

Weqas
Unit 6, Parc Tŷ Glas
Llanishen, Cardiff, CF14 5DU

Tel: 02920 314750
Fax: 02920 314760
Email: contact@weqas.com



EXTERNAL
QUALITY
ASSESSMENT



INTERNAL
QUALITY
CONTROL



REFERENCE
MEASUREMENT
SERVICES



EDUCATION &
TRAINING

Weqas

GLOBAL PROVIDER OF QUALITY
IN DIAGNOSTIC MEDICINE

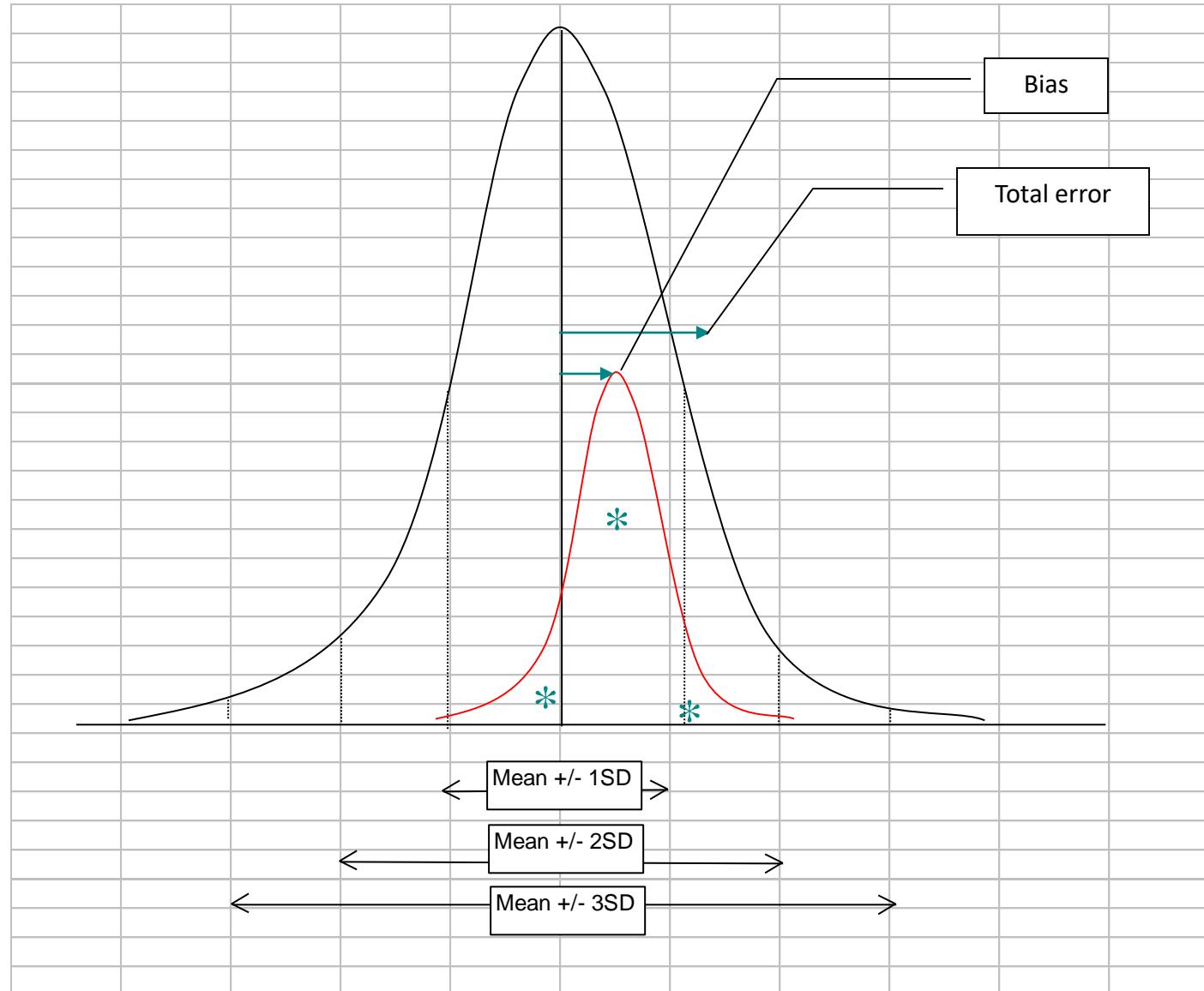
Error detection and Troubleshooting

Annette Thomas & Gareth Davies

Design - Why multiple samples are important

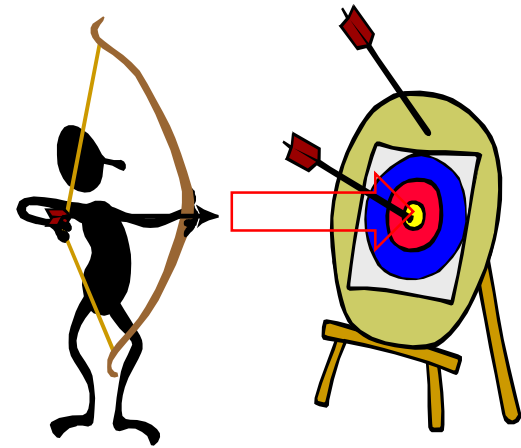
- Identifies components of both Imprecision and Inaccuracy
- Identifies systematic errors
- Assesses method linearity – required for ISO 15189
- Powerful error detection tool

Gaussian Distribution



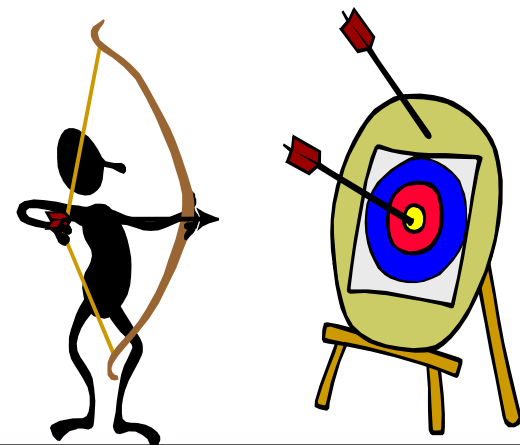
The Target Value?

Determining the 'right', 'true', 'correct' value?



Reference Measurement Targets

- “True” value traceable to higher order method.
- Establishes method traceability for the lab– requirement of ISO 15189.
- Independent assessment of manufacturer traceability claims.
- Highlights the pitfalls of using the trimmed overall mean as an accuracy target in EQA Schemes. Is not influenced by peer group numbers.
- Overall mean and method mean may not be traceable, may not be stable, may be influenced by large numbers from one manufacturer.
- Useful in the post market vigilance of the IVD - Directive
- **Expensive**



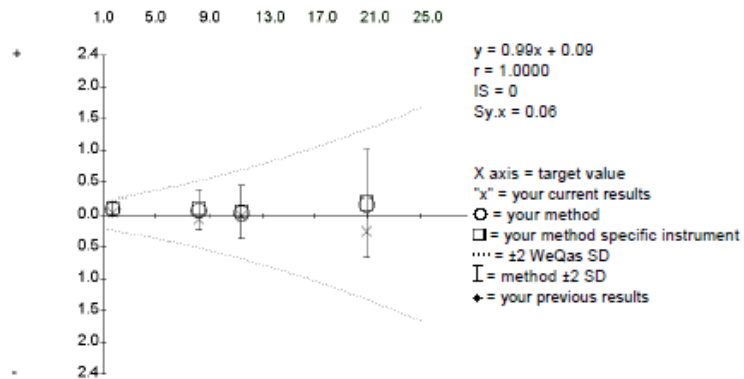
Traceability

Scheme: Serum Chemistry. Distribution Code: RH. Distribution Date: 2/01/18. Final Report Issued: 24/01/18					
Glucose (mmol/l)	1	2	3	4	Analyte SDI
Reported Result	11.4	8.1	20.7	1.8	
Method Corrected Result	11.40	8.10	20.70	1.80	
Hexokinase	Mean	11.42	8.21	21.11	1.85
	SD	0.20	0.15	0.41	0.05
	Number	170	172	169	168
	Uncert.	0.015	0.012	0.032	0.004
Cobas C Module	Mean	11.45	8.26	21.13	1.88
	SD	0.17	0.13	0.31	0.04
	Number	91	95	92	91
	Uncert.	0.018	0.013	0.033	0.004
Overall	Mean	11.39	8.21	21.05	1.86
	SD	0.22	0.15	0.46	0.06
	Number	191	188	188	186
	Uncert.	0.016	0.011	0.033	0.004
Reference Values ID-GCMS	11.40	8.15	20.95	1.76	
Ref. Value Uncertainty	0.100	0.070	0.150	0.020	
Non-scoring Reference Values					
WeQas SD	0.34	0.25	0.65	0.12	
SDI	0.00	-0.20	-0.38	0.34	0.23
Sigma Metrics					
Critical Level 1: 7 mmol/l					
Minimum Acceptable score	1.62	Critical Level 1 Sigma score			7.4
MAPS Allowable TE	6.9%				
MAPS Allowable bias %	2.20%	Lab [bias] %			0.2%
MAPS Allowable CV %	2.90%	Lab CV %			0.9%

Please note: Linear regression uses CF corrected data.

This Distribution RH

Prev



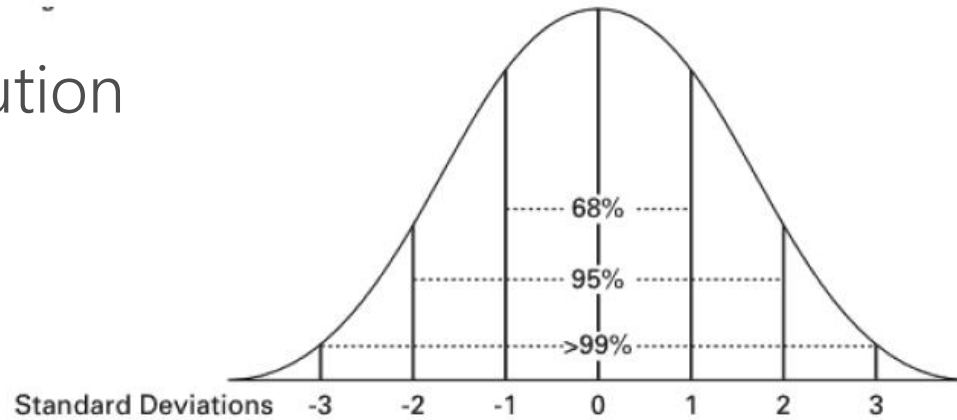
Reference measurement values shown on report (and reference value uncertainty). Full traceability chain to SI units available.

Lab results compared directly to reference values

SDI scores, Sigma scores and bias plot based on reference values

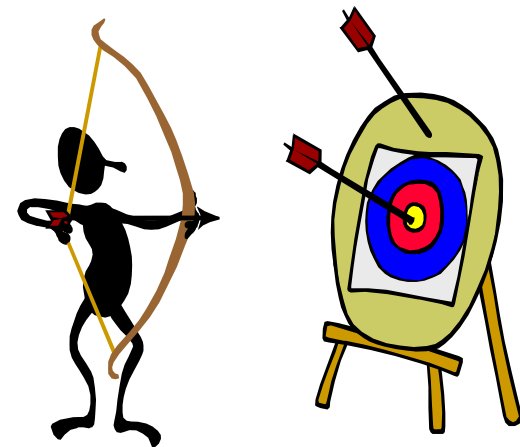
Using Statistical Comparison

e.g Distribution
Mean



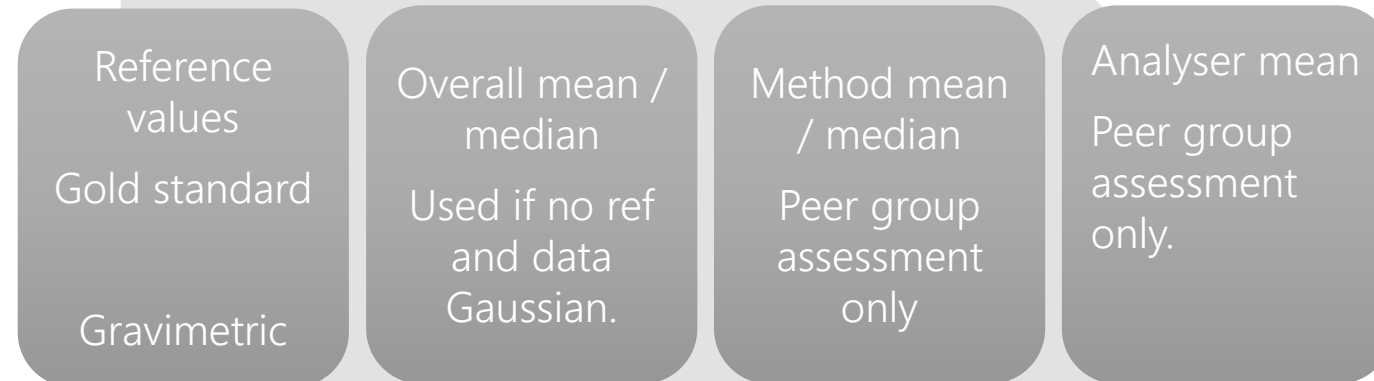
Where Overall Mean, Median, Method or instrument mean is used as the target.

- Cheap, quick and easy to do.
- Calculation (and uncertainty) of the Mean is influenced by outliers, number of results and spread of results.
- Gives no indication of the “true” result.
- May not be stable over time.
- May not provide context to clinical utility of the investigation especially where
- global targets are used for the clinical management of the patient.



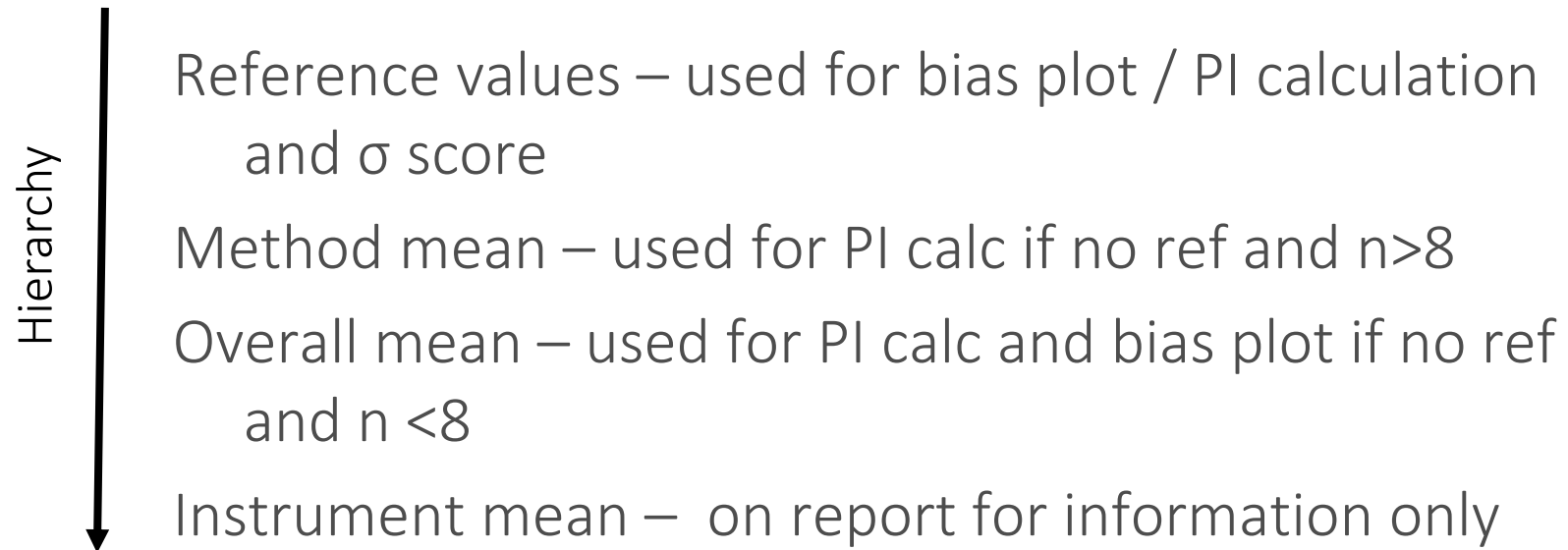
Target values used in Quantitative EQA

Loss of information for Assessment of accuracy



The Weqas Report

Target values used in Statistical Analysis



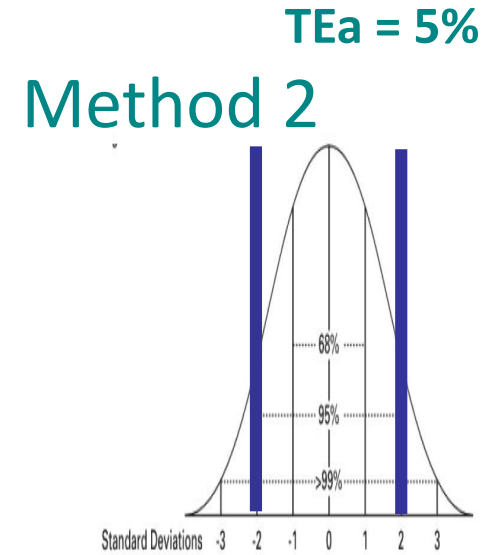
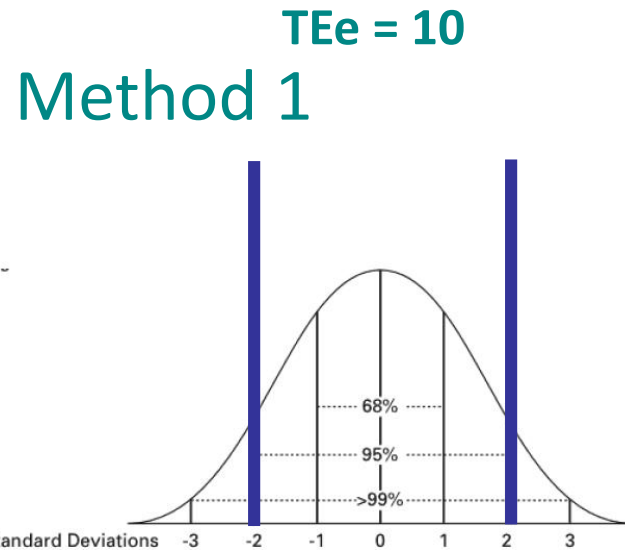
Determining Performance Specifications

Acceptable Performance Specification

A range of values around the target value that is considered clinically acceptable.

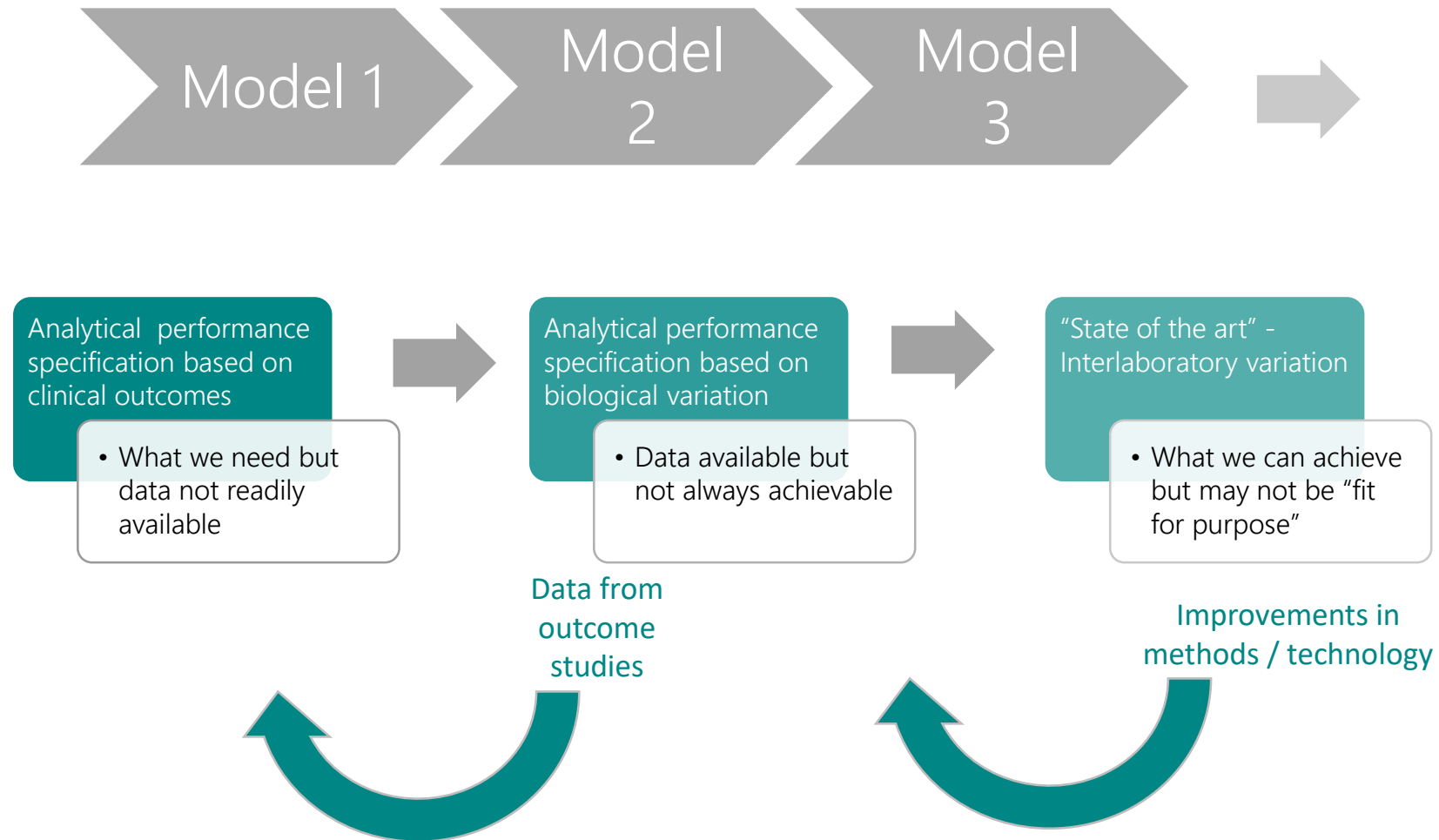
- Provides a simple tool to allow a rapid, standardized assessment of EQA results in both numerical and graphical report formats.
- A result outside the acceptable range should alert the laboratory that their assay may produce results that are at risk of detrimentally affecting clinical decision making.

Using Statistical Comparison



Mean \pm 2 SD = 95% returned results are usually used
Provides information on whether your result is in agreement with the peer group used
May not be clinically relevant
May not be stable from one distribution to another
Influenced by outliers

Specification Hierarchy



From Biological goals

Test	I (%)	B (%)	TE (%) (0.01)
Glucose	2.2	1.9	7.0
HbA1c	1.7	1.5	5.5

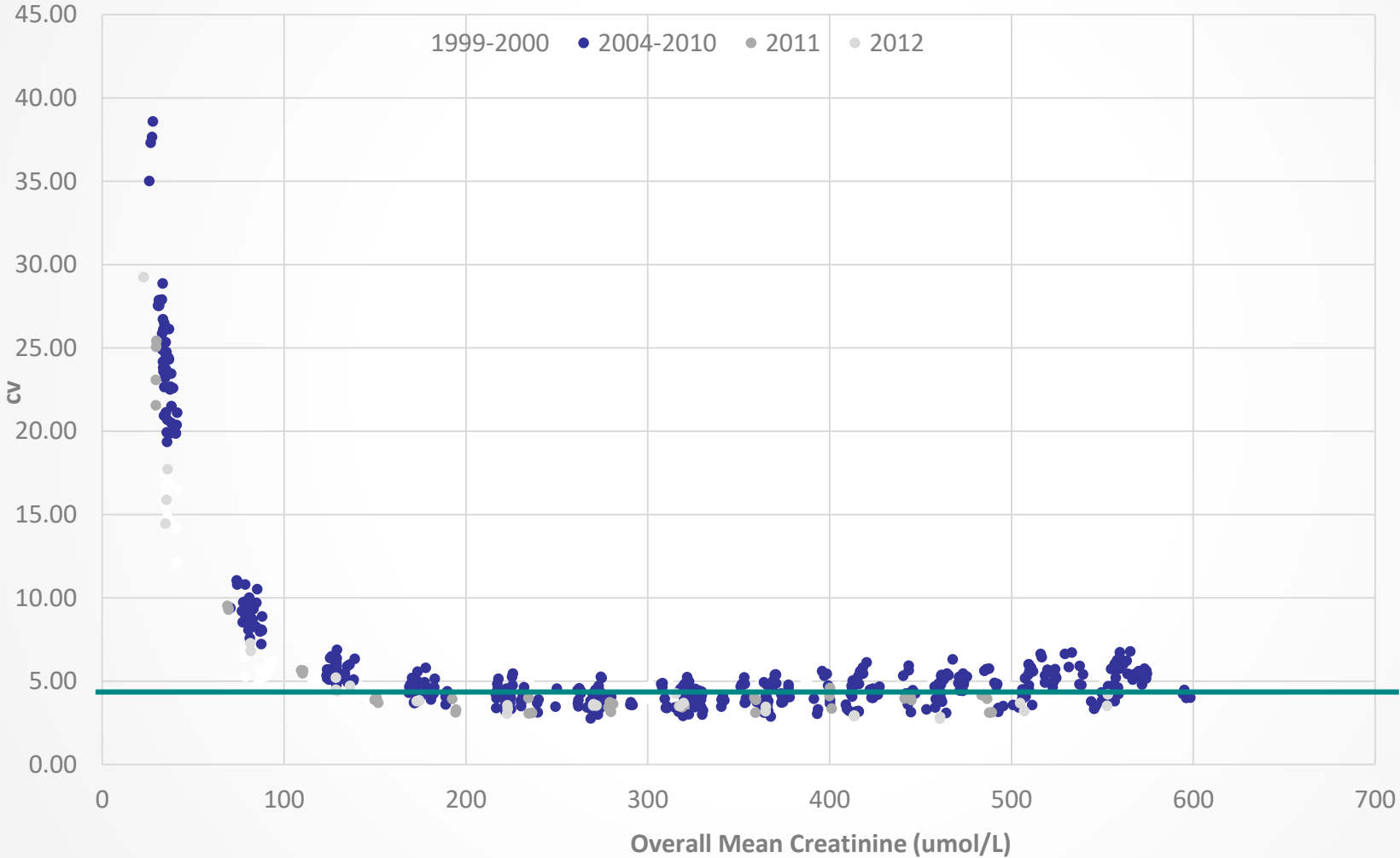
Desirable quality specification can be calculated from:

$$I < 0.5CV_w$$

$$B < 0.25 (CV_w^2 + CV_b^2)^{1/2}$$

$$TE = 2.33 I + B (a < 0.01) \text{ for EQA}$$

Creatinine Precision Profile (CV %)



Determining analytical quality specifications

Allowable Total Analytical Error (TEa) encompasses both imprecision and inaccuracy.

Shown as TAE (Total Allowable Error) on Weqas Reports

The WEQAS Report Statistical Indices

- Imprecision: $S_{y.x}$, r , IS
- Inaccuracy: Bias plots (absolute & relative), $y=mx+c$

Interpretation of Imprecision

Sy.x is the deviation around the best fit line and is an indication of scatter. It is used as an index of within run imprecision. This is given in the units of the analyte in question.

Correlation coefficient (**r value**) is also an index of within run imprecision. The closer to 1.0 the value is, the better the precision (less scatter about the best fit line).

IS score is derived from the correlation coefficient.

'r' value	Imprecision score	
0.9990 to 1.0000	0 to 10	- Good
0.9850 to 0.9989	11 to 150	- Acceptable to Warning level
< 0.9850	> 150	- Unacceptable (including Curvilinear Data)

Imprecision indices

Standard deviation

$$SD = \sqrt{\frac{\sum (\bar{y} - y)^2}{d.f.}}$$

where

y = observed value

\bar{y} = expected value

d.f. = degrees of freedom

Standard dev of residuals

$$S_{y.x} = \sqrt{\frac{\sum (\tilde{y} - y)^2}{d.f.}}$$

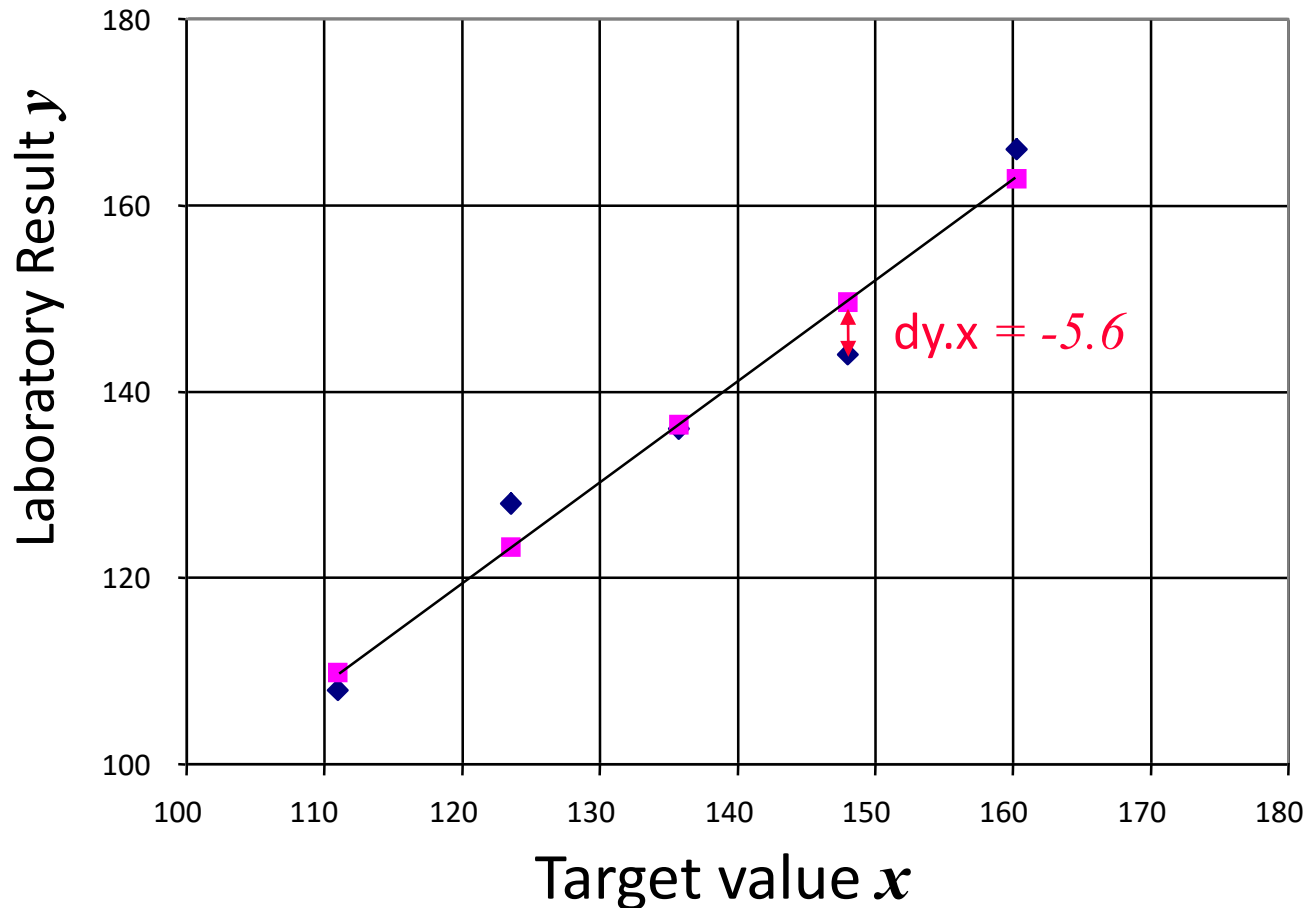
where

\tilde{y} = the value on the
line of best fit

Imprecision – Scatter around the “best fit line”, $Sy.x$

Sodium (mmol/l)

Measurement of scatter



■
 $r = 1.000$
 $Sy.x = 0$

All reported results are on the “best fit” line – no scatter

◆
 $r = 0.9812$
 $Sy.x = 4.1$

Reported results are scattered around the “best fit” line – standard deviation of 4.1 mmol/L

Imprecision – how to calculate $S_{y.x}$

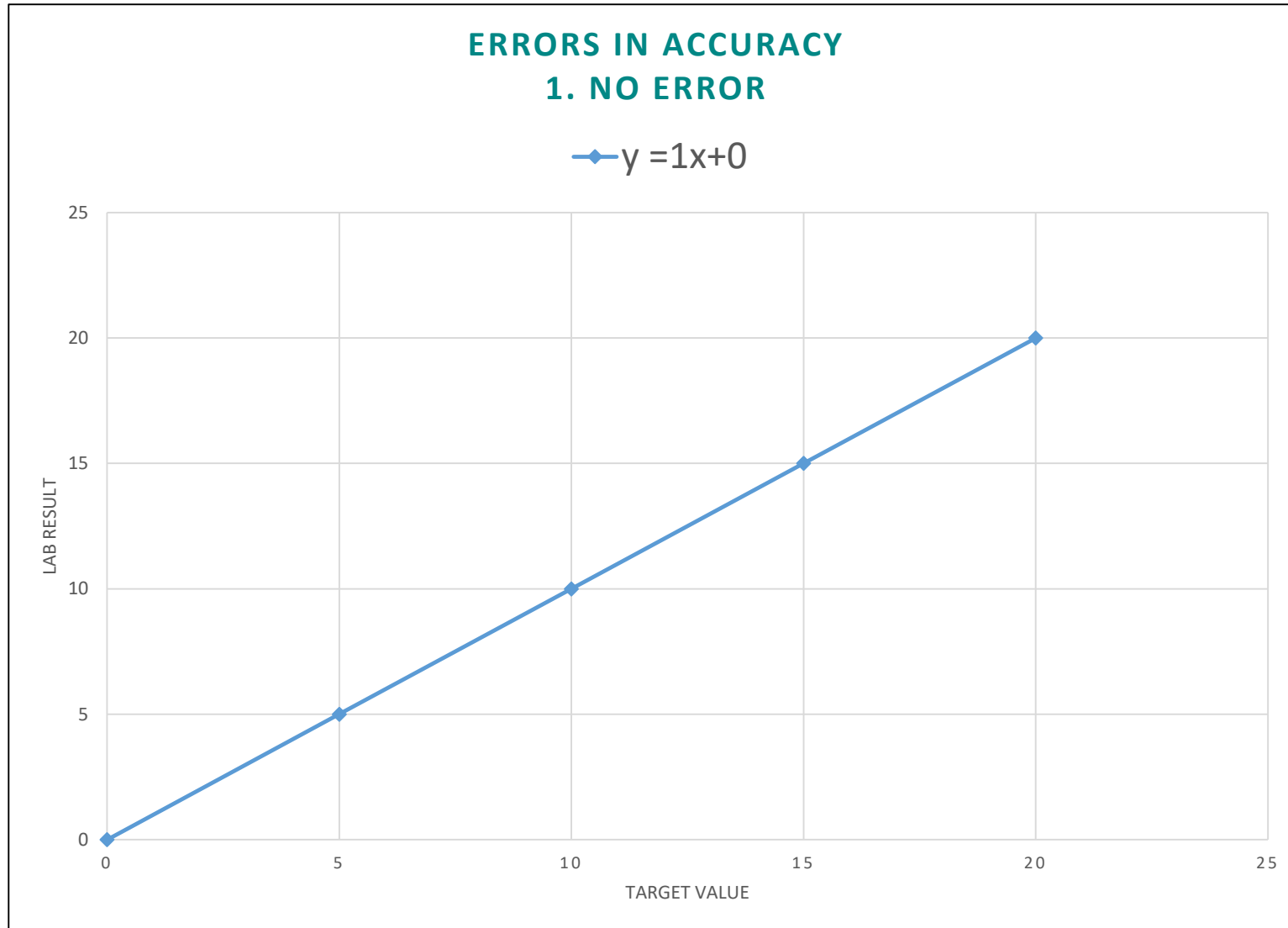
Target value	Lab result	Line of best fit	Deviation	
x	y	\tilde{y}	$y - \tilde{y} = dy.x$	$dy.x^2$
111	108	109.9	-1.9	3.62
123.5	128	123.3	4.7	21.97
135.7	136	136.4	-0.4	0.16
148	144	149.6	-5.6	31.30
160.3	166	162.8	3.2	10.31
slope	1.07		$\sum dy.x$	$\sum dy.x^2$
int	-9.17		0.0	67.36
			$d.f = n-1 = 4$	
	$S_{y.x} =$	$\sqrt{\sum dy.x^2 / d.f}$	$\sqrt{67.4/4}$	4.10

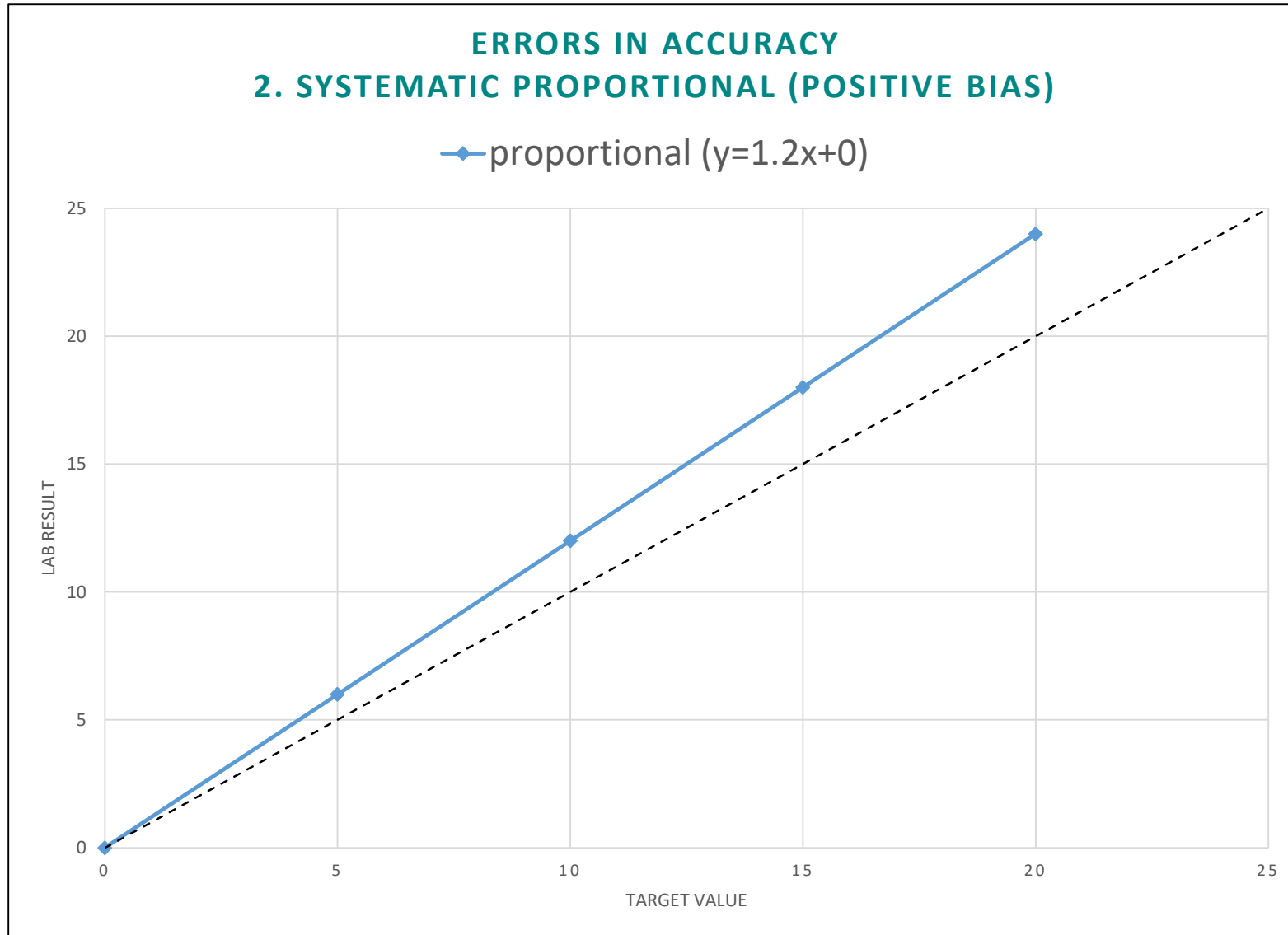
Interpretation of Inaccuracy

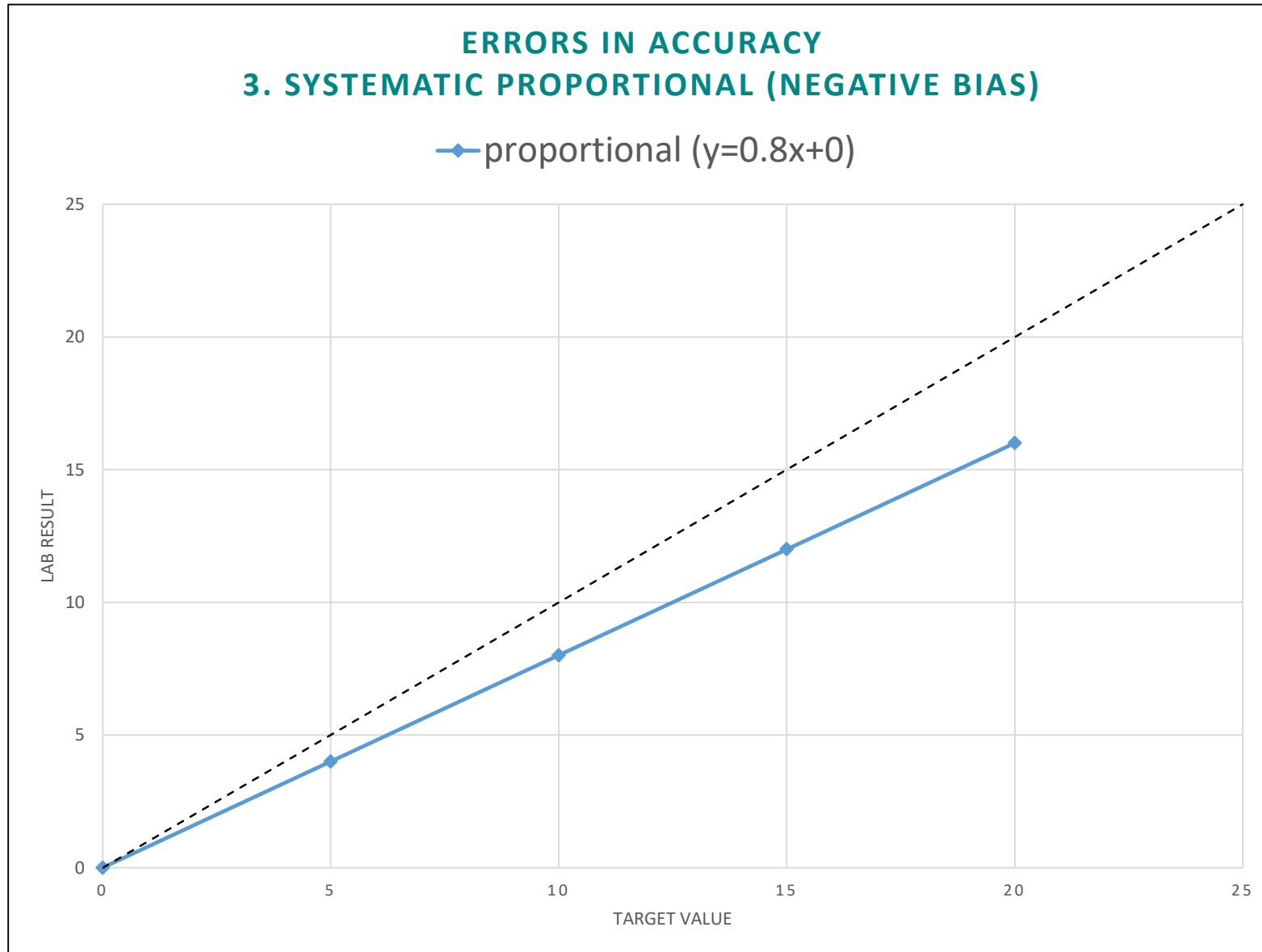
Represents the point at which the line crosses the y axis. This is shown in the units of measurement of each analyte. In the example this is 12.04nmol/L. If deemed significant, this indicates a constant error.

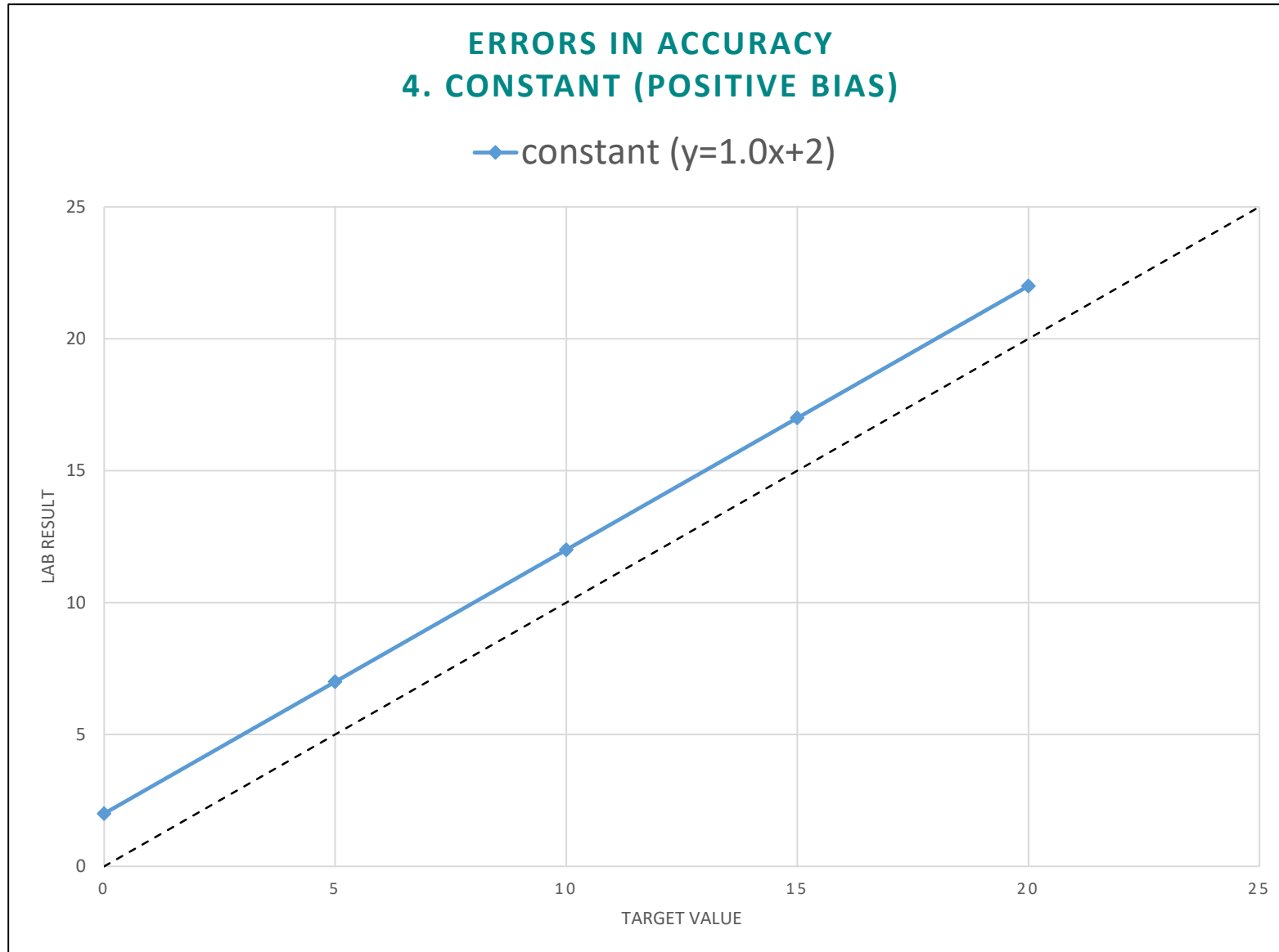
$$y = mx + c$$

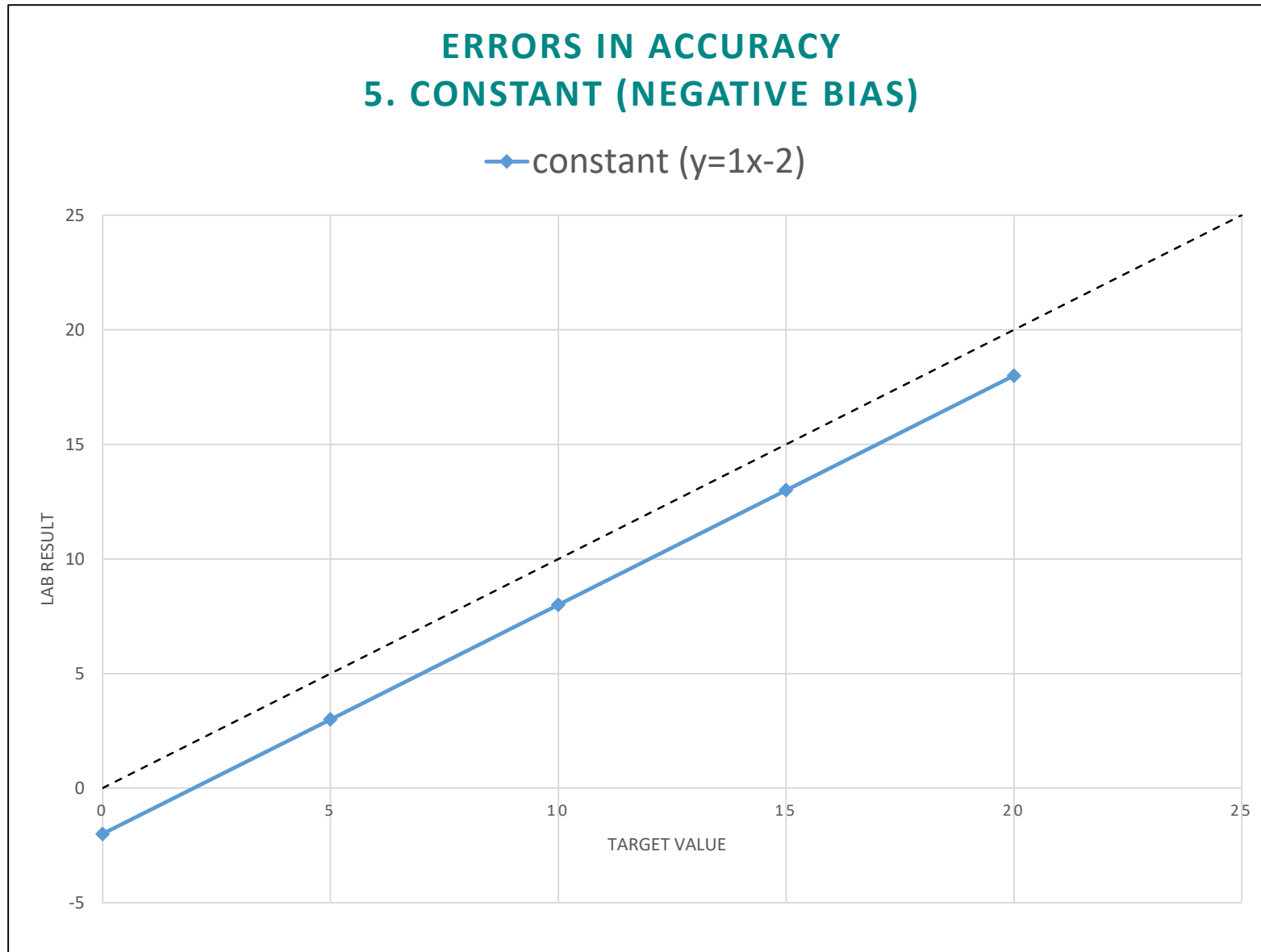
Represents the slope – in the example this is 0.97 which shows a 3% negative proportional bias. If deemed significant indicates a proportional error.

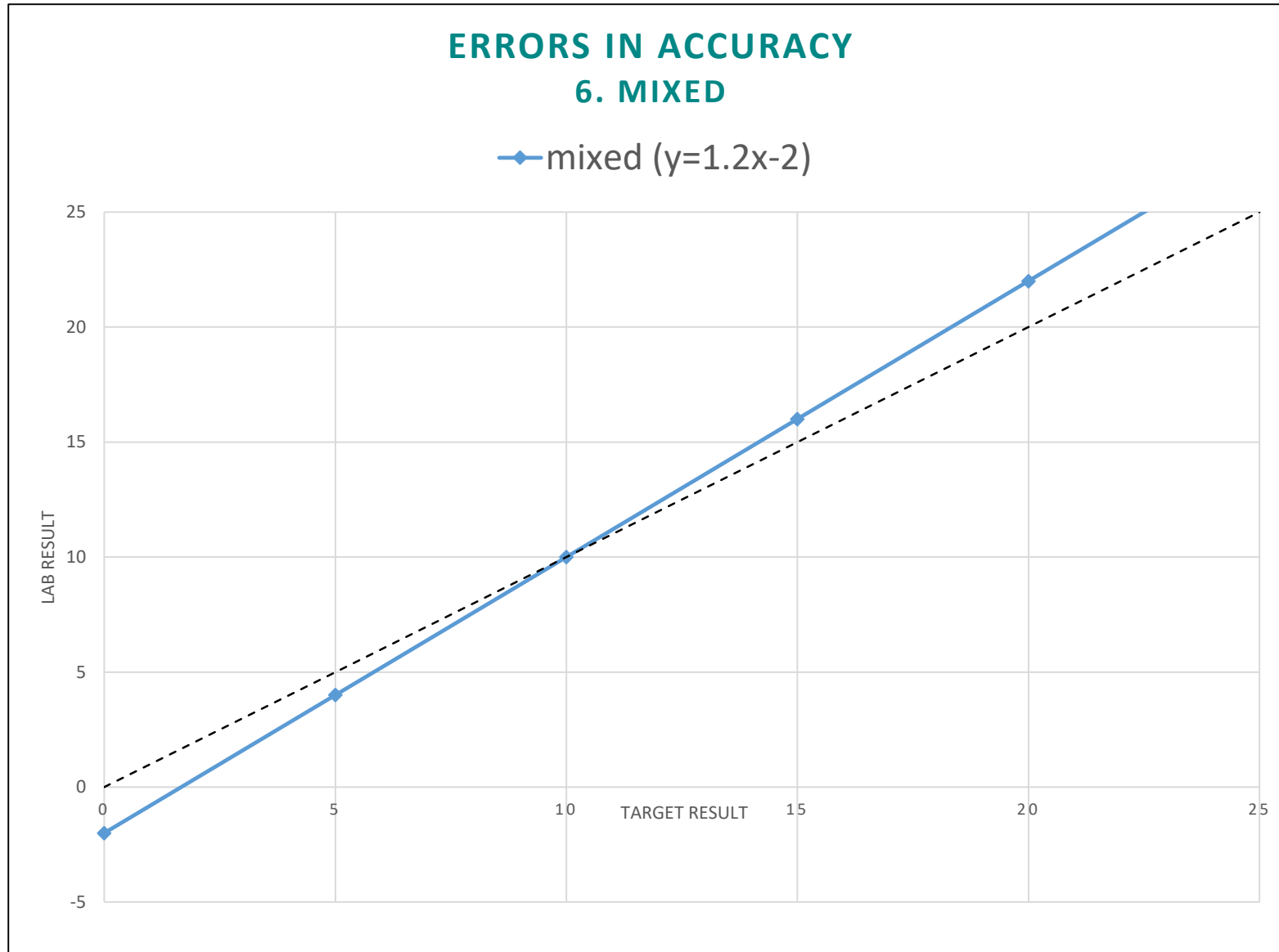


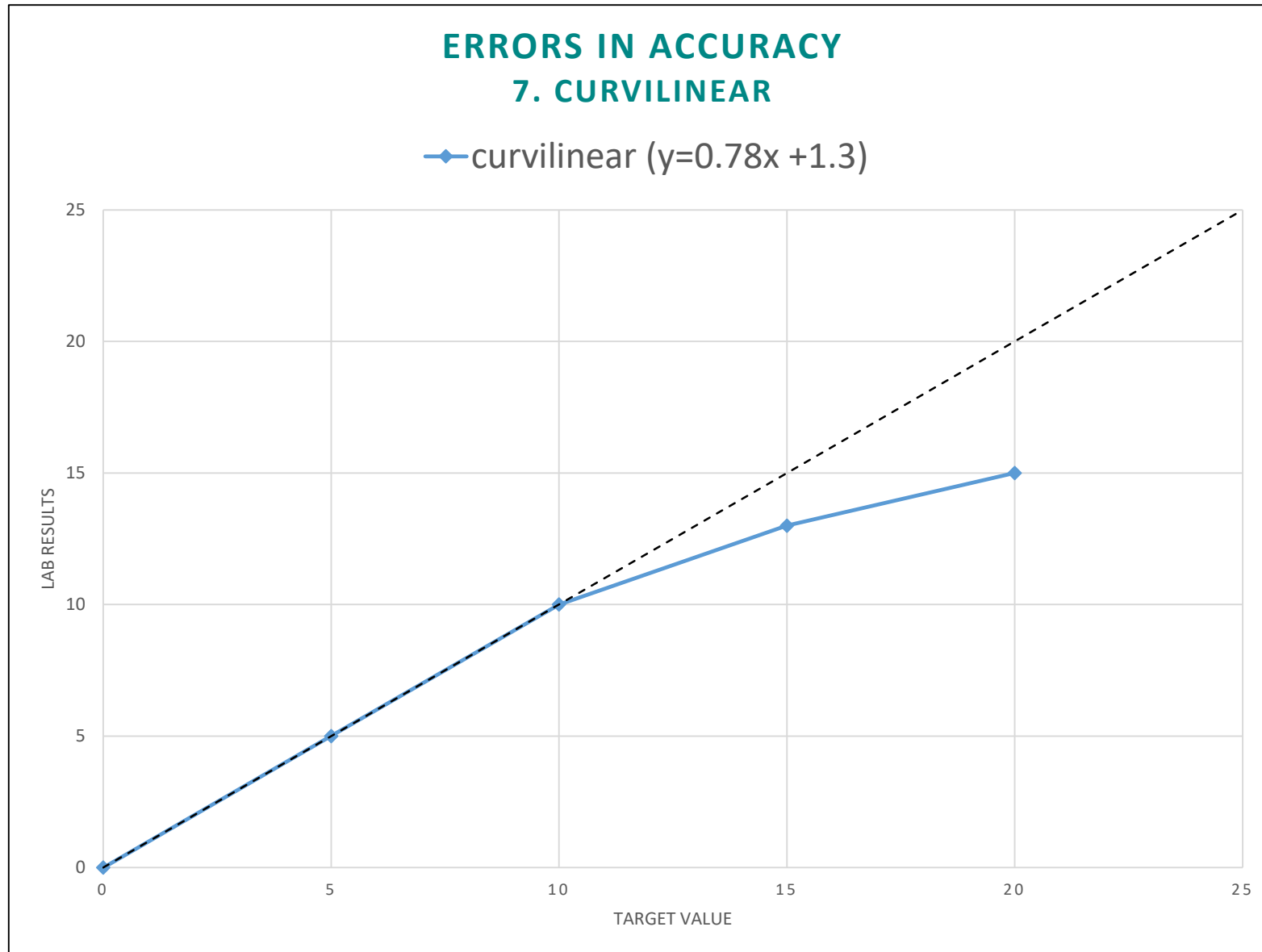




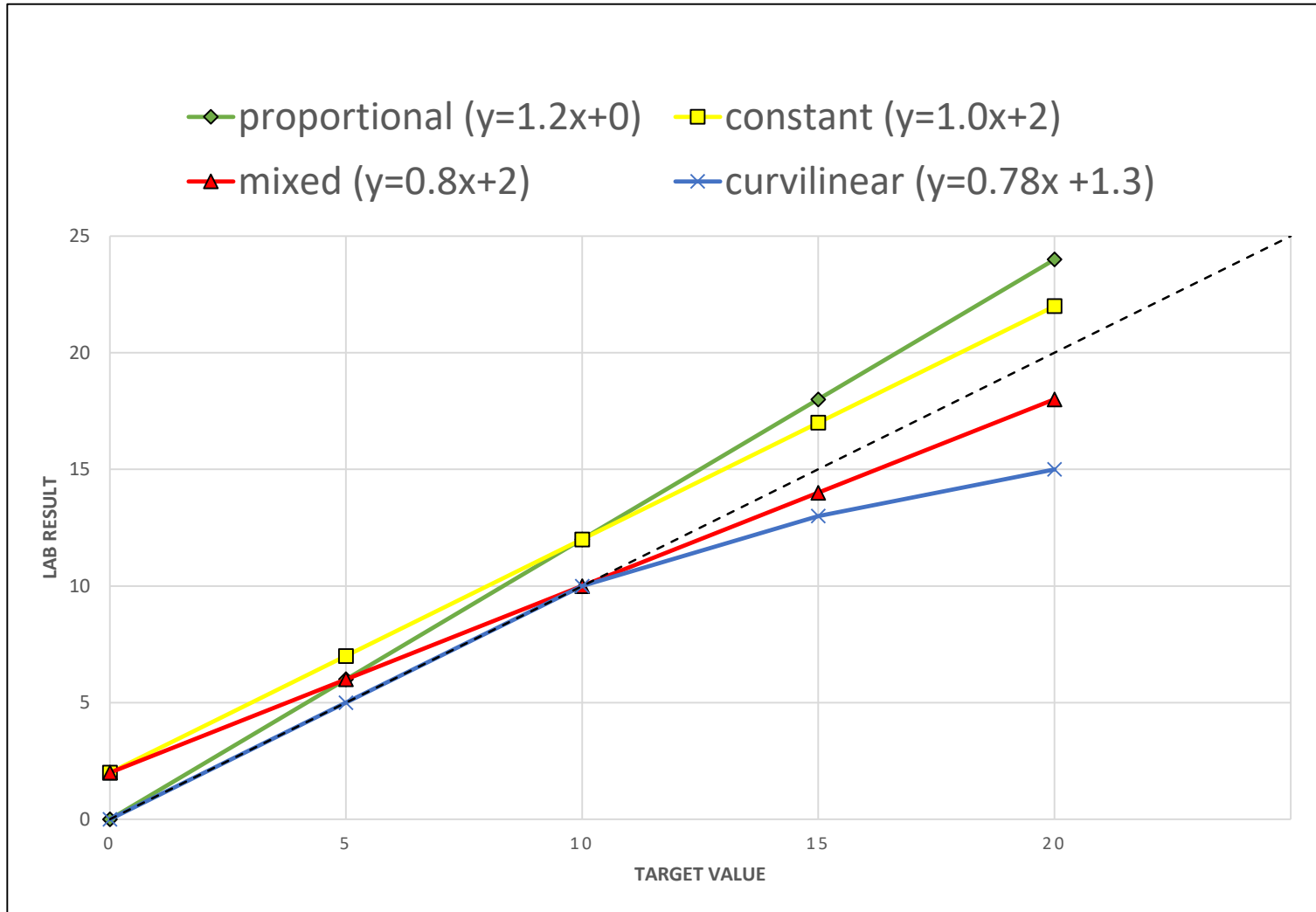








Types of Errors



Types of Errors

	Imprecision		Inaccuracy		
	Random	Curvilinear	Prop	Mixed	Constant
Slope	No	Yes/No	Yes	Yes	No
Intercept	No	Yes/No	No	Yes	Yes
$S_{y,x}$	Yes	Yes	No	No	No
r	Yes	Yes	No	No	No

Overall Performance

Traffic light colour	Performance category	Description
Red	Non-Return	(Any number of samples in distribution) and (No results submitted for any samples)
	Poor	(Any number of sample in distribution) and (one or more $ PI > 3$)
		(number of samples in distribution = 1) and ($2 < PI \leq 3$)
		(number of samples in distribution > 1) and (2 or more $ PI > 2$) (<i>Westgard 2_{2s}</i>)
(number of samples in distribution > 1) AND (sign $x_i \neq$ sign x_j) AND $ x_i > 2$ AND $ x_j > 2$ * for at least one pair of scores x_i and x_j where x_n with $i \neq j$ are the individual sample-analyte scores for the instrument in question (<i>Westgard R_{4s}</i>)		
Orange	Warning	(number of samples in distribution > 1) and (single sample with $2 < PI \leq 3$) and (no sample with $ PI > 3$)
Yellow	Acceptable	(any number of samples in distribution) AND ($1 < \text{Max } PI \leq 2$)
Green	Good	$ PI < 1$ for all samples Green is only assigned if all the individual samples are good.

Troubleshooting - Problem Solving Flow Chart

START HERE



IMPRECISION

INACCURACY

[1]

*Are you satisfied with
your imprecision values?
($S_{y.x}$, r)*

YES

[2]

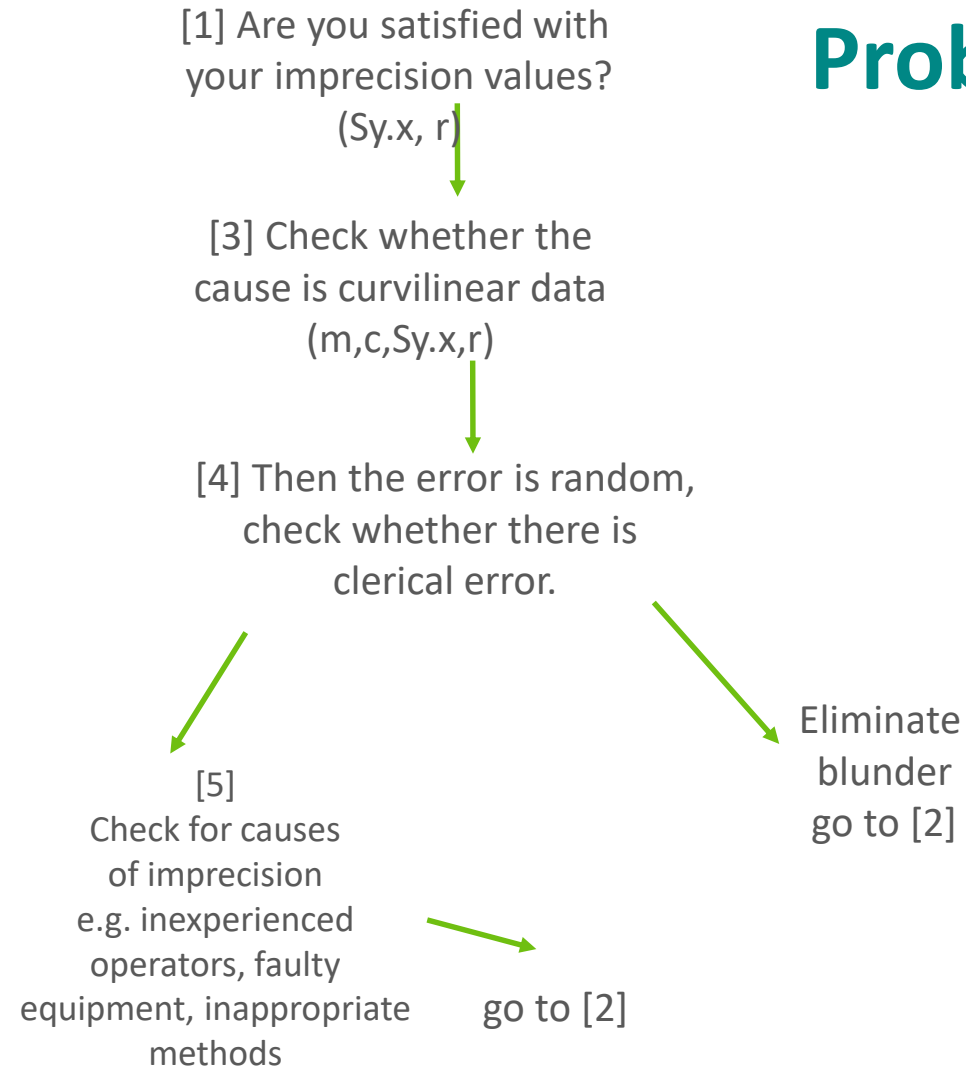
*Are you satisfied with
slope and intercept?
(m , c)*

YES



Problem Solving Flow Chart

IMPRECISION



Problem Solving Flow Chart

START HERE



IMPRECISION

INACCURACY

[1]

Are you satisfied with
your imprecision values?
($S_{y.x}$, r)

YES

[2]

Are you satisfied with
slope and intercept?
(m , c)

YES



NO

[6]

Identify type of error

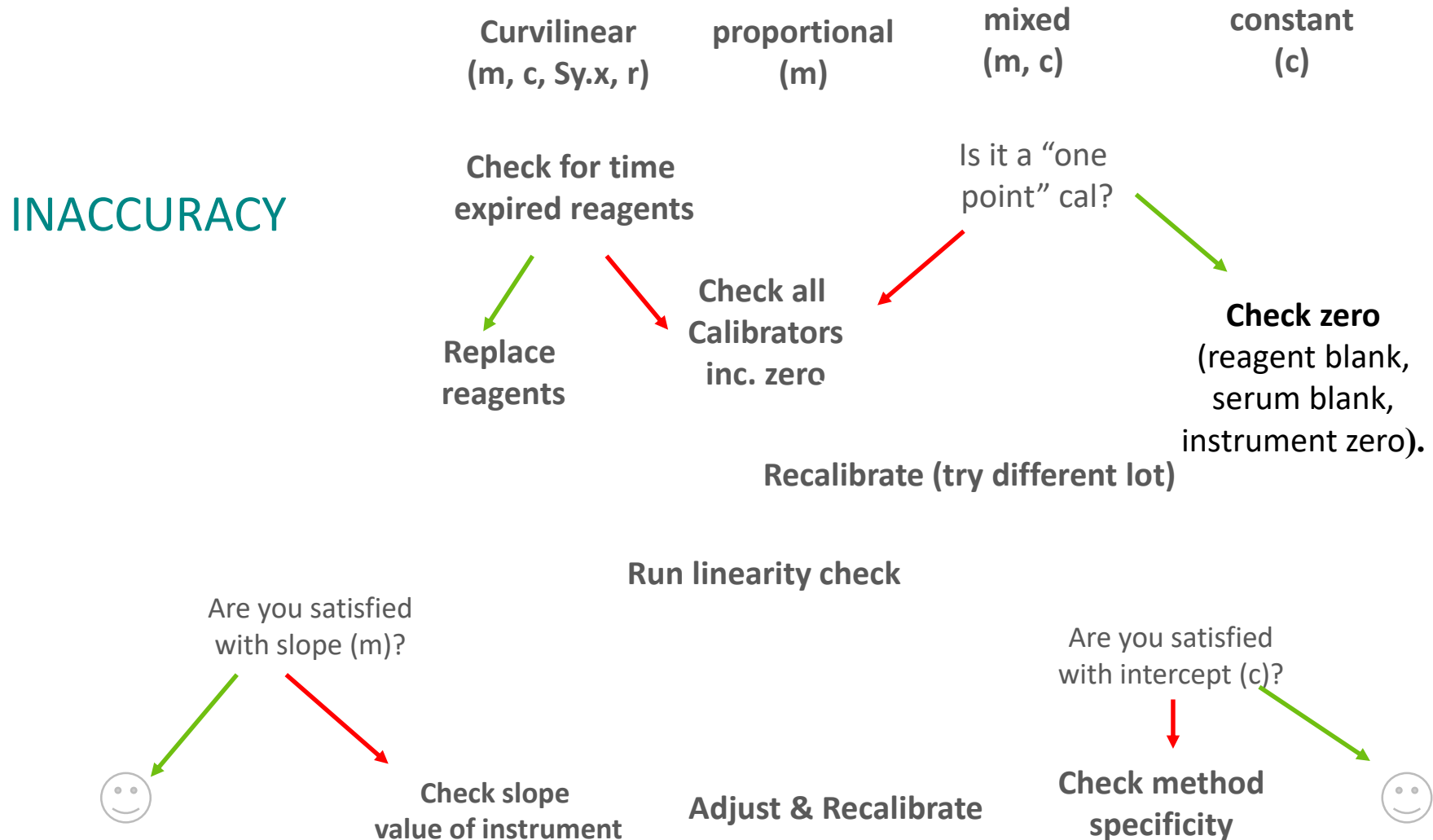
curvilinear
(m , c , $S_{y.x}$, r)

proportional
(m)

mixed
(m, c)

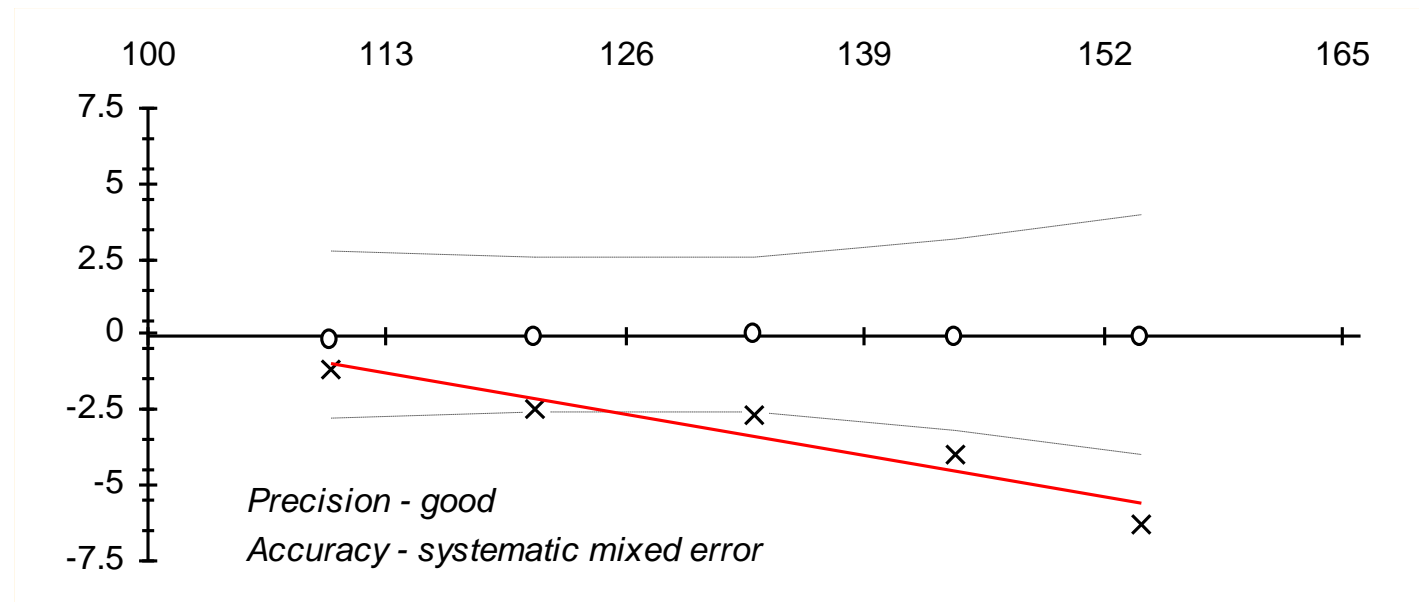
constant
(c)

Problem Solving Flow Chart



Bias plot (1)

Sodium (mmol/l)



$$y = 0.9x + 9.6$$

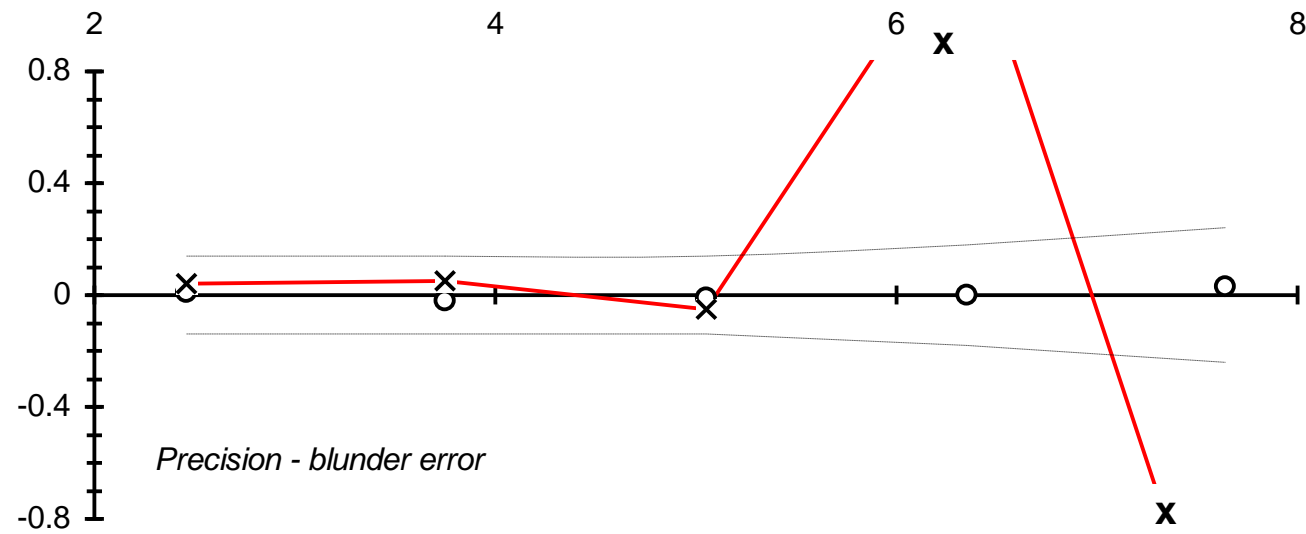
$$r = 0.9995$$

$$IS = 5$$

$$S_{y.x} = 0.63$$

Bias plot (2)

Potassium (mmol/l)



Precision - blunder error

y = slope not calculated

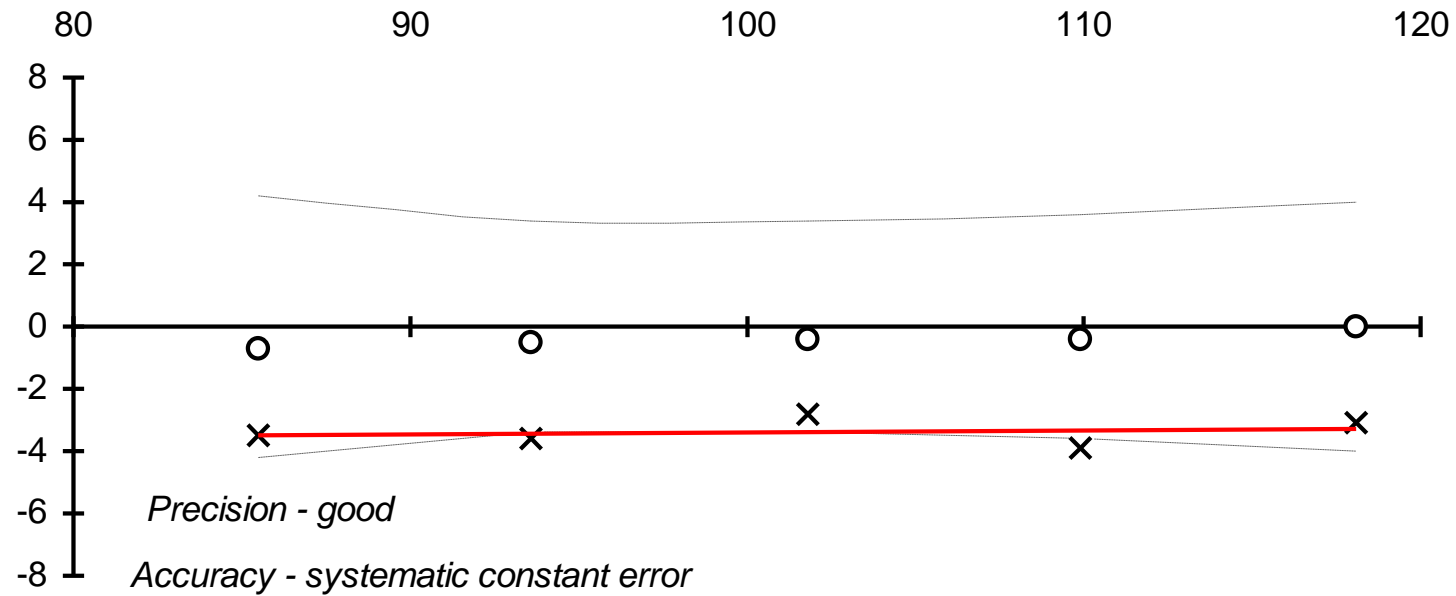
r = 0.8826

IS = 1174

Sy.x = 1.10

Bias plot (3)

Chloride (mmol/l)



$$y = 1.01x - 4.01$$

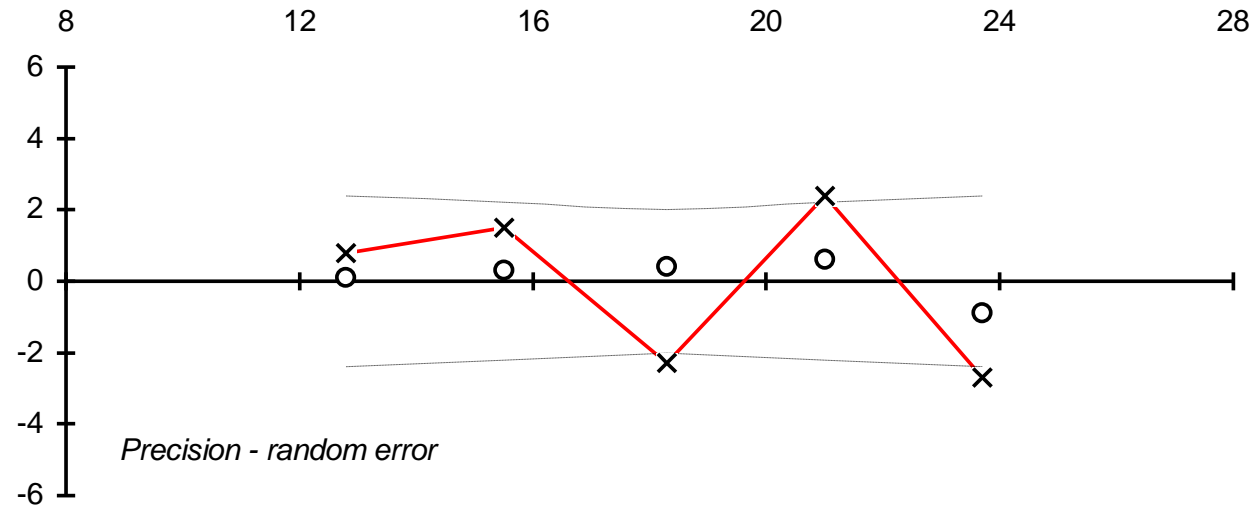
$$r = 0.9995$$

$$IS = 5$$

$$Sy.x = 0.49$$

Bias plot (4)

Bicarbonate (mmol/l)



y = slope not calculated

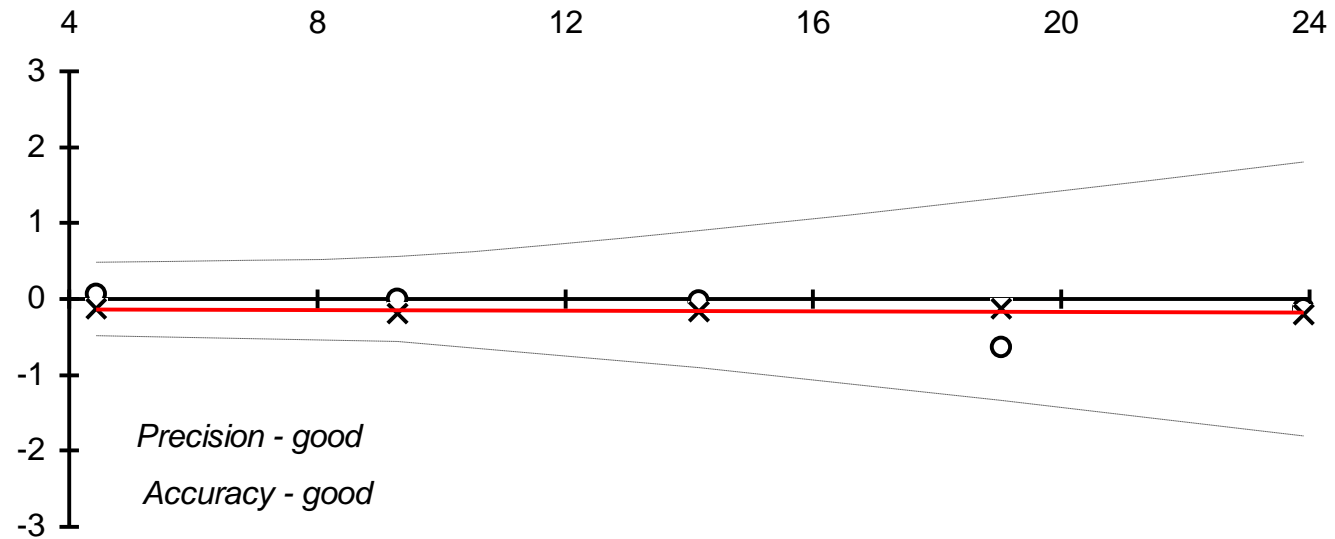
r = 0.8484

IS = 1516

Sy.x = 2.41

Bias plot (5)

Urea (mmol/l)



$$y = 1.00x - 0.14$$

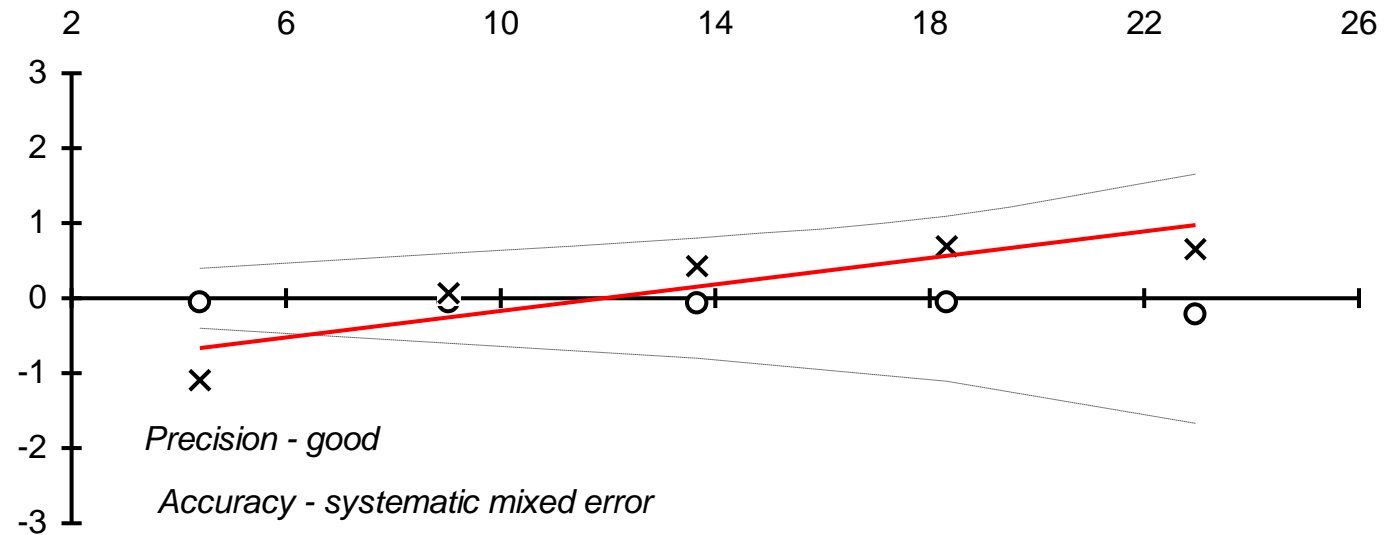
$$r = 1.000$$

$$IS = 0$$

$$Sy.x = 0.03$$

Glucose (mmol/l)

Bias plot (6)



$$y = 1.09x - 1.06$$

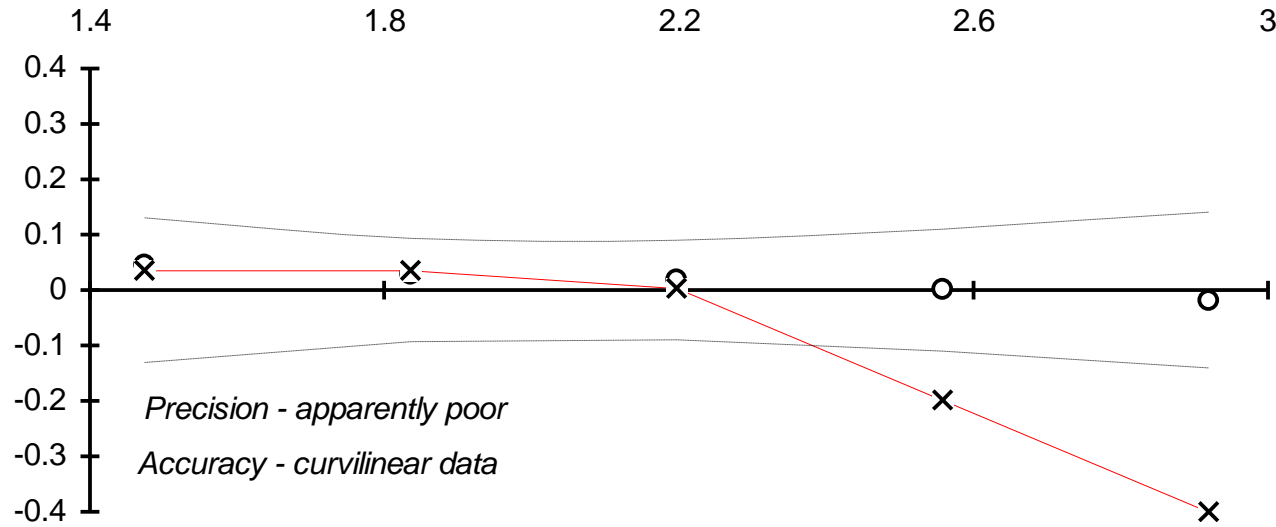
$$r = 0.9991$$

$$IS = 9$$

$$Sy.x = 0.40$$

Calcium (mmol/l)

Bias plot (7)



y = slope not calculated

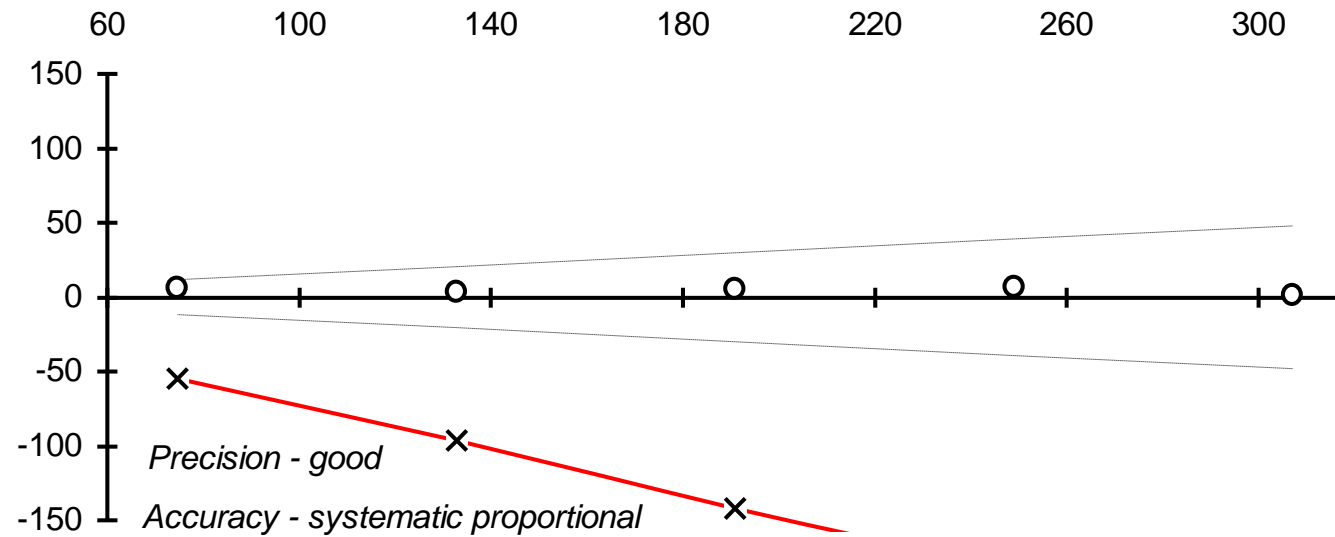
r = 0.9810

IS = 190

Sy.x = 0.09

Bias plot (8)

ALP (IU/L)



$$y = 0.50 x + 1.16$$

$$r = 0.9999$$

$$IS = 1$$

$$S_{y.x} = 1.30$$

Problem Solving Checklist

Analyte	Overall Performance	Results & Scoring Tables	Running PI	Precision (r, Sy.x, IS)	Accuracy (m,c, bias plots)	Sample Histograms	Identify Error & Possible Cause