Hvordan sette fornuftige kvalitetskrav?

Fagmøte Noklus September 2021

Sverre Sandberg, Noklus

Why do we need

Analytical Performance Specifications (APS)

Six sigma /Quality control rules / total error /Prec/trueness
Meausurement uncertainty/ EQAS / Lot to lot variation
Clinical guidelines

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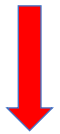
Models for APS

”submodels” to set APS (principles for calculations)



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When you see a ”six sigma plot” do you ever ask:

- ✓What performance specifications are used?
- ✓What are the reasons for using these performance specifications?
- ✓How subjective are they?
- ✓Could we have used completely different performance specifications?
- ✓If based on ”biology” what source, what mathematics are used to calculate ”total errors”?

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Analytical performance specifications Consensus statement

Model 1. Based on the effect of analytical performance on clinical outcomes

1a. Direct outcome studies

1b. Indirect outcome studies

Model 2. Based on components of biological variation of the measurand

Model 3. Based on state of the art

Model 1. Based on the effect of analytical performance on clinical outcomes

This can, in principle, be done using different types of studies:

1a. Direct outcome studies – investigating the impact of analytical performance of the test on clinical outcomes.

1b. Indirect outcome studies – investigating the impact of analytical performance of the test on clinical classifications or decisions and thereby on the probability of patient outcomes, e.g. by simulation or decision analysis.

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The advantage of this approach is that it addresses the influence of analytical performance on clinical outcomes that are relevant to patients and society. The primary disadvantage is that it is only useful for examinations where the links between the test, clinical decision making and clinical outcomes are straightforward and strong.

So Model, type 1 is difficult to perform and will take a lot of ressourses.

However type 1b is not that difficult – but we still have to concentrate on one clinical condition

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Model 1b

Indirect outcome studies

– investigating the impact of analytical performance of the test on

clinical classifications or decisions and thereby on the

probability of patient outcomes, e.g., by

simulation or **decision** analysis*

*to address how to take important decisions in a formal manner.

This approach is usually used in clinical guidelines or when clinicians set performance specifications

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Model 2. Based on components of biological variation of the measurand

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Model 2. Based on components of biological variation of the measurand

This attempts to minimize the ratio of ‘analytical noise’ to the biological signal.

The advantage is that it can be applied to most measurands for which population based or subject-specific biological variation data can be established.

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This approach is usually used in laboratory medicine for setting performance specifications

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Model 3. Based on state-of-the-art

This relates to the highest level of analytical performance technically achievable. Alternatively, it could be defined as the analytical performance achieved by a certain percentage of laboratories.

The advantage of this model is that state-of-the-art performance data are readily available. The disadvantage is that there may be no relationship between what is technically achievable and what is needed to minimize the ratio of ‘analytical noise’ to the biological signal or needed to obtain an improved clinical outcome.

Model Based on	Study/principles	Advantage	Disadvantage
Clinical outcomes			
Biological variation			
State of the art			

Explanatory notes

- It should be noted that the three models use different principles.
- The hierarchy assumes that high quality studies or data are available for each model.
- Proposed analytical performance specifications should therefore always be accompanied by a statement of the rationale, the source and the quality of the evidence behind the recommendation.

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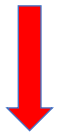
Models for APS

”submodels” to set APS (principles for calculations)



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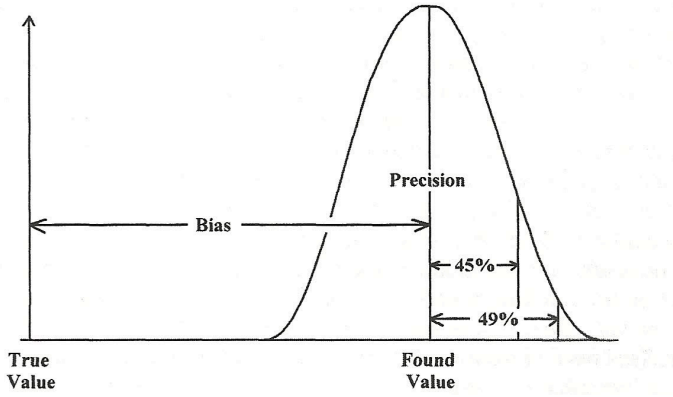
Some common "submodels" / "formulas"

Imprecision

$CV_A < 0.5\ CV_I$

CV_I ~ choose wisely –



Bias

$IBI < 0.25\ [CV_I{}^2 + CV_G{}^2]^{1/2}$

CV_G ~ variable – depends on partition – do we really need?

Total analytical error

$TEa < 1.65 \times 0.5\ CV_I + 0.25\ [CV_I{}^2 + CV_G{}^2]^{1/2}$

With permission from: Callum Fraser

APS for Measurement Uncertainty

DE GRUYTER

Clin Chem Lab Med 2016; aop

Opinion Paper

Ian Farrance*, Tony Badrick and Kenneth A. Sikaris

Uncertainty in measurement and total error – are they so incompatible?

So finally, what performance specifications (quality goals) can supporters of the GUM approach use as a guide to actual or comparative performance? Biological variation may be used for the evaluation of uncertainty derived by GUM procedures.

Or

Imprecision

- $CV_A < 0.5$ (or another factor) x CV_I

Bias – MU means account for or minimize or eliminate bias

- $IBI \sim 0$

Measurement Uncertainty

- $MU < 1.65$ (or another factor) x $0.5\ CV_I$

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Pragmatic model where you add analytical CV to within-subject or between subeject variation

(Oosterhuis et al/ Hoetzel et al – Clin Chem Lab Med 2015)

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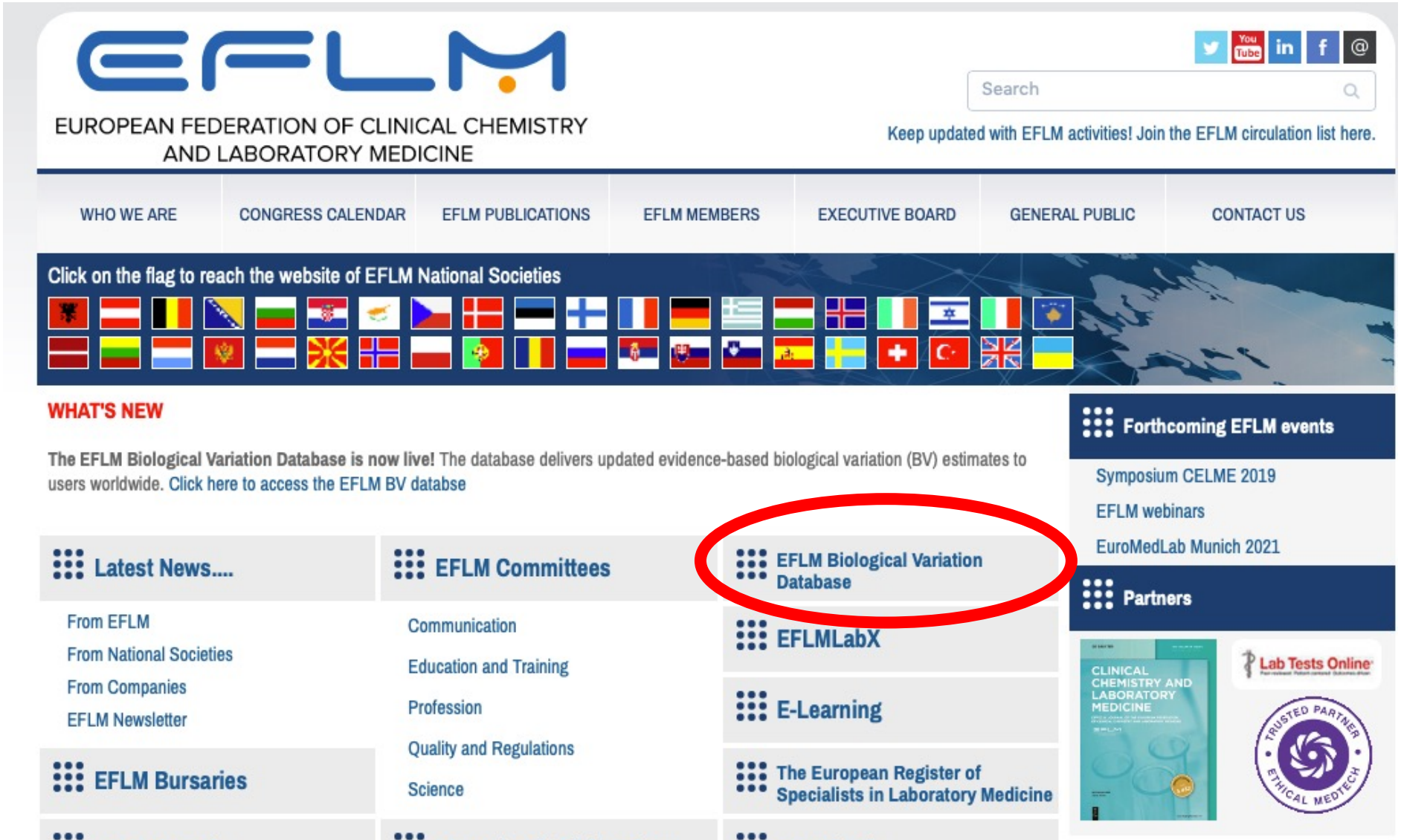
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EFLM Biological Variation Database

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Please note that we are in the process of reviewing and adding BV studies into the database, thus data may be subject to change. It will in the future be possible to sign up for update alerts.

Quick Links

List of BV estimates

Show All Measurands

Referencing the work

If using data from this website for scientific, commercial or other purposes, it should be referenced as:

Aarsand AK, Fernandez-Calle P, Webster C, Coskun A, Gonzales-Lao E, Diaz-Garzon J, Jonker N, Minchinela J, Simon M, Braga F, Perich C, Boned B, Roraas T, Marques-Garcia F, Carobene A, Aslan B, Barlett WA, Sandberg S. The EFLM Biological Variation Database. https://biologicalvariation.eu/ [time of access].

Summary Of Data

Number of Papers Referenced	Number of Biological Variation Records	Number of Analytes with Records
539	2,581	233

Found **Albumin** in database

Meta Analysis

Matrix: Serum/plasma

TYPE	MEDIAN CV ESTIMATE	LOWER CI LIMIT	HIGHER CI LIMIT	LAST UPDATED	TOOLS
Between-subject	4.9	2.2	6.3	2021-07-13 11:31:02 UTC	APS
Within-subject	2.5	2.5	3.2	2021-07-13 11:31:01 UTC	RCV

References

No meta analysis | Reference included in meta calculation | Reference not included in meta calculation

LINK	ESTIMATE OF CVI	ESTIMATE OF CVG	GENDER	STATE OF WELL BEING	MATRIX
Evaluation of biological variation of glycated albumin (GA) and fructosamine in healthy subjects, Montagnana M, Paleari R, Danese E, Salvagno GL, Lippi G, Guidi GC and Mosca A, 2013, Clin Chim Acta, 423, 1-4	2.3	2.9	Mixed	Healthy (excl pregnant)	Plasma

c0008 AU1

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Biological Variation and Analytical Performance Specifications

Sverre Sandberg, Thomas Røraas, and Aasne Karine Aarsand

AU2

s0010 **ABSTRACT**

s0015 **Background**

p0010 There are many sources of variation in numerical results generated by examinations performed in laboratory medicine. Some measurands have biological variations over the span of life and others have predictable cyclical or seasonal variations. Most measurands in an individual display random variation around homeostatic set points and this is termed within-subject biological variation. The homeostatic set points vary

variation are usually generated by prospective studies; series of specimens from a cohort of individuals are examined, followed by statistical analysis to identify and quantify the different types of variation. Furthermore, sources of evidence-based data on biological variation and tools for the appraisal of the quality of biological variation studies is presented. The chapter also provides an overview of what applications biological variation data have in laboratory

New edition of Tietz – 2022, in press

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Conclusions

- Analytical performance specifications are important.
- Three completely different principles
  - Outcome
  - Biological variation
  - State of the art
- Different submodels and mathematic to calculate Analytical Performance specifications

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Thank you!!