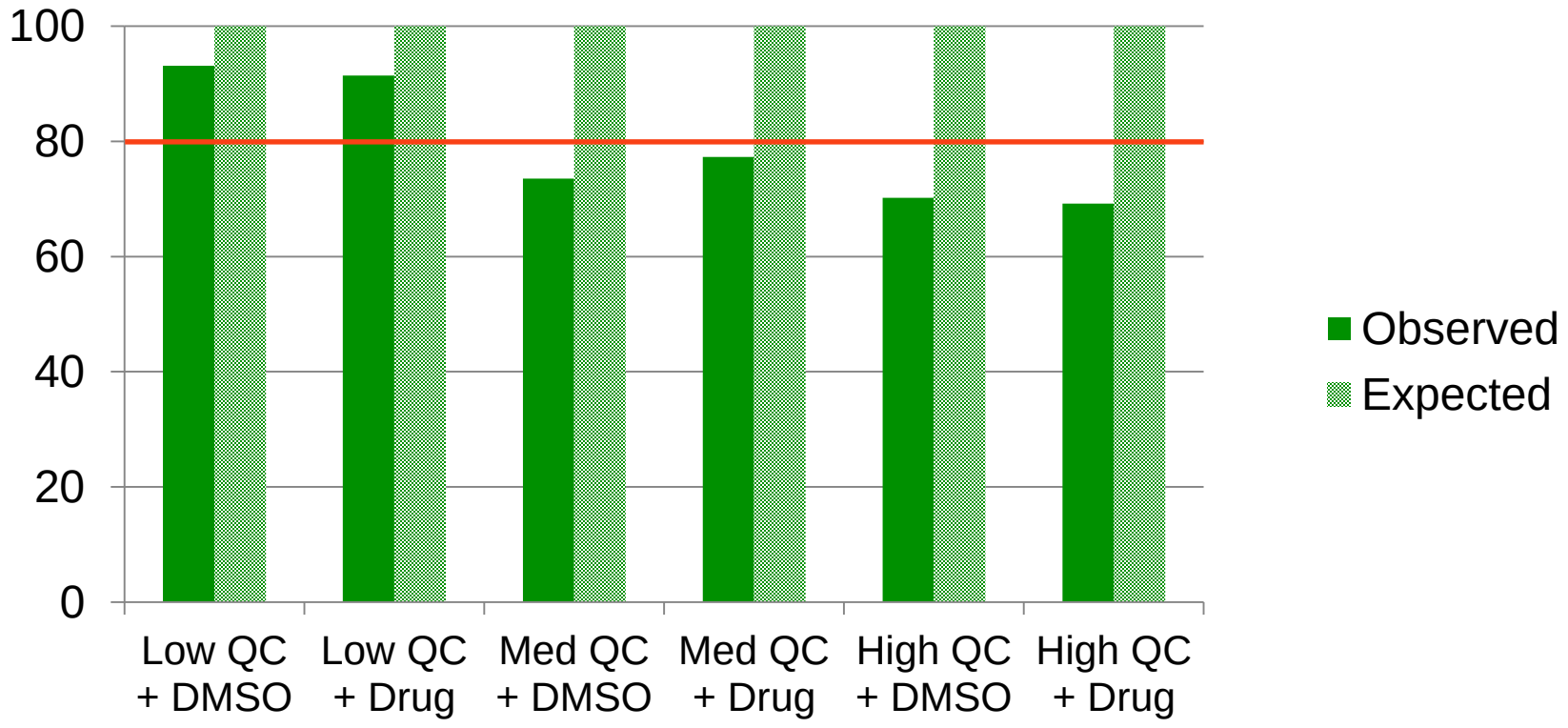
Unilabs
York Bioanalytical Solutions

2. Med QCs spiked with Drug in DMSO or DMSO alone
at 5% spike volume
Accuracy (%) from nominal



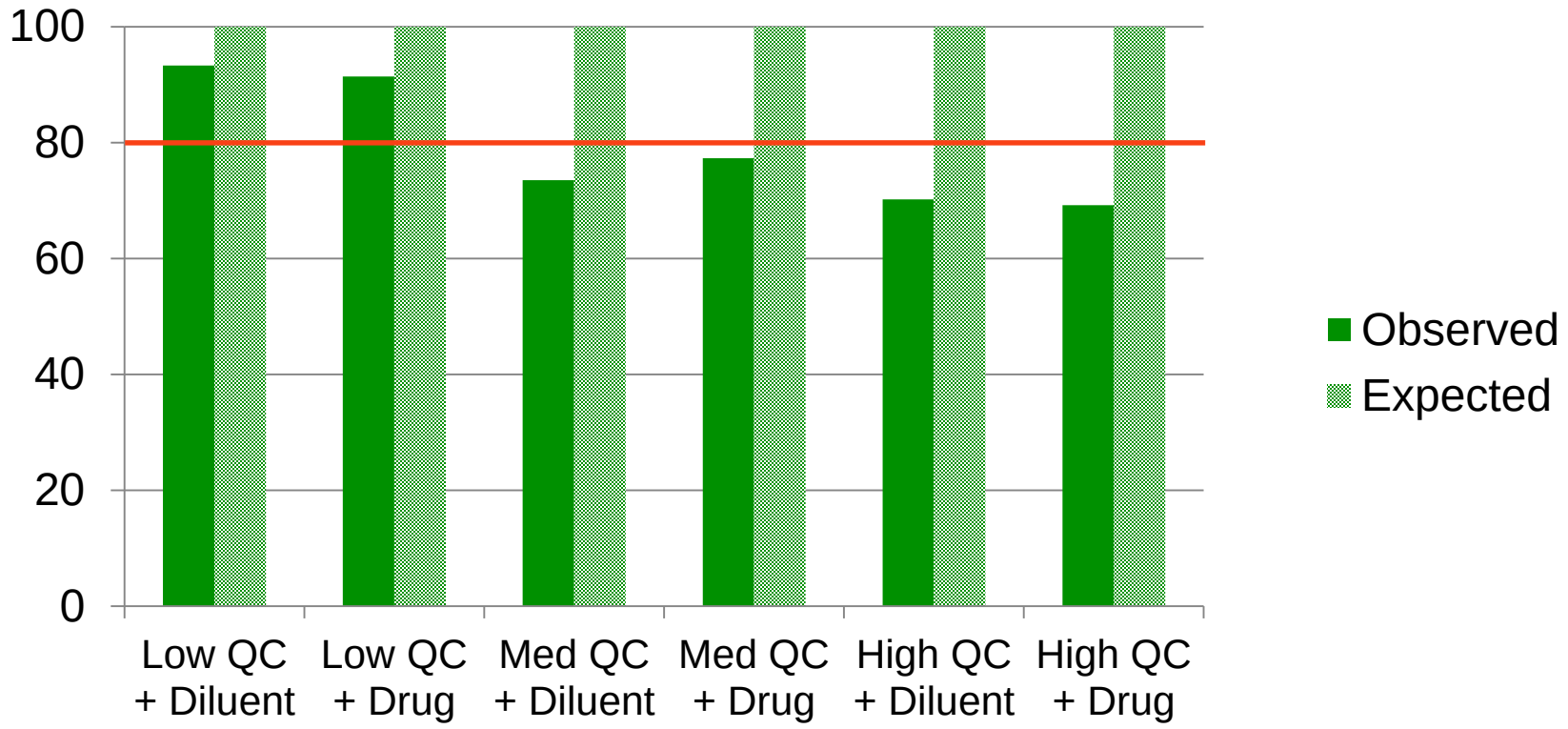
Specificity in the presence of Drug - continued

3. Low, Med and High QCs spiked with Drug in DMSO or DMSO alone at 2% spike volume
Accuracy (%) from nominal



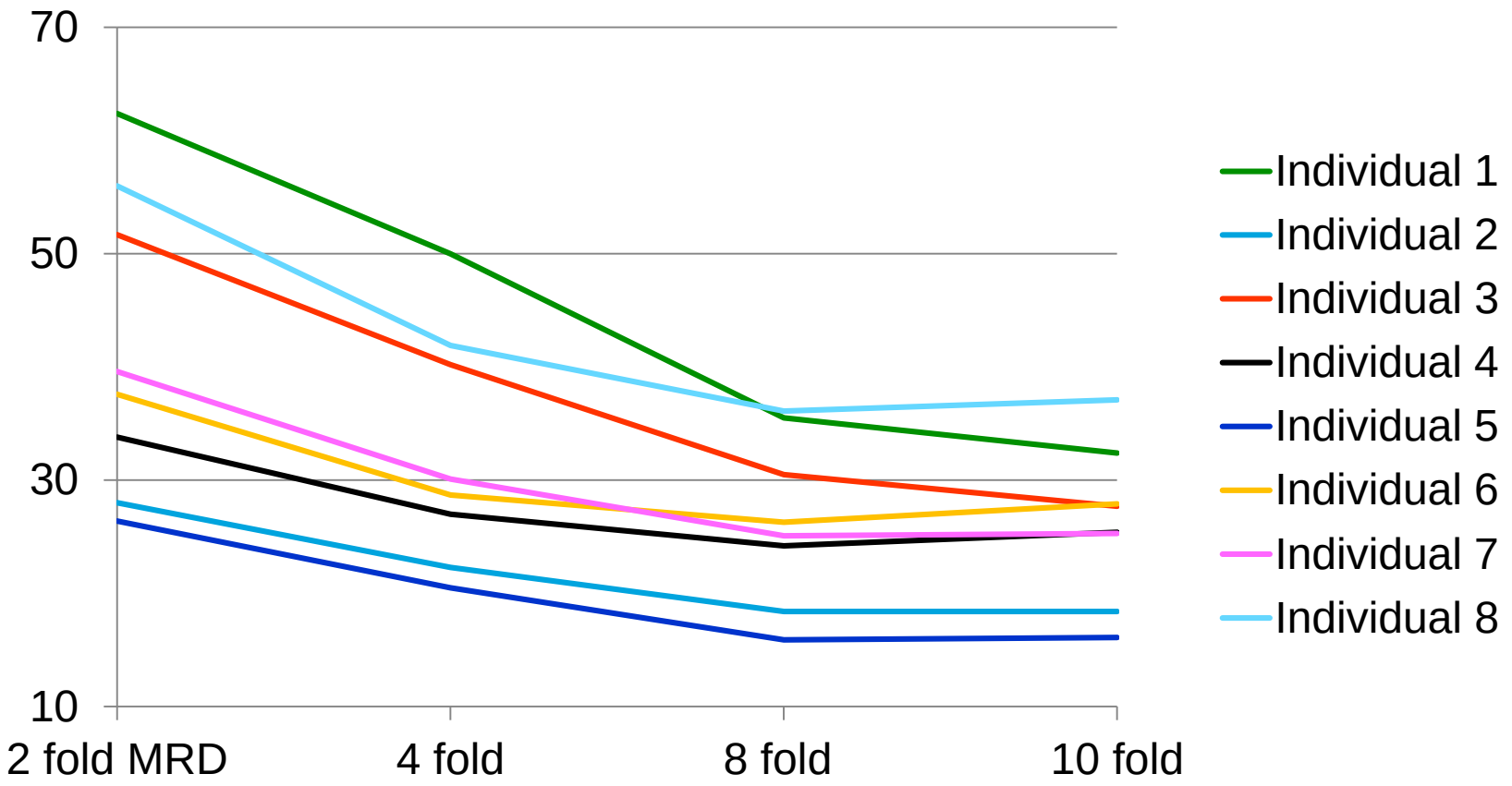
Specificity in the presence of Drug - continued

Tested at expected Drug Cmax concentration
4. Low, Med and High QCs spiked with Drug in Diluent or Diluent alone at 5% spike volume



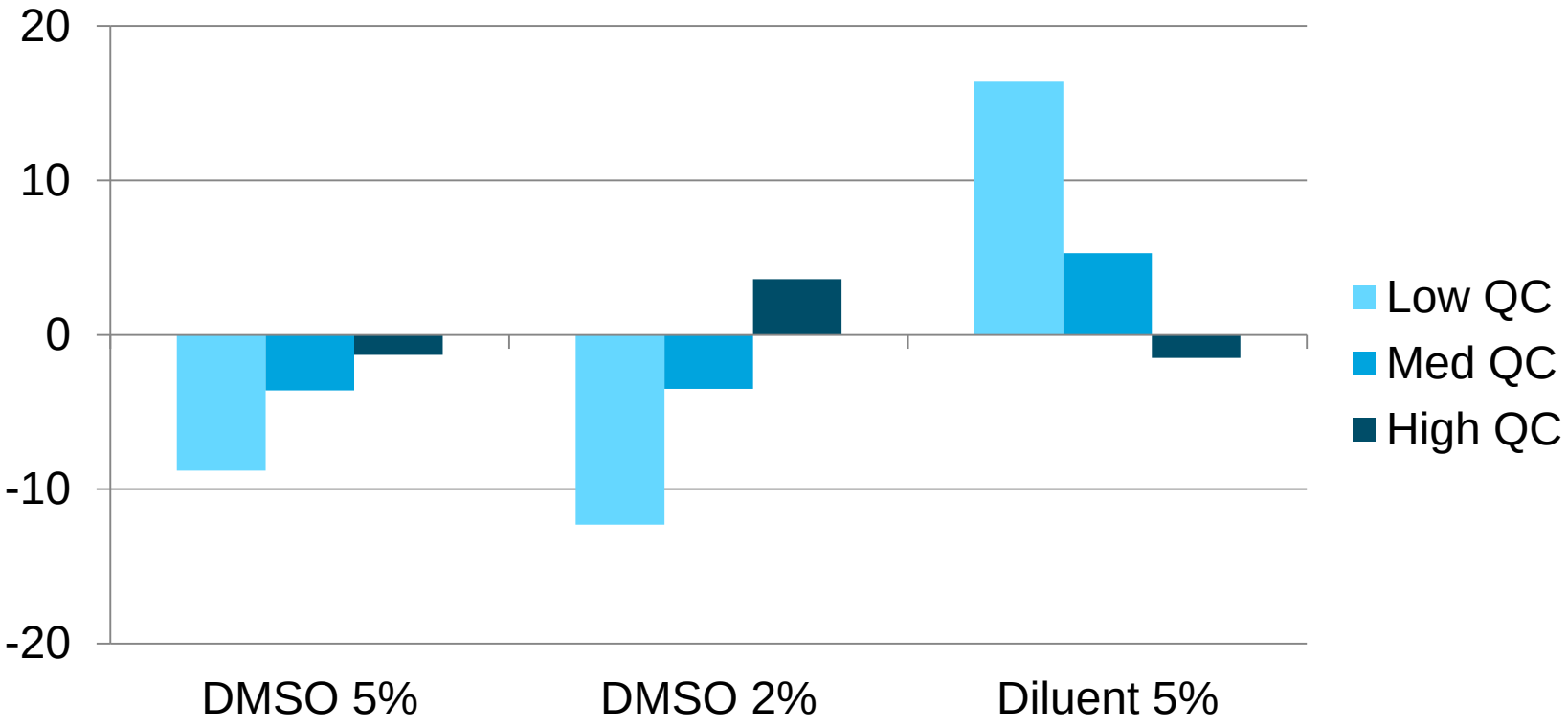
Parallelism data

Dilution corrected parallelism data of measured GLP-1 (pg/mL) from 8 individuals after dilution



Specificity: Spiked vs. Un-spiked

Bias calculated as Drug spiked concentration over Non-drug spiked concentrations



THANK YOU, ANY QUESTIONS?

Thanks to –
Colin Farrell, Unilabs York Bioanalytical Solutions
Elise Jones, Unilabs York Bioanalytical Solutions