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Pragmatism in Laboratory Medicine – Focus on Type II analytes and how they might be calibrated and harmonised

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Birmingham Quality

Aim

To present the argument of *why* we need *pragmatism* in laboratory medicine, and the *need* to focus on measurands other than Type I

…. I am not giving you the answer to this problem !

Introduction

- We, the scientific community, like to look at the bias of results compared to a Target value
- This is usually the relative bias between methods, but with commutable materials and reference method input this can be the absolute bias
- But this isn’t the full picture …
- We should be looking at the spread of the results, across multi specimens at multi concentrations at multi time points.

Type I and Type II analytes

Urea

Glucose

Cortisol

Creatinine

Free hormones

Calcium

Sodium

Type I
(Type A)

TSH

Ferritin

Thyroglobulin

Lipids

B12

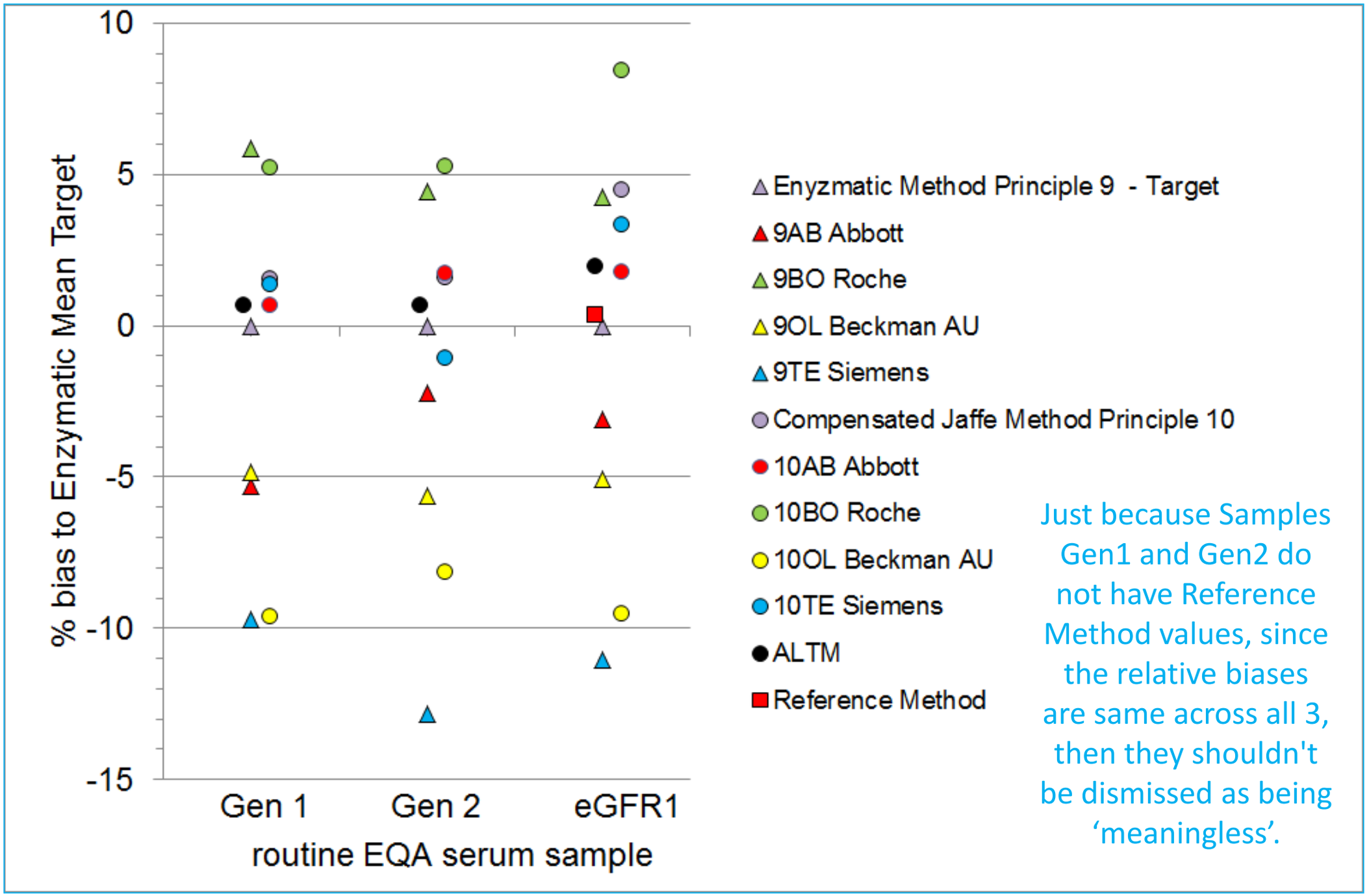
Proteins

Gentamicin

hCG

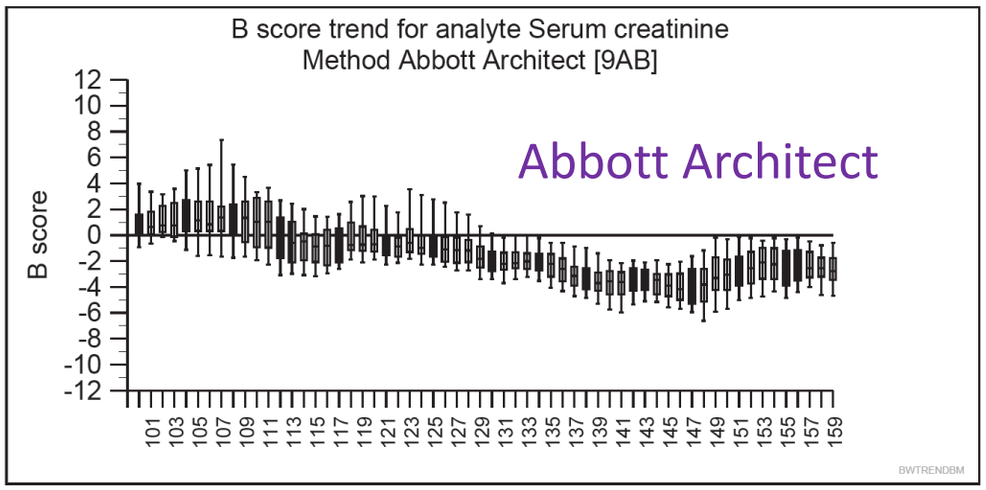
Type II
Type B

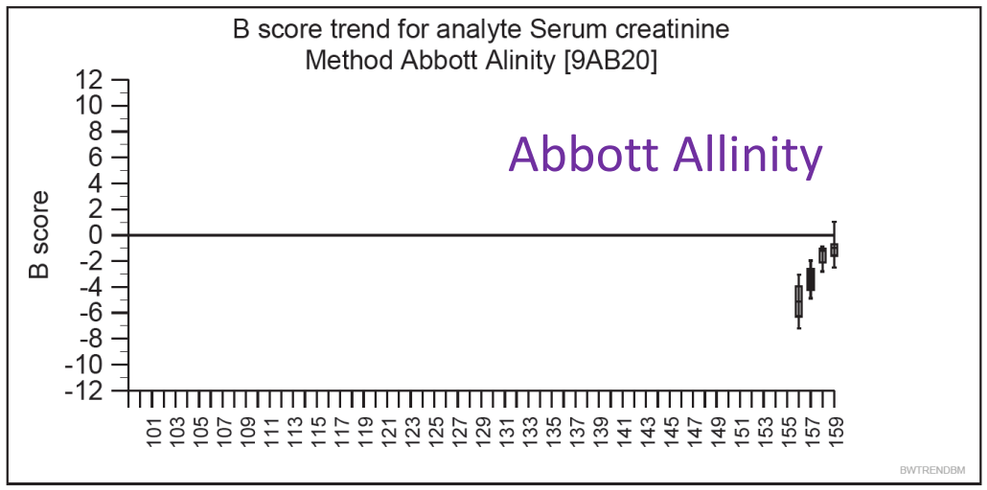
Creatinine

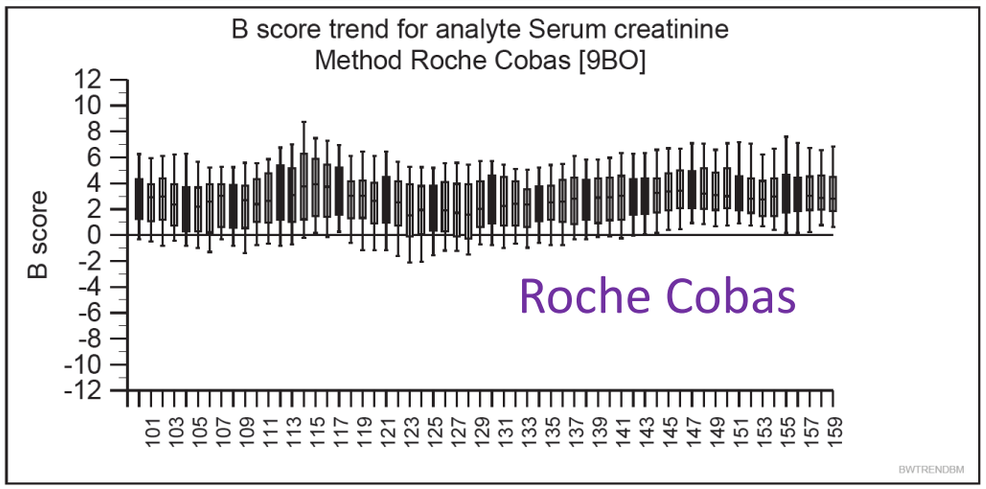


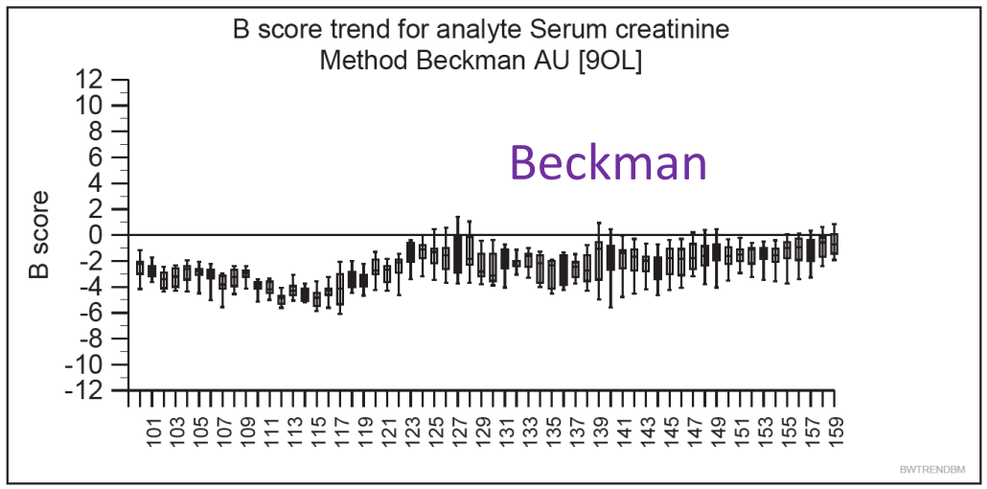
Just because Samples Gen1 and Gen2 do not have Reference Method values, since the relative biases are same across all 3, then they shouldn't be dismissed as being 'meaningless'.

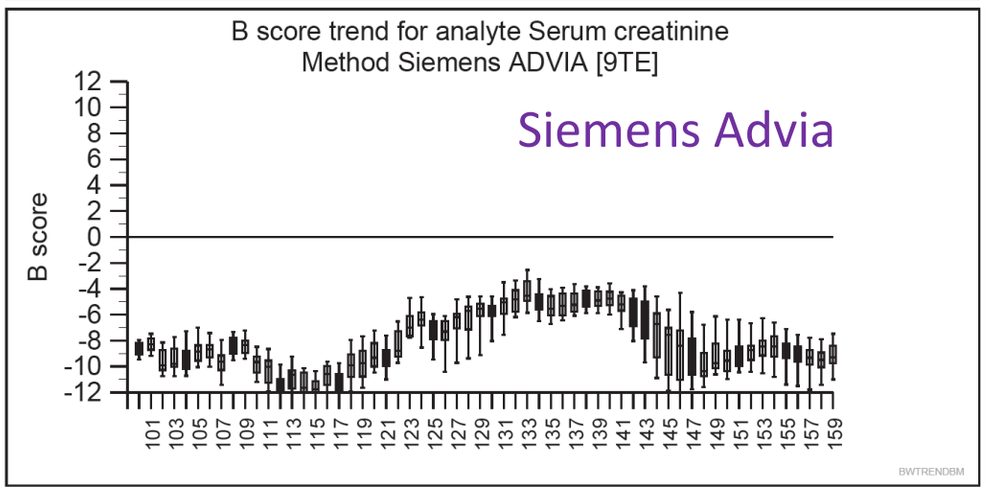
Creatinine


B score trend for analyte Serum creatinine
Method Abbott Architect [9AB]
Abbott Architect
B score
BWTRENDBM


B score trend for analyte Serum creatinine
Method Abbott Alinity [9AB20]
Abbott Allinity
B score
BWTRENDBM


B score trend for analyte Serum creatinine
Method Roche Cobas [9BO]
Roche Cobas
B score
BWTRENDBM


B score trend for analyte Serum creatinine
Method Beckman AU [9OL]
Beckman
B score
BWTRENDBM


B score trend for analyte Serum creatinine
Method Siemens ADVIA [9TE]
Siemens Advia
B score
BWTRENDBM

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fT3

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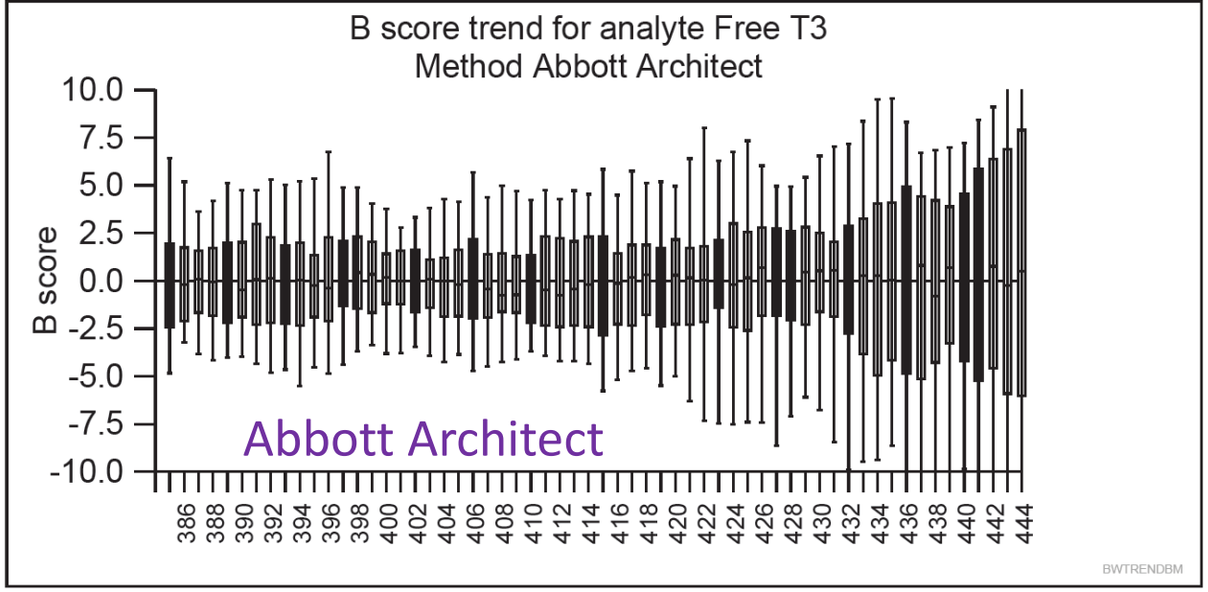
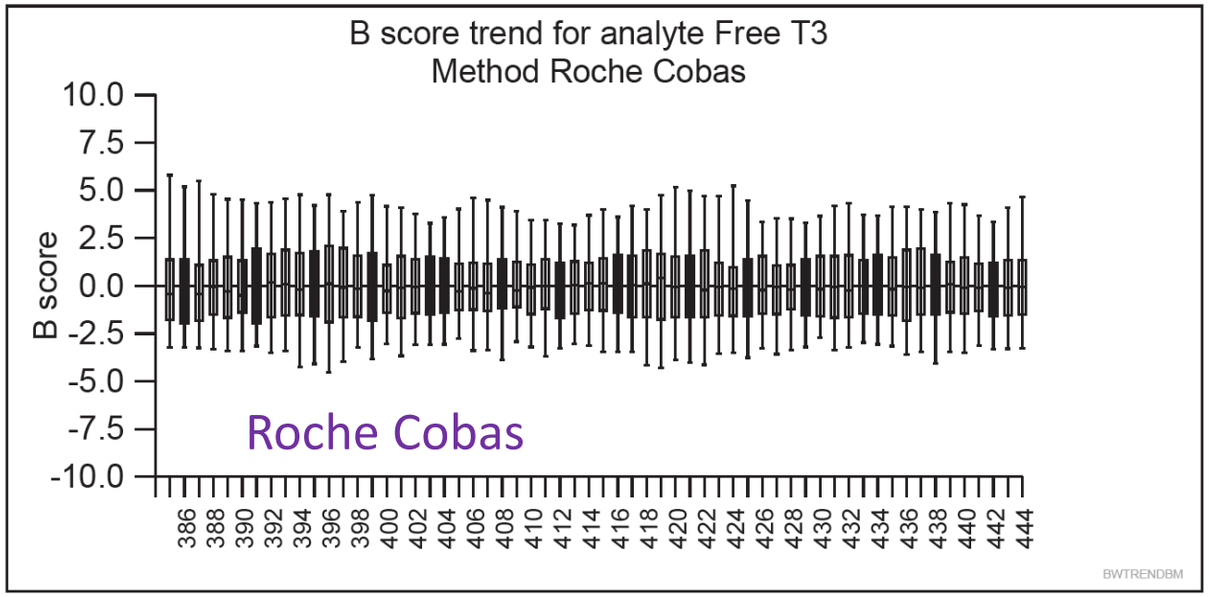
UK NEQAS for Thyroid Hormones

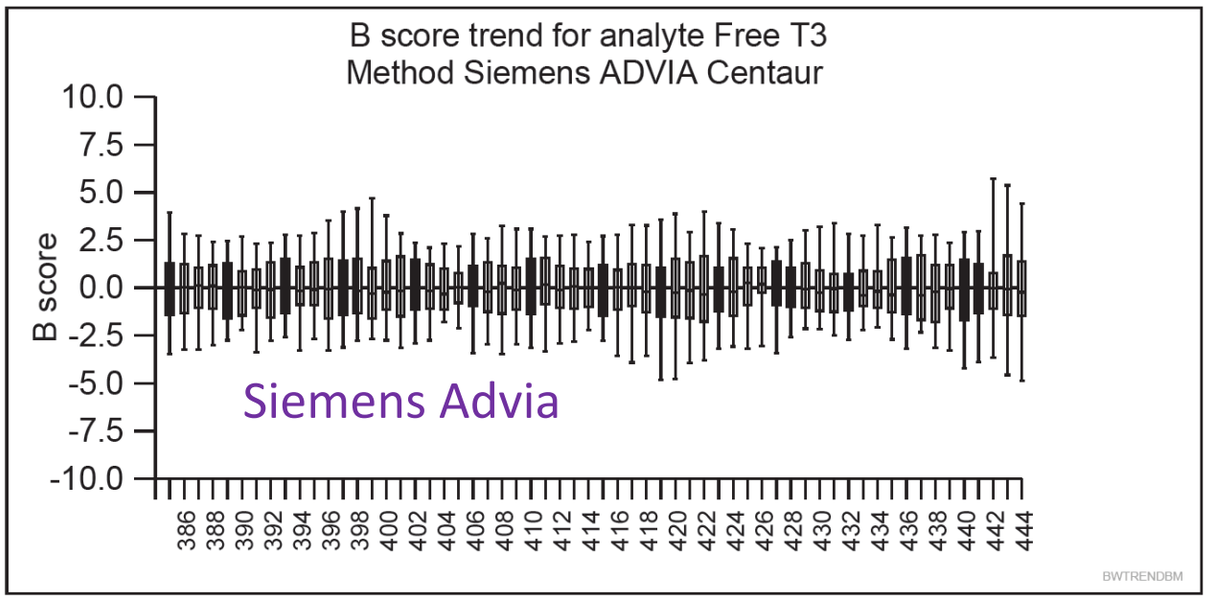
Seismograph Plot

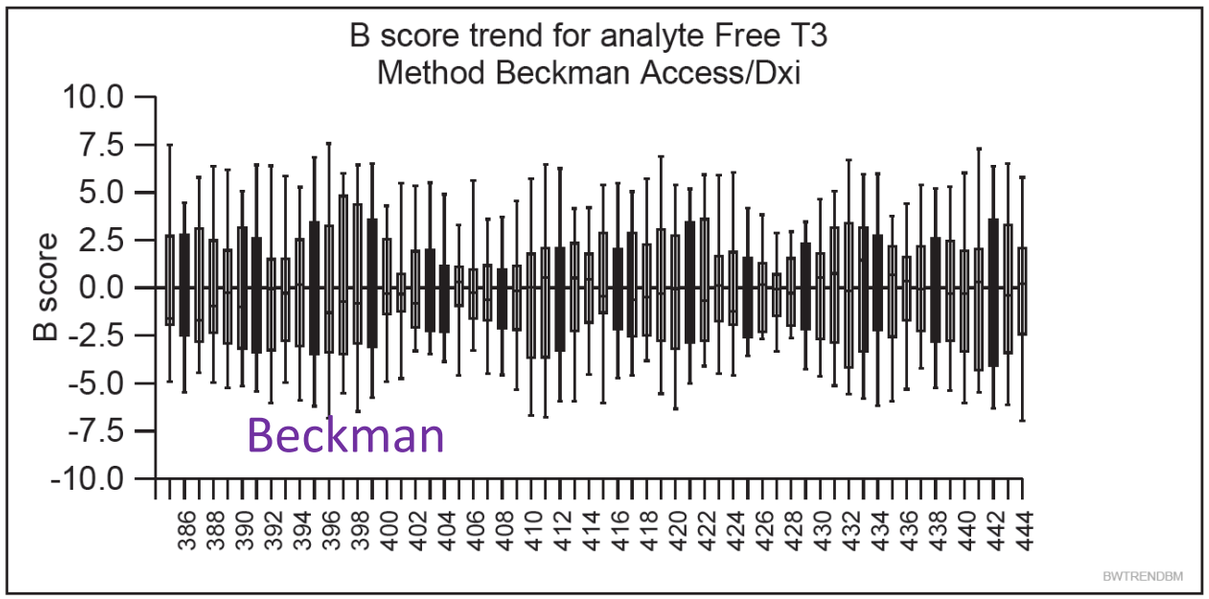
Distribution : **444** Date : 22-Oct-2019

Free T3 (pmol/L)



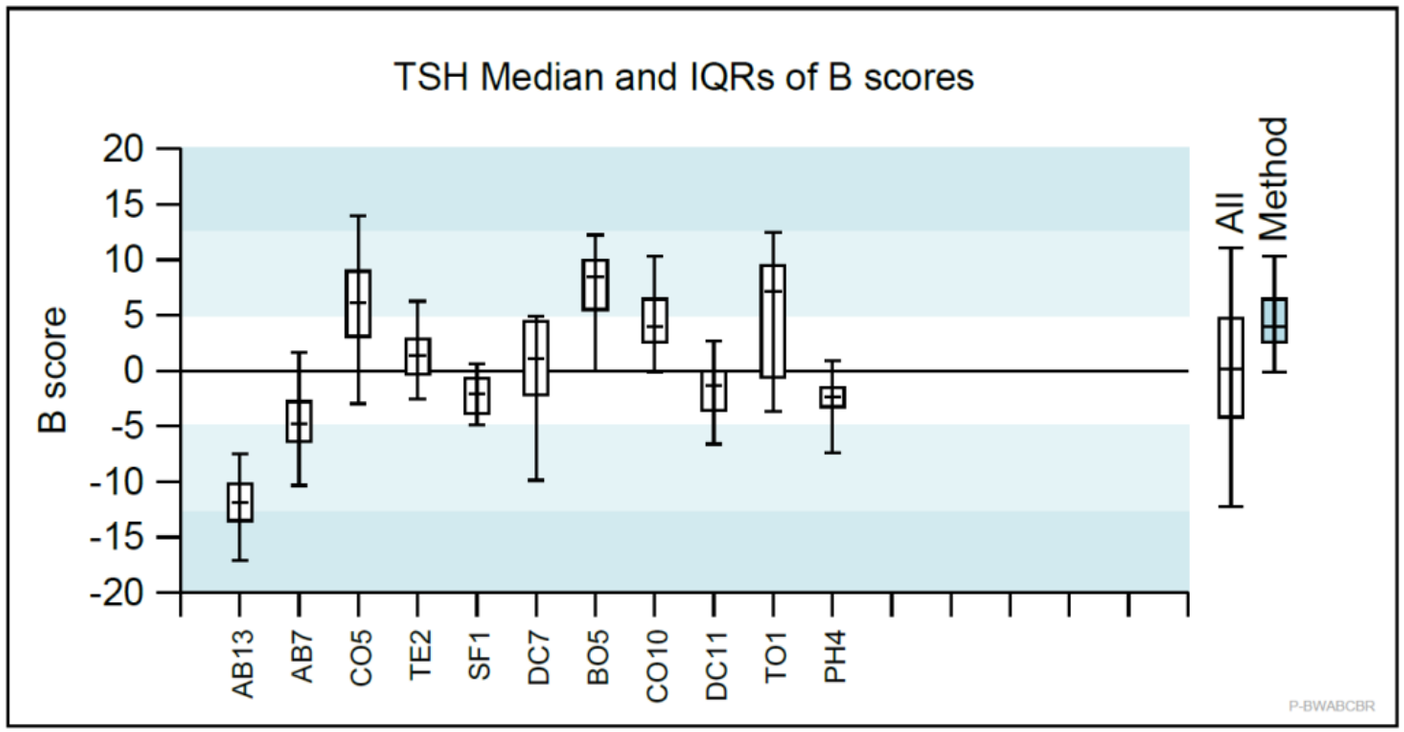




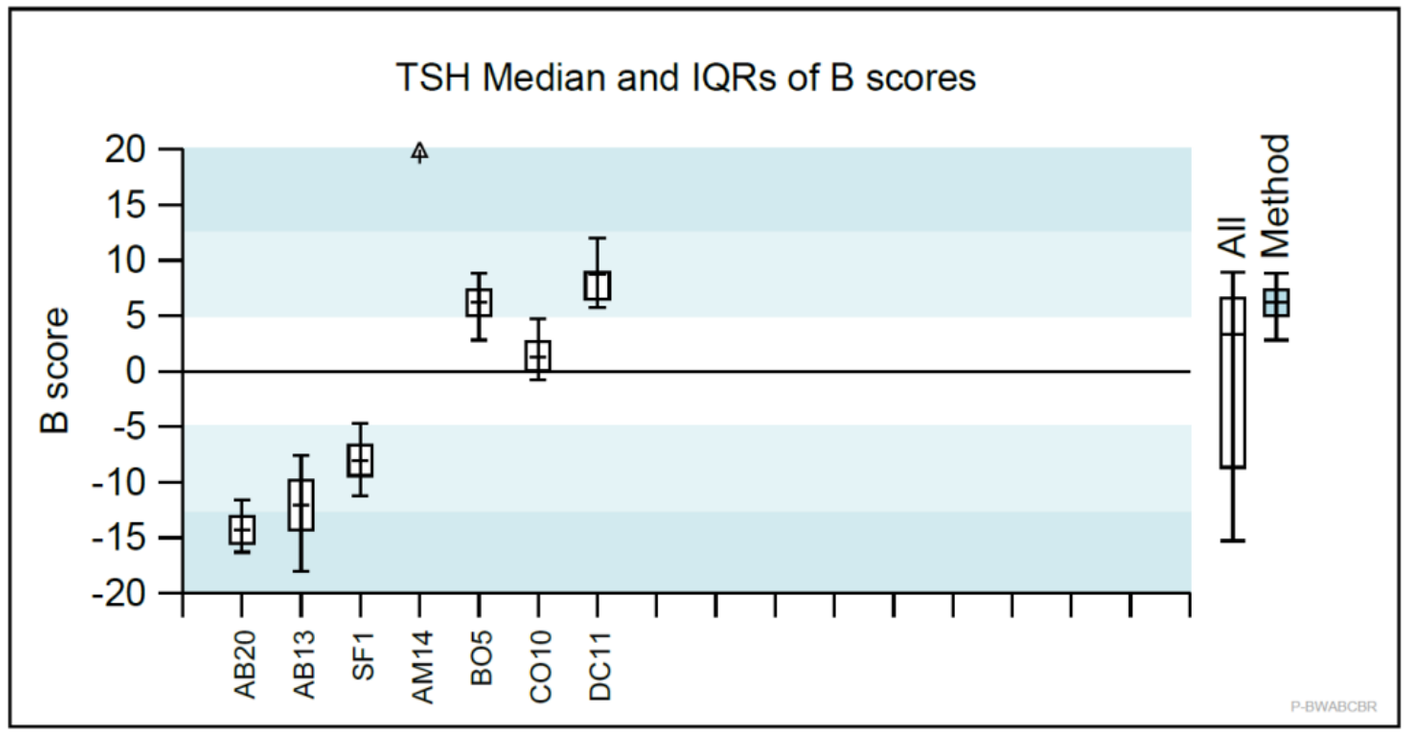


TSH

TSH September 2006

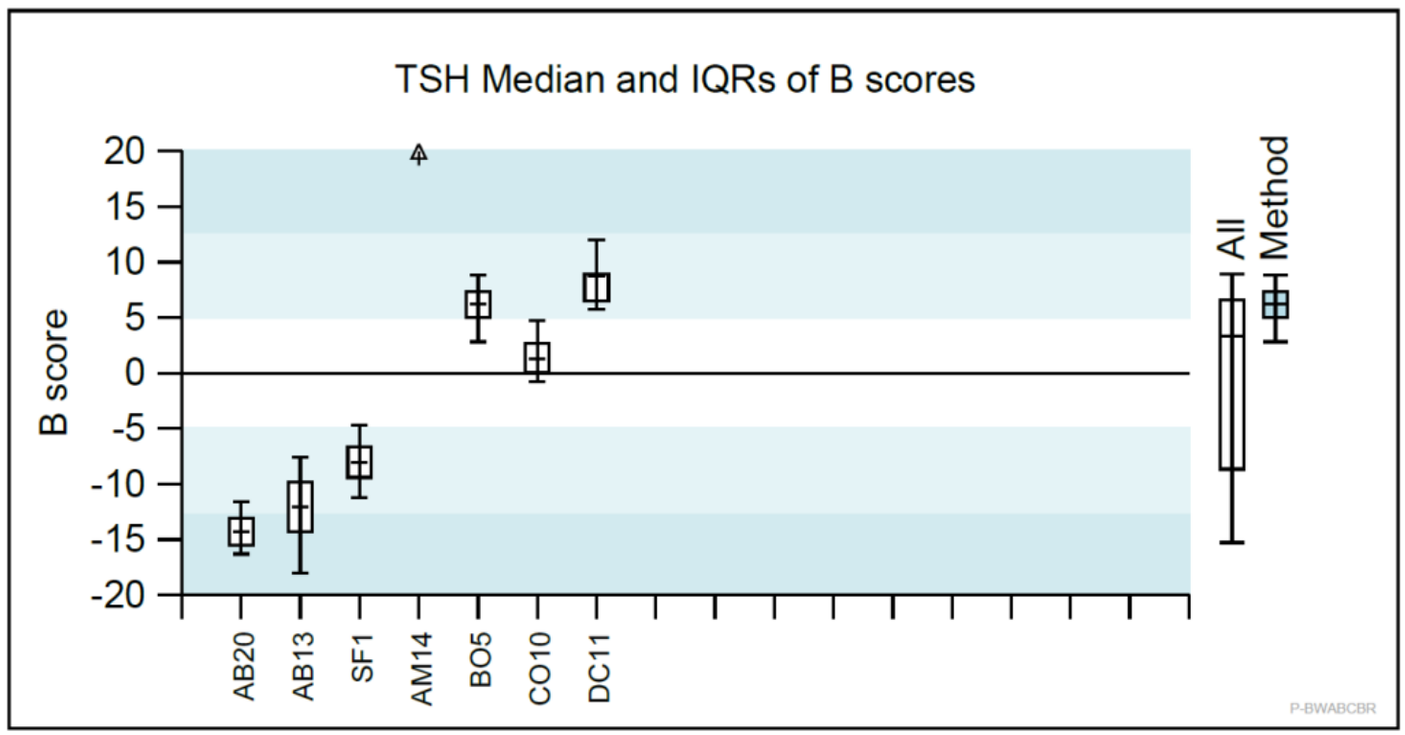


TSH October 2019

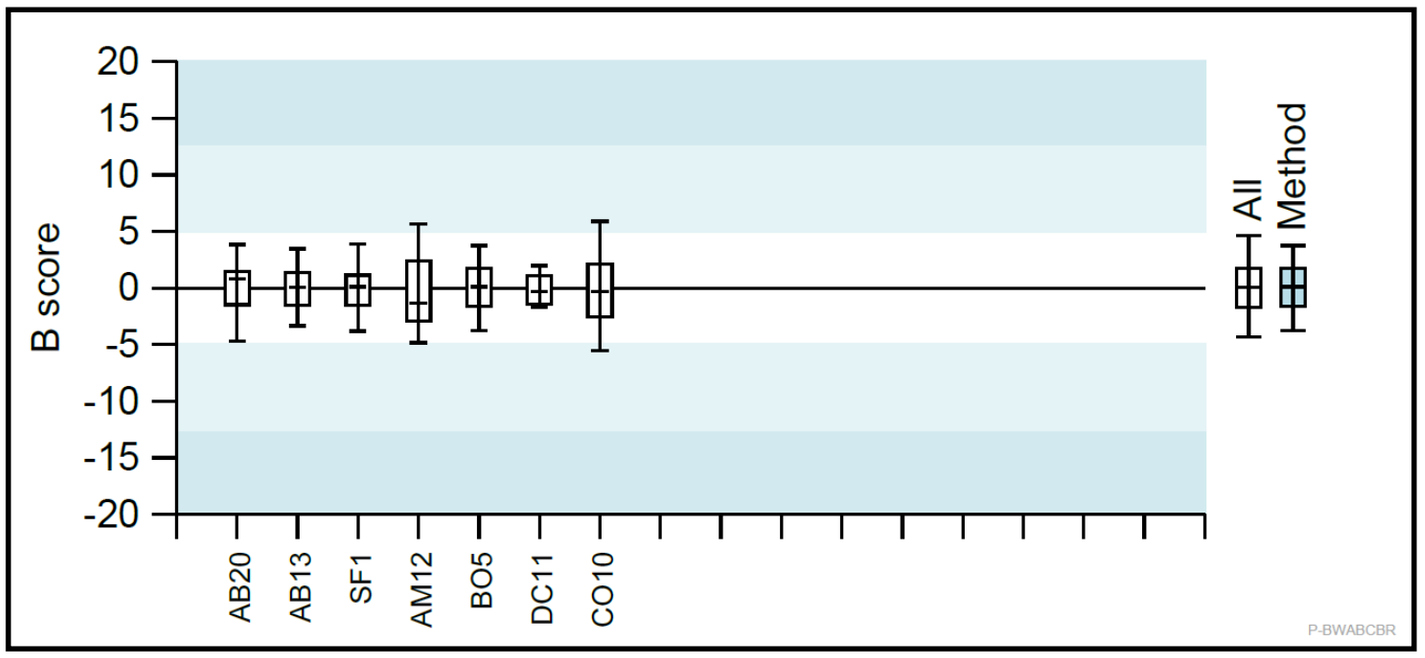


TSH

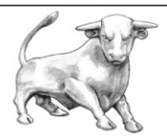
TSH October 2019



Where we want to be …



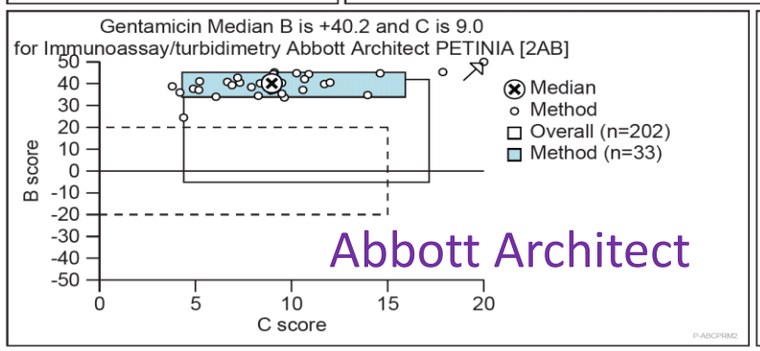
Gentamicin

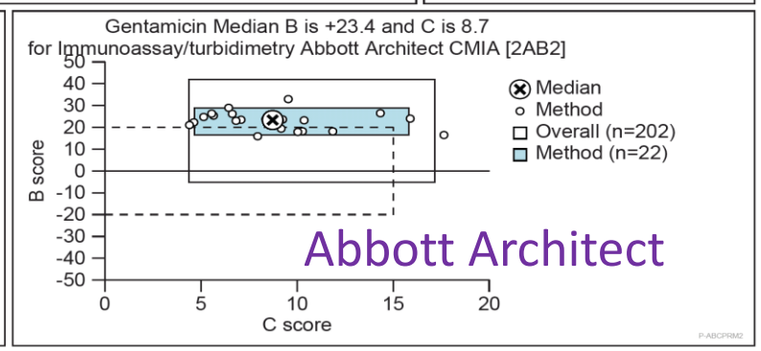


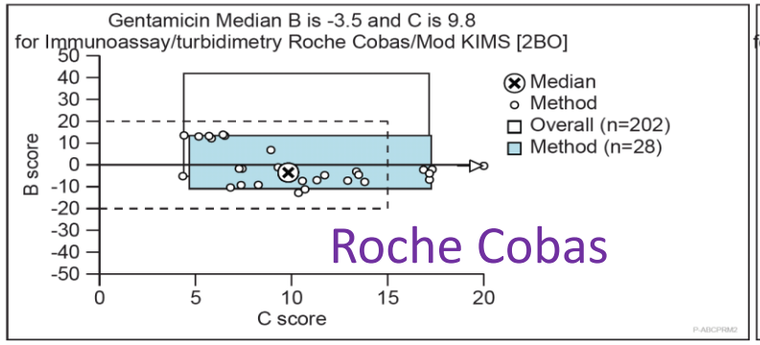
UK NEQAS for Antibiotic Assays | Method Report

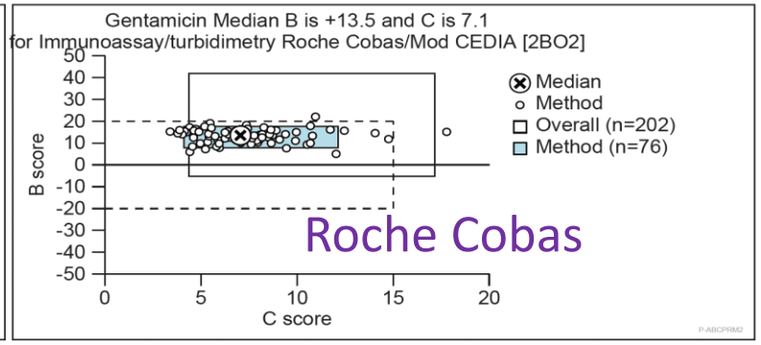
Distribution : **232** Date : 29-Sep-2019

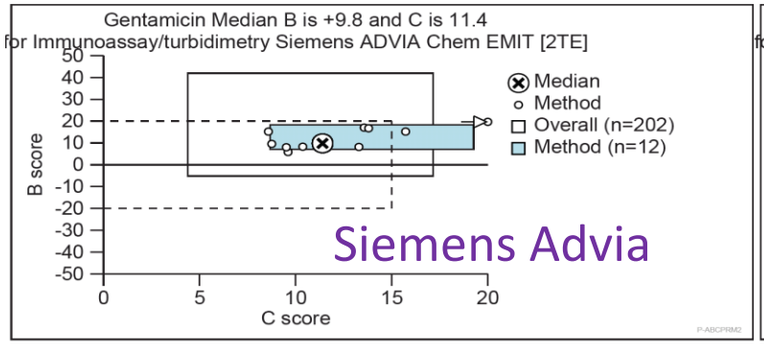
Gentamicin (mg/L)

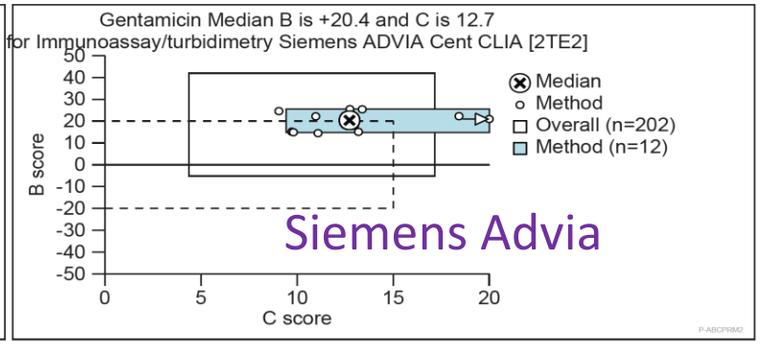


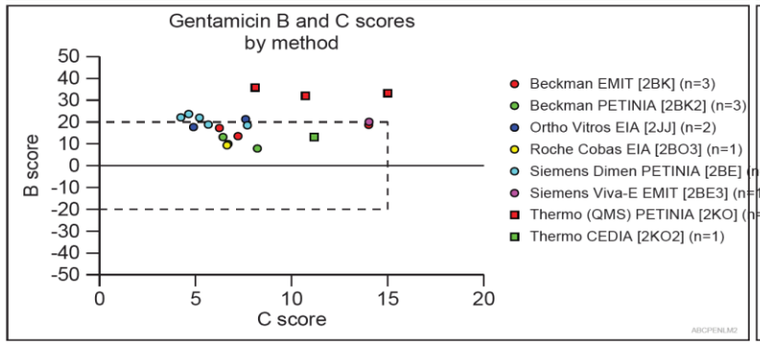










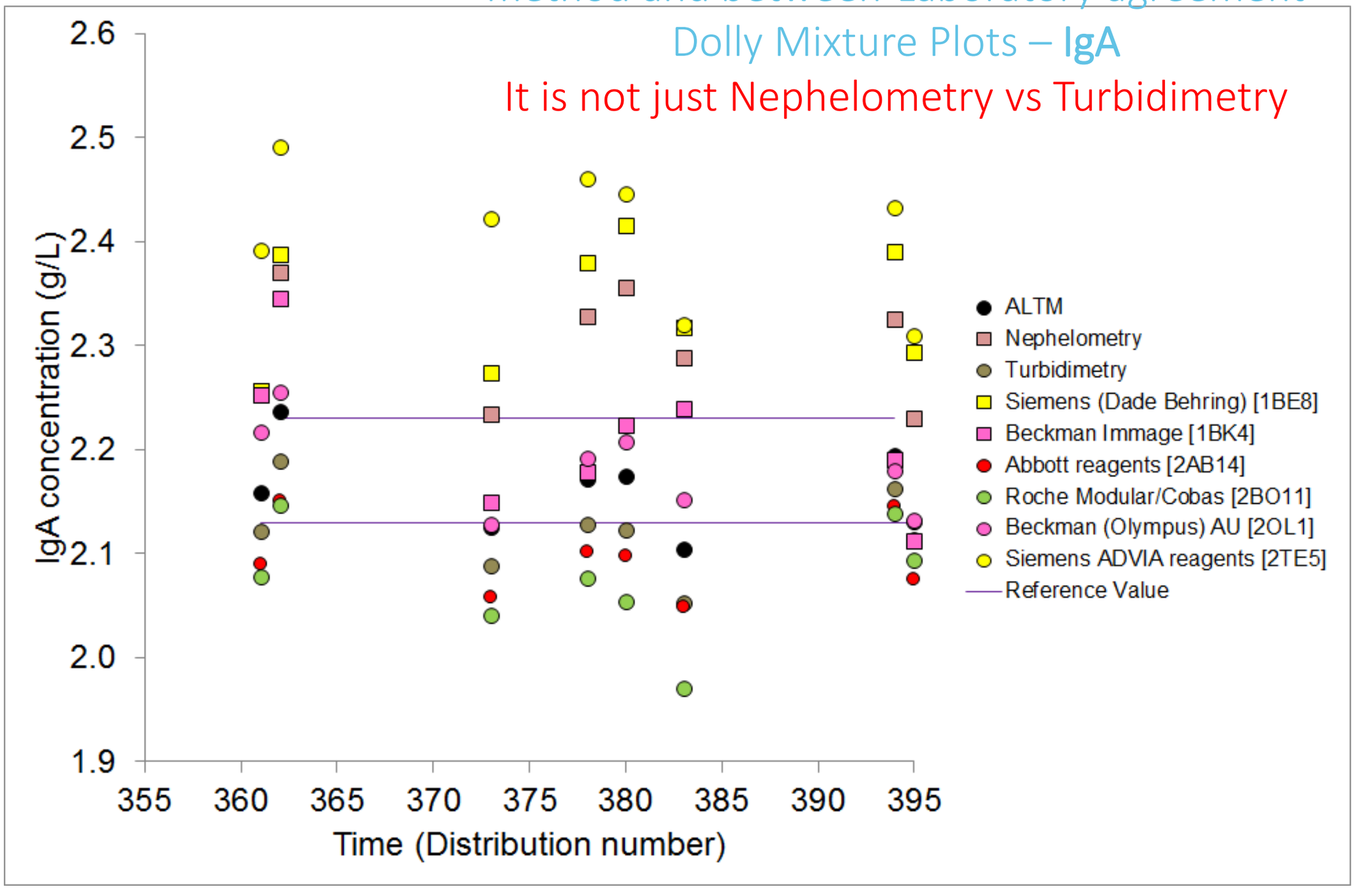


Proteins

Impact of the CRM 470 standards on between-method and between-Laboratory agreement

Dolly Mixture Plots – **IgA**

It is not just Nephelometry vs Turbidimetry



Proteins

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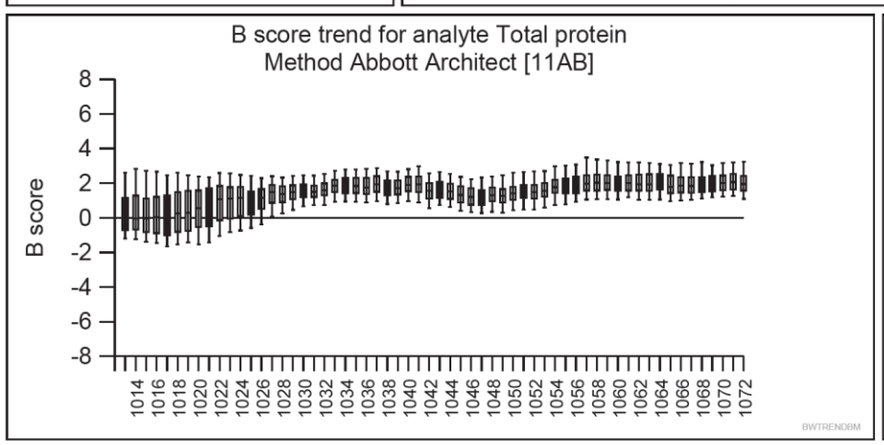
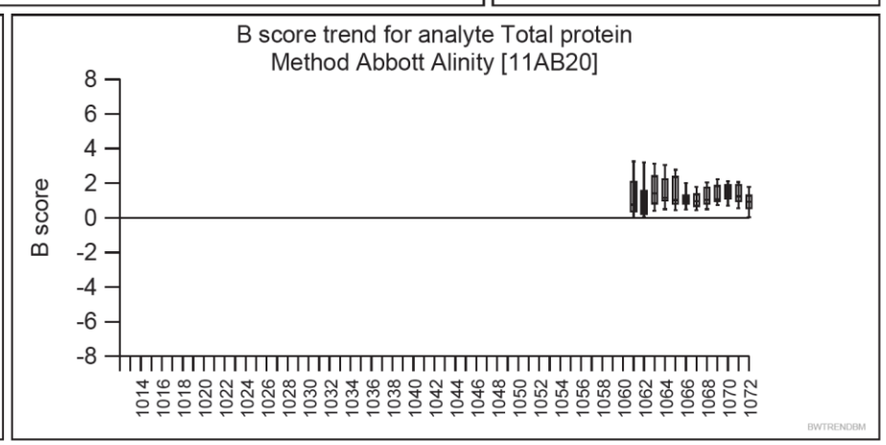
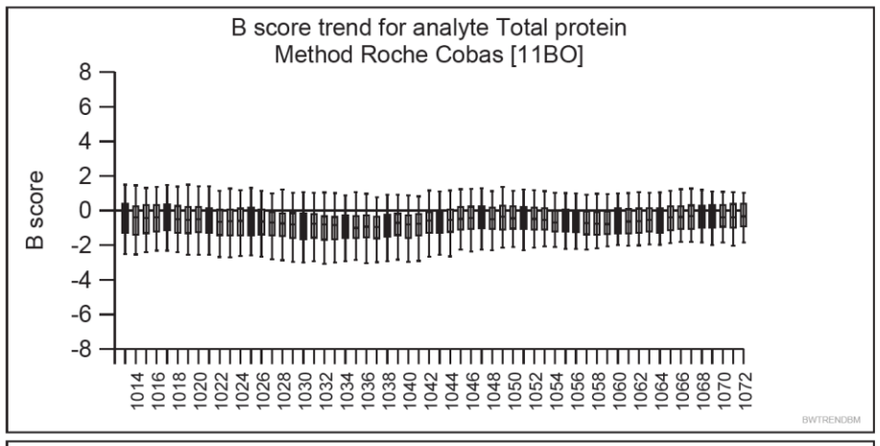
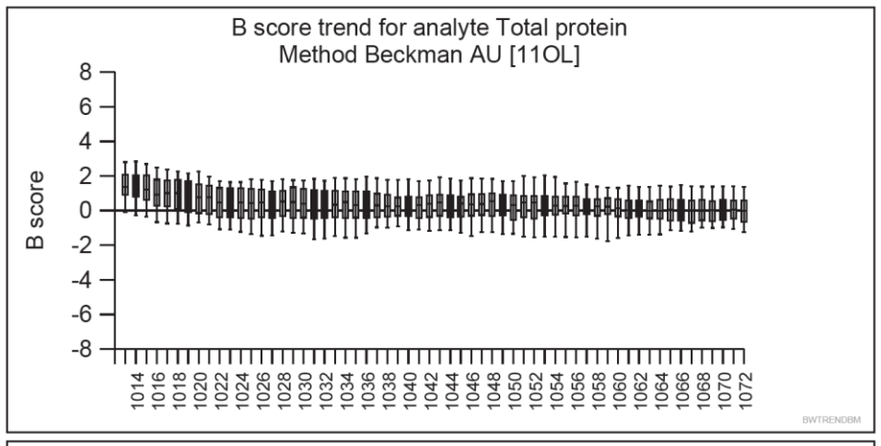
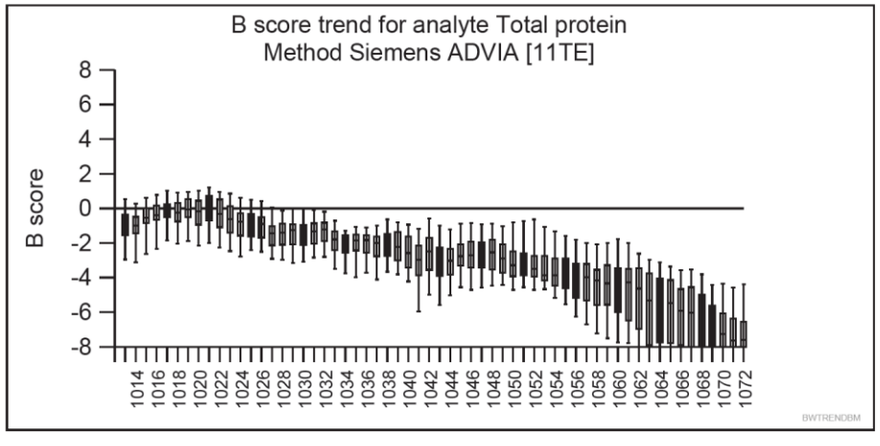
UK NEQAS for Clinical Chemistry	Method Report
Distribution : **1072** Date : 17-Nov-2019	
Total protein (g/L)	

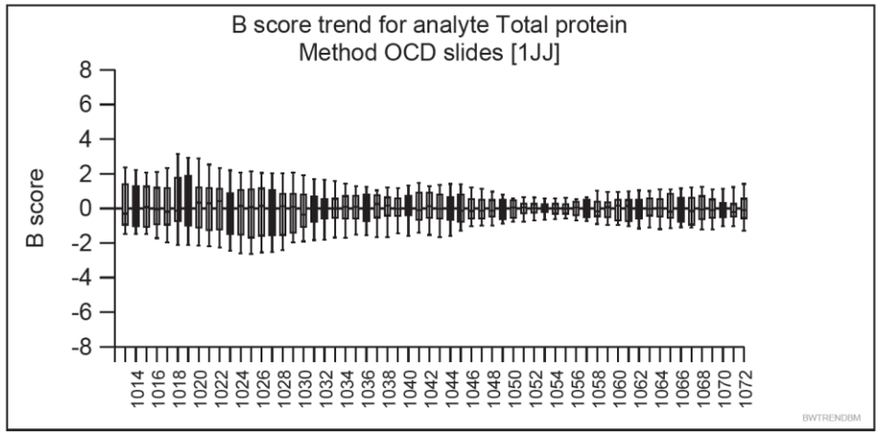












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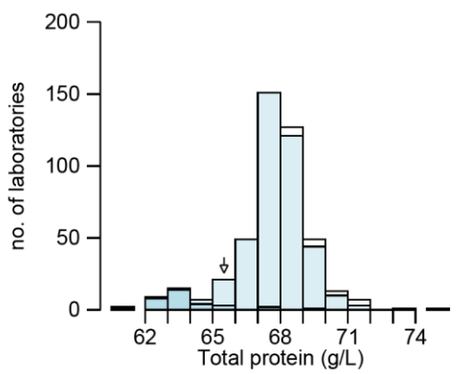
Total Protein and Albumin

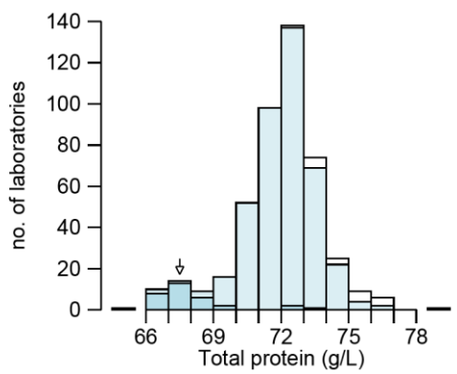
Specimen : 1073A

	n	Mean	SD	CV(%)
All methods [ALTM]	434	68.1	1.3	2.0
Dry slide / Sensor	18	70.2	1.3	1.9
OCD slides [1JJ]	18	70.2	1.3	1.9
Biuret	434	68.1	1.3	2.0
Abbott Alinity [11AB20]	18	67.5	1.1	1.6
Abbott Architect [11AB]	97	68.5	0.7	1.1
Beckman AU [11OL]	47	67.9	1.4	2.1
In-house [11OO]	5	67.7	3.0	4.4
Roche Cobas [11BO]	223	68.3	1.0	1.5
Siemens ADVIA [11TE]	33	64.2	1.3	2.1
non-numeric results	1			



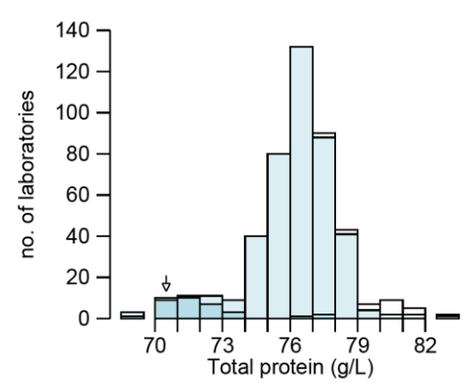
Specimen : 1073B

	n	Mean	SD	CV(%)
All methods [ALTM]	435	72.3	1.5	2.1
Dry slide / Sensor	18	75.3	1.4	1.9
OCD slides [1JJ]	18	75.3	1.4	1.9
Biuret	435	72.3	1.5	2.1
Abbott Alinity [11AB20]	18	71.6	1.1	1.6
Abbott Architect [11AB]	97	72.9	0.9	1.2
Beckman AU [11OL]	48	72.1	1.4	1.9
In-house [11OO]	5	72.3	1.0	1.4
Roche Cobas [11BO]	223	72.6	1.2	1.7
Siemens ADVIA [11TE]	33	68.3	1.4	2.0



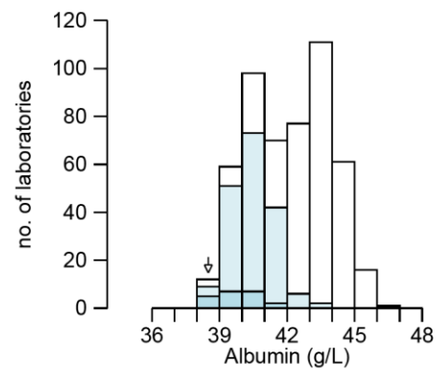
Specimen : 1073C

	n	Mean	SD	CV(%)
All methods [ALTM]	434	76.7	1.6	2.1
Dry slide / Sensor	18	80.4	1.4	1.7
OCD slides [1JJ]	18	80.4	1.4	1.7
Biuret	434	76.7	1.6	2.1
Abbott Alinity [11AB20]	18	76.4	1.2	1.6
Abbott Architect [11AB]	97	77.3	1.0	1.3
Beckman AU [11OL]	48	76.5	1.5	2.0
In-house [11OO]	5	76.3	1.0	1.3
Roche Cobas [11BO]	222	76.8	1.3	1.6
Siemens ADVIA [11TE]	33	72.3	1.6	2.2



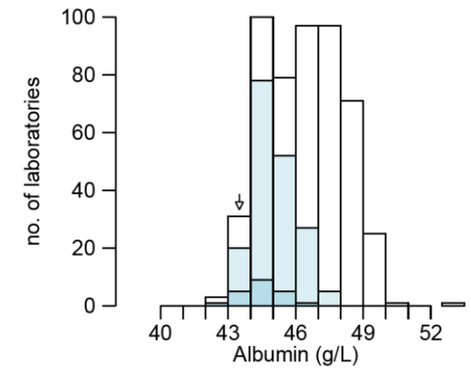
Specimen : 1073A

	n	Mean	SD	CV(%)
Dry slide / Sensor	20	42.9	1.2	2.8
OCD slides [1JJ]	20	42.9	1.2	2.8
BCP	183	40.9	0.9	2.2
Abbott Alinity [12AB20]	18	40.8	0.5	1.3
Abbott Architect [12AB]	85	41.2	0.9	2.2
Roche Cobas [12BO]	44	40.4	0.8	1.9
Siemens ADVIA [12TE]	21	40.2	1.0	2.6
BCG	301	43.5	1.4	3.1
Abbott Architect [13AB]	27	42.9	0.2	0.6
Beckman AU [13OL]	48	41.1	0.9	2.2
Randox [13RX]	6	43.5	0.7	1.7
Roche Cobas [13BO]	196	44.1	0.9	2.0
Siemens ADVIA [13TE]	20	43.7	0.8	1.8



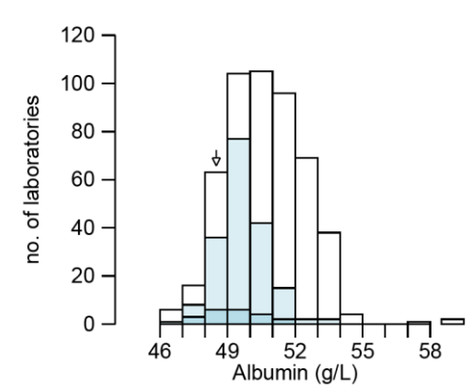
Specimen : 1073B

	n	Mean	SD	CV(%)
Dry slide / Sensor	20	46.9	1.3	2.8
OCD slides [1JJ]	20	46.9	1.3	2.8
BCP	183	45.4	1.0	2.2
Abbott Alinity [12AB20]	18	45.2	0.6	1.4
Abbott Architect [12AB]	85	45.8	1.0	2.2
Roche Cobas [12BO]	44	45.0	0.8	1.7
Siemens ADVIA [12TE]	21	45.0	1.0	2.1
BCG	301	47.6	1.4	3.0
Abbott Architect [13AB]	27	47.1	0.4	0.9
Beckman AU [13OL]	48	45.2	1.0	2.3
Randox [13RX]	6	47.7	0.6	1.3
Roche Cobas [13BO]	196	48.2	1.0	2.0
Siemens ADVIA [13TE]	20	47.7	1.1	2.3



Specimen : 1073C

	n	Mean	SD	CV(%)
Dry slide / Sensor	20	50.7	1.3	2.6
OCD slides [1JJ]	20	50.7	1.3	2.6
BCP	183	50.1	1.0	2.0
Abbott Alinity [12AB20]	18	49.7	0.5	1.1
Abbott Architect [12AB]	85	50.3	1.1	2.1
Roche Cobas [12BO]	44	49.9	0.7	1.3
Siemens ADVIA [12TE]	21	49.8	1.3	2.6
BCG	300	51.7	1.7	3.2
Abbott Architect [13AB]	27	50.9	0.3	0.5
Beckman AU [13OL]	48	48.9	0.8	1.6
Randox [13RX]	6	55.9	5.5	9.8
Roche Cobas [13BO]	195	52.4	1.1	2.0
Siemens ADVIA [13TE]	20	51.6	1.0	1.9



Spec.	Pool	Pool description / Treatments / Additions
1073A	583	Pooled Human Serum
1073B	584	Pooled Human Serum + 5 g/L Albumin
1073C	585	Pooled Human Serum + 10 g/L Albumin

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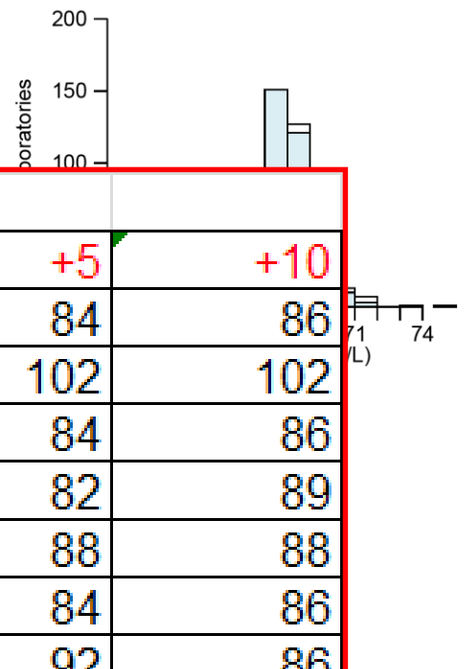
Total Protein and Albumin

Specimen : 1073A

	n	Mean	SD	CV(%)
All methods [ALTM]	434	68.1	1.3	2.0
Dry slide / Sensor	18	70.2	1.3	1.9
OCD slides [1JJ]	18	70.2	1.3	1.9
Biuret	434	68.1	1.3	2.0



Total Protein Recovery %

	+5	+10
ALTM	84	86
Dry Slide	102	102
Biuret	84	86
Abbott Alinity	82	89
Abbott Architect	88	88
Beckman AU	84	86
In-house	92	86
Roche Cobas	86	85
Siemens ADVIA	82	81

	n	Mean	SD	CV(%)
All methods [ALTM]	434	76.7	1.6	2.1
Dry slide / Sensor	18	80.4	1.4	1.7
OCD slides [1JJ]	18	80.4	1.4	1.7
Biuret	434	76.7	1.6	2.1
Abbott Alinity [11AB20]	18	76.4	1.2	1.6
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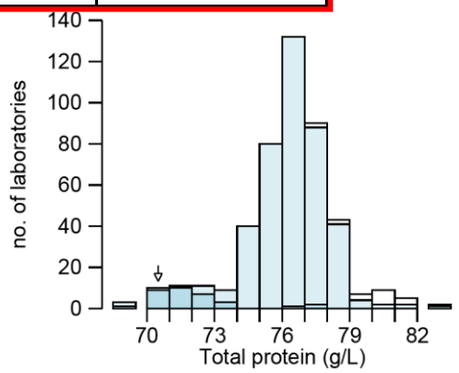

Specimen : 1073A

	n	Mean	SD	CV(%)
Dry slide / Sensor	20	42.9	1.2	2.8
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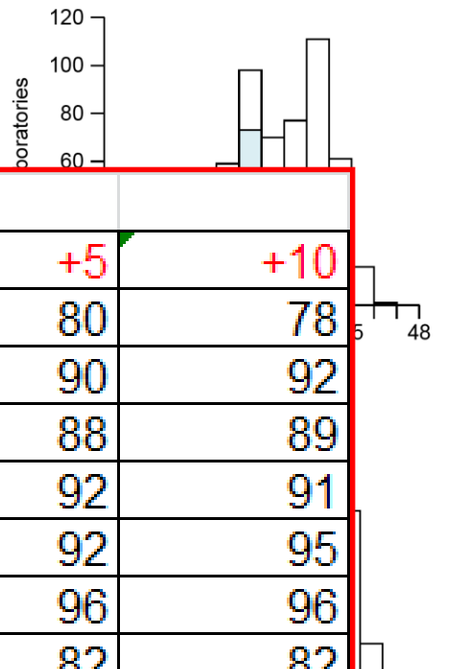
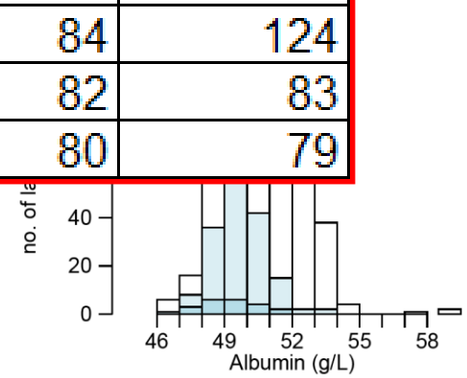
Abbott Alinity [12AB20]	18	40.8	0.5	1.3
Abbott Architect [12AB]	85	41.2	0.9	2.2
Roche Cobas [12BO]	44	40.9	0.7	1.5
Siemens ADVIA [12TE]	21	49.8	1.3	2.6
BCG	300	51.7	1.7	3.2
Abbott Architect [13AB]	27	50.9	0.3	0.5
Beckman AU [13OL]	48	48.9	0.8	1.6
Randox [13RX]	6	55.9	5.5	9.8
Roche Cobas [13BO]	195	52.4	1.1	2.0
Siemens ADVIA [13TE]	20	51.6	1.0	1.9



Albumin Recovery %

	+5	+10
Dry Slide	80	78
BCP	90	92
Abbott Alinity	88	89
Abbott Architect	92	91
Roche Cobas	92	95
Siemens ADVIA	96	96
BCG	82	82
Abbott Architect	84	80
Beckman AU	82	78
Randox	84	124
Roche Cobas	82	83
Siemens ADVIA	80	79



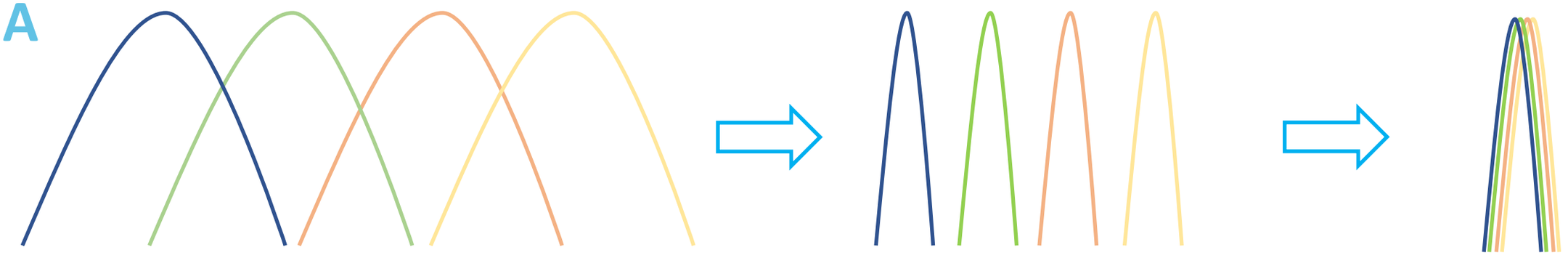
Spec.	Pool	Pool description / Treatments / Additions
1073A	583	Pooled Human Serum
1073B	584	Pooled Human Serum + 5 g/L Albumin
1073C	585	Pooled Human Serum + 10 g/L Albumin

What do we do about calibration and harmonisation of Type II analytes?

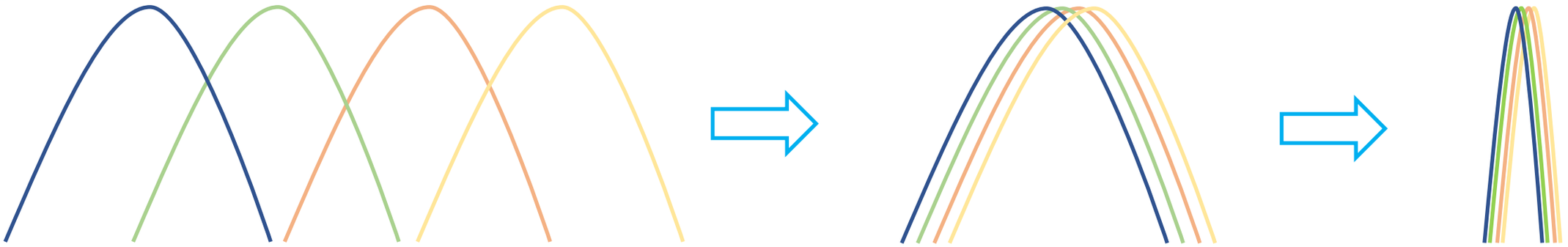
- Triage against clinical need
- Look at analytes where there is large difference between numerical results
- But because what you are measuring is a heterogeneous mixture you have to compromise on a representative and commutable material
- Define your measurand (which definition of *measurand* are we talking about?)
- Knowing what you are measuring – epitope mapping
- Know when to stop!

Assay Performance

A



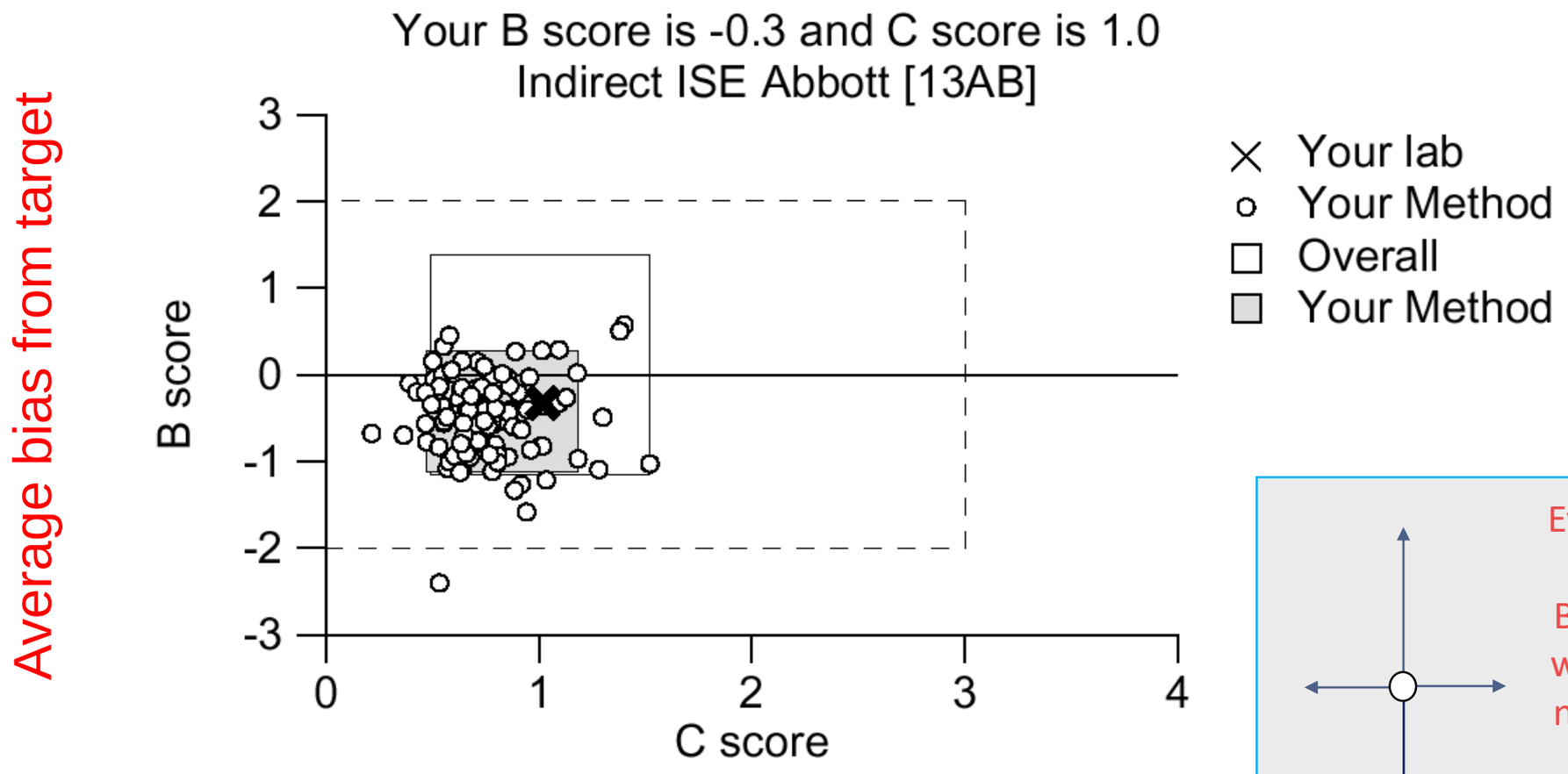
B



This works for a single specimen, at a single concentration, at a single time point

Penalty Box Plot

(rolling time-window data; one data point per laboratory)
each point is calculated from all the data specimens
distributed in the last 6 months which is usually 6 x 3 = 18)

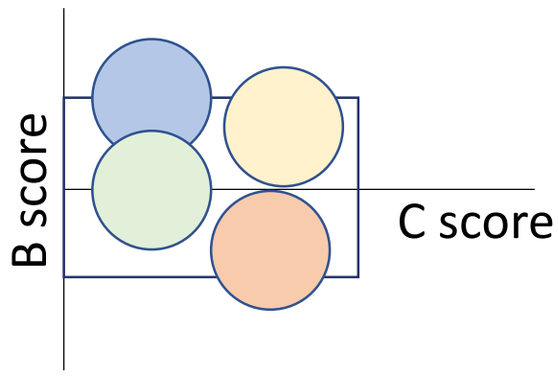


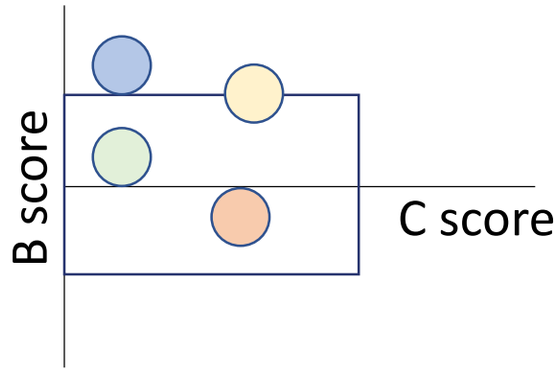
Consistency of bias

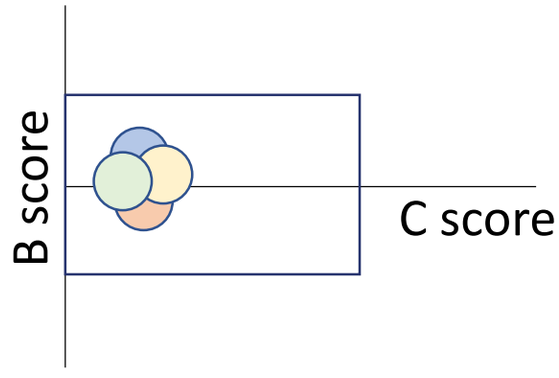
Every data point has its own B wobble and C wobble, but the number of data points clearly shows the domain

Assay Performance

A

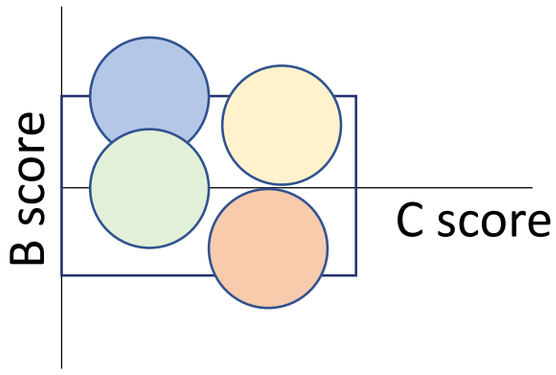


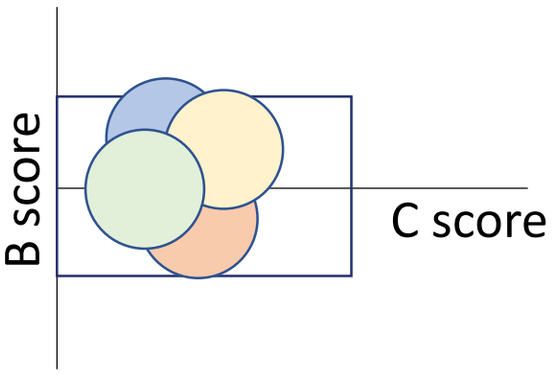


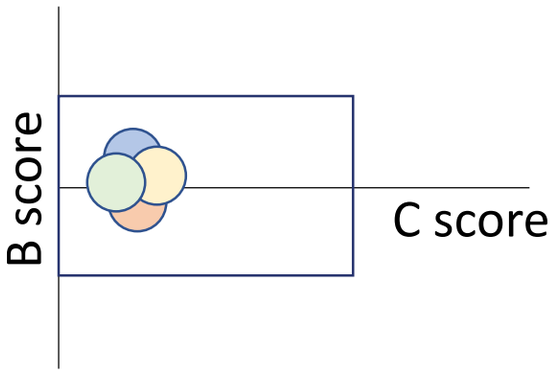


VS

B







Summary

- We should be looking at how analytes perform in the field that they are being used, taking into account within day/batch imprecision, between batch imprecision, concentration dependent biases and biases that differ due to the matrix of the sample (cross reactivity and interferences etc etc)

- EQA is crucial to post market surveillance and ensuring that there isn’t insidious drift in performance

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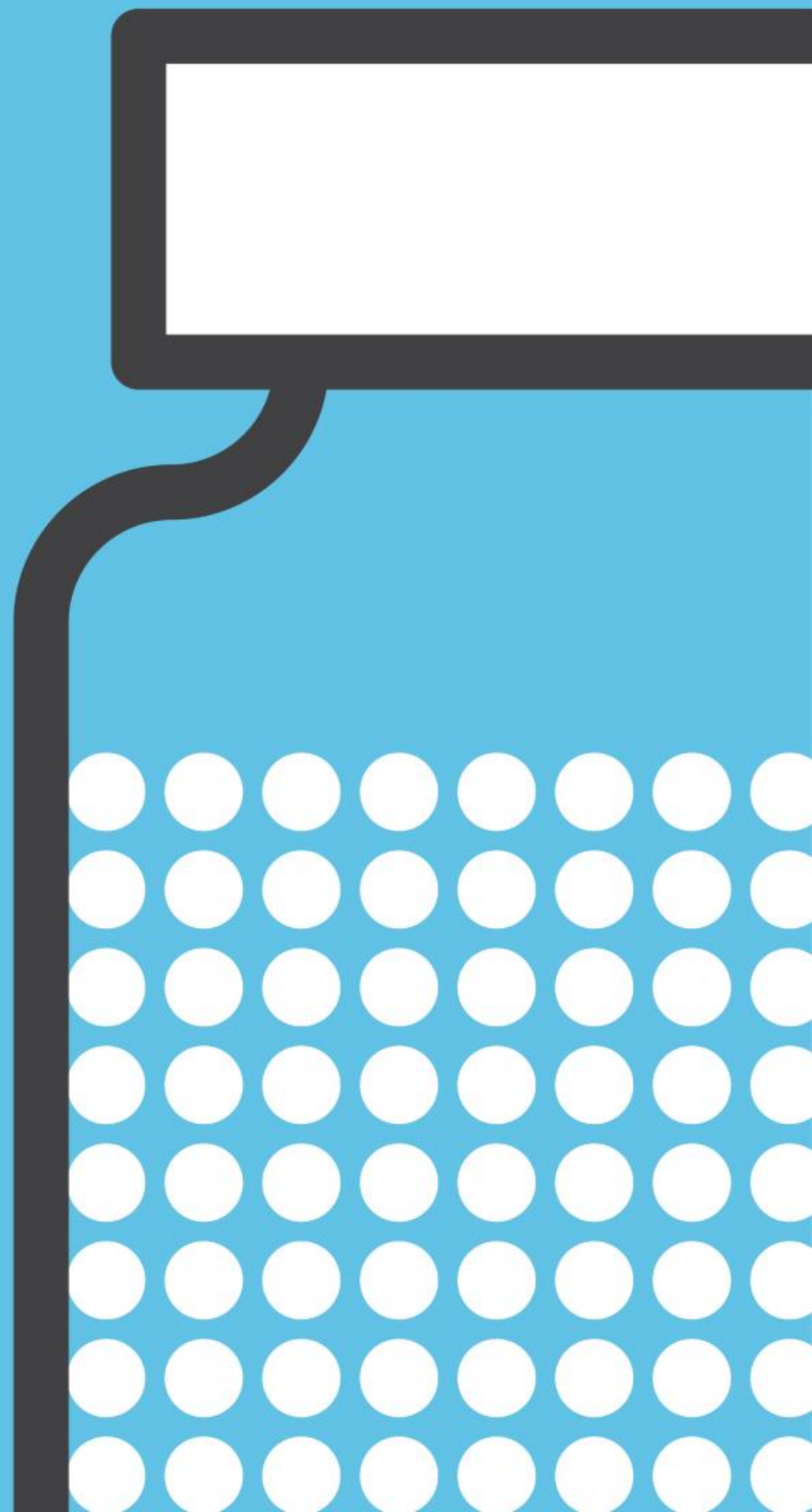
Thank You.



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