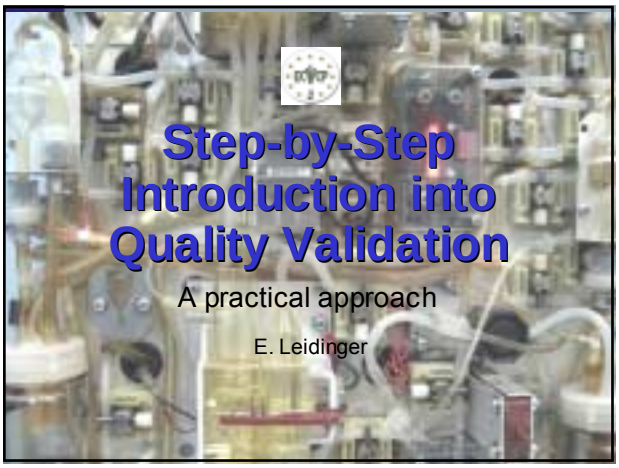


Step-by-Step Introduction into Quality Validation

A practical approach

E. Leidinger

INTRODUCTION

DEFINITION & TERMS

QC-Validation (QV): approach of evaluating the process of statistical QC by determining:

a) QC appropriate for detecting medically important errors
b) QC needed to detect variation affecting clinical interpretation
c) Overall quality of performance
d) If QC rules can be simplified

INTRODUCTION

DEFINITION & TERMS

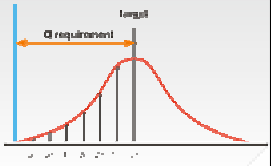
- Total allowable error (TE_a): performance characteristic that mathematically combines random and systematic error. "worst case"
- Desirable TE_a: set quality requirements for test performance, based on published data, clinical decision making, expert opinion
- Calculated TE_c: calculated from own measurements

$$TE_c = Bias_c + 1.65\ CV_c$$

INTRODUCTION

DEFINITION & TERMS

- Sigma metrics: numerical quality characteristic; measures performance in terms of the number of SD (s) fitting within the quality requirement of a test
- s <3 unstable performance; not suitable
- s >6 "world class quality"



INTRODUCTION

DEFINITION & TERMS

- Normalised operation points ($NOP_{x,y}$): x, y coordinates that define the operating point for OpSpecs charts

$$NOP_x = CV_c/TE_a \times 100$$
$$NOP_y = Bias_c/TE_a \times 100$$

INTRODUCTION

Define requirements

Calculate parameters

Identify candidate QC proc.

Predict IQC perform. (P_{ed}, P_{fr})

Define performance goals

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DEFINE REQUIREMENTS

QUALITY VALIDATION

Criteria to define (usually published data)

- CV_{max} - max. (allowed) random error
- $Bias_{max}$ - max. (allowed) systematic error
- Total allowable error (TE_a)
- Other (Sigma metric, OpSpecs)

Freeman KP, Guenwaldt J. (1999). Quality control validation in veterinary laboratories. VCP 28:159-155.
Rishniw M etal. The quality of veterinary in-clinic and reference laboratory biochemical testing. VCP 41:93-109

DEFINE REQUIREMENTS

CRITERIA FROM LITERATURE

Assumption: haematology analyser

Parameter	CV_{max} %	$Bias_{max}$ %	TE_a %	Source
WBC	5.5	5.6	14.6	1)
RBC	2.8	1.7	6.3	CV[2], Bias[1]
Hb	2.9	1.8	7.0	TE_a CV[2], Bias[1]
Hct	1.4	1.7	4.1	Bias[1], TE_a[2]
MCV	0.7	1.2	2.3	1)
PLT	4.6	5.9	25.0	CV, Bias[1] TE_a[3]

1) Ricós C, Alvarez V, Cava F, García-Lario JV, Hernández A, Jiménez CV, Minchinela J, Perich C, Simón M. (1999): Current databases on biological variation: pros, cons and progress. Scand J Clin Lab Invest 59:491-500.
2) Jensen, AL (2008): Lecture on biological variation. VIN-CE course
3) CLIA Analytical Quality Requirements. retrieved from www.westgard.com

DEFINE REQUIREMENTS

CRITERIA FROM LITERATURE

Parameter	CV_{max} %	$Bias_{max}$ %	TE_a %	$TE_{c\,max}$ %
WBC	5.5	5.6	14.6	14.7

Note: $Bias_{max} + 1.65 \times CV_{max} \neq TE_a\%$
different publications, different criteria

1) Ricós C, Alvarez V, Cava F, García-Lario JV, Hernández A, Jiménez CV, Minchinela J, Perich C, Simón M. (1999): Current databases on biological variation: pros, cons and progress. Scand J Clin Lab Invest 59:491-500.
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CALCULATE

COLLECT OWN DATA VALIDATION

- Collect and tabulate 30-60 IQC data sets for each QC level (usually 2-3)
- If possible: same lot
  Otherwise: t-test
- Eliminate apparent outliers (e.g., wrong QC material level)

CALCULATE

CALCULATE PARAMETERS

Control Level: LOW

	$\bar{x}_{arg}$	$\bar{x}_c$	CV_c%	Bias$_c$%	TE_c	NOP		TE_a	© QC Rule
Lot	0144L	n=32				x	y		
WBC	2.5	2.54	2.4	2.0	6.0	10	8	14.6	
RBC	2.45	2.50	2.7	2.0	6.5	43	32	6.3	
Haemoglobin	8.0	8.1	0.6	2.5	3.5	9	36	7.0	
Haematocrit	23.7	24.2	1.9	2.5	7.3	17	22	6.0	
MCV	96.7	96.1	1.0	0.6	2.3	7	5	2.3	
PLT	72.0	67.9	12.7	5.7	30.4	51	23	25.0	

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IDENTIFY

IDENTIFY CANDIDATE PROC

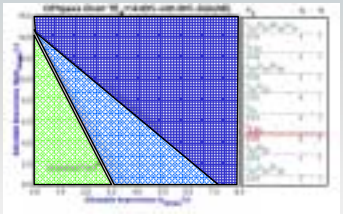
Can QV be done with the TE_a from literature by EZRules 3® if:

- High P_{ed}, low P_{fr}
- QC materials (N) 2/3 per day
- Control runs (R): 1 per day
- CV, bias considered constant in the beginning?

IDENTIFY

IDENTIFY CANDIDATE PROC

Control rule WBC



Charts by EZRules3®
Westgard QC Inc (2005)
Startup procedure
CV: 2.4%
Bias: 2.0%

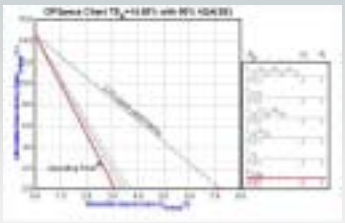
$1_{2.5s}$-rule: at 90% AQA (P_{ed}) the P_{fr} is 3.0%

http://westgard.com/downloads/cat_view/53-worksheets

IDENTIFY

IDENTIFY CANDIDATE PROC

Control rule RBC



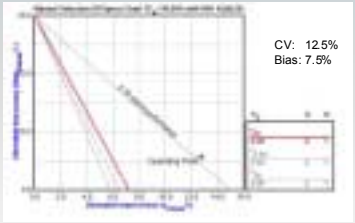
CV: 2.7%
Bias: 2.1%

at 90% AQA, TE_a=6.3%: no control rule applicable
Question: would a TE_a=15% trigger a clinical decision?

IDENTIFY

IDENTIFY CANDIDATE PROC

Control rule PLT



CV: 12.5%
Bias: 7.5%

at 90% & 50% AQA, TE_a=30%: NO stat QC!

IDENTIFY

IDENTIFY CANDIDATE PROC

What can you do in a case like this?

- Apply statistical methods
  - Improve CV, bias
  - Adapt TE_a (own data, clinical decision level)
  - Increase # of N, R
  - Apply multi-rule QC
  - AQA(SE) 50%

AQA(SE) = analytical quality

IDENTIFY

IDENTIFY CANDIDATE PROC

What else can you do?

- Ignore problem
- Consider new analyser
- Use non-statistical P_{ed} strategy
  - PLT estimate - smear
  - PLT clumps

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PREDICT

PREDICT Ped & Pfr

- Solution at 90% AQA ➞ HI P_{ed} strategy
  Example: WBC, Hb
- Solution at 50% AQA ➞ MOD P_{ed} strategy
  Example: RBC
- No solution at 50% AQA ➞ LOW P_{ed} strategy
  Example: PLT_{low}
- P_{fr} (usually <5%: determined by control rule)

PREDICT

P_{ed} & P_{fr}

Simple approach: TQC strategy

Strategy	HI-P_{ed} ☺	MOD-P_{ed} 😐	LO-P_{ed} ☹
Stat QC	++++	++	+
Nonstat QC	+	++	+++
Need for QI	+	++	++++
Costs	+	++	+++

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Define performance goals

DEFINE GOALS

PERFORMANCE GOALS

Control level: LOW, stable conditions

Parameter	CV%	Bias%	calc TE	OPSpec TE	Iit TE_a	©	QC rule	P_{ed} strat.	P_s %
WBC	2.4	2.0	6.0	14.6	14.6	5.04	$1_{2.5s}$	HI	3
RBC	2.4	2.0	6.5	14.5	6.3	5.25	$1_{2.5s}$	MOD	3
Hb	0.6	3.5	4.6	7.0	7.0	7.50	$1_{3.5s}$	HI	<1
Hct	1.9	2.1	7.3	12.0	6.0	5.21	1_{3s}	MOD	<1
MCV	1.0	0.6	2.3	6.1	2.3	5.50	1_{3s}	MOD	<1
PLT	12.7	5.7	30.4	--	25.0	1.65	*	LO	--

*EZRules 3® suggests max. QC rule: $1_{3s}/2_{2s}/R_{4s}/4_{1s}/8_x$ N=4

DEFINE GOALS

CONCLUSIONS

QV can be done in a five-step process with EZRules 3®

- High to medium P_{ed}, low P_{fr}
- Possible to stay within limits (given N, R)
- Few different rules ($1_{2.5s}$ fits most)
- Critical parameters: MOD/LO P_{ed} strategies

DEFINE GOALS

CONCLUSIONS

- Problem with IQC PLT_{low} evident
- Problems with control material?
- TE_a from literature too stringent?
- All results based analyser validated