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METHODOLOGIES FOR THE PRACTICAL DETERMINATION AND USE OF METHOD DETECTION LIMITS

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Method detection limits have often been misunderstood and misused. The basic definitions developed by Lloyd Currie and others have been combined with assumptions that are inappropriate for many types of radiochemical analyses. A practical way for determining detection limits based on Currie's basic definition is presented that removes the reliance on assumptions and that accounts for the total measurement uncertainty. Examples of proper and improper use of detection limits are also presented, including detection limits reported by commercial software for gamma spectroscopy and neutron activation analyses.

The concept of method detection limits (MDLs) [also known as minimum detection level (MDL), minimum detectable activity (MDA), and lower limit of detection (LLD)] has long been established. As early as 1968, Lloyd Currie[1] helped to bring a standard definition to the detection limit concept and to develop a consistent statistical approach to the determination of limits for qualitative detection and quantitative determination. Currie gave the symbol L_d to the detection limit, which is defined as the smallest quantity of radioactive material that can be detected (distinguished from background) with some specified degree of confidence. The detection limit is useful in comparing different method's measurement capabilities and ability to show compliance with regulatory limits.

Currie also developed an associated concept, the critical level (L_c) (also know as decision level), which is defined as the net counts that must be exceeded before there is a specific degree of confidence that the sample contains radioactive material (above background). These two concepts are graphically depicted in Figure 1 in relation to the measurement uncertainties as defined below:

$$L_c = k_\alpha \sigma_0 \tag{1}$$

and

$$L_d = k_\alpha \sigma_0 + k_\beta \sigma_d \tag{2}$$

where:

k_α & k_β = the abscissas of the standardized normal distribution for the corresponding probabilities

σ_0 = the standard deviation of the net measurement result when the sample contains zero radioactivity, and

σ_d = the standard deviation of the net measurement result when sample contains radioactivity at the level of the L_d.

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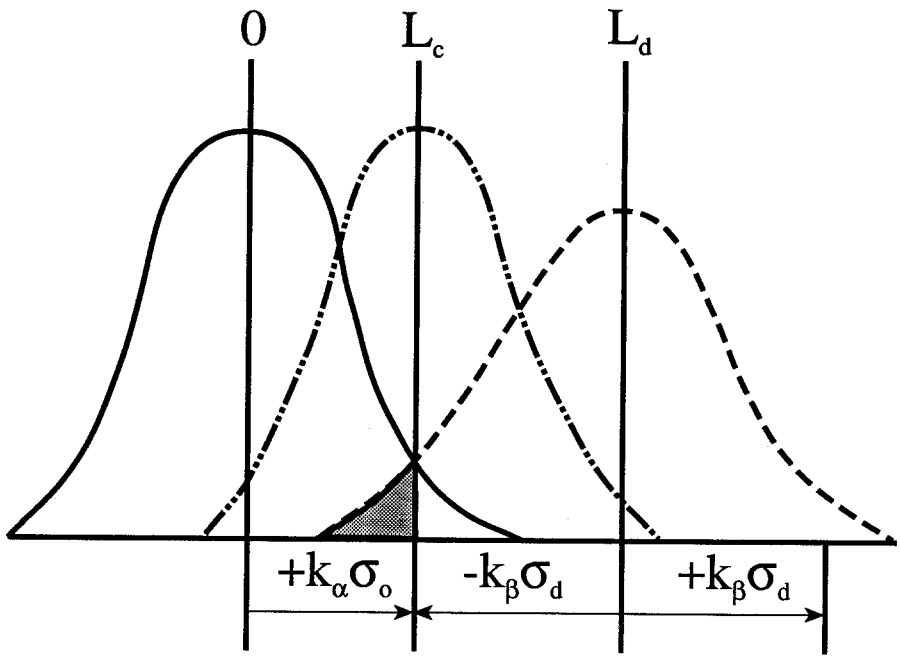

Figure 1. Detection Limit and Critical Level

Many others[2,3] have elaborated on Currie's definitive work, and today his concepts are generally regarded as the standard approach. However, practical application of Currie's concepts to radiochemical analyses have taken many different paths and have been combined with various assumptions, resulting in confusion on the part of many as to their calculation and use. These assumptions have generally been made in order to simplify the application of these concepts to practical measurements, and they generally relate to the determination of the standard deviation of the measurements. The typical use of the Currie equations has generally included only the counting uncertainty in the standard deviation of the measurement, since it is easily estimated (by taking the square root of the background counts). However, the counting uncertainty may be only a portion of the total random uncertainty for many radiological analyses that involve sample preparation and chemical separation steps.

Currie[4] and others[5] have attempted to include other uncertainties, particularly systematic errors (such as calibration uncertainties), in the calculation. However, systematic errors contribute to bias rather than to enlarging the standard deviation of a process. Therefore, systematic errors have little effect on the detection decision.

Overly optimistic estimates of detection limits can lead to unrealistic and nonconservative decisions about a method's capabilities and the confidence of detection. A straightforward approach is presented here that includes all random uncertainties and experimentally determines the standard deviations in order to avoid making assumptions about them.

Experimental

Currie's definition of detection limit has frequently been represented by the following formula:

$$L_d = 2.71 + 4.65\sigma_b \quad (3)$$

where σ_b is the standard deviation of the background (usually estimated by the square root of the background counts). This gives L_d in terms of counts that would need to be converted to activity and/or concentration units by division by such factors as efficiency, counting time, and sample size. For simplicity, the formulas in this paper will be left in terms of counts. This form of Currie's equation is obtained from equation 1 by making a number of assumptions, as shown in the development of Equations (4) through (6) as follows:

if $\sigma_0 = \sigma_d$

and if $k_\alpha = k_\beta = k_{.05} = 1.65$
(for 95% confidence level)

then

$$L_d = 2k\sigma_0 = 3.3\sigma_0 \quad (4)$$

However, the assumption that $\sigma_0 = \sigma_d$ is not a good assumption, especially at very small background count rates. Currie has shown that a correction for the difference can be made by adding a k^2 term as follows:

$$L_d = k^2 + 2k\sigma_0 = 2.71 + 3.3\sigma_0 \quad (5)$$

If the net counts are obtained by subtraction of a well-known background (insignificant uncertainty), then it is assumed that σ_0 equals the standard deviation of the gross sample measurement result. However, if the net counts are obtained by paired observation of the sample and background, then it is assumed that $\sigma_0 = \sqrt{2}\sigma_b$ and

$$L_d = k^2 + 2k\sqrt{2}\sigma_b = 2.71 + 4.65\sigma_b \quad (6)$$

This is the form of the L_d equation that has typically been referenced in most procedure manuals and regulatory guidance documents. In addition, most users have determined σ_b by taking the square root of the gross background counts. Lochamy[3] has shown this formula can be modified to use count rate rather than total counts. Further modification can be made by including efficiency, sample size, recovery, and other unit conversion factors, which has led to other names being used for L_d such as minimum detectable concentration.

As discussed earlier, the typical use of the equations has generally included only the counting uncertainty in the standard deviation of the measurement. However, the counting uncertainty may be only a portion of the total random uncertainty for many radiological analyses. Therefore, it is proposed that the best way to obtain an estimate of σ_0 is to analyze a number of blanks and determine their standard deviation, s_0. If this estimate of σ_0 is to be used, then a t factor from the "Student's t Table" should be used in place of the k factor in the

L_d equation. Substituting s_0 for σ_0 and t for k in equation (5) gives:

$$L_d = t^2 + 2ts_0 \tag{7}$$

where:

s_0 = the standard deviation of a number of net blank results, and
t = the student's t factor for the number of blank samples used to determine s_0 and the desired confidence level.

This equation is applicable regardless of whether the net blank result was determined using a well-known background or using paired observations because the background deviation is included in the net blank result. Furthermore, detection limits determined in this manner include all of the random uncertainty of the analysis, not just the counting uncertainty. The standard deviation can be easily calculated on some regular basis, such as from the previous quarter's laboratory blanks, and used to determine the L_d *a priori.*

Results

From Currie's definition of L_d, it should be obvious that its application should be *a priori* (i.e., used to state something about a measurement process's capabilities before the measurement is made). The detection limit is useful in comparing different methods' measurement capabilities and ability to show compliance with regulatory limits. The calculation of the detection limit from a number of laboratory blanks fits well with this use.

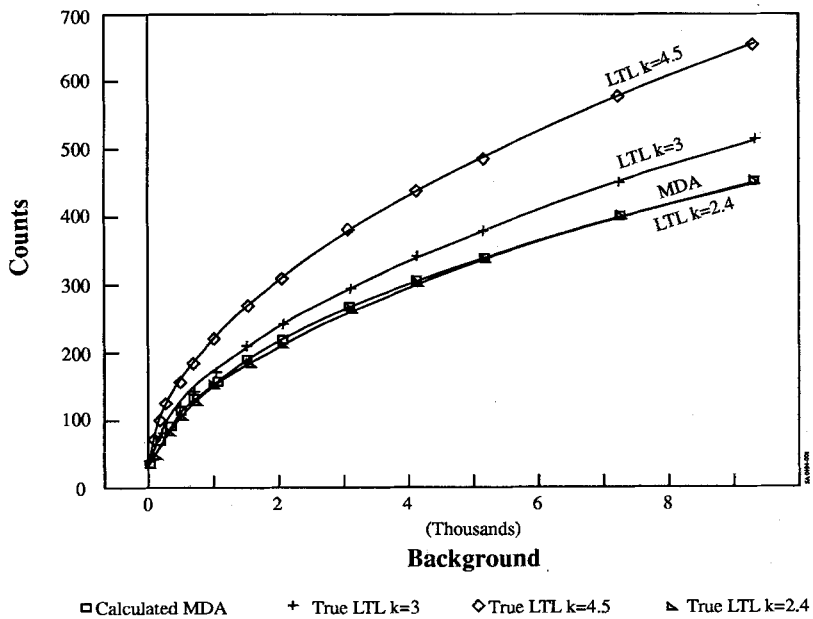

Figure 2. Comparison of Software Calculated MDA and True Maximum Less-Than Level

In determining the detection limit *a priori*, the capabilities of the measurement process are determined for a given set of nominal experimental conditions and, in particular, a certain background count rate. The estimation of the detection limit for a specific type of sample may require that a blank of that matrix type be used to calculate the standard deviation. However, the detection limit should not be calculated for each sample measurement. This practice has been traditionally performed so that it can be reported to the client or recorded in a data base in lieu of a measured activity as a less-than value. The inappropriateness of this type of application of the detection limit has been discussed by other authors.[6]

Measurements below the detection limit may still be statistically meaningful, and all actual measurement results should be used when computing sums and averages of data with the uncertainties propagated appropriately. This has been difficult to do in the past for gamma spectroscopy and neutron activation measurements. This is because the commercial software developed for gamma spectra data reduction did not allow a determination of net peak area when no peak was detected by the peak search algorithm, but did allow a calculation of the detection limit. However, most commercial gamma spectroscopy software currently available for purchase does allow a net peak area to be determined for selected target radionuclides.

When the detection limit is reported as a "less than" value (a value which represents an upper limit to the true value within a specified level of confidence), the upper confidence limit is overestimated in most cases. However, an example is shown in Figure 2 where the MDA reported by a ND 6620 gamma spectroscopy system results in an underestimate of the actual upper limit for the 95% confidence less-than value when the selected sensitivity parameter (which controls the peak size threshold for reporting) is set to values above 2.5. This is because the software calculated MDA does not take into consideration this threshold.

On the other hand, L_c is an *a posteriori* concept and may be used to determine when a specific level of confidence has been obtained that a sample contains radioactive material above background. It should be recognized that results below the critical level do not provide confidence that there is no radioactive material above the background; rather, results above the critical level provide confidence that radioactive material is present above background.

If "background" is interpreted to mean "detector background," then σ_0 can be estimated by taking the square root of the background counts. This may be appropriate for gamma spectroscopy measurements where there is minimal sample processing and the counting uncertainty accounts for most of the random uncertainty. However, for measurements involving chemical separations and other sample manipulations, the background to be differentiated from may be better represented by the reagent blank or matrix blanks. However, the counting uncertainty portion of the total random uncertainty may vary from sample to sample due to background variations from matrix and isotopic interferences. This is particularly true for gamma spectroscopy measurements, where other radioisotope gamma emission add to the Compton background under a peak. Therefore, it is recommended that the standard deviation used to calculate L_c be separated into two components: one from counting uncertainty (including sample specific Compton background), and the other from random uncertainties determined from routine blanks. L_c would then be represented by:

$$L_c = \sqrt{k^2 Ct_b + t^2 s_b^2} \tag{8}$$

where:

Ct_b = the background counts

s_b = the standard deviation estimated from a number of blanks after factoring out the counting uncertainty.

In this way, L_c has both *a priori* and *a posteriori* components.

Discussion

Since overly optimistic estimates of detection limits and critical levels can lead to unrealistic and nonconservative decisions about a method's capabilities and the confidence of detection, it is recommended that standard deviations of blank populations used to calculate these levels be estimated experimentally in order to include all random uncertainties. The resulting *a priori* detection limit should not be calculated for each sample measurement nor reported to the client or recorded in a data base in lieu of a measured activity as a less-than value since measurements below the detection limit may still be statistically meaningful. All actual measurement results should be used when computing sums and averages of data with the uncertainties propagated appropriately.

The critical level should be used for decisions about confidence of detection and may be estimated from the detector background counts for direct counting measurements that require no chemical processing (such as may be the case with many gamma spectroscopy measurements). However, for other types of measurements it is recommended that the standard deviation used to calculate L_c be separated into two components: one from counting uncertainty, and the other from random uncertainties determined from routine blanks. These can then be propagated to obtain an L_c that has both *a priori* and *a posteriori* components.

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