Consensus Statement

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Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine

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The Organisers and the Scientific Programme Committee (SPC) of the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) on 'Defining analytical performance goals 15 years after the Stockholm Conference on Quality Specifications in Laboratory Medicine', held in Milan (IT) on November 24–25, 2014, are pleased to report on the success of the Conference.

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The primary aim was to revisit the 'Consensus Agreement' from the Stockholm Conference investigating to what extent the advocated hierarchy is still valid or if it should be changed. A revision of the original hierarchy established by the Stockholm Conference was presented to the meeting with opportunity for discussion and feedback by conference participants. This revision further underwent modification and explanatory additions by the SPC in an attempt to simplify the hierarchy and improve its application by various stakeholders.

Consensus statement

Analytical performance specifications

In this revision, the hierarchy is simplified and represented by three different models to set analytical performance specifications. There is general agreement that some of these are better suited for certain measurands than for others.

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

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

1. Direct outcome studies – investigating the impact of analytical performance of the test on clinical outcomes;
2. 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.

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. Furthermore, analytical specifications derived in direct or indirect outcome studies will often be influenced by the current measurement quality and results may vary according to the actual test method used, the investigated population and healthcare settings.

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. There are limitations to this approach, including the need to carefully assess the relevance and validity of the biological variation data, e.g., the presence of 'steady state', the appropriate time intervals, effect of inter-current illness and effect of measurand concentrations.

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. If the best laboratories can only achieve a certain quality and better quality is needed (according to models 1 or 2), then improvements are required in the technology. If most laboratories can achieve a certain quality, then laboratories not meeting this level may need to change their practice.

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.

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.

Some models will be better suited for certain measurands than for others. It is therefore recommended that a list be made allocating measurands to different models. Preference should be given to models 1 and 2. In some situations, it can be advantageous to combine the different models.

Some measurands could have different performance specifications defined when the test has multiple intended clinical applications. For example, performance specifications could be defined for blood glucose in a critical care setting by simulation of the impact of the test on probable patient outcomes (model 1b), for self-monitoring of blood glucose in type 1 diabetes by clinical outcome studies (model 1a) or by a more general approach based on biological variation (model 2).

The application of the analytical performance specification can be modulated depending on its use. For example, users can be reference material providers, in vitro diagnostics manufacturers who produce calibrators, organizations who distribute materials for external quality assessment or individual laboratories who provide patient results.

Models for setting performance specifications of examinations using ordinal and ratio scales should follow one of the three models outlined above.

Performance specifications for pre- and post-analytical phases

It is acknowledged that, for patient care, optimizing the quality of the total (pre-analytical/analytical/post-analytical) examination process is the ultimate goal and therefore it would be desirable to go beyond setting analytical performance specifications and to establish examination performance specifications. In principle, the performance specifications for the pre- and post-analytical laboratory processes should follow the same models as for analytical performance specifications. When components of these additional phases can be expressed in numerical terms, they should be added in defining examination performance specifications. In other situations, pre- and post-analytical performance specifications will be best represented by separate quality indicators that should reflect models 1 and 3 listed above.

The SPC of the 1st EFLM Strategic Conference proposes a simplified hierarchy with three models for defining analytical performance specifications. The SPC encourages users to expand those specifications to the total examination process. It is desirable that analytical performance is defined by the highest possible hierarchical model. This approach acknowledges that the intended use of the test, the actual purpose of using the analytical performance

specification by various stakeholders and the quality of the available evidence behind each model may modulate the selection of the best approach.

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