codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 6 **CX/MAS 01/7**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING
Twenty-Third Session
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HARMONIZATION OF ANALYTICAL TERMINOLOGY IN ACCORDANCE WITH INTERNATIONAL STANDARDS: "MEASUREMENT LIMITS"[1]

At the twenty-second session of the Codex Committee of Methods of Analysis and Sampling, the United States, Finland, France and Spain were requested to supply a document discussing the need for the attributes of Limit of Determination and Limits of Detection. A previous document supplying a vocabulary of terms for methods of analysis discussed this matter and concluded that for enforcement of CODEX specification these attributes were unnecessary. We have reconsidered this matter and again conclude that although these properties may be valuable for the selection of methods of analysis to ensure that the method is "fit for the purpose," once the method is selected, these attributes are no longer necessary as adjuncts to providing a decision as to whether or not a lot of food complies with a Codex Specification. As stated in the Procedural Manual (10th edition, 1997**, p.58),** "All proposed methods of analysis must have direct pertinence to the Codex Standard to which they are directed."

The primary properties of an analytical chemical method with direct pertinence to compliance with Codex Standards are accuracy (how close are the method's estimates to the true concentration), precision (how closely clustered are the method's estimates), and selectivity (avoiding response from other entities). These properties are principally a function of concentration and secondarily a function of the instruments, reagents, operations, and various other aspects of the method protocol. Not routinely determined in inter-laboratory (collaborative) method performance studies are two elusive properties: (a) the limit of detection and (b) the limit of determination. To avoid disputed decisions, methods must operate well above these limiting values.

Good reasons exist for NOT routinely determining these two limits:

1. The definitions of the limit of detection and limit of determination are subject to varying interpretations.
2. Rigorous estimates are tedious and expensive to obtain and the mathematics can confuse the chemist.
3. These criteria are by definition located at low concentration levels, where replication in the same laboratory, by the same analyst, and in the same series can lead to DRASTICALLY different answers. Pinning down values for the limits under such conditions may require so many INDEPENDENT estimates that the costs would be prohibitive.
4. For regulatory agencies, often the key question is "What is the largest true concentration consistent with a FOUND VALUE (ESTIMATE) of zero concentration?" This "largest true concentration" is <u>not</u> the limit of detection <u>nor</u> is it the limit of determination. Rather, it is a quantity best determined on the spot, for the particular analyte of interest in the matrix of interest, by the preparation of multiple matrices with <u>known</u> low concentrations, including zero concentration. These blanks serve to estimate the false positive rate.

[1] Prepared by the United States in collaboration with other countries

5. Limits of detection and determination serve as a warning to keep away from certain concentration regions where concentration estimates will be highly variable. A rough statement as to the region of validity would often be just as useful as a more rigorous explicit statement of the values for the limit of detection and limit of determination.
6. If the reported concentration estimates were bracketed by appropriate confidence (uncertainty) intervals, then for most purposes you would not need to know the values for the limit of detection and the limit of determination. The confidence intervals would automatically address the concerns about the reliability of the estimates by not bracketing zero.

Therefore, tabulating the limit of detection and the limit of determination would needlessly complicate the compilation of method performance characteristics for most cases. A more tractable secondary "statistical" parameter to report would be "the lowest concentration for which collaborative results were satisfactory." This value should mean in practical terms the true verified (validated) limit of determination or limit of applicability of the method. It is suggested that CCMAS consider adopting the term "Lowest Validated Level (LVL)" for this value, which would be defined as "the lowest validated level established in collaborative studies." Since the term "Lowest Validated Level" is familiar to the European Committee for Standardization (CEN Report CR 13505), adopting this term for Codex purposes might help avoid any misunderstanding.

It may also be expected that an individual laboratory claims that it can achieve reliable results at levels which are lower than the estimated LVL. In that case it is the responsibility of that laboratory to present analytical data supporting such a claim.