The 1999 Stockholm Conference on Quality Specifications in Laboratory Medicine

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The Central Role of Analytical Performance Specifications

Needs for Analytical Performance Specifications

In introduction of an analytical system:

- *detailing the analytical requirements and assessing available systems,*
- *preparing a specification/tender and creating a short list for evaluation, and*
- *objectively assessing the evaluation data generated.*

For EQAS/PT organisers:

- *to set criteria for satisfactory performance.*

For manufacturers:

- *in designing, assessing and marketing systems and reagents.*

For laboratories and patients

- *to undertake objective quality planning, select those methods that need improvement and ensure that APS are met so that patient care is facilitated.*

Setting Analytical Performance Specifications

More than 50 years of effort:

- **1963 David Tonks**
  ALE = 2CV = [1/4 reference interval/mean] x 100% (biological)
- **1968 Roy Barnett**
  "Medically significant CV" – said to be "opinions of clinicians and laboratory specialists" (clinical)
- **1970 Cotlove, Harris and Williams**
  Biological variation - tolerable analytic variability
  CV < 1/2 CVwithin-subject (biological)
- **1976 CAP Aspen Conference (1977)** *(biological)*
- **1983 Review of work to date** - ***Adv Clin Chem 1983;23:299 -339.***

Setting Analytical Performance Specifications

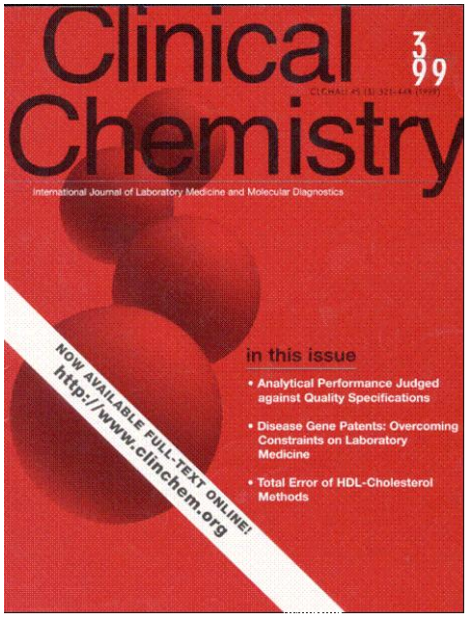
Then, intensive efforts:

- **1988 Odense Group**
  Specifications for acceptable bias (biological)
- **1980s Analysis of clinical situations** *[Nordic countries] (clinical)*
- **1980s Accumulation of data on biological variation** *(biological)*
- **1997 Fraser, Hytoft Petersen, Libeer, Ricos**
  Three levels of quality (biological)
- **1990s EGE-Lab Working Group**
  Biological variation and state of the art (biological and state of the art)

  European EQA Organisers Working Groups *(biological)*

  ISO TC 212/WG3 ISO 15196
  Analytical Performance Goals Based on Medical Needs

Evidence-Based Medicine



Editorial:

Fraser CG, Hyltoft Petersen P.

Analytical performance characteristics should be judged against objective quality specifications.

***Clin Chem* 1999;45:321-3**

The 1999 Stockholm Consensus Conference

ifcc
International Federation of Clinical Chemistry and Laboratory Medicine

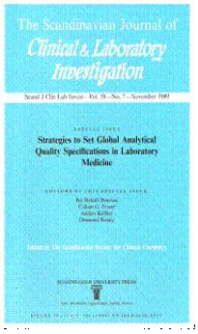
IUPAC
International Union of Pure and Applied Chemistry

Dr Anders Kallner

World Health Organization

The 1999 Stockholm Consensus Conference

- ***sponsored by IFCC, IUPAC, and WHO***
- ***24-26 April, 1999***
- ***more than 100 participants from 27 countries***
- ***22 formal presentations from the opinion leaders in the field***
- ***publication - in Scand J Clin Lab Invest 1999;57:475-585***
- ***Many discussions led by Dr Desmond Kenny, 1941-2006.***



It was said, at his funeral, "Desmond Kenny was a good man and did good work". So he was, and so he did.

The Consensus Hierarchy

1. Evaluation of the effect of analytical performance on clinical outcomes in specific clinical settings

2. Evaluation of the effect of analytical performance on clinical decisions in general:

a. Data based on components of biological variation
b. Data based on analysis of clinicians' opinions

3. Published professional recommendations:

a. From national and international expert bodies
b. From expert local groups or individuals

4. Performance goals set by:

a. Regulatory bodies
b. Organizers of External Quality Assessment (EQA) schemes

5. Goals based on the current state of the art:

a. As demonstrated by data from EQA or Proficiency Testing scheme
b. As found in current publications on methodology.

The Consensus Hierarchy

- *The above hierarchy includes currently available models; however, new useful concepts will undoubtedly evolve. Implementation of any of the models should use well-defined and described procedures.*
- *To facilitate the future debate on the setting of analytical quality specifications, there is a need for agreement on concepts, definitions and terms.*
- *There is a need for continuous improvement in the exchange of information on quality issues: between clinical laboratory professionals and the diagnostics industry, and between clinical laboratory professionals and the users of the laboratory service.*

Success or Failure?

Google scholar

Consensus agreement

D Kenny, CG Fraser, PH Petersen… - … Journal of Clinical & …, 1999 – informahealthcare.com

...

The **Stockholm Consensus Conference** on Quality Specifications in Laboratory Medicine, 25-26 April 1999; Introduction: Strategies to set global quality specifications in laboratory medicine; **...**

Cited by 130 (November 2104)

Success or Failure?

Some EQS organisers have adopted: RCPAQAP

The Allowable Limits of Performance have been set using the Stockholm criteria hierarchy.

www.rcpaqap.com.au/chempath/assessment-of-performance/

SKML Stichting Kwaliteitsbewaking Medische Laboratoriumdiagnostiek

MUSE

The TEa tolerance range… is determined according to the Stockholm Conference criteria, whereby biological variation data take the most important place……

What was not achieved in Stockholm?

There was no discussion about matrix-effects and consequently no specifications for allowable matrix

There was no discussion about measurements on ordinal scale

There was no conclusion about absolute and relative quality:

- **Deviation from a 'true' value**
- **Deviation from the method mean**

There was no agreement on which level of quality should be achieved

There was no agreement on consequences of poor quality

There was no agreement on the relation between clinical/biological specifications and specifications for EQAS and PT

Thanks to Per Hyltoft Petersen

Success?

BIO-RAD Convocations of Experts on Laboratory Quality

Burnett D, Ceriotti F, Cooper G, Parvin C, Plebani M, Westgard J. Collective opinion paper on findings of the 2009 convocation of experts on quality control. Clin Chem Lab Med 2010;48:41–52.

Cooper G, DeJonge N, Ehrmeyer S, Yundt-Pacheco J, Jansen R, Ricós C, et al. Collective opinion paper on findings of the 2010 convocation of experts on laboratory quality. Clin Chem Lab Med 2011;49:793-802.

Adams O, Cooper G, Fraser C, Hubmann M, Jones G, Plebani M, et al. Collective opinion paper on findings of the 2011 convocation of experts on laboratory quality. Clin Chem Lab Med 2012;50:1547-58.

Most experts used hierarchy and most used Level 2a

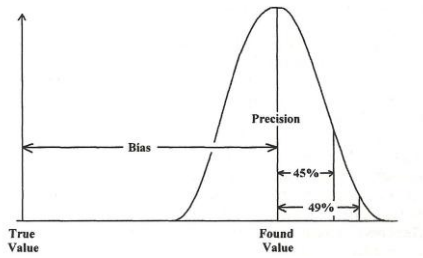
Level 2a – Biological Variation: Logical, Clinically-based and Simple

Imprecision

- $CV_A < 0.5\ CV_I$

Bias

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



Total analytical error

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

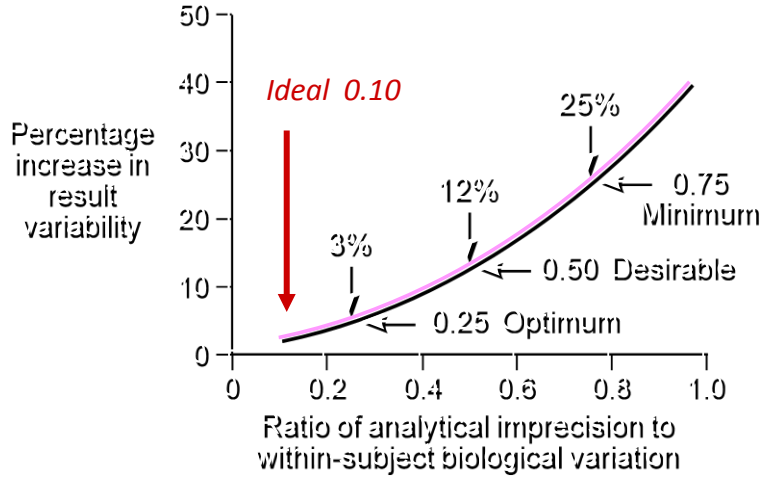
Database on Biological Variation

Westgard QC

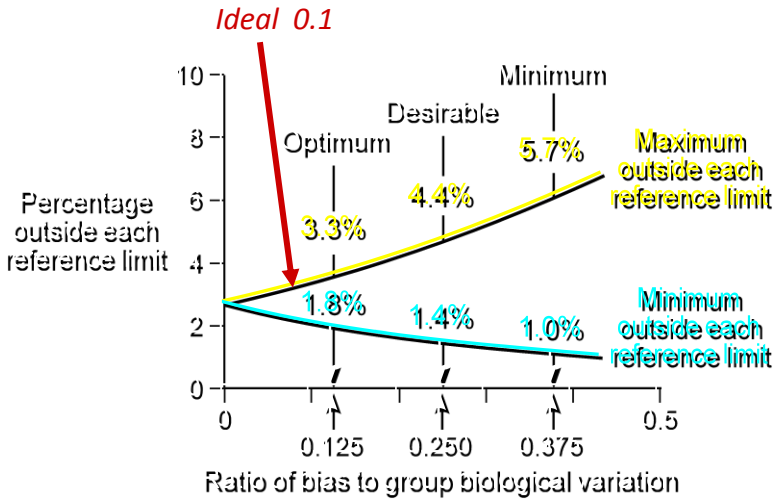
Updated for 2014! Desirable Specifications for imprecision, inaccuracy, and total allowable error, calculated from data on within-subject and between-subject biologic variation. This database is updated and compiled by ***Dr Carmen Ricos and colleagues****. We are honored to be able to host this database*.

http://www.westgard.com/biodatabase1.htm

BV and Test Result Variation



BV and Effect on Reference Values



BUT - Further Developments

Haeckel R, Wosniok W. A new concept to derive permissible limits for analytical imprecision and bias considering diagnostic requirements and technical state-of-the-art. Clin Chem Lab Med 2011;49:623–35.

Simple equations were derived from the relationship between biological variation and the analytical imprecision to calculate permissible imprecision and bias. Five quality classes are proposed for the various analytes reflecting the false-positive error rates (FPR). The new approach combines the theoretical base of biological variation with the technical state-of-the-art.

Haekel R, et al. Clin Chem Lab Med. 2012 25;50:833-9.

Further Developments

Klee GG. Establishment of outcome-related analytic performance goals. Clin Chem 2010;56:714–22.

Six approaches :

(a) limits defined by regulations and external assessment programs,

(b) limits based on biologic variation,

(c) limits based on surveys of clinicians about their needs,

(d) limits based on effects on guideline driven medical decisions,

(e) limits based on analysis of patterns for ordering follow-up clinical tests, and

(f) limits based on formal medical decision models.

Whatever Happened to ISO 15196?

A "Technical Report – Type 2" was produced - 2001-06-18 - but not widely circulated. This did essentially reproduce the 1999 Stockholm consensus hierarchical approach …… BUT

ISO/TC 212 N116 MEETING SUMMARY

Sydney, Australia, 19 and 21 May 2003

One project, ISO 15196 on performance goals, has been cancelled, with the expectation that WG3 will reconsider the need for the project and reaffirm its scope; if deemed appropriate by the TC, a new work item proposal will be circulated for vote.

Conclusions

Much work has been done over the last 50 years on setting analytical performance specifications.

Consensus was achieved at the 1999 Stockholm Conference on Strategies to Set Global Quality Specifications in Laboratory Medicine. The concept has been widely applied, particularly Level 2a, but there are caveats and deficiencies. New models have been developed but are not widely used.

Laboratory medicine has changed marked over the last 15 years. The time is right to re-evaluate the 1999 concept – that is our current goal.