The role of EQA providers in the harmonization process:

A Plea for Using Native Sera in External Quality Assurance

Adam Uldall Lecture
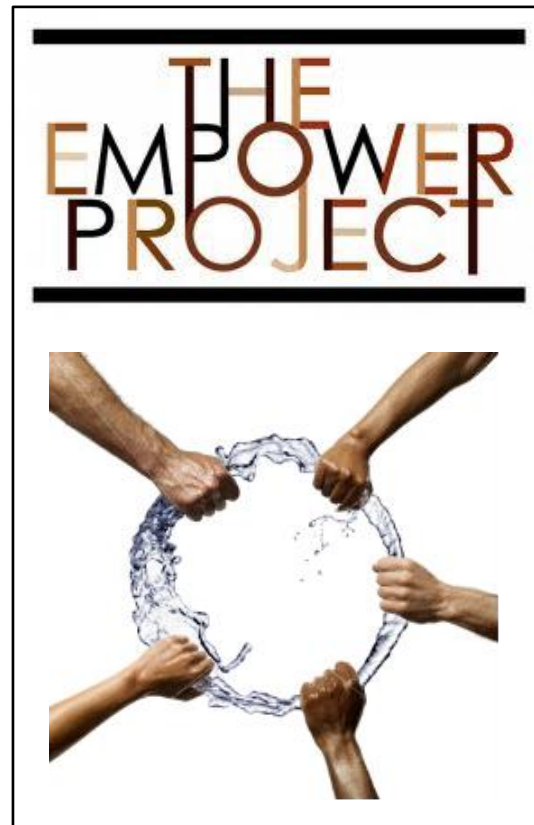**EQALM Symposium Bucharest 2013**

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Introduction

Empower project

Conceptual integration of assessment of analytical quality

Introduction

MASTER COMPARISONS
EQA with panels of fresh frozen single donation (commutable) sera

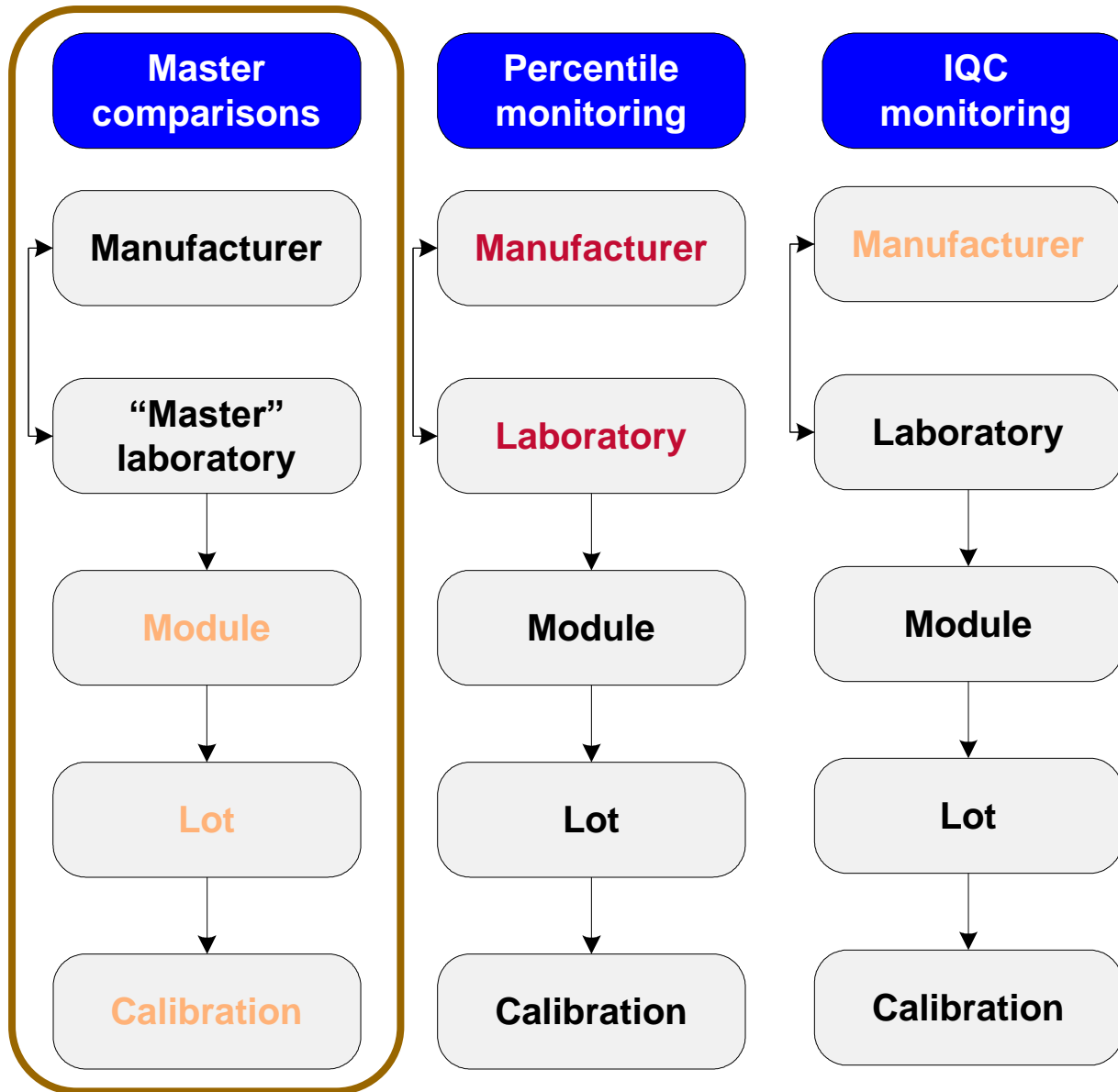**VIRTUAL EQA-1 (Percentiles)**
Mid- to long-term monitoring of patient percentiles across laboratories and manufacturers

THE EMPOWER PROJECT

EDUCATION
Conceptual and statistical education about analytical quality in the medical laboratory

VIRTUAL EQA-2 (IQC monitoring)
Mid- to long-term monitoring of IQC data across laboratories and manufacturers

Assessment of quality components

Master comparisons	Percentile monitoring	IQC monitoring
Manufacturer	Manufacturer	Manufacturer
"Master" laboratory	Laboratory	Laboratory
Module	Module	Module
Lot	Lot	Lot
Calibration	Calibration	Calibration

Harmonization & native samples

"PARADIGM"

"Good samples make good assays"

In

Calibration

as well as

Assessment

Native samples in calibration

Björkhem et al.
Assay of cortisol with a radioimmunoassay method calibrated by isotope dilution-mass spectrometry.
Scand J Clin Lab Invest 1983;43:433-7

"The **calibration standards** used in the RIA method … were replaced by a **series of human serum samples**, in which the concentration of cortisol had been determined by the reference ID-MS method"
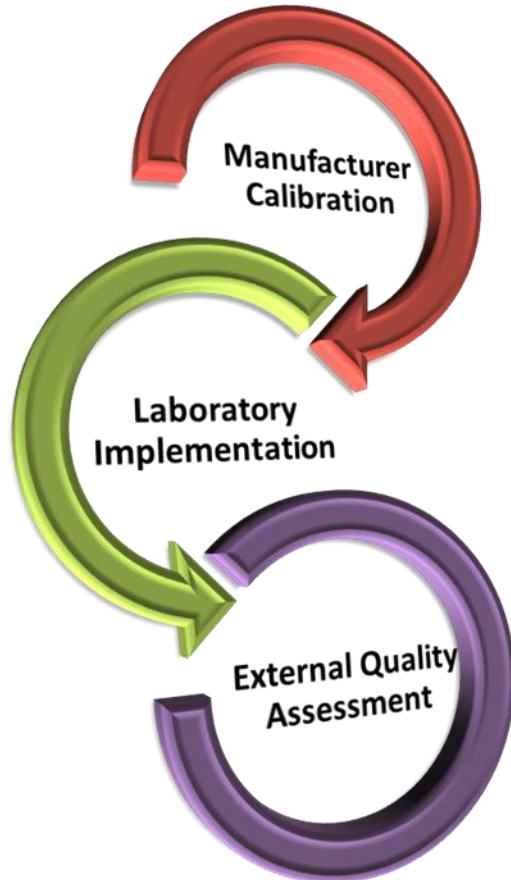
Native samples in EQA

Stöckl D, Thienpont LM. The Combined Target Approach – A Way Out of the Proficiency Testing Dilemma. Arch Pathol Lab Med 1994;118:775

"Method assessment based on patients' serum samples provided with reference method values"

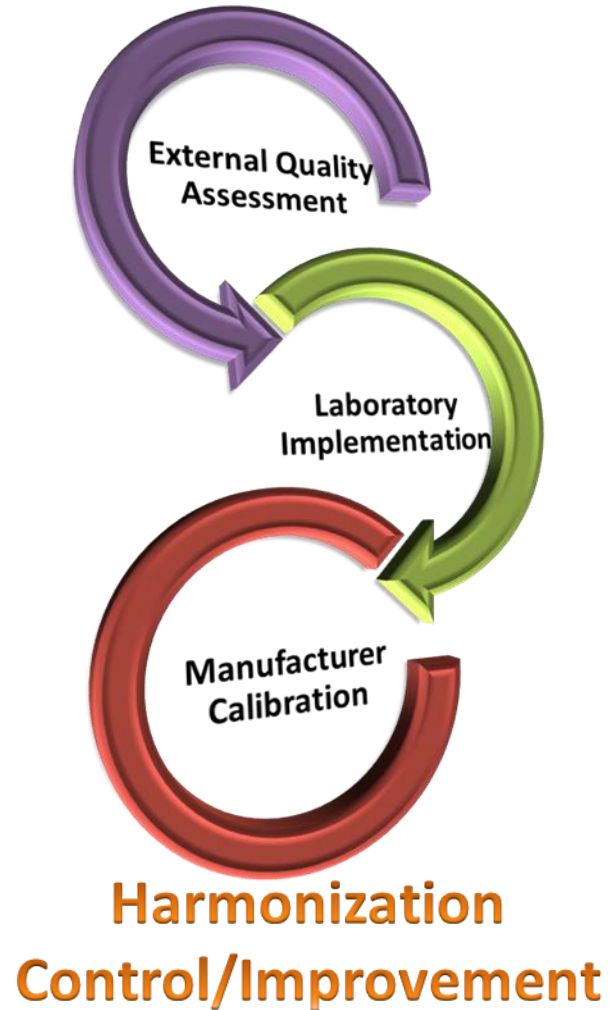**"Lyophilized control materials and PT-method means could be used for participant assessment"**
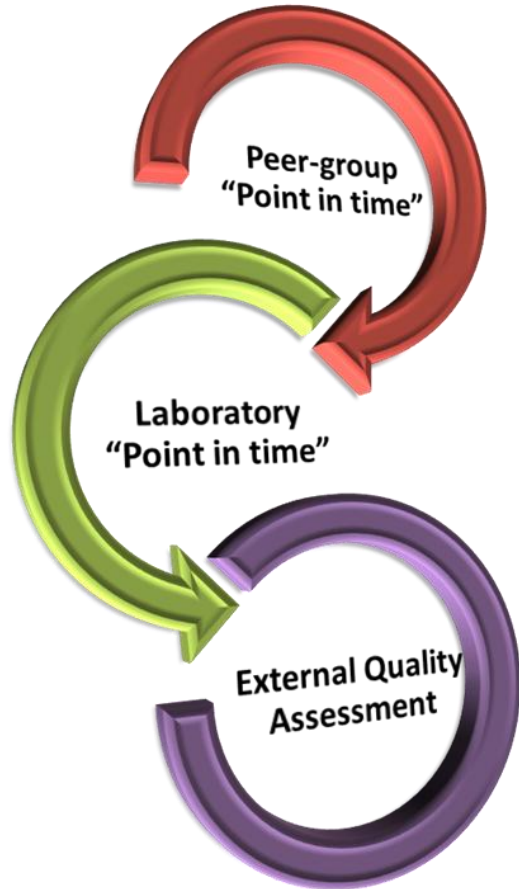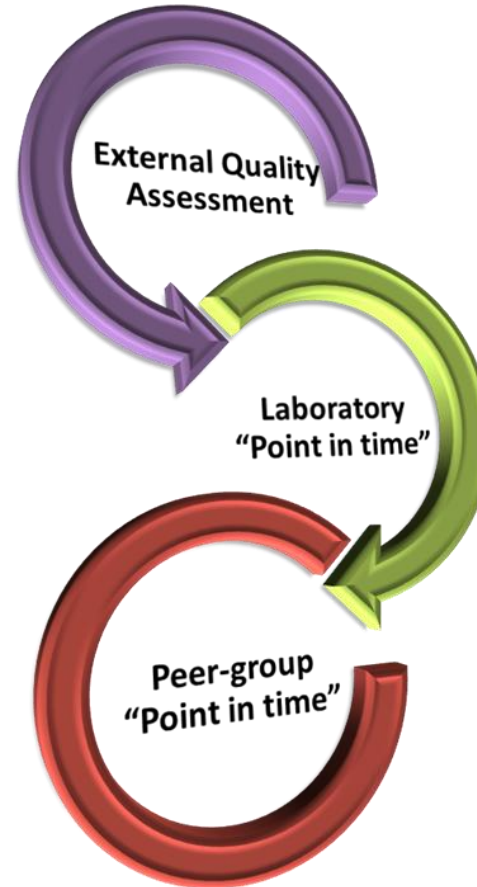
Manufacturer assessment

Laboratory assessment

Native sample master comparisons

Design

Interpretation

Results
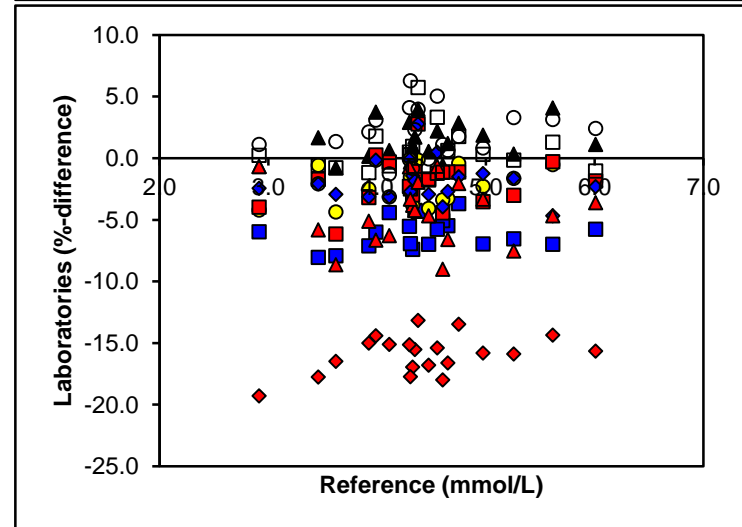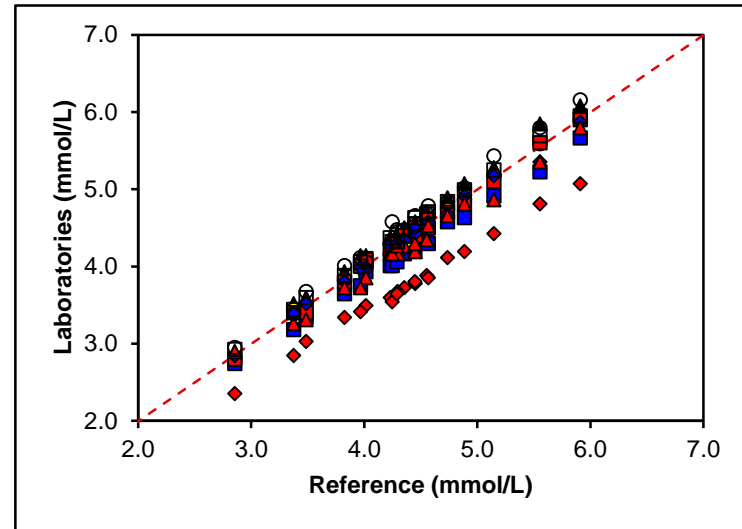
Design

EQA with fresh frozen, single donation sera

• **Twenty sera (commutable)**

• **Twenty "master" laboratories for each manufacturer**

• **Manufacturers' in-house laboratories**

• **Target = All Manufacturers' Trimmed Mean (AMTM)**

• **Reference measurement procedure targets only when needed**

Three already performed: Argentina[1], Norway[2] & Finland[3]

[1]Clin Chem Lab Med 2011;49:1829-36
[2]Clin Chem 2012;58:1597-9.
[3]In preparation.

Interpretation

Manufacturer & "master" laboratory

• **Quality ("master" laboratory & manufacturer)**

• **Versus Peer Group & Reference**

Quality indicators (FAIL-limits)
Sy/x (%) versus Peer
   FAIL
Peer Bias ±CI (><±3%)
        PASS
Peer Bias ±CI at range limits (><±3%)
     LOW   HIGH
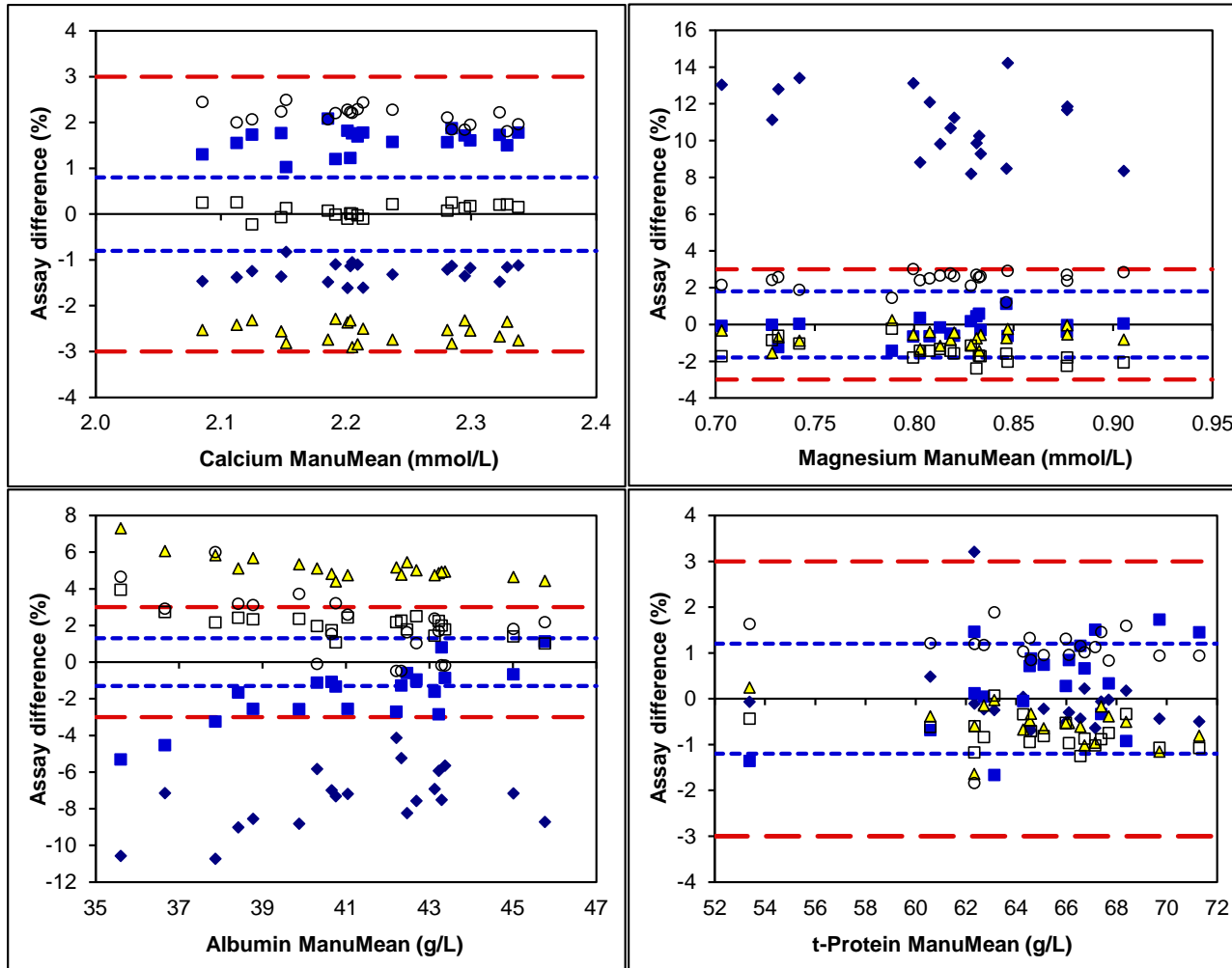   PASS   PASS
Peer total error (>=3 samples ><±5%)
      PASS

Results survey 2011 (with NKK)

Assay comparability

◆ Abbott ■ Ortho △ Roche Modular ○ Siemens □ Roche Cobas

Difference (%) of peer group means from the ManuMean.
Generic (3%; - - -) and biological limits (- - -) for bias
(Van Houcke et al. Clin Chem 2012;58:1597-9.)

Results survey 2011

Master laboratory assessment

	Calcium	Magnesium	Albumin	t-Protein	Mean
Fail percentages for run-to-run quality and peer group performance (%)					
CV	6.5	8.8	8.5	0.0	**6.0**
Difference replicate	6.5	2.9	4.3	4.9	**4.6**
Difference peer	8.7	5.9	8.5	4.9	**7.0**
Trend	2.2	5.9	0.0	2.4	**2.6**
Outlier	8.7	0.0	3.2	4.9	**4.2**
Mean	**6.5**	**4.7**	**4.9**	**3.4**	**4.9**
Fail percentages for overall performance (%)					
Correlation	2.2	2.9	0.0	0.0	**1.3**
Bias	17	18	36	7.3	**20**
Bias at range limits	17	24	49	10	**25**
Total error	15	24	43	4.9	**22**
Slope	0.0	0.0	6.4	0.0	**1.6**
Mean	**13**	**16**	**34**	**5.5**	**17**

Master comparison survey 2012

Survey 2012 (with Labquality)

- **Eight analytes: HDL-cholesterol, LDL-cholesterol, cholesterol, triacylglycerides, glucose, creatinine, uric acid, phosphate**

- **Reference measurement procedure values for creatinine, uric acid, cholesterol (CDC)**

- **Sample volume 1 mL**

Participants

- **At least 8 participants in 6 peer groups: Abbott/Architect, Beckman/Olympus, Ortho/Vitros, Roche/Cobas, Siemens/Advia, Thermo/Konelab**

- **All 6 manufacturers participated with 3 (or more) in-house systems**

Future master comparison surveys

Survey 2014

ST*T* Consulting/Laboratory for Analytical Chemistry

Future frequency

1 – 2 times per year

>Approximately 3 years to "work through" a clinical chemistry menu

Master comparisons – Special aspect

## Commutability assessment (survey 2011)
Mainly sample 2: Magnesium & Albumin

Table 1 Prediction intervals (%) and commutability data ($) for the EQA sera #1 & #2

	Calcium			Magnesium			Albumin			t-Protein		
	PI§	#1	#2	PI	#1	#2	PI	#1	#2	PI	#1	#2
Abbott Architect	0.4	0.6	**1.4**	**3.4**	ok£	*[3.1]*	**3.2**	ok	**5.1**	0.7	0.7	ok
Ortho Vitros	0.5	ok	ok	**2.0**	ok	**5.4**	**2.1**	ok	**7.2**	**1.8**	ok	ok
Roche Cobas	0.3	ok	ok	1.2	ok	ok	1.0	ok	ok	0.7	ok	ok
Roche Modular	0.5	0.5	ok	0.6	0.7	ok	0.8	ok	ok	0.5	ok	ok
Siemens Advia	0.4	ok	ok	1.4	ok	**2.6**	**3.1**	ok	ok	0.6	0.8	ok

$Deviation (%) of the EQA samples from the native samples at the concentration of the EQA-samples.

§Prediction interval (%) at the mean of the data.

£Data are within the prediction interval.

Linda Thienpont - Adam Uldall Lecture EQALM 2013

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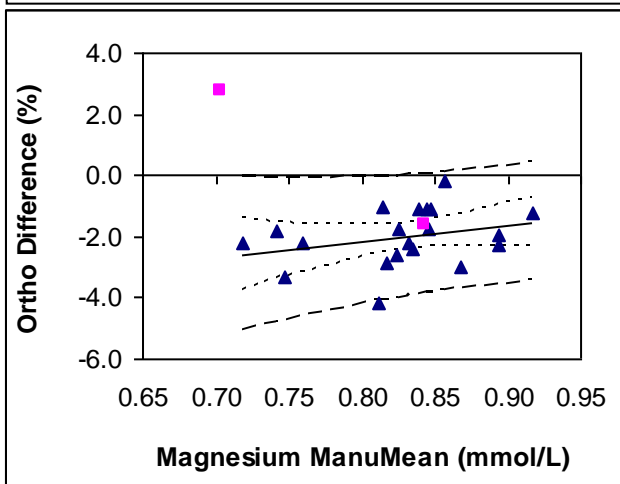
Master comparisons

Benefits

- **Create evidence about the quality of commercial assays, their standardization status and comparability between manufacturers**

- **Define the "master" laboratory calibration set-point**

- **Are an excellent management tool for the laboratory and the manufacturer**

- **Can serve as major input for health economy planning for the government (for example, interchangeability of electronic health-care records)**

Native sera in EQA

Conceptual integration in general assessment strategy

Interested to join?

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