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A New Look at the Limits of Detection (L_D), Quantification (L_Q) and Power of Definition (PD)

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Summary: The relationship between the concentration of the analyte and the imprecision of an analytical method can be displayed by the precision profile in which the coefficient of variation (relative standard deviation) is plotted against the concentration of the analyte. The function of the curve of the profile and its confidence limits can easily be assessed by a computer program developed by *W. A. Sadler & M. H. Smith* (Clin. Chem. *36* (1990), 1346–1350). For the assessment of limits of detection and of quantification the following procedure is proposed:

The lower (and upper) limit of the measuring interval is defined by the point at which an acceptable CV-line intersects the confidence limit. If, in the variance function one sets the concentration to zero, the normal distribution of the random errors of the blank will result. The mean of the next adjacent normal distribution, following the variance formula and overlapping the "zero-distribution" by a defined amount, represents the limit of detection. Within the described measuring interval, or within a fraction of it, one might construct overlapping normal distributions in an analogous manner. Their number represents the "power of definition" (PD) (instead of the "analytical sensitivity"), which also depends on the concentration of the determinand according to the variance function.

We tested these hypotheses by a comparison of two methods for the determination of cyclosporin A (ciclosporin, INN). Our results demonstrate that the data of the lower limits of the measuring interval and of the limit of detection agree well with data from the literature obtained in extensive interlaboratory surveys.

Introduction

The three most important characteristics of the efficiency of analytical methods, particularly in the field of instrumental chemical analysis, are[1]):

(i) limit of detection (L_D),

(ii) lower (and upper) limit of the quantification interval (LL_Q and UL_Q respectively), and

(iii) its "analytical sensitivity".

Instead of this ambiguous expression, we prefer the term "power of definition" (PD), characterizing the smallest difference of analyte concentration (or signal-difference) which can be discriminated with a defined statistical confidence.

Today, the definitions of limits for "... qualitative detection and quantitative determination ..." given by *Currie* (1) are widely accepted. The statistics of detection and determination deal specifically with the observed signal and its associated random fluctuations, in other words with the analytical imprecision, which *Currie* assumes to be constant (homoscedastic).

It is a common occurrence in many analytical assays that the distribution of random errors varies with the

[1]) List of abbreviations used:
L_D = Limit of detection
L_C = Critical limit
LL_Q = Lower limit of quantification interval
UL_Q = Upper limit of quantification interval
PD = Power of definition