Define Analytical Quality: A Professional Challenge

Rethinking Quality Control in the Traceability Era

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Overview

Introduction

Desirable Quality

Relative (State-of-the-art) Quality

Quality – Where are we?

Outlook

Introduction

Rethinking Quality Control In the Traceability Era

Define Analytical Quality: A Professional Challenge

Introduction

The central topics to be emphasized

Rethinking Quality Control
In the **Traceability** Era

Define **Analytical Quality:**
A Professional Challenge

Traceability era?

When you want traceability (to reference method values)

Standardize the market

Tin Can Series (ST*T* Consulting)

Consolidation

Traceability era?

When you want traceability assessment

Use commutable samples

Traceability era?

Traceability to which extent?

When you want to talk about quality

Agree on quality specifications

“Traceability Era”?

We are NOT yet there!

What is quality?

Quality

"A degree to which a set of inherent characteristics fulfils requirements" (ISO 9000:2005)

→ "Minimum philosophy"? Who defines requirements? More economic view?

Quality ("the good old days")

"The totality of characteristics of an entity that bear on its ability to satisfy stated and implied needs" (ISO 8402:1994)

→ "Maximum philosophy"? "As good as you can"? "More patient view"?

http://www.clsi.org/Content/NavigationMenu/Resources/HarmonizedTerminologyDatabase/Harmonized_Terminolo.htm

Desirable Quality

Hierarchy of models for desirable numbers

- **Clinical concepts ⇦**
- **Questionnaires to clinicians ⇦**
- **Concepts based on biological variation ⇦**
- **Expert opinion/Regulations**
- **“State-of-the-art”**

Current discussion focuses on those ⇦

#Consensus Statement (Stockholm 1999). Scand J Clin Lab Invest 1999;59:585 (in hierarchical order).

Desirable Quality

Relation of the analytical error (SD_A) to a biological standard deviation (SD_{Biol})

$$SD_A \leq 0.5\ SD_{Biol}$$

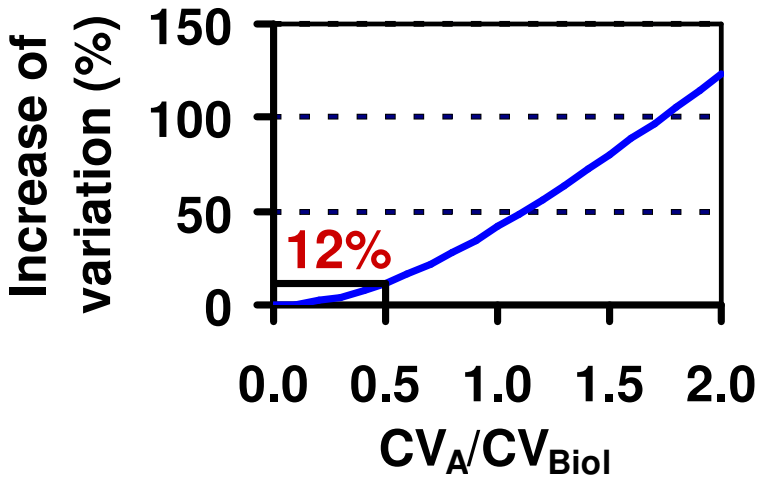
Statistical background (in CV-terms)

$CV_A = 0.5 \cdot CV_{Biol}$

➔CV_A adds only 12% to the total test variability (CV_T)

$CV_T = [(0.5\ CV_{Biol})^2 + CV_{Biol}^2]^{1/2}$

$CV_T = 1.12\ CV_{Biol}$



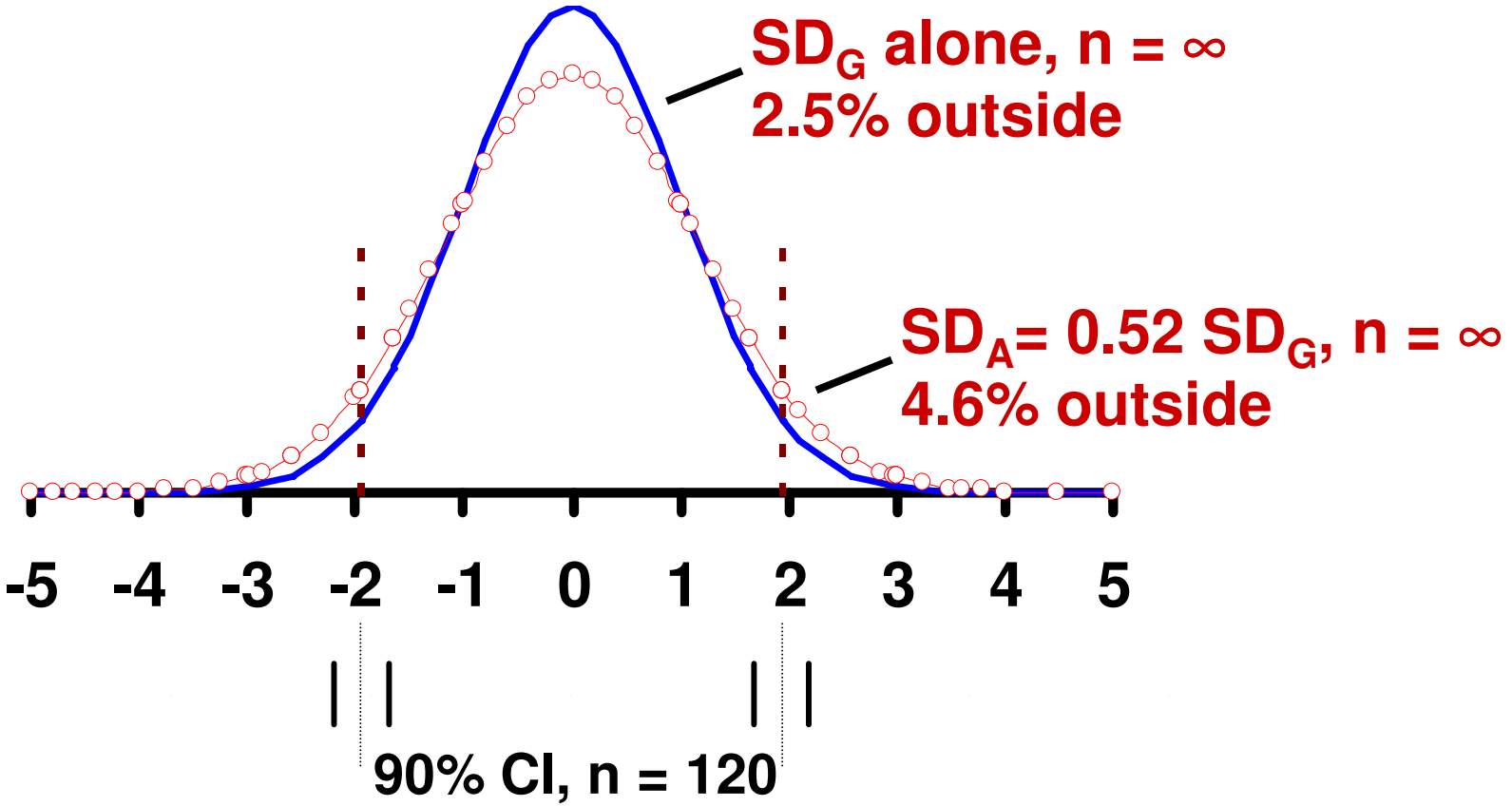
Desirable Quality

Statistical background for reference intervals

Confidence interval n = 120 instead of n = ∞

translated into increase of SD_G by SD_A:

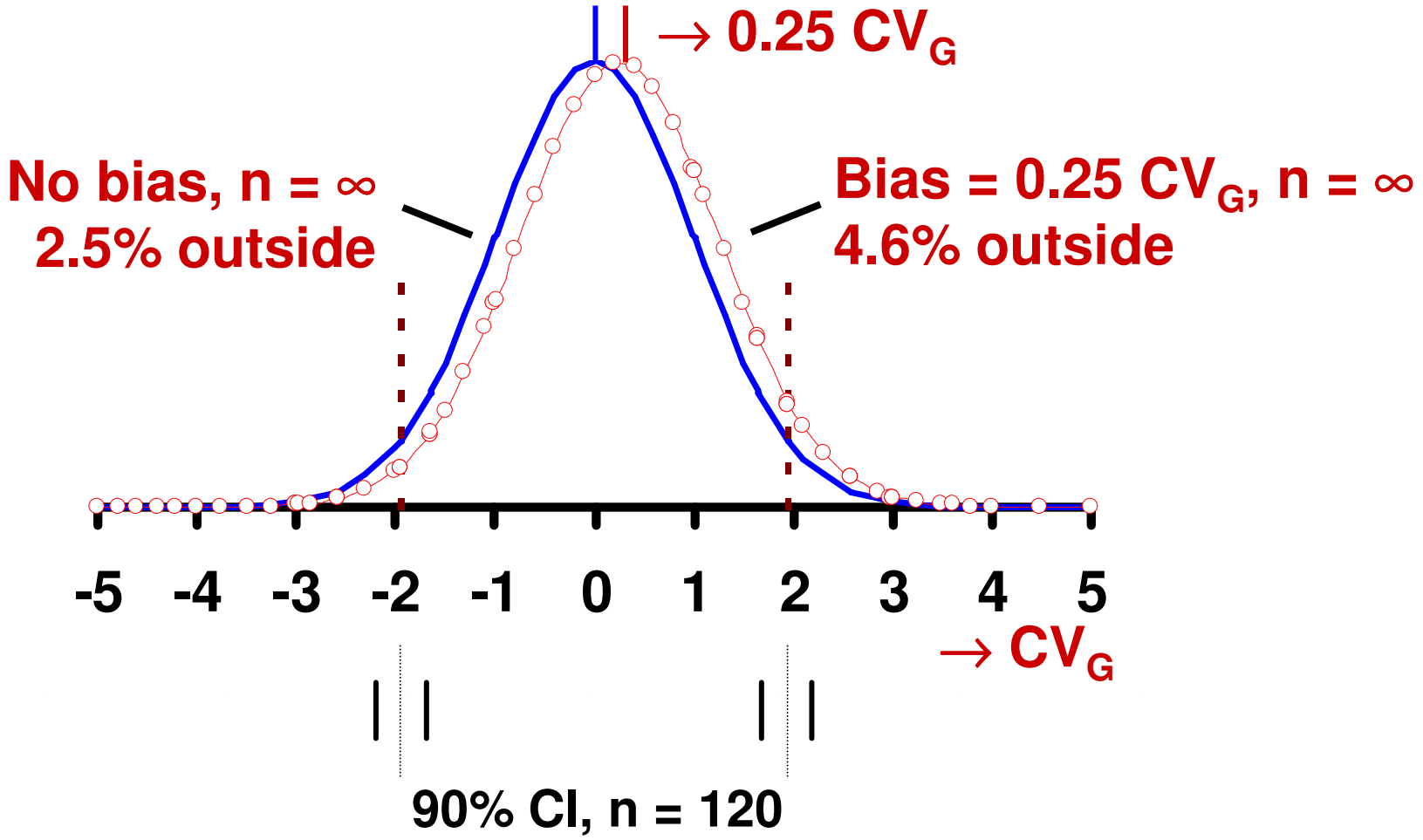
$SD_T = SQRT[SD_G^2 + SD_A^2]$



Desirable Quality

Statistical background of reference intervals

Confidence interval n = 120 translated into bias goal



Desirable Quality

We are fairly "there"

CAVEAT: We lack goals for TE including

- Bias (traceability)/SE
- Sample-related effects (overall matrix)
- Specificity (cross-reactions)
- Common interferences (lipemia, etc.)
- Effects of drugs
- Effects of auto-/heterophilic antibodies
- Effects of genetic variants

➔Define the quality for analysis of the individual sample!

But, do we not focus too much on the aforementioned scientific models?

Relative Quality

Hierarchy of models for desirable numbers

- Clinical concepts
- Questionnaires to clinicians
- Concepts based on biological variation
- Expert opinion/Regulations

- **"State-of-the-art" ⇦**

Focus more on the "lowest level concept", on "relative" quality!

Relative Quality

State-of-the-art versus state-of-the-art

Comparison of imprecision data (instrument generation 2001)

Manufacturer	Clinical chemistry	Immunoassays
Beckman	Synchron LX20	Access
Bayer	---	Advia Centaur
Abbott	Aeroset	Architect
Roche	Modular	Elecsys
Ortho	Vitros 700	Vitros ECi

Relative Quality

Imprecision, Chemistry (instrument generation 2001)

Analyte	Level	total-CV (%) Best	Worst	Analyte	Level	total-CV (%) Best	Worst
Na	120	0.5	1.1	Mg	0.6	3	4
mmol/l#	145	0.7	1.2	mmol/l	0.9	2	4.4
	160	0.8	1.2		2	1	3.5
Cl	85	0.8	1.4	Crea	0.9	1.1	5
mmol/l	100	0.8	1.5	mg/dl	1.5	1	3.6
	120	0.6	1.4		6	1.1	3
Ca	2	1.3	1.8	K	3	1.1	2
mmol/l	2.4	1.2	2	mmol/l	4.5	1	2
	3.4	1.2	2.3		7	0.6	1.3
Prot	4	1.1	2	Gluc	90	1.2	2.2
g/dl	5.5	1	2	mg/dl	150	1.5	2.2
	7	1.1	2.5		300	1.2	2.3
Alb	2.5	0.9	2.3	Chol	100	1.5	1.8
g/dl	3	0.8	2	mg/dl	150	1.6	1.8
	4.5	0.6	1.7		250	0.8	2
#Note: SI Units, except when all used conventional				ALP	100	3	4.5
				U/l	250	1.1	3
					600	2.5	3

Major differences for certain analytes

Relative Quality

Imprecision, Immunoassay (instrument generation 2001)

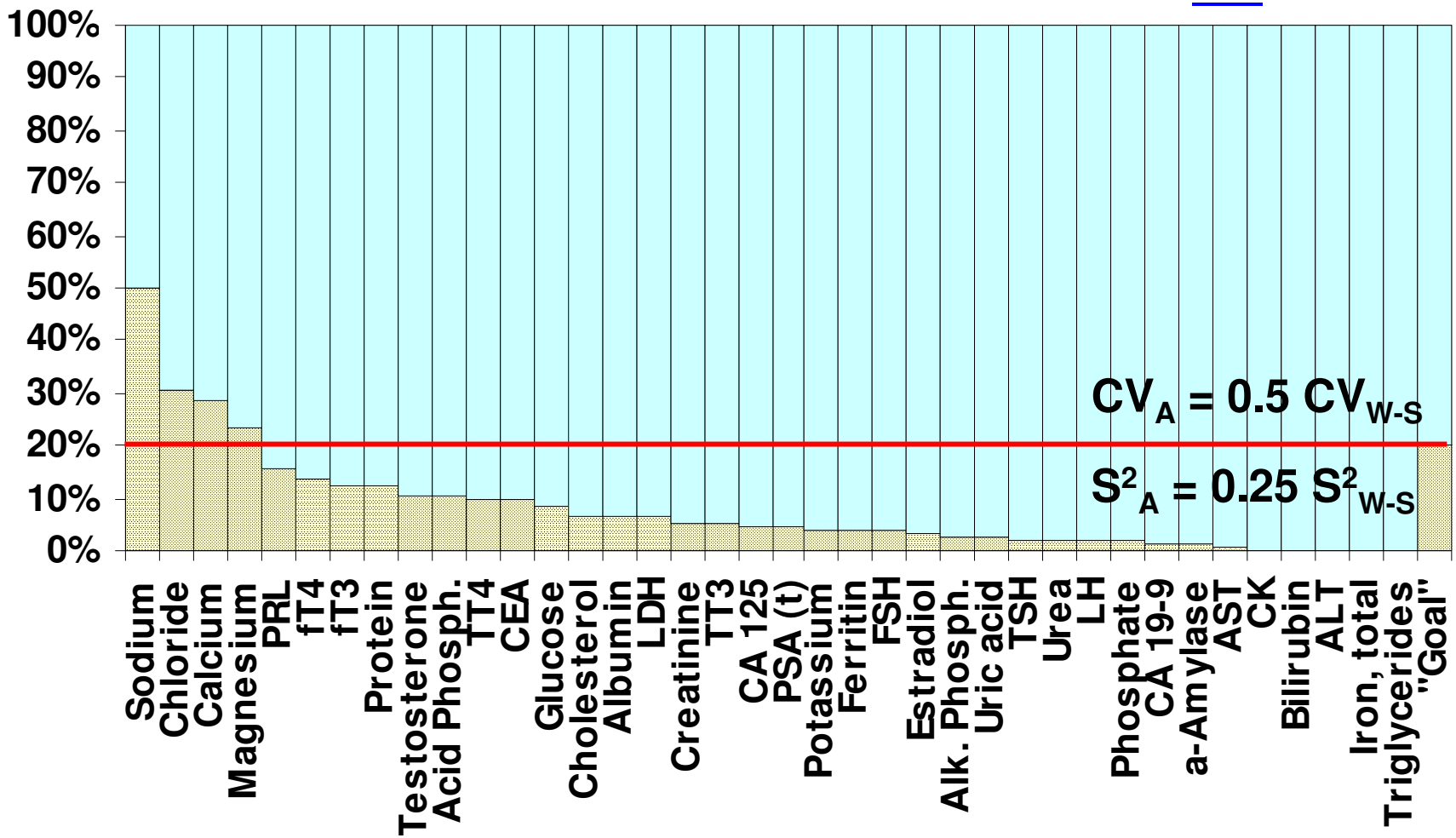
Analyte	Level	total-CV (%) Best	Worst	Analyte	Level	total-CV (%) Best	Worst
TSH	0.1	2	7	Prog	3	6	13
µIU/ml#	5	2	4	nmol/l	40	3	8
	30	3	5		85	3	8
TT4	50	5	7	E2	150	6	20
nmol/l	100	2	6	pmol/l	500	4	8
	200	3	8		2000	3	6
fT4	6	4	10	Testo	2	7	8
pmol/l	15	3	7	nmol/l	15	3	6
	40	4	6		40	3	6
TT3	1	3	8	LH	5	3	9
nmol/l	2	2	5	mIU/ml	50	2	4
	5	2	5		100	2	5
fT3	3	4	15	FSH	5	4	7
pmol/l	10	3	9	mIU/ml	30	2	5
	20	3	8		80	3	6
#Note: SI Units, except when all used conventional				PRL	60	4	8
				mIU/l	400	3	5
					2000	4	6

Major differences for certain analytes

Quality – Where are we?

Variance in % of total variance (analytical & biological)

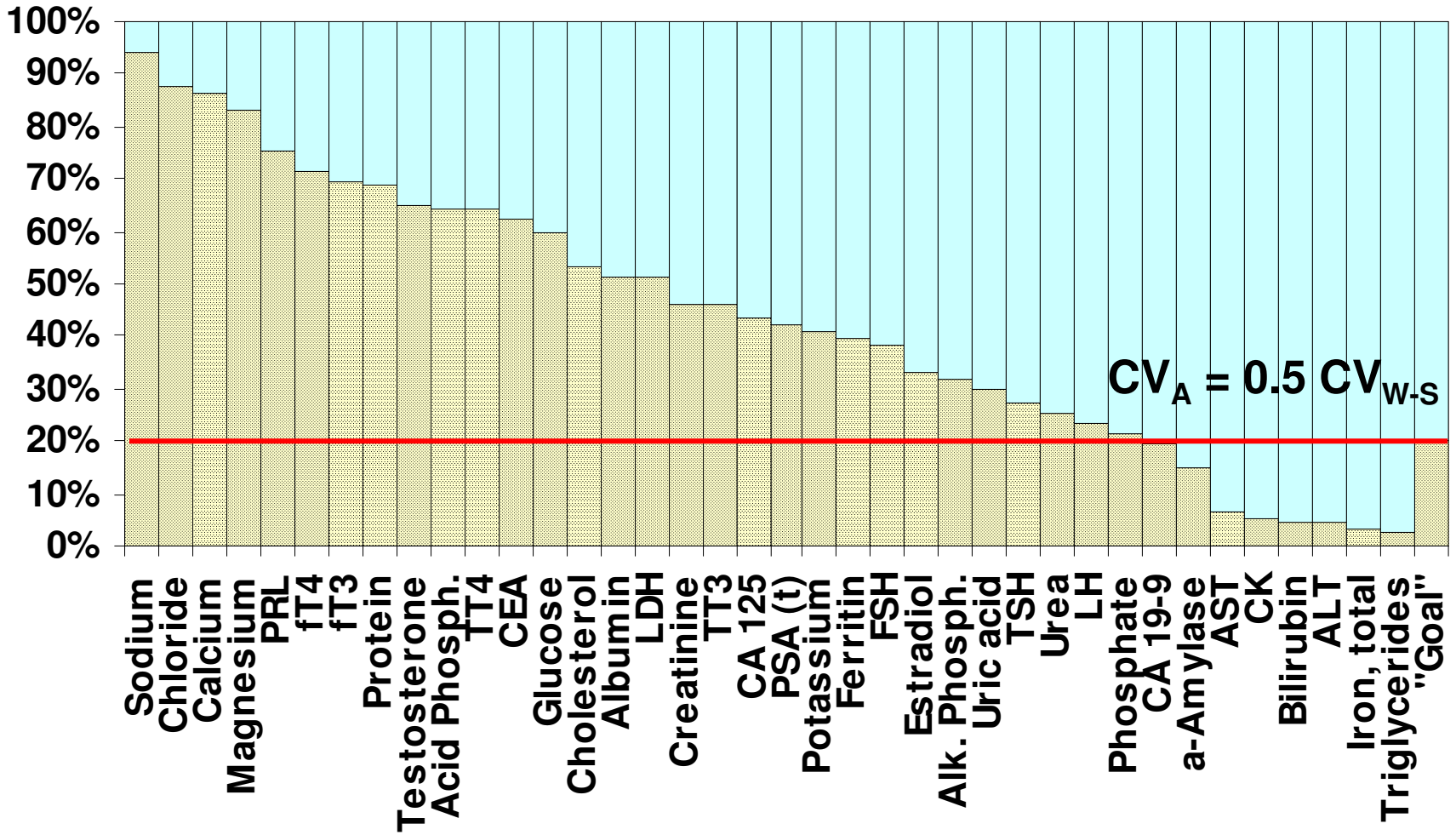
Basis: Best Manufacturer CV_A and $CV_{W\text{-}S}$



Quality – Where are we?

Variance in % of total variance (analytical & biological)

Laboratory uncertainty$ = 4 x best CV_A and CV_{W-S}



$Lab performance, bias, sample-related effects, specificity, effects of drugs …

Quality – Where are we?

The discussion will continue!

Outlook

When you want to enter the traceability era

Take care that ALL elements are in place

Traceability

Only after standardization

Only with native materials

Only with accepted quality specifications

Only with clinical support

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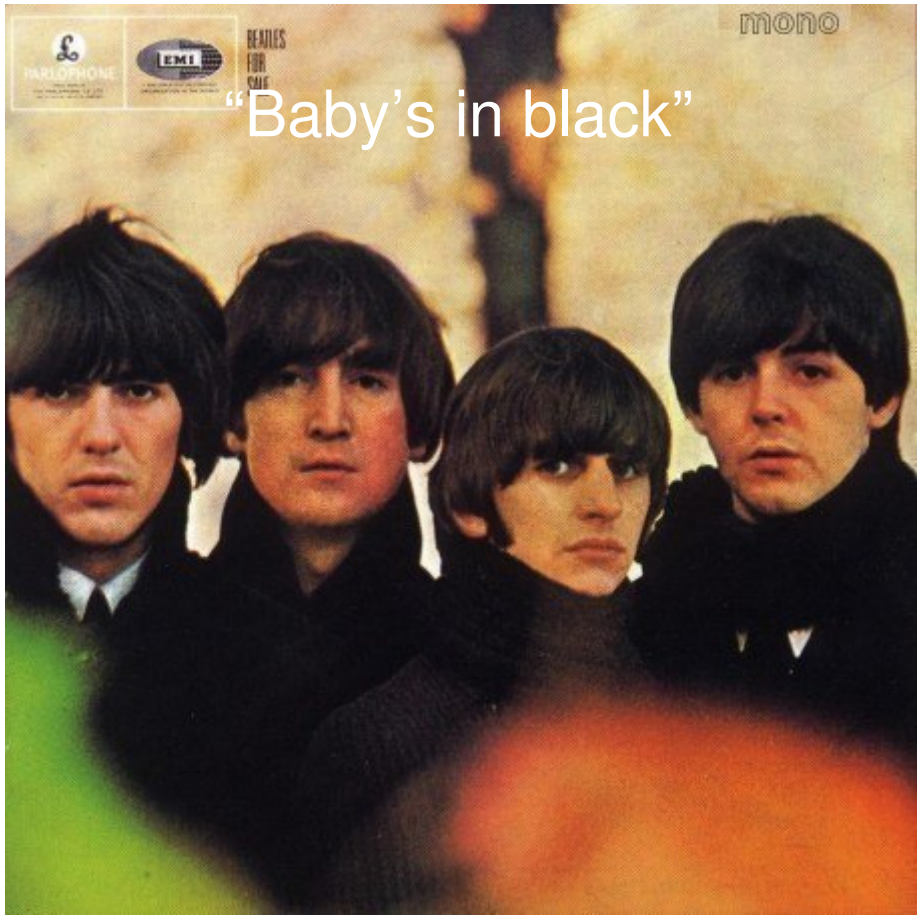
Outlook

Oh, how long will it take?



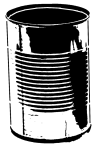
Beware of Snails!

The goal Snail

Tonks DB. A study of the accuracy and precision of clinical chemistry determinations in 170 Canadian laboratories. Clin Chem 1963;9:217-33.

Kenny D, Fraser CG, Hyltoft Petersen P, Kallner A. Strategies to set global quality specifications in laboratory medicine. Stockholm, 24-26 April 1999. Consensus agreement. Scand J Clin Lab Invest 1999;59:585.

Still not fully appreciated



Common Snails

The commutability Snail*

*Also known under the name “matrix-effect” Snail

Charles F. Fasce, Jr., Robert Rej, William H. Copeland, and Raymond E. Vanderlinde. A Discussion of enzyme Reference Materials: applications and specifications. Clin Chem 1973;19:5-9.

Stöckl D, Thienpont LM. The combined-target approach: a way out of the proficiency testing dilemma. Arch Pathol Lab Med 1994;118:775-6.

Many PT surveys use materials not tested for commutability

Common Snails

Another Snail

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

SCIENTIFIC DIVISION

PROJECT PROPOSAL

1. Title of Project:

IFCC–Master Comparisons (IFCC*MC*)

2. Submitted by:

Prof. Dr. LM Thienpont (coordinates on last page)

3a. Aims of project (definition of problem)

To promote quality, metrological traceability, and standardization of in vitro diagnostic measurement procedures.

Relative Quality, try it since 7 years

Summary

Traceability era – We are not yet there

Quality – What about “implied needs”?

Desirable quality – We are fairly there

Relative quality – Much more should be done

Quality – Where are we? The discussion will continue!

Outlook – Oh, how long will it take? Beware of Snails!