

20 DETECTION AND QUANTIFICATION CAPABILITIES

20.1 Overview

This chapter discusses issues related to analyte detection and quantification capabilities. The topics addressed include methods for deciding whether an analyte is present in a sample as well as measures of the detection and quantification capabilities of a measurement process.

Environmental radioactivity measurements may involve material containing very small amounts of the radionuclide of interest. Measurement uncertainty often makes it difficult to distinguish such small amounts from zero. So, an important performance characteristic of an analytical measurement process is its *detection capability*, which is usually expressed as the smallest concentration of analyte that can be reliably distinguished from zero. Effective project planning requires knowledge of the detection capabilities of the analytical procedures that will be or could be used. This chapter explains the performance measure, called the *minimum detectable concentration* (MDC), or the *minimum detectable amount* (MDA), that is used to describe radio-analytical detection capabilities, as well as some proper and improper uses for it. The chapter also gives laboratory personnel methods for calculating the minimum detectable concentration.

Project planners may also need to know the *quantification capability* of an analytical procedure, or its capability for precise measurement. The quantification capability is expressed as the smallest concentration of analyte that can be measured with a specified relative standard deviation. This chapter explains a performance measure called the *minimum quantifiable concentration* (MQC), which may be used to describe quantification capabilities. (See Chapter 3 and Appendix C for explanations of the role of the minimum detectable concentration and minimum quantifiable concentration in the development of measurement quality objectives.)

Section 20.2 presents the concepts and definitions used throughout the chapter. The major recommendations of the chapter are listed in Section 20.3. Section 20.4 presents the mathematical details of calculating critical values, minimum detectable values, and minimum quantifiable values. Attachment 20A describes issues related to analyte detection decisions in low-background radiation counting and how the issues may be dealt with mathematically.

20.2 Concepts and Definitions

20.2.1 Analyte Detection Decisions

An obvious question to be answered following the analysis of a laboratory sample is: "Does the sample contain a positive amount of the analyte?" Uncertainty in the measured value

Contents	
20.1	Overview 20-1
20.2	Concepts and Definitions 20-1
20.3	Recommendations 20-11
20.4	Calculation of Detection and Quantification Limits 20-12
20.5	References 20-33
Attachment 20A: Low-Background Detection Issues 20-37	

often makes the question difficult to answer. There are different methods for making a *detection decision*, but the methods most often used in radiochemistry involve the principles of statistical hypothesis testing.

To “detect” the analyte in a laboratory sample means to decide on the basis of the measurement data that the analyte is present. The detection decision involves a choice between two hypotheses about the sample. The first hypothesis is the “null hypothesis” H_0 : The sample is analyte-free. The second hypothesis is the “alternative hypothesis” H_1 : The sample is not analyte-free. The null hypothesis is presumed to be true unless there is sufficient statistical evidence to the contrary. If the evidence is strong enough, the null hypothesis is rejected in favor of the alternative hypothesis. (See Attachment 3B of Chapter 3 for an introduction to these concepts.)

The methods of statistical hypothesis testing do not guarantee correct decisions. In any hypothesis test there are two possible types of decision errors. An error of the first type, or Type I error, occurs if one rejects the null hypothesis when it is true. An error of the second type, or Type II error, occurs if one fails to reject the null hypothesis when it is false. The probability of a Type I error is usually denoted by α , and the probability of a Type II error is usually denoted by β . In the context of analyte detection decisions, to make a Type I error is to conclude that a sample contains the analyte when it actually does not, and to make a Type II error is to fail to conclude that a sample contains the analyte when it actually does.¹

A Type I error is sometimes called a “false rejection” or “false positive,” and a Type II error is sometimes called a “false acceptance” or “false negative.” Recently the terms “false positive” and “false negative” have been losing favor, because they can be misleading in some contexts.

The use of statistical hypothesis testing to decide whether an analyte is present in a laboratory sample is conceptually straightforward, yet the subject still generates confusion and disagreement among radiochemists and project managers. Hypothesis testing has been used for analyte detection in radiochemistry at least since 1962. Two influential early publications on the subject were Altshuler and Pasternack (1963) and Currie (1968). Other important but perhaps less well-known documents were Nicholson (1963 and 1966). Most approaches to the detection problem have been similar in principle, but there has been inadequate standardization of terminology and methodology. However, there has been recent progress. In 1995, the International Union of Pure and Applied Chemistry (IUPAC) published “Nomenclature in Evaluation of Analytical Methods Including Detection and Quantification Capabilities” (IUPAC, 1995), which recommends a uniform approach to defining various performance characteristics of any chemical measurement process, including detection and quantification limits; and in 1997 the International Organization for Standardization (ISO) issued the first part of ISO 11843 “Capability of Detection,” a multi-

¹ Note that in any given situation, only one of the two types of decision error is possible. If the sample *does not* contain the analyte, a Type I error is possible. If the sample *does* contain the analyte, a Type II error is possible.

part standard which deals with issues of detection in an even more general context of measurement. Part 1 of ISO 11843 includes terms and definitions, while Parts 2–4 deal with methodology. Although members of the IUPAC and ISO working groups collaborated during the development of their guidelines, substantial differences between the final documents remain. MARLAP follows both the ISO and IUPAC guidelines where they agree but prefers the definitions of ISO 11843-1 for the critical value and minimum detectable value, relating them to the terminology and methodology already familiar to most radiochemists.

In July 2000, ISO also published the first three parts of ISO 11929 “Determination of the Detection Limit and Decision Threshold for Ionizing Radiation Measurements.” Unfortunately, ISO 11929 is not completely consistent with either the earlier ISO standard or the IUPAC recommendations.

In the terminology of ISO 11843-1, the analyte concentration of a laboratory sample is the *state variable*, denoted by Z , which represents the state of the material being analyzed. Analyte-free material is said to be in the *basic state*. The state variable cannot be observed directly, but it is related to an observable *response variable*, denoted by Y , through a *calibration function* F , the mathematical relationship being written as $Y = F(Z)$. In radiochemistry, the response variable Y is most often an instrument signal, such as the number of counts observed. The inverse, F^{-1} , of the calibration function is sometimes called the *evaluation function* (IUPAC, 1995). The evaluation function, which gives the value of the net concentration in terms of the response variable, is closely related to the *mathematical model* described in Section 19.4.2 of Chapter 19.

The difference between the state variable, Z , and its value in the basic state is called the *net state variable*, which is denoted by X . In radiochemistry there generally is no difference between the state variable and the net state variable, because the basic state is represented by material whose analyte concentration is zero. In principle the basic state might correspond to a positive concentration, but MARLAP does not address this scenario.

20.2.2 The Critical Value

In an analyte detection decision, one chooses between the null and alternative hypotheses on the basis of the observed value of the response variable, Y . The value of Y must exceed a certain threshold value to justify rejection of the null hypothesis and acceptance of the alternative: that the sample is not analyte-free. This threshold is called the *critical value* of the response variable and is denoted by y_c .

The calculation of y_c requires the choice of a *significance level* for the test. The significance level is a specified upper bound for the probability, α , of a Type I error (false rejection). The significance level is usually chosen to be 0.05. This means that when an analyte-free sample is analyzed, there should be at most a 5 % probability of incorrectly deciding that the analyte is present. In principle other values of α are possible, but in the field of radiochemistry, α is often

implicitly assumed to be 0.05. So, if another value is used, it should be explicitly stated. A smaller value of α makes type I errors less likely, but also makes Type II errors more likely when the analyte concentration in the laboratory sample is positive but near zero.

The *critical value of the analyte concentration*, x_c , as defined by MARLAP, is the value obtained by applying the evaluation function, F^{-1} , to the critical value of the response variable, y_c . Thus, $x_c = F^{-1}(y_c)$. In radiochemistry, when y_c is the gross instrument signal, this formula typically involves subtraction of the blank signal and division by the counting efficiency, test portion size, chemical yield, decay factor, and possibly other factors. In ANSI N42.23, "Measurement and Associated Instrument Quality Assurance for Radioassay Laboratories," the same value, x_c , is called the *decision level concentration*, or DLC.

A detection decision can be made by comparing the observed gross instrument signal to its critical value, y_c , as indicated above. However, it has become standard practice in radiochemistry to make the decision by comparing the *net* instrument signal to its critical value, S_c . The net signal is calculated from the gross signal by subtracting the estimated blank value and any interferences. The critical net signal, S_c , is calculated from the critical gross signal, y_c , by subtracting the same correction terms; so, in principle, either approach should lead to the same detection decision.

Since the term "critical value" alone is ambiguous, one should specify the variable to which the term refers. For example, one may discuss the critical (value of the) analyte concentration, the critical (value of the) net signal, or the critical (value of the) gross signal.

It is important to understand that there is no single equation for the critical value that is appropriate in all circumstances. Which equation is best depends on the structure of the measurement process and the statistics of the measurements. Many of the commonly used expressions are based on the assumption of Poisson counting statistics and are invalid if that assumption is not a good approximation of reality. For example, if the instrument background varies between measurements or if it is necessary to correct the result for sample-specific interferences, then expressions for the critical value based on the Poisson model require modification or replacement. If the analyte is a naturally occurring radionuclide that is present at varying levels in reagents, then a correction for the reagent contamination is necessary and expressions based on the Poisson model may be completely inappropriate. In this case the critical value usually must be determined by repeated measurements of blanks under conditions similar to those of the sample measurement.

Generally, the clients of a laboratory do not have the detailed knowledge of the measurement process that is necessary to choose a specific equation for the critical value; however, clients may specify the desired Type I error rate (5 % by default).

Section 20.4.1 and Section 20A.2 of Attachment 20A provide more information on the calculation of critical values.

20.2.3 The Blank

In radiochemistry, the response variable is typically an instrument signal, whose mean value generally is positive even when analyte-free material is analyzed. The gross signal must be corrected by subtracting an estimate of the signal produced by analyte-free material. This estimate may be obtained by means of any of several types of radiochemical blanks, including blank sources and reagent blanks (Chapter 18). The radiochemical blank is chosen to provide an estimate of the mean signal produced by an analyte-free sample, whether the signal is produced by the instrument background, contaminated reagents, or other causes. The most appropriate type of blank depends on the analyte and on the method and conditions of measurement. Some analytes, including many anthropogenic radionuclides, are unlikely to occur as contaminants in laboratory reagents. For these analytes the radiochemical blank may be only a blank source that mimics the container, geometry, and physical form of a source prepared from a real sample. On the other hand, many naturally occurring radionuclides may be present in laboratory water, reagents, and glassware, and these analytes often require the laboratory to analyze reagent blanks or matrix blanks to determine the distribution of the instrument signal that can be expected when analyte-free samples are analyzed.

20.2.4 The Minimum Detectable Concentration

The *power* of any hypothesis test is defined as the probability that the test will reject the null hypothesis when it is false.² So, if the probability of a Type II error is denoted by β , the power is $1 - \beta$. In the context of analyte detection, the power of the test is the probability of correctly detecting the analyte (concluding that the analyte is present), which happens whenever the response variable exceeds its critical value. The power depends on the analyte concentration of the sample and other conditions of measurement; so, one often speaks of the “power function” or “power curve.” Note that the power of a test for analyte detection generally is an increasing function of the analyte concentration — i.e., the greater the analyte concentration the higher the probability of detecting it.

The *minimum detectable concentration* (MDC) is the minimum concentration of analyte that must be present in a sample to give a specified power, $1 - \beta$. It may also be defined as:

- The minimum analyte concentration that must be present in a sample to give a specified probability, $1 - \beta$, of detecting the analyte; or

² Some authors define *power* more simply as the probability that the null hypothesis will be rejected — regardless of whether it is true or false. However, the concept of power is more relevant when the null hypothesis is false.

- The minimum analyte concentration that must be present in a sample to give a specified probability, $1 - \beta$, of measuring a response greater than the critical value, leading one to conclude correctly that there is analyte in the sample.

The value of β that appears in the definition, like α , is usually chosen to be 0.05 or is assumed to be 0.05 by default if no value is specified. The minimum detectable concentration is denoted in mathematical expressions by x_D . In radiochemistry the MDC is usually obtained from the *minimum detectable value of the net instrument signal*, S_D , which is the smallest mean value of the net signal at which the probability that the response variable will exceed its critical value is $1 - \beta$. The relationship between the critical net signal, S_C , and the minimum detectable net signal, S_D , is shown in Figure 20.1.

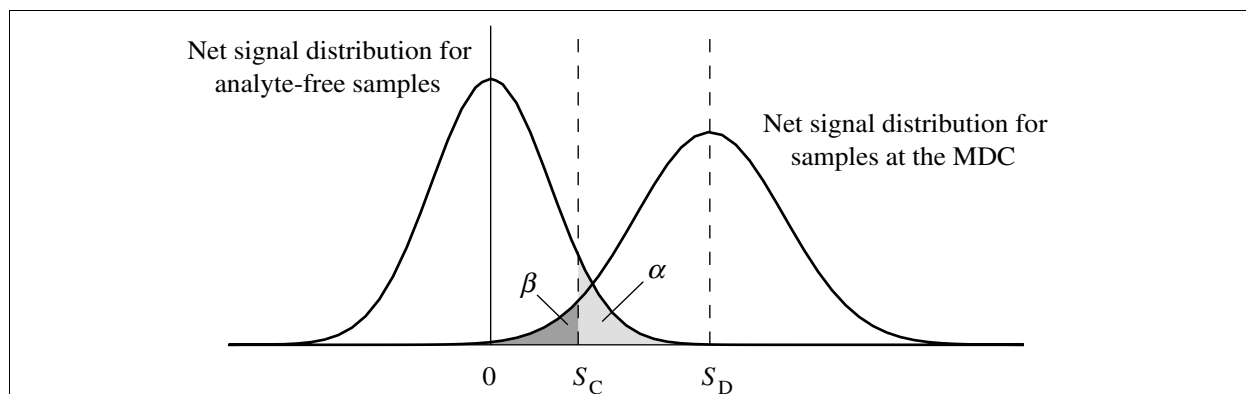


FIGURE 20.1 — The critical net signal, S_C , and minimum detectable net signal, S_D

Sections 20.4.2 and 20A.3 provide more information about the calculation of the minimum detectable concentration.

The minimum detectable value of the activity or mass of analyte in a sample is sometimes called the *minimum detectable amount*, which may be abbreviated as MDA (ANSI N13.30 and N42.23). This chapter focuses on the MDC, but with few changes the guidance is also applicable to any type of MDA.

While project planners and laboratories have some flexibility in choosing the significance level, α , used for detection decisions, the MDC is usually calculated with $\alpha = \beta = 0.05$. The use of standard values for α and β allows meaningful comparison of analytical procedures.

The MDC concept has generated controversy among radiochemists for years and has frequently been misinterpreted and misapplied. The term must be carefully and precisely defined to prevent confusion. The MDC is by definition an estimate of the *true* concentration of analyte required to give a specified high probability that the *measured* response will be greater than the critical

value. Thus, the common practice of comparing a measured concentration to the MDC to make a detection decision is incorrect.

There are still disagreements about the proper uses of the MDC concept. Some define the MDC strictly as an estimate of the nominal detection capability of a *measurement process*. Those in this camp consider it invalid to compute an MDC for each *measurement* using sample-specific information such as test portion size, chemical yield, and decay factors (e.g., ANSI N42.23). The opposing view is that the “sample-specific” MDC is a useful measure of the detection capability of the measurement process, not just in theory, but as it actually performs. The sample-specific MDC may be used, for example, to determine whether an analysis that has failed to detect the analyte of interest should be repeated because it did not have the required or promised detection capability.

Neither version of the MDC can legitimately be used as a threshold value for a detection decision. The definition of the MDC presupposes that an appropriate detection threshold (i.e., the critical value) has already been defined.

Many experts strongly discourage the reporting of a sample-specific MDC because of its limited usefulness and the likelihood of its misuse. Nevertheless, this practice has become firmly established at many laboratories and is expected by many users of radioanalytical data. Furthermore, NUREG/CR-4007 states plainly that “the critical (decision) level and detection limit [MDC] really do vary with the nature of the sample” and that “proper assessment of these quantities demands relevant information on each sample, unless the variations among samples (e.g., interference levels) are quite trivial” (NRC, 1984).

Since a sample-specific MDC is calculated from measured values of input quantities such as the chemical yield, counting efficiency, test portion size, and background level, the MDC estimate has a combined standard uncertainty, which in principle can be obtained by uncertainty propagation (see Chapter 19).

In the calculation of a sample-specific MDC, the treatment of any *randomly varying but precisely measured* quantities, such as the chemical yield, is important and may not be identical at all laboratories. The most common approach to this calculation uses the measured value and ignores the variability of the quantity. For example, if the chemical yield routinely varies between 0.85 and 0.95, but for a particular analysis the yield happens to be 0.928, the MDC for that analysis would be calculated using the value 0.928 with no consideration of the typical range of yields. A consequence of this approach is that the MDC varies randomly when the measurement is repeated under similar conditions; or, in other words, the sample-specific MDC with this approach is a random variable. An MDC calculated in this manner may or may not be useful as a predictor of the future performance of the measurement process.

If sample-specific MDCs are reported, it must be clear that no measured value should ever be compared to an MDC to make a detection decision. In certain cases it may be valid to compare the sample-specific MDC to a required detection limit to determine whether the laboratory has met contractual or regulatory requirements (remembering to consider the uncertainty of the MDC estimate), and in general it may be informative to both laboratory personnel and data users to compare sample-specific MDCs to nominal estimates, but other valid uses for the sample-specific MDC are rare.

20.2.5 The MARLAP Approach to Critical Values and Detection Limits

Historically, detection in radiochemistry has often been based on the distribution of the instrument signal obtained by counting analyte-free *sources*; however, in principle it should be based on the distribution obtained when analyte-free *samples* are analyzed, which is often affected by the processing of samples before instrumental analysis. There is more than one valid approach for dealing with the effects of sample processing. One approach, which is recommended by IUPAC (1995), makes the detection decision for a sample using the critical concentration, x_c , which is calculated on the basis of the distribution of the measured analyte concentration, $\hat{x}$, under the null hypothesis of zero true concentration in the sample. Similarly, the IUPAC approach determines the MDC on the basis of the distribution of $\hat{x}$ as a function of the true concentration.

The approach of this chapter makes detection decisions using the critical net signal, S_c , which is calculated on the basis of the distribution of the net signal, $\hat{S}$, under the same null hypothesis (zero true concentration in the sample). This approach requires one to consider all sources of variability in the signal, including any due to sample processing. So, for example, if the presence of analyte in the reagents causes varying levels of contamination in the prepared sources, this variability may increase the variance of the blank signal and thereby increase the critical net signal.

The MARLAP approach to detection decisions ignores the variability of any term or factor in the measurement model that does not affect the distribution of the instrument signal obtained from samples and blanks. For example, measurement errors in the counting efficiency may increase the variability of the measured concentration, but since they have no effect on the distribution of the signal, they do not affect the critical value, S_c .

The MARLAP approach to the calculation of the MDC also takes into account all sources of variability in the signal, including those related to sample processing, but it ignores any additional sources of variability in the measured concentration that do not affect the distribution of the signal. For example, variability in the true yield from one measurement to another affects the distribution of $\hat{S}$ and thereby increases the MDC, but measurement error in the estimated yield typically does not. The estimated yield is applied as a correction factor to $\hat{S}$; so, errors in its measurement contribute to the variability of the calculated concentration but do not affect the variability of $\hat{S}$ or the true value of the MDC. (On the other hand, yield measurement errors may

make precise determination of the MDC more difficult because they make it harder to determine the distribution of yields.)

20.2.6 Other Detection Terminologies

Another term frequently used for a measure of detection capability is the “lower limit of detection,” or LLD (Altshuler, 1963; EPA, 1980; NRC, 1984). Unfortunately this term has been used with more than one meaning. In *Upgrading Environmental Radiation Data* (EPA, 1980), the LLD is defined as a measure of the detection capability of an instrument and is expressed as an activity. However, the Nuclear Regulatory Commission defines the LLD to be identical to the MDC when $\alpha = \beta = 0.05$ (see, for example, NUREG/CR-4007). It is thus a measure of the detection capability of a measurement process and is expressed as an activity *concentration*.

The term “detection limit” is often used as a synonym for “minimum detectable concentration” or for “minimum detectable value” of any other measured quantity.

Many other terms have been used to describe detection capabilities of measurement procedures. Most of them will not be listed here, but one term deserves attention because of the possibility of its confusion with the MDC. The *method detection limit*, or MDL, is a measure of detection capability used routinely in the context of analyzing samples for chemical contaminants.

The term “method detection limit” is defined in the Code of Federal Regulations. In Title 40 CFR Part 136, Appendix B, the following definition appears:

The method detection limit (MDL) is defined as the minimum concentration of a substance that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.

The definition is later clarified somewhat by a statement that the MDL “is used to judge the significance of a single measurement of a future sample.” Thus, the MDL serves as a critical value; however, it is also used as a measure of detection capability, like an MDC. Note that, in MARLAP’s usage, the “method detection limit” is not truly a detection limit.

In March 2003, the Federal Register published a proposed revision of the definition of MDL, which would make it clear that the MDL serves as a critical value. The proposed new definition is:

The method detection limit (MDL) is an estimate of the measured concentration at which there is 99 % confidence that a given analyte is present in a given sample matrix. The MDL is the concentration at which a decision is made regarding

whether an analyte is detected by a given analytical method. The MDL is calculated from replicate analyses of a matrix containing the analyte and is functionally analogous to the “critical value” described by Currie (1968, 1995 [IUPAC, 1995]) and the Limit of Detection (LOD) described by the American Chemical Society (Keith et al, 1980, McDougal et al., 1983).

At the time of this writing, the proposed revision had not been approved.

The similarity between the abbreviations MDC and MDL tends to produce confusion. The term “method detection limit” is seldom used in the context of radiochemistry except when the analytical method is one that is commonly used to measure stable elements (e.g., ICP-MS methods), or when the term is misused by those who are more familiar with the terminology of hazardous chemical analysis. The confusion is made worse by the fact that “MDL” is sometimes interpreted by radiochemists as an abbreviation for nonstandard terms such as “minimum detectable level” and “minimum detectable limit,” the use of which MARLAP strongly discourages.

20.2.7 The Minimum Quantifiable Concentration

The *minimum quantifiable concentration*, or the *minimum quantifiable value* of the analyte concentration, is defined as the concentration of analyte in a laboratory sample at which the measurement process gives results with a specified relative standard deviation.³ A relative standard deviation of 10 % is usually specified, although other values are possible (see for example MARLAP Appendix C). Since ISO 11843 addresses detection capability but not quantification capability, MARLAP follows IUPAC guidance in defining “minimum quantifiable value” (IUPAC, 1995). IUPAC defines both the minimum quantifiable instrument signal and the minimum quantifiable concentration, although MARLAP considers only the latter. In this document the minimum quantifiable concentration will be abbreviated as MQC and denoted in equations by x_Q .

The term “quantification limit” may be used as a synonym for “minimum quantifiable concentration” or for “minimum quantifiable value” of any other measured quantity.

Section 20.4.3 provides more information about the calculation of the minimum quantifiable concentration.

Historically much attention has been given to the detection capabilities of radiochemical measurement processes, but less attention has been given to quantification capabilities, although for some analytical projects, quantification capability may be a more relevant issue. For example, suppose the purpose of a project is to determine whether the ²²⁶Ra concentration in soil from a

³ The MQC is defined in terms of the relative standard *deviation* of the estimator — not the relative standard *uncertainty* of the measured result. The standard uncertainty is generally an estimate of the standard deviation.

site is below an action level. Since ^{226}Ra occurs naturally in almost any type of soil, the analyte may be assumed to be present in every sample, making detection decisions irrelevant. The MDC of the measurement process obviously should be less than the action level, but a more important question is whether the MQC is less than the action level (see also Chapter 3 and Appendix C).

20.3 Recommendations

MARLAP makes the following recommendations.

- When an analyte detection decision is required, it should be made by comparing the gross signal, net signal, or measured analyte concentration to its corresponding critical value.
- The laboratory should choose expressions for the critical value and minimum detectable value that are appropriate for the structure and statistics of the measurement process. The client may specify the desired Type I and Type II error rates (both 5 % by default) but should not require particular equations for the critical value or the minimum detectable value without detailed knowledge of the measurement process.
- The laboratory should use an appropriate radiochemical blank to predict the signal produced by a sample that contains no analyte. The most appropriate type of blank for this purpose depends on the analyte and on the method and conditions of measurement. Depending on the circumstances, it may be a blank source, reagent blank, or other process blank that accounts for instrument background as well as any contaminants introduced during the processing of the sample.
- The laboratory should confirm the validity of the Poisson approximation for the measurement process before using an expression for the critical value that is based on Poisson statistics. When the analyte is present at observable levels in the water, reagents, and lab ware used in the analysis, the Poisson approximation is often inappropriate. In these cases replicated blanks may be used to determine the critical value.
- The laboratory should consider all sources of variance in the instrument signal (or other response variable) when calculating the critical value and minimum detectable value.
- The minimum detectable value (MDC or MDA) should be used only as a performance characteristic of the measurement process.
- A measurement result should never be compared to the minimum detectable value to make a detection decision.

- The laboratory should report each measurement result and its uncertainty as obtained (as recommended in Chapter 19) even if the result is less than zero. The laboratory should never report a result as “less than MDC.”
- The minimum detectable value should not be used for projects where the issue is quantification of the analyte and not detection. For these projects, MARLAP recommends the minimum quantifiable value as a more relevant performance characteristic of the measurement process.

MARLAP neither encourages nor discourages the reporting of sample-specific MDCs with measurement results, so long as the recommendations stated above are followed.

20.4 Calculation of Detection and Quantification Limits

20.4.1 Calculation of the Critical Value

In Section 20.2.2, the *critical value* of the response variable (or gross instrument signal), denoted by y_C , was defined as the response threshold used to decide whether the analyte concentration of a laboratory sample is greater than that of the blank. The critical value of the net instrument signal, denoted by S_C , was similarly defined as the net signal threshold that may be used for the same purpose.

The critical value of the net signal, S_C , is defined symbolically by the relation

$$\Pr[\hat{S} > S_C | X = 0] = \alpha \quad (20.1)$$

where $\Pr[\hat{S} > S_C | X = 0]$ denotes the probability that the observed net signal, $\hat{S}$, exceeds its critical value, S_C , when the true analyte concentration, X , is zero, and α denotes the significance level, or the specified probability of a Type I error. When the signal assumes only discrete values (e.g., numbers of counts), there may be no value S_C that satisfies Equation 20.1 exactly. The critical value in this case is defined as the smallest value, S_C , such that $\Pr[\hat{S} > S_C | X = 0] \leq \alpha$.

Determining a value of S_C which satisfies the definition requires knowledge of the distribution of the net signal, $\hat{S}$, under the assumption that the analyte concentration in the laboratory sample is zero (the null hypothesis). The measured net signal may be written as $\hat{S} = \hat{Y} - \hat{B}$, where $\hat{Y}$ denotes the measured gross signal and $\hat{B}$ denotes the estimated value of the gross signal under the null hypothesis H_0 . In the absence of interferences, the value of $\hat{B}$ is usually estimated by measuring one or more blanks using the same procedure used to measure the test sample, and the distribution of $\hat{Y}$ under H_0 is determined from that of $\hat{B}$. In other cases, however, the value of $\hat{B}$ includes estimated baseline and other interferences that are present only during the measurement of the sample and cannot be determined from the blank.

Since S_C , not y_C , has traditionally been used for analyte detection decisions in radiochemistry, the following presentation focuses primarily on S_C . However, conversion of either of these values to the other is simple, because $y_C = S_C + \hat{B}$.

20.4.1.1 Normally Distributed Signals

If the distribution of the net signal $\hat{S}$ under H_0 is approximately normal with a well-known standard deviation, σ_0 , the critical value of $\hat{S}$ is

$$S_C = z_{1-\alpha} \sigma_0 \quad (20.2)$$

where $z_{1-\alpha}$ denotes the $(1 - \alpha)$ -quantile of the standard normal distribution. Table G.1 in Appendix G shows that $z_{1-\alpha} \approx 1.645$ when $\alpha = 0.05$. Attachment 20A describes the calculation of S_C when the standard deviation is not well-known.

The blank signal, $\hat{B}$, and its standard deviation, σ_B , may be estimated by replicate blank measurements, but at least 20 measurements are generally needed to ensure that the experimental standard deviation, s_B , is an accurate estimate of σ_B . (If fewer than 20 measurements are made, see Attachment 20A.) Given σ_B , the standard deviation, σ_0 , of the net signal, $\hat{S} = \hat{Y} - \hat{B}$, under the null hypothesis is equal to

$$\sigma_0 = \sigma_B \sqrt{1 + \frac{1}{n}} \quad (20.3)$$

where n denotes the number of replicate blank measurements. So, the critical net signal is given by

$$S_C = z_{1-\alpha} \sigma_B \sqrt{1 + \frac{1}{n}} \quad (20.4)$$

The preceding equation is valid only if the blank measurements are made in the same manner and under the same conditions as the sample measurement. In particular, count times should be identical for the sample and the blanks.

20.4.1.2 Poisson Counting

Radionuclide analyses typically involve radiation counting measurements. Although radiation counting data never follow the Poisson model exactly, the model may be a useful approximation in some situations, especially those where the mean blank count is extremely low and the observed count therefore does not follow a normal distribution. At somewhat higher count levels, features from both models are often used, since the Poisson distribution may be approximated by a normal distribution. In this case the Poisson model allows one to estimate σ_0 without replication, because one blank measurement provides an estimate of σ_B .

Generally the pure Poisson model is inappropriate when one analyzes for radionuclides that are found in observable quantities in the water, reagents, and lab ware used in the analysis. Some radionuclides, such as the naturally occurring isotopes of uranium, thorium, and radium, may be present as interfering contaminants in the laboratory and require blank corrections that account for their presence and variability in prepared sources. The variability of these contaminant levels usually must be determined by replicate measurements. If variability is found, one may either abandon the Poisson model (in this case see Section 20.4.1.1) or modify it by including additional non-Poisson variance terms (as shown in the next subsection, “The Poisson-Normal Approximation,” and in Section 19.5.4 of Chapter 19).

When a test source is analyzed in a radiation counting measurement, either the gross count or the gross count rate may be considered the instrument signal $\hat{Y}$. In this section, it is assumed that the instrument signal is the gross count. Therefore, if there are no interferences, the estimated gross and blank signals are

$$\hat{Y} = N_S \quad \text{and} \quad \hat{B} = N_B \frac{t_S}{t_B} \quad (20.5)$$

where

- N_S is the gross count (source count);
- N_B is the blank count;
- t_S is the count time for the test source; and
- t_B is the count time for the blank.

If there are interferences, the blank signal is

$$\hat{B} = \left(\frac{N_B}{t_B} + \hat{R}_I \right) t_S \quad (20.6)$$

where $\hat{R}_I$ denotes the estimated count rate due to the interferences. In either case the net instrument signal is the *net count*, defined as $\hat{S} = N_S - \hat{B}$. The net signal is always assumed to have zero mean when analyte-free samples are analyzed.

THE POISSON-NORMAL APPROXIMATION

Suppose the distribution of the blank signal can be estimated using the Poisson model, possibly with an additional small non-Poisson variance component and perhaps a correction for known interferences, and the instrument background remains at a level where the Poisson distribution is approximately normal. Then the critical net count is given approximately by the equation

$$S_C = z_{1-\alpha} t_S \sqrt{\frac{R_B + R_I}{t_S} + \frac{R_B}{t_B} + \zeta_B^2 + \sigma^2(\hat{R}_I)} \quad (20.7)$$

where

- R_B is the (true) mean count rate of the blank;
- R_I is the mean interference count rate;
- ζ_B^2 is the non-Poisson variance in the blank (count rate) correction (see Section 19.5.4 of Chapter 19); and
- $\sigma^2(\hat{R}_I)$ is the variance of the estimator for R_I .

When there are no interferences and no non-Poisson blank variance, Equation 20.7 becomes

$$S_C = z_{1-\alpha} \sqrt{R_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.8)$$

The preceding formula is equivalent to “Currie’s equation” $L_C = 2.33 \sqrt{\mu_B}$ when $t_B = t_S$, $\alpha = 0.05$, and the symbols L_C and μ_B are identified with S_C and $R_B t_S$, respectively (Currie, 1968).

In Equation 20.8, R_B denotes the *true* mean blank count rate, which can only be estimated. In practice one must substitute an estimated value, $\hat{R}_B$, for R_B , as shown in the following equation.

$$S_C = z_{1-\alpha} \sqrt{\hat{R}_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.9)$$

Equation 20.9 resembles Equation 20.8 but involves the estimated count rate, $\hat{R}_B$, which varies with repeated measurements. The value of $\hat{R}_B$ is usually estimated from the same blank value N_B used to calculate the net instrument signal. (See Attachment 20A for other possible estimators.)

$$\hat{R}_B = \frac{N_B}{t_B} \quad (20.10)$$

The resulting formula, shown below, is equivalent to equations published by several authors (Currie, 1968; Lochamy, 1976; Strom and Stansbury, 1992; ANSI N13.30).

$$S_C = z_{1-\alpha} \sqrt{N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \quad (20.11)$$

Note that this is a commonly used expression for the critical net count, but its validity depends on the assumption of pure Poisson counting statistics. If the variance of the blank signal is affected by sample processing, interferences, or background instability, then Equation 20.11 may be invalid (but Equation 20.7 may be appropriate).

If $\alpha = 0.05$ and $t_B = t_S$, Equation 20.11 leads to the well-known expression $2.33\sqrt{N_B}$ for the critical net count.

When the blank count is high (e.g., 100 or more), Equation 20.11 works well. At lower blank levels, it can produce a high rate of Type I errors. For example, if the true mean blank count is 0.693, there is a 25 % chance of observing 0 blank counts and a positive number of test source counts in paired measurements of equal duration. In this case, a critical value calculated by Equation 20.11 produces Type I errors more than 25 % of the time regardless of the chosen significance level α . Attachment 20A describes several expressions for S_C that have been proposed for use in situations where the mean blank count is less than 100.

EXAMPLE 20.1

Problem: A 6000-second blank measurement is performed on a proportional counter and 108 beta counts are observed. A test source is to be counted for 3000 s. Estimate the critical value of the net count when $\alpha = 0.05$. (See also Example 20.10.)

Solution:

$$\begin{aligned} S_C &= z_{1-\alpha} \sqrt{N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\ &= 1.645 \sqrt{108 \left(\frac{3000 \text{ s}}{6000 \text{ s}} \right) \left(1 + \frac{3000 \text{ s}}{6000 \text{ s}} \right)} \\ &= 14.8 \text{ net counts.} \end{aligned}$$

EXAMPLE 20.2

Problem: Repeat the same problem assuming the blank correction, expressed as a count rate, has a non-Poisson uncertainty component of $\zeta_B = 0.001 \text{ s}^{-1}$ (see Section 19.5.4 of Chapter 19).

Solution:

$$\begin{aligned}
S_C &= z_{1-\alpha} \sqrt{N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right) + \zeta_B^2 t_S^2} \\
&= 1.645 \sqrt{108 \left(\frac{3000 \text{ s}}{6000 \text{ s}} \right) \left(1 + \frac{3000 \text{ s}}{6000 \text{ s}} \right) + (0.001 \text{ s}^{-1})^2 (3000 \text{ s})^2} \\
&= 15.6 \text{ net counts.}
\end{aligned}$$

20.4.1.3 Batch Blanks

Equation 20.11 is derived with the assumption that a detection decision is based on counts obtained from a single radiation counter. When laboratory samples are analyzed in batches, it is common to analyze a single blank per batch, so that the measurement conditions for the blank may differ somewhat from those of the samples. In particular, the counts for the laboratory samples and the blank may be measured using different detectors. If detection in a laboratory sample is defined relative to a blank counted on a different instrument, Equation 20.11 is inappropriate. Even if a single instrument is used, the presence of positive amounts of analyte in the reagents probably invalidates the (pure) Poisson assumption. In principle, $\hat{B}$ should be estimated by converting the absolute activity of the blank Z_B to an estimated gross count on the instrument used to measure the laboratory sample. Thus,

$$\hat{B} = F(Z_B) \quad (20.12)$$

where

- F is the calibration function for the laboratory sample measurement, whose parameters include the instrument background, counting efficiency, chemical yield, and any estimated interferences and
- Z_B is the estimated absolute activity of the blank.

Then the net count is $\hat{S} = \hat{Y} - \hat{B}$, whose critical value is

$$S_C = z_{1-\alpha} \sqrt{\sigma^2(\hat{Y}_0) + \sigma^2(\hat{B})} \quad (20.13)$$

where

- $\sigma^2(\hat{Y}_0)$ is the variance of the gross count $\hat{Y}$ in the test source measurement when the sample is analyte-free and
- $\sigma^2(\hat{B})$ is the variance of the estimator $\hat{B}$.

If Poisson counting statistics are assumed, then $\sigma^2(\hat{Y}_0)$ may be estimated by $\hat{B}$ (assuming $\hat{B} > 0$), but estimating $\sigma^2(\hat{B})$ still requires a more complicated expression, which may be based on uncer-

tainty propagation or replication. The variance of $\hat{B}$ may be difficult to estimate if positive blank values are caused not by the presence of the analyte in reagents but by contaminated glassware or instruments, which may represent a loss of statistical control of the analytical process.

A valid alternative to the approach just described is to use replicate blank measurements to determine the distribution of the measured total activity and to calculate the critical net (absolute) activity using an equation similar to Equation 20.4. The critical net activity is given by

$$\text{Critical Net Activity} = z_{1-\alpha} \sigma_{\text{blank}} \sqrt{1 + \frac{1}{n}} \quad (20.14)$$

where σ_{blank} denotes the standard deviation of the blank activity and n denotes the number of replicate blank measurements. Then a detection decision is made for a real sample by comparing the measured net activity to the critical net activity.

This approach should work best if all samples and blanks are analyzed under very similar conditions, using instruments with similar counting efficiencies and background levels. (Each sample result and each blank result must still be corrected for instrument background.) If the instruments are significantly different, special care may be needed to ensure that the replicate blank measurements are made using all the available instruments and that samples are assigned to instruments randomly so that the variance of the blank results is similar to the variance observed when analyte-free samples are analyzed.

20.4.2 Calculation of the Minimum Detectable Concentration

The *minimum detectable concentration* (MDC) is defined as the concentration of analyte x_D that must be present in a laboratory sample to give a specified probability, $1 - \beta$, of obtaining a measured response greater than its critical value, leading one to conclude correctly that there is analyte in the sample. In other words, the MDC is the analyte concentration at which the type II error rate is β .

The MDC may also be defined as the analyte concentration x_D that satisfies the relation

$$\Pr[\hat{S} \leq S_C | X = x_D] = \beta \quad (20.15)$$

where the expression $\Pr[\hat{S} \leq S_C | X = x_D]$ is read as “the probability that the net signal $\hat{S}$ does not exceed its critical value S_C when the true concentration X is equal to x_D .”

The MDC is often used as a performance measure for an analytical process for the purpose of comparing different analytical procedures or evaluating a laboratory’s capabilities against specified requirements. The calculation of the “nominal” MDC is complicated by the fact that some

input quantities in the mathematical model, such as interferences and the chemical yield, which have a substantial impact on the MDC, may vary significantly from measurement to measurement. Other quantities that may have similar effects include the decay time, counting efficiency, and instrument background. Because of these variable quantities, determining the value of x_D that satisfies Equation 20.15 in practice may be difficult. One common approach to this problem is to make conservative choices for the values of the variable quantities, which tend to increase the value of x_D .

The MDC is also commonly used in radiochemistry to describe the detection capability of the analytical process as implemented in a particular instance. In this case, the need for conservative choices is reduced. Instead, the measured values of the variable quantities may be used. However, since the measured values have uncertainties, their uncertainties contribute to a combined standard uncertainty in the calculated value of x_D . To ensure compliance with regulatory or contractual requirements, an uncertainty interval or conservative upper bound for x_D may still be useful (see NRC, 1984).

20.4.2.1 The Minimum Detectable Net Instrument Signal

The traditional method for calculating the MDC involves first calculating the *minimum detectable value of the net instrument signal* and then converting the result to a concentration using the mathematical measurement model. The minimum detectable value of the net instrument signal, denoted by S_D , is defined as the mean value of the net signal that gives a specified probability, $1 - \beta$, of yielding an observed signal greater than its critical value S_C . Thus,

$$\Pr[\hat{S} \leq S_C | S = S_D] = \beta \quad (20.16)$$

where S denotes the true mean net signal.

In radiochemistry the mean net signal, S , is usually directly proportional to X , the true analyte concentration in the sample. So, there is a “sensitivity” constant, A , such that $S = AX$. The constant A typically is the mean value of the product of factors such as the source count time, decay-correction factor, yield, counting efficiency, and test portion size (e.g., mass or volume). Its value in some cases may be sample-dependent, but it is essentially independent of the analyte concentration over a wide range of values. Combining Equation 20.16 with the relation $S = AX$ gives

$$\Pr[\hat{S} \leq S_C | X = S_D / A] = \beta \quad (20.17)$$

A comparison of Equation 20.17 to Equation 20.15, the defining relation of the minimum detectable concentration, x_D , shows that

$$x_D = \frac{S_D}{A} \quad (20.18)$$

The preceding equation is only true if all sources of variability are accounted for when determining the distribution of the net signal, $\hat{S}$. If sample-processing effects are ignored, the expression S_D / A may underestimate the MDC. Note that ensuring the MDC is not underestimated also requires that the value of A not be overestimated.

Certain variations of this procedure for calculating S_D and x_D may also be useful. As an example, suppose

$$A = t_S \mu_Y \mu_V \mu_\epsilon \mu_D \mu_{F_S} \quad (20.19)$$

where

- t_S the source count time;
- μ_Y the mean chemical yield;
- μ_V the mean test portion size (mass or volume);
- μ_ϵ the mean counting efficiency;
- μ_D the mean decay-correction factor; and
- μ_{F_S} the mean “subsampling factor,” defined in Chapter 19 as the ratio of analyte concentration in a subsample to that in a sample (μ_{F_S} is assumed to be 1).

Much of the guidance given later for calculating S_D presumes that the distribution of the signal is normal, but the distribution tends not to be normal if the true yield (Y), test portion size (V), counting efficiency (ϵ), decay-correction factor (D), or subsampling factor (F_S) is not normally distributed, or if the total relative variance of the product of these factors is large. For example, suppose the yield and decay factor vary over large ranges and are not normally distributed but the other factors are either constant or approximately normal. Then a reasonable method of calculating x_D is to ignore the variances of Y and D when calculating S_D but to compensate for their omission by replacing $\mu_Y \mu_D$ in the expression for the sensitivity factor, A , by a lower value, such as the β -quantile of the historical distribution of YD (i.e., the 5th percentile when $\beta = 0.05$). In general, the variance of any or all of the factors may be ignored if a sufficiently conservative value is substituted for the mean value of the product of those factors when estimating the sensitivity factor, A .

20.4.2.2 Normally Distributed Signals

If the net signal, $\hat{S}$, is normally distributed and its estimated standard deviation, σ_0 , under H_0 is well-known, the critical value of $\hat{S}$ is $S_C = z_{1-\alpha} \sigma_0$, as previously noted. Then the minimum detectable net signal, S_D , is determined implicitly by the equation

$$S_D = S_C + z_{1-\beta} \sqrt{\sigma^2(\hat{S} | S = S_D)} \quad (20.20)$$

where $\sigma^2(\hat{S} | S = S_D)$ denotes the variance of the measured signal, $\hat{S}$, when the true mean signal, S , equals S_D . If the function $\sigma^2(\hat{S} | S = S_D)$ is constant, Equation 20.20 gives the value of S_D immediately, but typically $\sigma^2(\hat{S} | S = S_D)$ is an increasing function of S_D .

If the function $\sigma^2(\hat{S} | S = S_D)$ has a simple form, it may be possible to transform Equation 20.20 by algebraic manipulation into an explicit formula for S_D . For example, the variance of $\hat{S}$ often has the form

$$\sigma^2(\hat{S}) = aS^2 + bS + c \quad (20.21)$$

where S denotes the true mean net signal and the constants a , b , and c do not depend on S (see Section 20.4.2.3, “Poisson Counting”). In this case the minimum detectable net signal is given by

$$S_D = \frac{1}{I_\beta} \left(S_C + \frac{z_{1-\beta}^2 b}{2} + z_{1-\beta} \sqrt{bS_C + \frac{z_{1-\beta}^2 b^2}{4} + aS_C^2 + I_\beta c} \right) \quad (20.22)$$

where $I_\beta = 1 - z_{1-\beta}^2 a$. When $\alpha = \beta$, the preceding equation can be simplified to the following.

$$S_D = \frac{bz_{1-\beta}^2 + 2S_C}{1 - z_{1-\beta}^2 a} \quad (20.23)$$

In Equations 20.21 and 20.22, the constant c equals σ_0^2 , the variance of the net signal, $\hat{S}$, when analyte-free samples are analyzed. If Poisson counting statistics are assumed (possibly with other sources of variance) and the signal S is the net count, as defined earlier, the constant b usually equals 1. In some situations, such as alpha-counting ^{222}Rn and its short-lived progeny in an alpha scintillation cell, a different value of b may be needed because of the different counting statistics.⁴

For typical radiochemistry measurement models, the value of the constant a is the relative variance (squared coefficient of variation) of the overall sensitivity, which is the product of factors such as the count time, yield, counting efficiency, and subsampling factor. In general the relative variance of a product of independent positive factors $F_1, F_2, \dots, F_N$ is given by

$$\varphi^2(F_1 F_2 \cdots F_N) = (1 + \varphi^2(F_1))(1 + \varphi^2(F_2)) \cdots (1 + \varphi^2(F_N)) - 1 \quad (20.24)$$

where φ^2 denotes relative variance, although an adequate approximation is usually given by

⁴ Note that b equals the “index of dispersion” of the counts produced by net sample activity (the ratio of the variance to the mean). See Lucas and Woodward (1964) for more information about the counting statistics of alpha-scintillation cells.

$$\varphi^2(F_1 F_2 \cdots F_N) \approx \varphi^2(F_1) + \varphi^2(F_2) + \cdots + \varphi^2(F_N) \quad (20.25)$$

when each coefficient of variation, $\varphi(F_i)$, is small. So, if the coefficients of variation of the yield, counting efficiency, subsampling factor, and other such factors are known, the value of a can be calculated.

EXAMPLE 20.3

Problem: Suppose the sensitivity is the product of the yield (Y), counting efficiency (ε), test portion size (V), count time (t_s), and subsampling factor (F_s), and that essentially all of the variance of this product is generated by the variances of the yield and subsampling factor. Assume the coefficients of variation of these two factors are

$$\begin{aligned} \varphi(Y) &= 0.06 \\ \varphi(F_s) &= 0.03 \end{aligned}$$

Assume the counts produced by the net sample activity follow Poisson counting statistics, and assume that σ_0^2 , the variance of the net count observed when analyte-free samples are analyzed, equals 209. Determine the values of the constants a , b , and c such that $\sigma^2(\hat{S}) = aS^2 + bS + c$.

Solution: The value of a is determined using Equation 20.24, as follows:

$$\begin{aligned} a &= \varphi^2(YF_s) = (1 + \varphi^2(Y))(1 + \varphi^2(F_s)) - 1 \\ &= (1 + 0.06^2)(1 + 0.03^2) - 1 \\ &= 0.0045 \end{aligned}$$

The value of b is 1, because Poisson counting statistics are assumed. The value of c equals σ_0^2 , or 209. So, the variance of the net signal, $\hat{S}$, is given by the equation

$$\sigma^2(\hat{S}) = (0.0045 \times S^2) + S + 209$$

ITERATIVE METHODS

If Equation 20.20 cannot be transformed algebraically, an iterative procedure, such as fixed-point iteration, may be used to solve the equation for S_D . An outline of fixed-point iteration is shown below.⁵

⁵ Fixed-point iteration, or functional iteration, is the term for a general technique for solving an equation of the form $x = f(x)$. The iteration produces a sequence $x_0, x_1, x_2, \dots$, where $x_{n+1} = f(x_n)$. Under certain conditions, the sequence converges to a fixed point of f , where $f(x) = x$. Newton's Method for finding a zero of a function $g(x)$ is one example

1. Initially calculate $S_D = S_C + z_{1-\beta} \sqrt{\sigma^2(\hat{S} | S = S_C)}$ (using $S = S_C$)
2. **repeat loop (Lines 3–4)**
3. Set $h = S_D$
4. Recalculate $S_D = S_C + z_{1-\beta} \sqrt{\sigma^2(\hat{S} | S = h)}$ (using $S = h$)
5. **until** $|S_D - h|$ is sufficiently small
6. **output** the solution S_D

In many cases, one iteration of the loop (Lines 3–4) provides an adequate approximation of S_D . In almost all cases, repeated iteration produces an increasing sequence of approximations converging upward to the solution; so, the stopping condition at Line 5 may be replaced by “**until** $S_D \leq h$ ” to obtain full machine precision in the result.

EXAMPLE 20.4

Problem: Assume the variance of the net signal, $\hat{S}$, is given by

$$\sigma^2(\hat{S}) = (0.0045 \times S^2) + S + 209$$

where 0.0045 is the value of the constant a determined in Example 20.3, assuming a 3 % coefficient of variation in the subsampling factor and a 6 % coefficient of variation in the yield. Let $\alpha = \beta = 0.05$. The critical net signal, S_C , is calculated as follows.

$$S_C = z_{1-\alpha} \sqrt{\sigma^2(\hat{S} | S = 0)} = 1.645 \sqrt{209} = 23.78$$

Use fixed-point iteration to calculate S_D .

Solution: The algorithm produces a sequence of approximations.

$$S_{D,0} = 23.78 + 1.645 \sqrt{\sigma^2(\hat{S} | S = 23.78)} = 49.02$$

$$S_{D,1} = 23.78 + 1.645 \sqrt{\sigma^2(\hat{S} | S = 49.02)} = 50.75$$

$$S_{D,2} = 23.78 + 1.645 \sqrt{\sigma^2(\hat{S} | S = 50.75)} = 50.88$$

of the technique.

$$S_{D,3} = 23.78 + 1.645\sqrt{\sigma^2(\hat{S} | S = 50.88)} = 50.89$$

$$S_{D,4} = 23.78 + 1.645\sqrt{\sigma^2(\hat{S} | S = 50.89)} = 50.89$$

The sequence converges to 50.89, which is the value of S_D .

Notice that the same value can be calculated using Equation 20.22 or 20.23 with the constants $a = 0.0045$, $b = 1$, $c = 209$.

20.4.2.3 Poisson Counting

If the following assumptions are true:

- The mean blank count is at least 100
- The only source of signal variance considered is Poisson counting statistics
- $\alpha = \beta$
- Equation 20.11 is used to calculate the critical net signal, S_C

then the minimum detectable net signal, S_D , is given by the following simple equation.⁶

$$S_D = z_{1-\beta}^2 + 2S_C \quad (20.26)$$

In the special case when $\alpha = \beta = 0.05$, Equation 20.26 becomes

$$S_D = 2.71 + 2S_C \quad (20.27)$$

In the case when $\alpha \neq \beta$, S_D is determined from Equation 20.22 using the following values for a , b , and c .

$$a = 0 \quad b = 1 \quad c = R_B t_S \left(1 + \frac{t_S}{t_B} \right)$$

The resulting formula for S_D is

⁶ Some references use the value 3 instead of $z_{1-\beta}^2$ in this formula. A straightforward derivation gives the value $z_{1-\beta}^2$, which is approximately 2.71 when $\beta = 0.05$, but replacing this value by $-\ln \beta$ (approximately 3 when $\beta = 0.05$) accounts for the fact that when the mean count is low, a Poisson distribution is only imperfectly approximated by a normal distribution. The value $-\ln \beta$ is the exact value of S_D when the mean blank count rate is zero, because in this case $S_C = 0$, and $\Pr[\hat{S} = 0] \leq \beta$ if and only if $S \geq -\ln \beta$. Note also that the equation in the text is valid only if $\alpha = \beta$. MARLAP considers either $z_{1-\beta}^2$ or $-\ln \beta$ to be an acceptable value in this case.

$$S_D = S_C + \frac{z_{1-\beta}^2}{2} + z_{1-\beta} \sqrt{\frac{z_{1-\beta}^2}{4} + S_C + R_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.28)$$

EXAMPLE 20.5

Problem: Consider Example 20.1 again, where a 6000-second blank measurement on a proportional counter produces 108 beta counts and a test source is to be counted for 3000 s. Assume this blank measurement gives the best available estimate of the true mean blank count rate, R_B , and use Equation 20.27 to calculate the minimum detectable net signal, S_D , using the default value, 0.05, for Type I and Type II error probabilities. Also use Equation 20.28 to calculate S_D for $\alpha = 0.05$ and $\beta = 0.10$.

Solution: As in Example 20.1, the critical net count, S_C , equals 14.8. The count times are $t_S = 3000$ s and $t_B = 6000$ s. The mean blank count rate, R_B , is estimated by

$$R_B \approx \frac{108}{6000 \text{ s}} = 0.018 \text{ s}^{-1}$$

For the first part of the problem, Equation 20.27 may be used, because $\alpha = \beta = 0.05$. It gives the result

$$S_D = 2.71 + 2(14.8) = 32.3 \text{ net counts}$$

For the second part of the problem, Equation 20.28 is used, because $\alpha \neq \beta$.

$$\begin{aligned} S_D &= S_C + \frac{z_{1-\beta}^2}{2} + z_{1-\beta} \sqrt{\frac{z_{1-\beta}^2}{4} + S_C + R_B t_S \left(1 + \frac{t_S}{t_B} \right)} \\ &= 14.8 + \frac{1.282^2}{2} + 1.282 \sqrt{\frac{1.282^2}{4} + 14.8 + (0.018 \text{ s}^{-1})(3,000 \text{ s}) \left(1 + \frac{3,000 \text{ s}}{6,000 \text{ s}} \right)} \\ &= 28.2 \text{ net counts} \end{aligned}$$

As previously noted, counting data never follow the Poisson model exactly. Variable factors such as the yield, counting efficiency, subsampling error, and source geometry and placement tend to increase a , while interferences and background instability tend to increase c . So, using any of Equations 20.26–28 to calculate S_D is only appropriate if a conservative value of the sensitivity factor, A , (such as the β -quantile of the distribution of the true sensitivity) is used when converting S_D to the MDC. The following example illustrates the calculation of S_D and x_D when both Poisson counting statistics and other sources of variance are considered.

EXAMPLE 20.6

Problem: Again consider the scenario of Example 20.5, where $t_B = 6000$ s, $t_S = 3000$ s, and $R_B \approx 0.018$ s⁻¹. Let the measurement model be

$$X = \frac{N_S - (N_B t_S / t_B)}{t_S \epsilon Y m_S D F_S}$$

where

- X is the specific activity of the radionuclide in the sample;
- ϵ is the counting efficiency;
- Y is the yield;
- m_S is the mass of the test portion;
- D is the decay-correction factor (calculated); and
- F_S is the subsampling factor.

Assume:

- the mass of the test portion is always between 0.98 g and 1.05 g
- the half-life of the analyte is 5.07 d, and decay times from collection to start of counting range from about 3 d to about 10 d
- the counting efficiency has mean 0.42 and a 2 % coefficient of variation
- the yield has approximate mean 0.85 and a 5 % coefficient of variation
- the subsampling factor, whose mean is assumed to be 1, has a 3 % coefficient of variation
- background instability contributes a non-Poisson standard deviation of 0.001 s⁻¹ to the blank correction, expressed as a count rate (see Section 19.5.4 of Chapter 19).

Calculate S_D and x_D using the value 0.05 for both the Type I and Type II error probabilities.

Solution: First determine how to handle each variable sensitivity factor. The following approach is reasonable.

- The source count time, t_S , has negligible variability; so, use the given value 3000 s and ignore the variance.
- The mass of the test portion, m_S , has only a little variability; so, use the lower bound, 0.98 g, and ignore the variance of m_S .
- The decay-correction factor, D , can vary significantly from sample to sample, but no information is given about the distribution except its range of values. Assume a rectangular distribution of decay times from 3 d to 10 d, and calculate the 95th percentile, $3 + 0.95(10 - 3) = 9.65$ d, which gives the 5th percentile of the decay-correction factor (calculated below).

- Use the stated mean values of the counting efficiency (ϵ), yield (Y), and subsampling factor (F_S) to calculate the sensitivity factor, and use the stated coefficients of variation for these factors when calculating S_D .

Next write an expression for the variance of the net signal, $\hat{S}$. The Poisson counting variance is given by

$$\text{Poisson variance of } \left(N_S - N_B \frac{t_S}{t_B} \right) = E(N_S) + E(N_B) \frac{t_S^2}{t_B^2} = (S + R_B t_S) + R_B \frac{t_S^2}{t_B}$$

where $E(\cdot)$ denotes expectation. The non-Poisson variance of the background contributes to $\hat{S}$ an additional variance component equal to $(0.001)^2 t_S^2$. The variability of the efficiency, yield, and subsampling factor contribute a variance component of

$$((1 + 0.02^2)(1 + 0.05^2)(1 + 0.03^2) - 1) \times S^2 = 0.0038 \times S^2$$

Therefore, the total variance of $\hat{S}$ is given by

$$\begin{aligned} \sigma^2(\hat{S}) &= (S + R_B t_S) + R_B \frac{t_S^2}{t_B} + (0.001 \text{ s}^{-1})^2 t_S^2 + (0.0038 \times S^2) \\ &= (0.0038 \times S^2) + S + R_B t_S \left(1 + \frac{t_S}{t_B} \right) + (0.001 \text{ s}^{-1})^2 t_S^2 \end{aligned}$$

So, let a , b , and c be as follows.

$$a = 0.0038 \quad b = 1 \quad c = R_B t_S \left(1 + \frac{t_S}{t_B} \right) + (0.001 \text{ s}^{-1})^2 t_S^2 = 90$$

As in Example 20.2, the critical net count, S_C , equals 15.6. Then Equation 20.23 gives the minimum detectable net signal, S_D .

$$S_D = \frac{(1)(1.645)^2 + 2(15.6)}{1 - (1.645)^2(0.0038)} = \frac{33.918}{0.9897} = 34.3 \text{ counts}$$

The value of the sensitivity factor, A , is obtained from the product of the chosen values for the count time, counting efficiency, yield, test portion size, decay factor, and subsampling factor. The decay constant, λ , must be calculated from the half-life, $T_{1/2} = 5.07 \text{ d}$.

$$\lambda = \frac{\ln 2}{T_{1/2}} = \frac{0.693147}{(5.07 \text{ d})(86,400 \text{ s/d})} = 1.582 \times 10^{-6} \text{ s}^{-1}$$

Then the decay-correction factor is calculated.

$$D = e^{-\lambda t_D} \frac{1 - e^{-\lambda t_S}}{\lambda t_S} = e^{-(1.582 \times 10^{-6} \text{ s}^{-1})(9.65 \text{ d})(86,400 \text{ s/d})} \frac{1 - e^{-(1.582 \times 10^{-6} \text{ s}^{-1})(3000 \text{ s})}}{(1.582 \times 10^{-6} \text{ s}^{-1})(3000 \text{ s})} = 0.2667$$

So, the sensitivity factor is

$$A = t_S \epsilon Y m_S DF_S = (3000 \text{ s})(0.42)(0.85)(0.98 \text{ g})(0.2667)(1) = 279.9 \text{ g} \cdot \text{s}$$

Therefore, the minimum detectable concentration is

$$x_D = \frac{S_D}{A} = \frac{34.3}{279.9} = 0.12 \text{ Bq/g}$$

20.4.2.4 More Conservative Approaches

More conservative (higher) estimates of the MDC may be obtained by following the recommendations of NUREG/CR-4007, in which formulas for MDC (LLD) include estimated bounds for relative systematic error in the blank determination (Δ_B) and the sensitivity (Δ_A). The critical net count S_C is increased by $\Delta_B \hat{B}$, and the minimum detectable net count S_D is increased by $2 \Delta_B \hat{B}$. The MDC is then calculated by dividing S_D by the sensitivity and multiplying the result by $1 + \Delta_A$. The NUREG's conservative approach treats random errors and systematic errors differently to ensure that the MDC for a measurement process is unlikely to be consistently underestimated, which is an important consideration if the laboratory is required by regulation or contract to achieve a specified MDC.

20.4.2.5 Experimental Verification of the MDC

To ensure that the MDC has been estimated properly, one may test the estimate experimentally by analyzing n identical control samples spiked with an analyte concentration equal to x_D . If the MDC has been determined properly (the null hypothesis), the probability of failing to detect the analyte in each control sample is at most β . Then the number of nondetectable results in the experiment may be assumed to have a binomial distribution with parameters n and β . If k nondetectable results are actually obtained, one calculates the cumulative binomial probability

$$P = \sum_{j=k}^n \binom{n}{j} \beta^j (1-\beta)^{n-j} \quad \text{or} \quad 1 - \sum_{j=0}^{k-1} \binom{n}{j} \beta^j (1-\beta)^{n-j} \quad (20.29)$$

and rejects the null hypothesis if P is smaller than the chosen significance level for the test (which may differ from the significance level for the analyte detection test).

NOTE: For any nonnegative integers n and j , the notation $\binom{n}{j}$ denotes a *binomial coefficient*, usually read “ n choose j ,” which is the number of possible combinations of n objects chosen j at a time. For $0 \leq j \leq n$, the value of $\binom{n}{j}$ equals $\frac{n!}{j!(n-j)!}$, where the symbol $!$ denotes the factorial operator. The number of combinations of n objects chosen j at a time is also denoted sometimes by ${}_nC_j$.

To make the test realistic, one should ensure that the physical and chemical characteristics of the control samples, including potential interferences, are representative of laboratory samples encountered in practice.

EXAMPLE 20.7

Problem: Assume x_D is estimated with $\beta = 0.05$. As a check, 10 control samples spiked with concentration x_D are analyzed and 3 of the 10 produce nondetectable results. Does x_D appear to have been underestimated (at the 10 % level of significance)?

Solution: The variables are $n = 10$, $\beta = 0.05$, and $k = 3$. Calculate the P -value

$$P = 1 - \sum_{j=0}^2 \binom{10}{j} (0.05)^j (0.95)^{10-j} = 1 - 0.9885 = 0.0115$$

Since $P \leq 0.10$, reject the null hypothesis and conclude that the MDC was underestimated.

20.4.3 Calculation of the Minimum Quantifiable Concentration

The *minimum quantifiable concentration* (MQC), or the *minimum quantifiable value* of the concentration, was defined in Section 20.2.7 as the analyte concentration in a laboratory sample that gives measured results with a specified relative standard deviation $1 / k_Q$, where k_Q is usually chosen to be 10.

Calculation of the MQC requires that one be able to estimate the standard deviation for the result of a hypothetical measurement performed on a laboratory sample with a specified analyte concentration. Section 19.5.13 of Chapter 19 discusses the procedure for calculating the standard deviation for such a hypothetical measurement.

The MQC is defined symbolically as the value x_Q that satisfies the relation

$$x_Q = k_Q \sqrt{\sigma^2(\hat{X} | X = x_Q)} \quad (20.30)$$

where $\sigma^2(\hat{X} | X = x_Q)$ denotes the variance of the estimator $\hat{X}$ when the true concentration X equals x_Q . If the function $\sigma^2(\hat{X} | X = x_Q)$ has a simple form, it may be possible to solve Equation 20.30 for x_Q using only algebraic manipulation. Otherwise, fixed-point iteration, which was introduced in Section 20.4.2, may be used. The use of fixed-point iteration for this purpose is shown below.

1. Initially calculate $x_Q = k_Q \sqrt{\sigma^2(\hat{X} | X = 0)}$ (using $X = 0$)
2. **repeat loop (Lines 3–4)**
3. Set $h = x_Q$
4. Recalculate $x_Q = k_Q \sqrt{\sigma^2(\hat{X} | X = h)}$ (using $X = h$)
5. **until** $|x_Q - h|$ is sufficiently small
6. **output** the solution x_Q

The sequence of values generated by the algorithm typically converges upward to the solution.

When Poisson counting statistics are assumed, possibly with excess variance components, and the mathematical model for the analyte concentration is $X = S / A$, where S is the net count, A denotes the overall sensitivity of the measurement, Equation 20.30 may be solved for x_Q to obtain the formula

$$x_Q = \frac{k_Q^2}{2AI_Q} \left(1 + \sqrt{1 + \frac{4I_Q}{k_Q^2} \left(R_B t_S \left(1 + \frac{t_S}{t_B} \right) + \zeta_B^2 t_S^2 + R_I t_S + \sigma^2(\hat{R}_I) t_S^2 \right)} \right) \quad (20.31)$$

where

- t_S is the count time for the test source;
- t_B is the count time for the blank;
- R_B is the mean blank count rate;
- ζ_B^2 is the non-Poisson variance component of the blank count rate correction;
- R_I is the mean interference count rate;
- $\sigma(\hat{R}_I)$ is the standard deviation of the measured interference count rate;
- ϕ_A^2 is the relative variance of the measured sensitivity, $\hat{A}$, including the subsampling variance; and

I_Q is equal to $1 - k_Q^2 \phi_A^2$.

If the true sensitivity A may vary, then a conservative value, such as the 0.05-quantile $A_{0.05}$, should be substituted for A in the formula. Note that ϕ_A^2 denotes only the relative variance of $\hat{A}$ due to subsampling and measurement error — it does not include the variance of the true sensitivity, A .

Note that Equation 20.31 defines the MQC only if $I_Q > 0$. If $I_Q \leq 0$, the MQC is infinite, because there is no concentration at which the relative standard deviation of $\hat{X}$ fails to exceed $1 / k_Q$. In particular, if the relative standard deviation of the measured sensitivity $\hat{A}$ or the subsampling standard deviation ϕ_{Samp} exceeds $1 / k_Q$, then $I_Q < 0$ and the MQC is infinite.

More generally, if the variance of the measured concentration $\hat{X}$ can be expressed in the form $\sigma^2(\hat{X}) = aX^2 + bX + c$, where a , b , and c do not depend on X , then the MQC is given by the formula

$$x_Q = \frac{k_Q^2}{2(1 - k_Q^2 a)} \left(b + \sqrt{b^2 + \frac{4c(1 - k_Q^2 a)}{k_Q^2}} \right) \quad (20.32)$$

For example, if pure Poisson counting statistics are assumed and there are no interferences, then $a = \phi_A^2$, $b = 1 / A$, and $c = R_B t_S (1 + t_S / t_B) / A^2$.

EXAMPLE 20.8

Problem: Refer once more to Examples 20.5 and 20.6, where the measurement model is given by

$$X = \frac{N_S - (N_B t_S / t_B)}{t_S \epsilon Y m_S D F_S}$$

where

- X is the specific activity of the radionuclide in the sample;
- N_S is the sample (gross) count;
- N_B is the blank count;
- t_S is the sample count time (s);
- t_B is the blank count time (s);
- ϵ is the counting efficiency;
- Y is the yield;
- m_S is the mass of the test portion (g);
- D is the decay-correction factor; and
- F_S is the subsampling factor.

Keep the same assumptions as in the earlier examples. Assume also that the relative standard deviation of the yield measurement (as opposed to that of the yield itself) is 3 %, and that the relative standard deviation of the efficiency measurement is 2 %. Use Equation 20.31 to calculate the minimum quantifiable concentration, x_Q , defined as the analyte concentration at which the relative standard deviation of the measurement process is 10 %.

Solution: The relative measurement variance of the sensitivity, ϕ_A^2 , is assumed to be the sum of the relative subsampling variance and the relative measurement variances of Y and ε , since the other sensitivity factors are measured with better relative precision. As in the earlier example, conservative values for m_s (0.98 g) and D (0.2667) will be used in the calculation of the sensitivity factor, A . However, for this problem, a somewhat conservative value of the yield will also be used, because the true yield has a 5 % relative standard deviation, which is not otherwise taken into account. Since the mean value of the yield is 0.85 and the relative standard deviation is 5 %, estimate the 0.05-quantile of the yield as follows:

$$Y = 0.85 \times (1 - 1.645 \times 0.05) = 0.78$$

The following values are also used in this problem.

$$\begin{aligned} t_S &= 3000 \text{ s} \\ t_B &= 6000 \text{ s} \\ R_B &= 0.018 \text{ s}^{-1} \\ \varepsilon &= 0.42 \\ R_I &= 0, \sigma^2(\hat{R}_I) = 0, \zeta_B = 0 \\ k_Q &= 10 \\ \phi_\varepsilon &= 0.02 \\ \phi_Y &= 0.03 \\ \phi_{\text{Samp}} &= 0.03 \\ \phi_A^2 &= \phi_\varepsilon^2 + \phi_Y^2 + \phi_{\text{Samp}}^2 = 0.02^2 + 0.03^2 + 0.03^2 \\ I_Q &= 1 - k_Q^2 \phi_A^2 = 1 - 100(0.02^2 + 0.03^2 + 0.03^2) = 0.78 \end{aligned}$$

The sensitivity factor, A , is now evaluated as follows.

$$A = t_S \varepsilon Y m_s D F_S = (3000 \text{ s})(0.42)(0.78)(0.98 \text{ g})(0.2667)(1) = 256.9 \text{ g} \cdot \text{s}$$

Next, the MQC can be calculated as shown below.

$$\begin{aligned}
 x_Q &= \frac{k_Q^2}{2AI_Q} \left(1 + \sqrt{1 + \frac{4I_Q}{k_Q^2} \left(R_B t_S \left(1 + \frac{t_S}{t_B} \right) + 0 \right)} \right) \\
 &= \frac{100}{2(256.9 \text{ g} \cdot \text{s})(0.78)} \left(1 + \sqrt{1 + \frac{4(0.78)}{100} \left((0.018 \text{ s}^{-1})(3000 \text{ s}) \left(1 + \frac{3000 \text{ s}}{6000 \text{ s}} \right) + 0 \right)} \right) \\
 &= 0.718 \text{ Bq/g}
 \end{aligned}$$

Now, as a check, one may use the procedure described in Section 19.5.13 of Chapter 19 to predict the combined standard uncertainty of a measurement made on a hypothetical sample whose analyte concentration is exactly x_Q .

$$\begin{aligned}
 N_B &= R_B t_B = (0.018 \text{ s}^{-1})(6000 \text{ s}) = 108 \\
 N_S &= x_Q A + R_B t_S = (0.718 \text{ Bq/g})(256.9 \text{ g} \cdot \text{s}) + (0.018 \text{ s}^{-1})(3000 \text{ s}) = 238.45 \\
 u_c(X) &= \sqrt{\frac{N_S + N_B t_S^2 / t_B^2}{A^2} + x_Q^2 \left(\frac{u^2(\varepsilon)}{\varepsilon^2} + \frac{u^2(Y)}{Y^2} + \phi_{\text{Samp}}^2 \right)} \\
 &= \sqrt{\frac{238.45 + (108)(3000 \text{ s})^2 / (6000 \text{ s})^2}{(256.9 \text{ g} \cdot \text{s})^2} + (0.718 \text{ Bq/g})^2 (0.02^2 + 0.03^2 + 0.03^2)} \\
 &= 0.0718 \text{ Bq/g}
 \end{aligned}$$

So, the combined standard uncertainty is predicted to be 0.0718 Bq/g, or 10 % of the true value, as expected.

20.5 References

20.5.1 Cited Sources

Altshuler, Bernard, and Bernard Pasternack. 1963. Statistical Measures of the Lower Limit of Detection of a Radioactivity Counter. *Health Physics* 9: 293–298.

American National Standards Institute (ANSI). 1996. *Performance Criteria for Radiobioassay*, N13.30.

American National Standards Institute (ANSI). 1996. *Measurement and Associated Instrument Quality Assurance for Radioassay Laboratories*, N42.23.

- CFR 136. 1999. U.S. Environmental Protection Agency. "Guidelines Establishing Test Procedures for the Analysis of Pollutants."
- Currie, Lloyd A. 1968. Limits for Qualitative Detection and Quantitative Determination: Application to Radiochemistry. *Analytical Chemistry* 40(3): 586–593.
- Currie, L.A. 1997. Detection: International Update, and Some Emerging Dilemmas Involving Calibration, the Blank, and Multiple Detection Decisions. *Chemometrics and Intelligent Laboratory Systems* 37: 151–181.
- U.S. Environmental Protection Agency (EPA). 1980. *Upgrading Environmental Radiation Data, Health Physics Society Committee Report HPSR-1*, EPA, 520/1-80-012, EPA, Office of Radiation Programs, Washington, DC.
- U.S. Environmental Protection Agency (EPA). 2000. *Guidance for Data Quality Assessment: Practical Methods for Data Analysis*. EPA QA/G-9, QA00 Version. EPA/600/R-96/084, EPA, Quality Assurance Division, Washington, DC. Available at www.epa.gov/quality1/qa_docs.html.
- Federal Register. 2003. "Proposed Rules." *Federal Register* 68(48):11786.
- International Organization for Standardization (ISO). 1993. *Statistics – Vocabulary and Symbols – Part 1: Probability and General Statistical Terms*. ISO 3534-1. ISO, Geneva, Switzerland.
- International Organization for Standardization (ISO). 1997. *Capability of Detection – Part 1: Terms and Definitions*. ISO 11843-1. ISO, Geneva, Switzerland.
- International Organization for Standardization (ISO). 2000. *Determination of the Detection Limit and Decision Threshold for Ionizing Radiation Measurements – Part 1: Fundamentals and Application to Counting Measurements without the Influence of Sample Treatment*. ISO 11929-1. ISO, Geneva, Switzerland.
- International Organization for Standardization (ISO). 2000. *Determination of the Detection Limit and Decision Threshold for Ionizing Radiation Measurements – Part 2: Fundamentals and Application to Counting Measurements with the Influence of Sample Treatment*. ISO 11929-2. ISO, Geneva, Switzerland.
- International Organization for Standardization (ISO). 2000. *Determination of the Detection Limit and Decision Threshold for Ionizing Radiation Measurements – Part 3: Fundamentals and Application to Counting Measurements by High-resolution Gamma Spectrometry, without the Influence of Sample Treatment*. ISO 11929-2. ISO, Geneva, Switzerland.

- International Union of Pure and Applied Chemistry (IUPAC). 1995. Nomenclature in Evaluation of Analytical Methods Including Detection and Quantification Capabilities. *Pure and Applied Chemistry* 67(10): 1699–1723.
- Keith, Lawrence H., et al. 1983. Principles of Environmental Analysis. *Analytical Chemistry* 55(14): 2210–2218.
- Lochamy, Joseph C. 1976. *The Minimum Detectable Activity Concept*. NBS Report No. NBS-SP456, National Bureau of Standards, Gaithersburg, MD.
- Lucas, H.F., Jr., and D.A. Woodward. 1964. *Journal of Applied Physics* 35: 452.
- McDougal, Daniel, et al. 1980. Guidelines for Data Acquisition and Data Quality Evaluation in Environmental Chemistry. *Analytical Chemistry* 52(14): 2242–2249.
- National Bureau of Standards (NBS). 1963. *Experimental Statistics*. NBS Handbook 91, National Bureau of Standards, Gaithersburg, MD.
- National Bureau of Standards (NBS). 1964. *Handbook of Mathematical Functions*. Applied Mathematics Series 55, National Bureau of Standards, Gaithersburg, MD.
- National Council on Radiation Protection and Measurements (NCRP). 1985. *Handbook of Radioactivity Measurement Procedures*. NCRP Report 58, 2nd ed., NCRP, Bethesda, MD.
- Nicholson, W.L. 1963. *Fixed Time Estimation of Counting Rates with Background Corrections*. AEC Research and Development Report HW-76279.
- Nicholson, W.L. 1966. Statistics of Net-counting-rate Estimation with Dominant Background Corrections. *Nucleonics* 24(8): 118–121.
- Nuclear Regulatory Commission (NRC). 1984. *Lower Limit of Detection: Definition and Elaboration of a Proposed Position for Radiological Effluent and Environmental Measurements*. NUREG/CR-4007. NRC, Washington, DC.
- Strom, Daniel J., and Paul S. Stansbury. 1992. Minimum Detectable Activity When Background Is Counted Longer than the Sample. *Health Physics* 63(3): 360–361.

20.5.2 Other Sources

- American Chemical Society (ACS). 1988. *Detection in Analytical Chemistry: Importance, Theory, and Practice*. ACS Symposium Series 361, ACS, Washington, DC.

ATTACHMENT 20A

Low-Background Detection Issues

20A.1 Overview

This attachment describes methods for determining critical values and minimum detectable concentrations (MDCs) when the standard deviation of the blank signal is not known precisely, which occurs for example when the blank is measured by low-background Poisson counting or when the standard deviation is estimated from a small number of replicate measurements. The methods described below are applicable more generally, even when the background is high or the number of degrees of freedom is large, but in these situations the simpler methods described previously should be adequate.

20A.2 Calculation of the Critical Value

The critical value of the net signal S_C was defined earlier by the relation

$$\Pr[\hat{S} > S_C | X = 0] = \alpha \quad (20.33)$$

When the signal assumes only discrete values (e.g., numbers of counts), there may be no value S_C that satisfies Equation 20.33 exactly. The critical value in this case is defined as the smallest value S_C such that $\Pr[\hat{S} > S_C | X = 0] \leq \alpha$.

20A.2.1 Normally Distributed Signals

If the distribution of the net signal $\hat{S}$ under H_0 is approximately normal with a well-known standard deviation, σ_0 , the critical value of $\hat{S}$ is

$$S_C = z_{1-\alpha} \sigma_0 \quad (20.34)$$

where $z_{1-\alpha}$ denotes the $(1 - \alpha)$ -quantile of the standard normal distribution. Typically the standard deviation σ_0 is not well-known and must therefore be replaced by an estimate, $\hat{\sigma}_0$. If $\hat{\sigma}_0$ is determined by a statistical evaluation with ν degrees of freedom, the multiplier $z_{1-\alpha}$ should be replaced by $t_{1-\alpha}(\nu)$, the $(1 - \alpha)$ -quantile of the t -distribution with ν degrees of freedom (cf. *Type A* evaluation of standard uncertainty in Section 19.4.2.1 of Chapter 19). Thus,

$$S_C = t_{1-\alpha}(\nu) \times \hat{\sigma}_0 \quad (20.35)$$

Table G.2 in Appendix G lists values of $t_{1-\alpha}(\nu)$. In general, $t_{1-\alpha}(\nu)$ is greater than $z_{1-\alpha}$, but the two values are approximately equal if ν is large.

When $\hat{B}$ is estimated by the average of n replicate blank measurements (assuming no interferences), the standard deviation $\hat{\sigma}_0$ of the net signal $\hat{S}$ under the null hypothesis may be estimated from the experimental standard deviation of the measured blank values, s_B . Specifically,

$$\hat{\sigma}_0 = s_B \sqrt{1 + \frac{1}{n}} \quad (20.36)$$

The number of degrees of freedom, ν , in this case equals $n - 1$; so, the critical value of $\hat{S}$ is

$$S_C = t_{1-\alpha}(n-1) \times s_B \sqrt{1 + \frac{1}{n}} \quad (20.37)$$

EXAMPLE 20.9

Problem: Suppose seven replicate blank measurements are made, producing the following results (total counts).

58 43 64 53 47 66 60

Assume the blank distribution is approximately normal and calculate the critical value of the net count (gross sample count minus average blank count) using a 5 % significance level.

Solution: First, calculate the mean blank count, $\bar{B}$.

$$\bar{B} = \frac{1}{n} \sum_{i=1}^n B_i = \frac{391}{7} = 55.857$$

Calculate the standard deviation of the blank counts, s_B .

$$s_B = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (B_i - \bar{B})^2} = \sqrt{\frac{442.857}{7-1}} = 8.5912$$

Find the 0.95-quantile of the t -distribution with $7 - 1 = 6$ degrees of freedom in Appendix G.

$$t_{1-\alpha}(n-1) = t_{0.95}(6) = 1.943$$

Calculate the critical net count using Equation 20.37.

$$S_C = t_{1-\alpha}(n-1) \times s_B \sqrt{1 + \frac{1}{n}} = 1.943 \times 8.5912 \sqrt{1 + \frac{1}{7}} = 17.85$$

Thus, the net count must exceed 17.85 to be considered detected.

Note that if $z_{1-\alpha}$ were used instead of $t_{1-\alpha}(n-1)$ in the equation, the critical value would be underestimated as

$$S_C = z_{1-\alpha} \times s_B \sqrt{1 + \frac{1}{n}} = 1.645 \times 8.5912 \sqrt{1 + \frac{1}{7}} = 15.11 \quad (\text{incorrect})$$

20A.2.2 Poisson Counting

It is assumed here, as in Section 20.4, that the instrument is a radiation counter and the instrument signal is the gross count. Therefore,

$$\hat{Y} = N_S \qquad \hat{B} = \left(\frac{N_B}{t_B} + \hat{R}_I \right) t_S \quad (20.38)$$

and the net instrument signal is the net count, which is given by

$$\hat{S} = N_S - \left(\frac{N_B}{t_B} + \hat{R}_I \right) t_S \quad (20.39)$$

where

- N_S is the gross count (source count);
- N_B is the blank count;
- $\hat{R}_I$ is the estimated count rate due to interferences;
- t_S is the count time for the test source; and
- t_B is the count time for the blank.

If t_B is much greater than t_S , generally at least 10 times greater, the blank count rate, R_B , can be considered to be “well-known,” because it contributes little variance to the net signal, $\hat{S}$. The value of R_B may be estimated from a single measurement of long duration or from an average of several measurements of shorter duration. Whenever R_B is well-known, if there are no interferences, then according to the Poisson model, the critical gross count, y_C , equals the smallest nonnegative integer n such that

$$e^{-R_B t_S} \sum_{k=0}^n \frac{(R_B t_S)^k}{k!} \geq 1 - \alpha \quad (20.40)$$

Then S_C , the critical net count, equals $y_C - R_B t_S$. Table 20.1 shows critical gross counts for $\alpha = 0.05$ for small values of $R_B t_S$ (adapted from NRC, 1984).⁷ To use the table, one calculates the

⁷ The breaks in the table occur at $R_B t_S = 0.5 \times \chi_{0.05}^2(2y_C)$ and $0.5 \times \chi_{0.05}^2(2y_C + 2)$.

value of $R_B t_S$, finds the appropriate line in the table, and compares the observed gross count N_S to the value of y_C read from the table. The analyte is considered detected if and only if $N_S > y_C$. When $R_B t_S$ is greater than about 20, y_C may be approximated by

$$y_C = \lfloor 0.5 + R_B t_S + z_{1-\alpha} \sqrt{R_B t_S} \rfloor \quad (20.41)$$

where $z_{1-\alpha}$ denotes the $(1 - \alpha)$ -quantile of the standard normal distribution, and for any number x , the expression $\lfloor x \rfloor$ denotes the largest integer not greater than x .

Note that these critical values are appropriate only under the assumption of Poisson counting statistics with no interferences.

TABLE 20.1 — Critical gross count (well-known blank)

$R_B t_S$	y_C	$R_B t_S$	y_C	$R_B t_S$	y_C
0.000–0.051	0	5.425–6.169	10	13.255–14.072	20
0.051–0.355	1	6.169–6.924	11	14.072–14.894	21
0.355–0.818	2	6.924–7.690	12	14.894–15.719	22
0.818–1.366	3	7.690–8.464	13	15.719–16.549	23
1.366–1.970	4	8.464–9.246	14	16.549–17.382	24
1.970–2.613	5	9.246–10.036	15	17.382–18.219	25
2.613–3.285	6	10.036–10.832	16	18.219–19.058	26
3.285–3.981	7	10.832–11.634	17	19.058–19.901	27
3.981–4.695	8	11.634–12.442	18	19.901–20.746	28
4.695–5.425	9	12.442–13.255	19	20.746–21.594	29

Figure 20.2 shows the Type I error rates produced by Table 20.1 for $\alpha = 0.05$ and three different count-time ratios, t_B / t_S . The error rates are much greater than 0.05 when the blank count time equals the sample count time, but they fall as the blank count time increases (and the blank count rate becomes better known). If the blank count rate were known perfectly, the Type I error rate would remain at or below 0.05 everywhere.⁸

⁸ Probabilities on the curves are calculated using the equation

$$P(\mu) = 1 - e^{-\mu(1+t_B/t_S)} \sum_{n=0}^{\infty} \frac{(\mu t_B/t_S)^n}{n!} \sum_{k=0}^{y_C(n)} \frac{\mu^k}{k!}$$

where $\mu = R_B t_S$ (the true mean gross count when the sample contains no analyte) and $y_C(n)$ denotes the critical gross count obtained from Table 20.1 when $R_B t_S$ is approximated by $n(t_S / t_B)$.

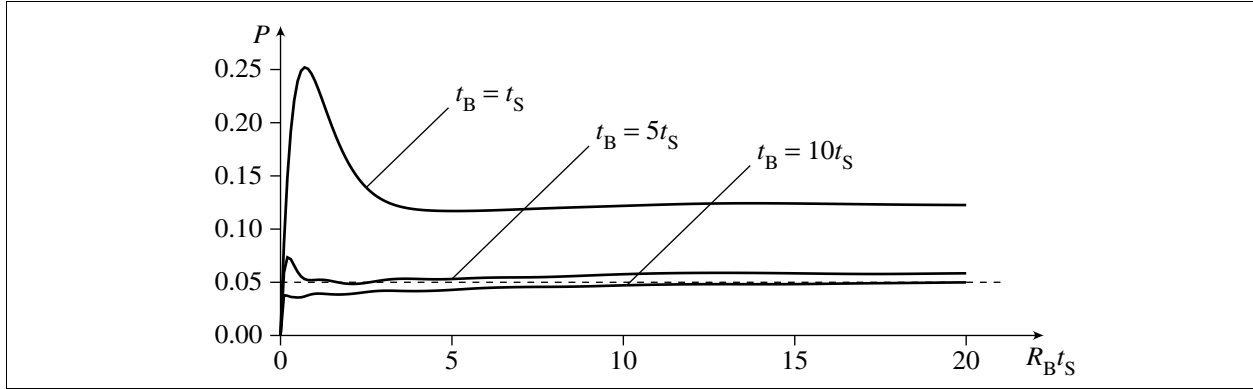


FIGURE 20.2 — Type I error rates for Table 20.1

Other commonly used methods for calculating the critical value when the blank count rate is not well-known are described below.

THE POISSON-NORMAL APPROXIMATION

As stated in Section 20.4.1.2, when Poisson counting statistics are assumed (possibly with additional variance components) and the instrument background remains stable between measurements at a level where the Poisson distribution is approximately normal, the critical net count is given approximately by the equation

$$S_C = z_{1-\alpha} t_S \sqrt{\frac{R_B + R_I}{t_S} + \frac{R_B}{t_B} + \zeta_B^2 + \sigma^2(\hat{R}_I)} \quad (20.42)$$

where R_B denotes the (true) mean count rate of the blank, R_I denotes the mean interference count rate, ζ_B^2 denotes non-Poisson variance in the blank (count rate) correction, and $\sigma^2(\hat{R}_I)$ denotes the variance of the estimator for R_I . When there are no interferences and no non-Poisson blank variance, this equation becomes

$$S_C = z_{1-\alpha} \sqrt{R_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.43)$$

Low mean blank levels cause the Poisson distribution to deviate from the normal model. Figure 20.3 shows the effects of these deviations on the Type I error rates for the Poisson-normal approximation when $t_B = t_S$ and $\alpha = 0.05$. The graph has discontinuities because of the discrete

nature of the Poisson distribution, but the Type I error rate is approximately correct (equal to 0.05) when the mean blank count is 10 or more.⁹

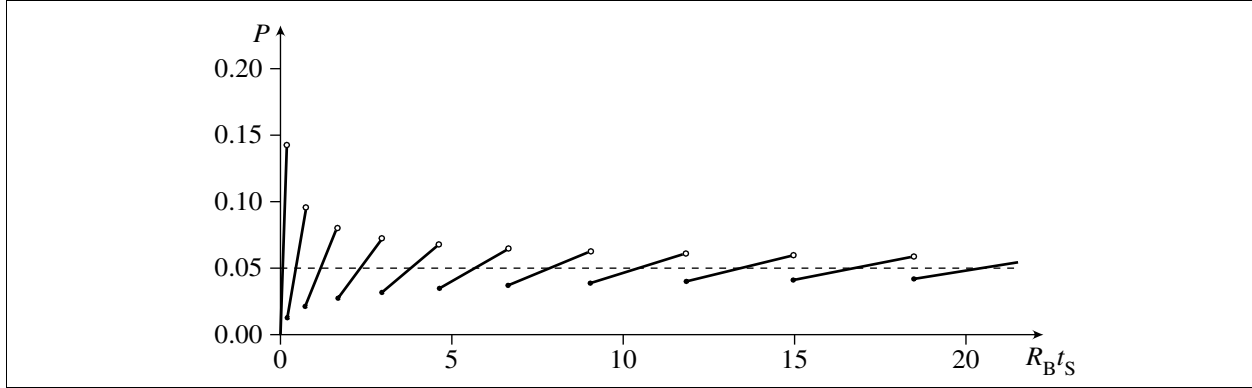


FIGURE 20.3 — Type I error rate for the Poisson-normal approximation ($t_B = t_S$)

In Equation 20.43, R_B denotes the *true* mean blank count rate. In practice, R_B is usually not well-known; so, one must substitute an estimated value, $\hat{R}_B$, as shown in the following equation.

$$S_C = z_{1-\alpha} \sqrt{\hat{R}_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.44)$$

The most frequently used expressions for S_C may be derived from Equation 20.44 using an estimator $\hat{R}_B$ that equals a weighted average of the measured blank count rate N_B / t_B and the measured source count rate N_S / t_S . A weighted average of both measured rates may be used here to estimate the true blank level for the purpose of the hypothesis test, because, under the null hypothesis of zero net source activity, both measured rates are unbiased estimates of the true blank count rate. Given nonnegative weights w_S and w_B such that $w_S + w_B = 1$, the mean blank count rate is estimated by

$$\hat{R}_B = w_S \frac{N_S}{t_S} + w_B \frac{N_B}{t_B} \quad (20.45)$$

⁹ Probabilities on the curve are calculated using the equation

$$P(\mu) = 1 - e^{-\mu} \sum_{n=0}^{\infty} \frac{\mu^n}{n!} \sum_{k=0}^{\lfloor n + 2.33\sqrt{\mu} \rfloor} \frac{\mu^k}{k!}$$

where μ denotes the (true) mean blank count. Terms of the infinite sum are accumulated until the cumulative Poisson probability, $e^{-\mu} \sum_{i=0}^n \mu^i / i!$, approaches 1. The calculated values agree with those listed in Table 1 of Brodsky (1992). The discontinuities occur at $\mu = k^2 / 2.33^2$ for $k = 1, 2, 3, \dots$

This estimator $\hat{R}_B$ is always unbiased under the null hypothesis of zero net activity and no interferences, but the choice of weights affects the variance of the estimator. (When interferences are present, this weighted average is inappropriate.)¹⁰

This attachment will use the notation $\tilde{S}_C$, which is nonstandard, to denote any version of the critical value that depends on the gross signal N_S (or $\hat{Y}$). Then Equations 20.44 and 20.45 imply the following.

$$\tilde{S}_C = z_{1-\alpha} \sqrt{\left(w_S \frac{N_S}{t_S} + w_B \frac{N_B}{t_B} \right) t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.46)$$

It is often convenient to eliminate N_S from the expression for $\tilde{S}_C$ (e.g., when calculating the MDC). When the same measured value of N_B is used to calculate both the critical value $\tilde{S}_C$ and the net signal $\hat{S}$, elimination of N_S from Equation 20.46 produces the following formula for an alternative critical value S_C .¹¹

$$S_C = \frac{z_{1-\alpha}^2 w_S}{2} \left(1 + \frac{t_S}{t_B} \right) + z_{1-\alpha} \sqrt{\frac{z_{1-\alpha}^2 w_S^2}{4} \left(1 + \frac{t_S}{t_B} \right)^2 + N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \quad (20.47)$$

It is not generally true that $S_C = \tilde{S}_C$ unless $w_S = 0$, but either critical value may be used to implement the same test for analyte detection, because $\hat{S} > S_C$ if and only if $\hat{S} > \tilde{S}_C$.

If there is additional non-Poisson variance associated with the blank correction, an extra term may be included under the radical (e.g., $\zeta_B^2 t_S^2$, where ζ_B^2 is as in Equation 20.42), although at very low blank levels the Poisson variance tends to dominate this excess component.

FORMULA A

The most commonly used approach for calculating S_C is given by Formula A (shown below).

¹⁰ The common practice of using the same Poisson measurement data to calculate both the net signal $\hat{S}$ and its critical value tends to produce a correlation between the two variables. This correlation does not exist when the critical value is determined by a statistical evaluation of normally distributed data as described earlier in the attachment.

¹¹ The critical value $\tilde{S}_C$ may be written as a function $f(\hat{S})$ of the observed net signal $\hat{S}$ and the blank count N_B . Then $\hat{S}$ exceeds $\tilde{S}_C$ if and only if it exceeds the fixed point of f , which is the value S_C where $f(S_C) = S_C$. The fixed point is a function of N_B but not of N_S .

$$S_C = z_{1-\alpha} \sqrt{N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \quad (20.48)$$

Formula A

If $\alpha = 0.05$ and $t_B = t_S$, Formula A leads to the well-known expression $2.33\sqrt{N_B}$ for the critical net count (e.g., see Currie, 1968).

Formula A may be derived from Equation 20.44 by using the blank measurement alone to estimate the true blank count rate — i.e., by using the weights $w_S = 0$ and $w_B = 1$.

As noted in Section 20.4.1.2, when the blank count is high (e.g., 100 or more), Formula A works well, but at lower blank levels, it can produce a high rate of Type I errors. Figure 20.4 shows Type I error rates for Formula A as a function of the mean blank count for count time ratios $t_B / t_S = 1$ and 5 when $\alpha = 0.05$.¹²

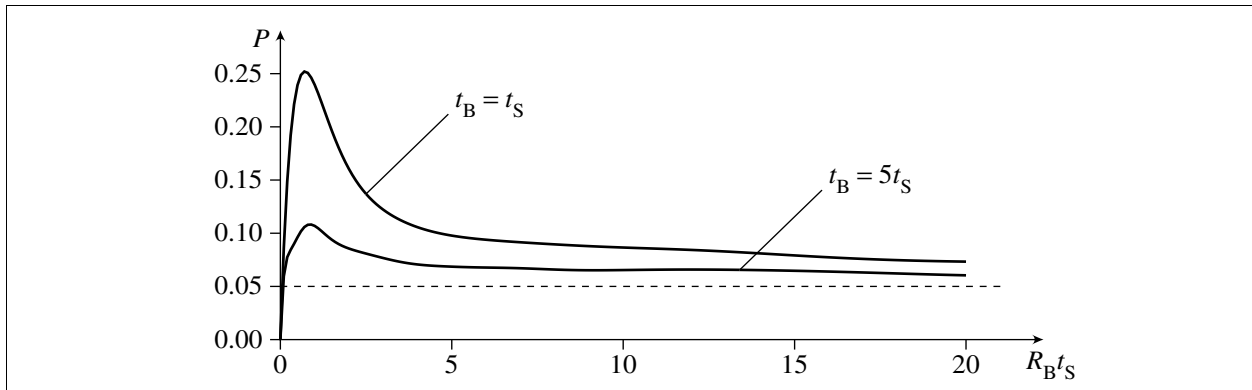


FIGURE 20.4 — Type I error rates for Formula A

¹² Probabilities on the two curves are calculated using the equation

$$P(\mu) = 1 - e^{-\mu(1+t_B/t_S)} \sum_{n=0}^{\infty} \frac{(\mu t_B / t_S)^n}{n!} \sum_{k=0}^{[y_C(n)]} \frac{\mu^k}{k!}$$

where $y_C(n) = S_C(n) + n(t_S / t_B)$ and $\mu = R_B t_S$ (the mean gross count when the sample contains no analyte). The same equation with different expressions for $S_C(n)$ is used to calculate the Type I error rates shown in Figures 20.5–8.

FORMULA B

Another published formula for the critical value is (equivalent to) the following (Nicholson, 1966).

$$\tilde{S}_C = z_{1-\alpha} \sqrt{N_S + N_B \frac{t_S^2}{t_B^2}} \quad (20.49)$$

The critical value calculated by Equation 20.49 equals $z_{1-\alpha}$ times the combined standard uncertainty of the net count. This fact is the basis for the original derivation of the formula, but the formula may also be derived from Equation 20.46 using the weights $w_S = t_B / (t_S + t_B)$ and $w_B = t_S / (t_S + t_B)$ to estimate $\hat{R}_B$. When N_S is eliminated from Equation 20.49, one obtains Formula B (below), which is equivalent to the equation for the critical value given in *Atoms, Radiation, and Radiation Protection* (Turner, 1995).

$$S_C = \frac{z_{1-\alpha}^2}{2} + z_{1-\alpha} \sqrt{\frac{z_{1-\alpha}^2}{4} + N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \quad (20.50)$$

Formula B

Type I error rates for Formula B are shown in Figure 20.5.

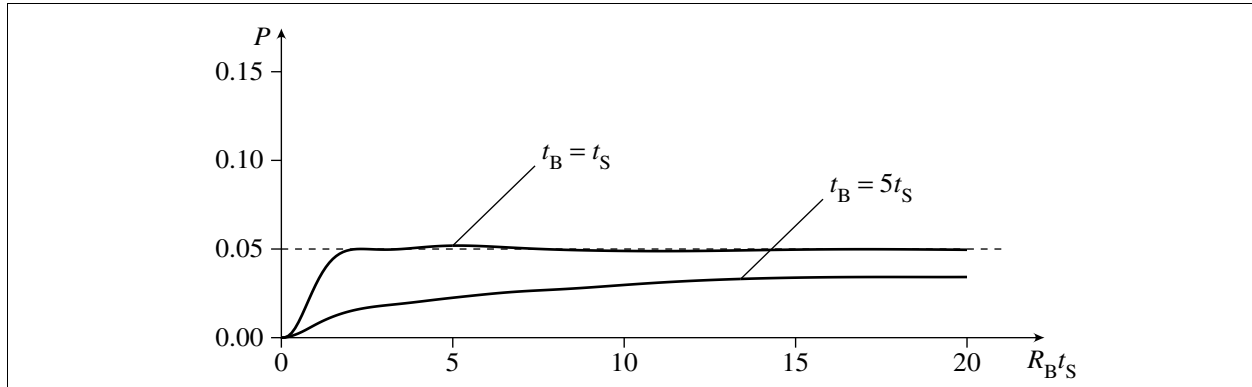


FIGURE 20.5 — Type I error rates for Formula B

Formula B appears natural and intuitive when it is derived in terms of the combined standard uncertainty of the net count, and it gives excellent results when $t_B = t_S$ and the pure Poisson model is valid. However, when the formula is derived using the weights w_S and w_B , as described

above, the expression seems much less natural, because the weights clearly are not optimal when $t_B \neq t_S$. Notice that when $t_B > t_S$, the Type I error rate tends to be less than α .

FORMULA C

If the pure Poisson model is valid, then under the null hypothesis, the weights $w_S = t_S / (t_S + t_B)$ and $w_B = t_B / (t_S + t_B)$ provide the minimum-variance unbiased estimator $\hat{R}_B$ for the mean blank count rate and lead to the following formula for the critical net count (Nicholson, 1963; 1966).¹³

$$\tilde{S}_C = z_{1-\alpha} \sqrt{(N_S + N_B) \frac{t_S}{t_B}} \quad (20.51)$$

Elimination of N_S from Equation 20.51 produces Formula C, shown below.

$$S_C = \frac{z_{1-\alpha}^2 t_S}{2t_B} + z_{1-\alpha} \sqrt{\frac{z_{1-\alpha}^2 t_S^2}{4t_B^2} + N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B}\right)} \quad (20.52)$$

Formula C

Formula C is equivalent to the equation for the “decision threshold” given in Table 1 of ISO 11929-1 for the case of fixed-time counting. Figure 20.6 shows Type I error rates for Formula C.

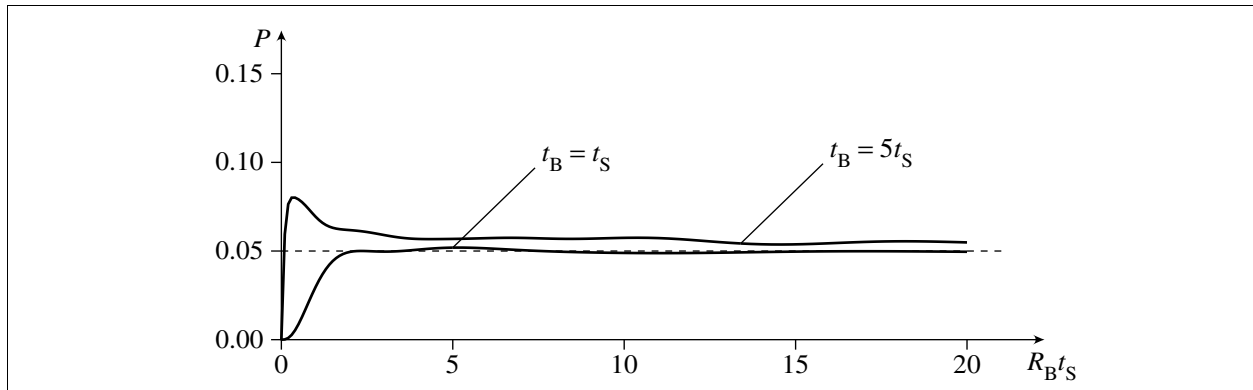


FIGURE 20.6 — Type I error rates for Formula C

¹³ The approach here is conceptually similar to that of a two-sample t -test, which employs a pooled estimate of variance in the comparison of two normal populations.

If the blank correction involves additional non-Poisson variance, an extra term may be included under the radical in Formula C; however, the weights w_S and w_B used to derive the formula are not necessarily optimal in this case. (See ISO 11929-2 for another approach.)

Note that Formulas B and C are equivalent when $t_B = t_S$, because both assign equal weights to the blank measurement and the source measurement. In this case, both formulas are also equivalent to the formula given by Altshuler and Pasternack (1963).

THE STAPLETON APPROXIMATION

When the mean counts are low and $t_B \neq t_S$, another approximation formula for S_C appears to outperform all of the approximations described above. For small values of the constant d , the statistic

$$Z = 2 \left(\sqrt{\frac{N_S + d}{t_S}} - \sqrt{\frac{N_B + d}{t_B}} \right) / \sqrt{\frac{1}{t_S} + \frac{1}{t_B}} \quad (20.53)$$

which involves variance-stabilizing transformations of the Poisson counts N_S and N_B , has a distribution that is approximately standard normal under the null hypothesis (Stapleton, 1999; Strom and MacLellan, 2001). So, the critical value of Z is $z_{1-\alpha}$, the $(1 - \alpha)$ -quantile of the standard normal distribution. From these facts one may derive the following expression for the critical net count as a function of N_B .

$$S_C = d \left(\frac{t_S}{t_B} - 1 \right) + \frac{z_{1-\alpha}^2}{4} \left(1 + \frac{t_S}{t_B} \right) + z_{1-\alpha} \sqrt{(N_B + d) \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \quad (20.54)$$

The Stapleton Approximation

When $\alpha = 0.05$, the value $d = 0.4$ appears to be a near-optimal choice. Then for $t_B = t_S$, the Stapleton approximation gives the equation

$$S_C = 1.35 + 2.33 \sqrt{N_B + 0.4} \quad (20.55)$$

Figure 20.7 shows the Type I error rates for the Stapleton approximation when $\alpha = 0.05$ and $d = 0.4$. This approximation gives Type I error rates almost identical to those of Formulas B and C when $t_B = t_S$, but it has an advantage when $t_B \neq t_S$.

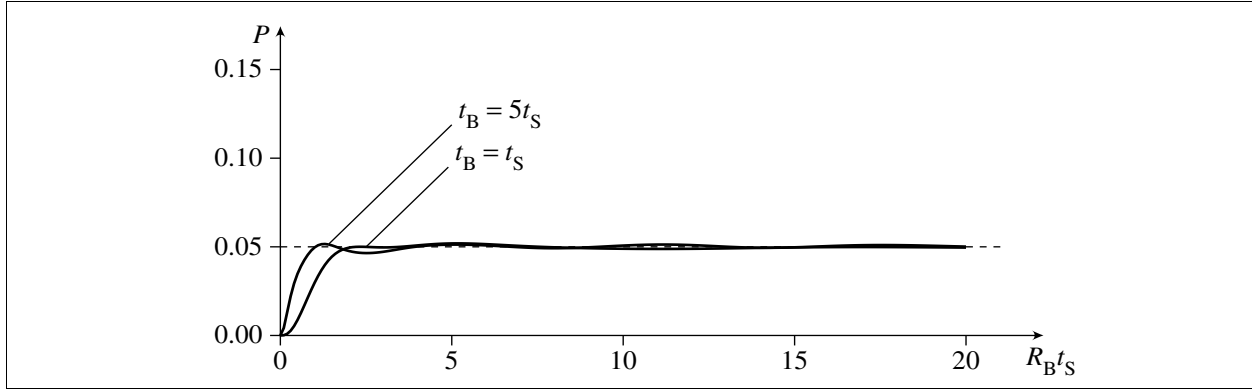


FIGURE 20.7 — Type I error rates for the Stapleton approximation

When $\alpha \neq 0.05$, the value $d = z_{1-\alpha} / 4.112$ appears to give good results ($4.112 = z_{0.95} / 0.4$).

When the blank correction involves a small non-Poisson variance component, a term ($\xi_B^2 t_S^2$) may be included under the radical in Equation 20.54 to account for it.

THE EXACT TEST

Poisson counting statistics also permit an “exact” test for analyte detection, whose Type I error rate is guaranteed to be *no greater than* the chosen value of α , although it may be less. A randomized version of the test can provide a Type I error rate *exactly equal to* α (Nicholson, 1963), but only the nonrandomized version will be considered here, since its outcome is always based solely on the data and not on a random number generator. The test is implemented by rejecting H_0 if and only if the following inequality is true.¹⁴

$$\sum_{k=N_S}^{N_S+N_B} \binom{N_S+N_B}{k} \left(\frac{t_S}{t_S+t_B} \right)^k \left(\frac{t_B}{t_S+t_B} \right)^{N_S+N_B-k} \leq \alpha \quad (20.56)$$

NOTE: For any nonnegative integers n and k , the notation $\binom{n}{k}$ denotes a *binomial coefficient*, usually read “ n choose k ,” which is the number of possible combinations of n objects chosen k at a time. For $0 \leq k \leq n$,

¹⁴ The left-hand side of the inequality is a cumulative binomial probability (see Attachment 19A of Chapter 19). It also equals

$$I_{\frac{t_S}{t_S+t_B}}(N_S, N_B+1)$$

where $I_x(a,b)$ denotes the incomplete beta function (NBS, 1964; Press et al., 1992).

the value of $\binom{n}{k}$ equals $\frac{n!}{k!(n-k)!}$, where the symbol ! denotes the factorial operator. The number of combinations of n objects chosen k at a time is also denoted sometimes by ${}_nC_k$.

Nicholson presents the test as a comparison of the gross count N_S to a critical value. The critical value $\tilde{y}_C$ is the smallest nonnegative integer n such that¹⁵

$$\sum_{k=0}^n \binom{N_S + N_B}{k} \left(\frac{t_S}{t_S + t_B} \right)^k \left(\frac{t_B}{t_S + t_B} \right)^{N_S + N_B - k} \geq 1 - \alpha \quad (20.57)$$

The same (nonrandomized) test is implemented by calculating a critical gross count, y_C , equal to the smallest nonnegative integer, n , such that

$$\sum_{k=0}^n \binom{N_B + k}{N_B} \left(\frac{t_S}{t_S + t_B} \right)^k \geq (1 - \alpha) \left(\frac{t_S + t_B}{t_B} \right)^{N_B + 1} \quad (20.58)$$

Then the critical net count, S_C , equals $y_C - N_B(t_S / t_B)$. (Note that Inequality 20.58 is intended for use when N_B is small.) Table G.4 in Appendix G lists critical values y_C for $\alpha = 0.01$ and 0.05 and for integral values of the count time ratio, t_B / t_S , ranging from 1 to 5.

Figure 20.8 shows the Type I error rates for the nonrandomized exact test. (The Type I error rate for the randomized version of the test equals 0.05 everywhere.)

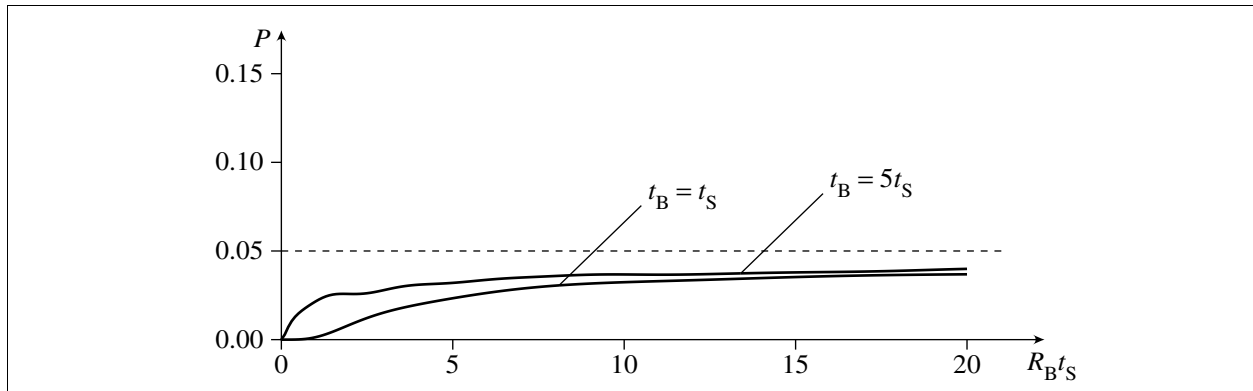


FIGURE 20.8 — Type I error rates for the nonrandomized exact test

¹⁵ To implement the randomized test, calculate the critical value $\tilde{y}_C$, and, if $N_S > \tilde{y}_C$, reject H_0 , as in the non-randomized test. If $N_S = \tilde{y}_C$, calculate a rejection probability P by subtracting $1 - \alpha$ from the sum on the left-hand side of the inequality (with $n = N_S$) and dividing the difference by the summation's last term

$$\binom{N_S + N_B}{N_S} \left(\frac{t_S}{t_S + t_B} \right)^{N_S} \left(\frac{t_B}{t_S + t_B} \right)^{N_B}$$

Then reject H_0 with probability P .

EXAMPLE 20.10

Problem: A 60,000-second blank measurement is performed on an alpha-particle spectrometer and 4 counts are observed in a region of interest. A test source is to be counted for 60,000 s. Use the methods described in this attachment to estimate the critical value of the net count when $\alpha = 0.05$.

Solution: Table 20.1 should not be used in this case, because the ratio of count times, t_B / t_S , is too small.

Formula A gives the result

$$\begin{aligned} S_C &= z_{1-\alpha} \sqrt{N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\ &= 1.645 \sqrt{4 \left(\frac{60,000 \text{ s}}{60,000 \text{ s}} \right) \left(1 + \frac{60,000 \text{ s}}{60,000 \text{ s}} \right)} \\ &= 4.65 \text{ net counts.} \end{aligned}$$

Formula B gives the result

$$\begin{aligned} S_C &= \frac{z_{1-\alpha}^2}{2} + z_{1-\alpha} \sqrt{\frac{z_{1-\alpha}^2}{4} + N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\ &= \frac{1.645^2}{2} + 1.645 \sqrt{\frac{1.645^2}{4} + 4 \left(\frac{60,000 \text{ s}}{60,000 \text{ s}} \right) \left(1 + \frac{60,000 \text{ s}}{60,000 \text{ s}} \right)} \\ &= 6.20 \text{ net counts.} \end{aligned}$$

Formula C gives the result

$$\begin{aligned} S_C &= \frac{z_{1-\alpha}^2 t_S}{2 t_B} + z_{1-\alpha} \sqrt{\frac{z_{1-\alpha}^2 t_S^2}{4 t_B^2} + N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\ &= \frac{1.645^2 (60,000 \text{ s})}{2 (60,000 \text{ s})} + 1.645 \sqrt{\frac{1.645^2 (60,000 \text{ s})^2}{4 (60,000 \text{ s})^2} + 4 \left(\frac{60,000 \text{ s}}{60,000 \text{ s}} \right) \left(1 + \frac{60,000 \text{ s}}{60,000 \text{ s}} \right)} \\ &= 6.20 \text{ net counts.} \end{aligned}$$

Notice that Formula B and Formula C give the same result, because $t_S = t_B$.

The Stapleton approximation (with $d = 0.4$) gives the result

$$\begin{aligned}
 S_C &= d \left(\frac{t_S}{t_B} - 1 \right) + \frac{z_{1-\alpha}^2}{4} \left(1 + \frac{t_S}{t_B} \right) + z_{1-\alpha} \sqrt{(N_B + d) \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\
 &= 0.4 \left(\frac{60,000}{60,000} - 1 \right) + \frac{1.645^2}{4} \left(1 + \frac{60,000}{60,000} \right) + 1.645 \sqrt{(4 + 0.4) \left(\frac{60,000}{60,000} \right) \left(1 + \frac{60,000}{60,000} \right)} \\
 &= 6.23 \text{ net counts.}
 \end{aligned}$$

The exact test gives the result $y_C = 11$ counts (the entry in Table G.4 for $\alpha = 0.05$, $t_B / t_S = 1$, and $N_B = 4$), which implies that

$$S_C = 11 - (4)(60,000 / 60,000) = 7 \text{ net counts.}$$

EXAMPLE 20.11

Problem: Consider again the problem presented in Example 20.1. A 6000-second blank measurement is performed on a proportional counter and 108 beta counts are observed. A test source is to be counted for 3000 s. Use the methods described in this attachment to estimate the critical value of the net count when $\alpha = 0.05$.

Solution: Again, Table 20.1 should not be used, because the ratio of count times, t_B / t_S , is too small.

Formula A gives the result

$$\begin{aligned}
 S_C &= z_{1-\alpha} \sqrt{N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\
 &= 1.645 \sqrt{108 \left(\frac{3000}{6000} \right) \left(1 + \frac{3000}{6000} \right)} \\
 &= 14.8 \text{ net counts.}
 \end{aligned}$$

Notice that this is the same result that was obtained in Example 20.1.

Formula B is not recommended. Since $t_B > t_S$ in this case, Formula B produces a Type I error rate that is less than α .

Formula C gives the result

$$\begin{aligned}
 S_C &= \frac{z_{1-\alpha}^2 t_S}{2t_B} + z_{1-\alpha} \sqrt{\frac{z_{1-\alpha}^2 t_S^2}{4t_B^2} + N_B \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B}\right)} \\
 &= \frac{(1.645)^2(3000)}{2(6000)} + 1.645 \sqrt{\frac{(1.645)^2(3000)^2}{4(6000)^2} + 108 \left(\frac{3000}{6000}\right) \left(1 + \frac{3000}{6000}\right)} \\
 &= 15.5 \text{ net counts.}
 \end{aligned}$$

The Stapleton approximation (with $d = 0.4$) gives the result

$$\begin{aligned}
 S_C &= d \left(\frac{t_S}{t_B} - 1 \right) + \frac{z_{1-\alpha}^2}{4} \left(1 + \frac{t_S}{t_B} \right) + z_{1-\alpha} \sqrt{(N_B + d) \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \\
 &= 0.4 \left(\frac{3000}{6000} - 1 \right) + \frac{1.645^2}{4} \left(1 + \frac{3000}{6000} \right) + 1.645 \sqrt{(108 + 0.4) \left(\frac{3000}{6000} \right) \left(1 + \frac{3000}{6000} \right)} \\
 &= 15.6 \text{ net counts.}
 \end{aligned}$$

The exact test gives the result $y_C = 70$ counts (the entry in Table G.4 for $\alpha = 0.05$, $t_B / t_S = 2$, and $N_B = 108$), which implies that

$$S_C = 70 - (108)(3000 / 6000) = 16 \text{ net counts.}$$

COMPARISONS AND RECOMMENDATIONS

Although Formula A gives the highest Type I error rates of all the formulas described above in the pure Poisson counting scenario, it is the formula that can be adapted most easily for dealing with interferences. It can also be modified to reduce the very high Type I error rates at low blank levels (by adding 1 or 2 to the number of blank counts N_B under the radical). Formula B cannot be recommended. When the pure Poisson model is valid, Formula C gives better results than either A or B, but the Stapleton approximation appears to give the most predictable Type I error rates of all. Nicholson's exact test is the only one of the tests whose Type I error rate is guaranteed not to exceed the chosen significance level, but it is also the most complicated of the tests and requires either software or lookup tables to be practical. Furthermore, the nonrandomized version of the test has relatively low power. Achieving the chosen significance level exactly

appears to require the randomized version of Nicholson's test. Using critical values from Table 20.1 is appropriate when the blank is counted much longer than the sample and the expected count for an analyte-free sample is very low.

MARLAP makes the following recommendations regarding the use of the various equations for the critical value when Poisson statistics are assumed:

- A laboratory should confirm the validity of the Poisson approximation before using Table 20.1, Formula A, Formula C, Stapleton's approximation, Nicholson's exact test, or any other detection criterion that is based on pure Poisson counting statistics. (If the Poisson approximation is invalid, the blank distribution should be determined by repeated measurements.)
- If the blank count time is at least 10 times longer than the sample count time, the critical gross counts in Table 20.1 can be used.
- If the mean blank count is at least 100, Formula A can be used and may be preferred for its relative simplicity.
- Formula B for the critical value should not be used.
- If the ratio of count times, t_B / t_S , is not large, and if the mean blank count is less than 100, either Formula C or Stapleton's approximation should be used. Stapleton's approximation seems to have an advantage over Formula C when $t_S \neq t_B$.
- Nicholson's exact test may be used to compare the means of two Poisson distributions when a high level of statistical rigor is required, but it is more complicated than necessary for routine laboratory analyses and lacks the power of Formula C and Stapleton's approximation.¹⁶

20A.3 Calculation of the Minimum Detectable Concentration

The minimum detectable concentration, or MDC, was defined earlier as the concentration of analyte, x_D , that must be present in a laboratory sample to give a probability $1 - \beta$ of obtaining a measured response greater than its critical value. Equivalently, the MDC is defined as the analyte concentration x_D that satisfies the relation

$$\Pr[\hat{S} \leq S_C | X = x_D] = \beta \quad (20.59)$$

where the expression $\Pr[\hat{S} \leq S_C | X = x_D]$ may be read as "the probability that the net signal $\hat{S}$ does not exceed its critical value S_C when the true concentration X is equal to x_D ."

The MDC may be estimated by calculating the minimum detectable value of the net instrument signal, S_D , and converting the result to a concentration. Recall that the minimum detectable value

¹⁶ The reduced power of the exact test at low blank levels is evident from the low Type I error rates shown in Figure 20.8.

of the net instrument signal is defined as the mean value of the net signal that gives a specified probability, $1 - \beta$, of yielding an observed signal greater than its critical value S_C . Thus,

$$\Pr[\hat{S} \leq S_C | S = S_D] = \beta \quad (20.60)$$

where S denotes the true mean net signal.

20A.3.1 Normally Distributed Signals

If the net signal, $\hat{S}$, is normally distributed and its estimated standard deviation, $\hat{\sigma}_0$, under H_0 is determined from a statistical evaluation with ν degrees of freedom (e.g., $n = \nu + 1$ replicate blank measurements), then the critical value of $\hat{S}$ is

$$S_C = t_{1-\alpha}(\nu) \times \hat{\sigma}_0 \quad (20.61)$$

Then, if the variance of $\hat{S}$ is constant at all concentrations – or at least can be considered constant at sufficiently low concentrations – the minimum detectable value of the signal is given by

$$S_D = \delta_{\alpha,\beta,\nu} \sigma_0 \quad (20.62)$$

where $\delta_{\alpha,\beta,\nu}$ denotes the noncentrality parameter of a noncentral t -distribution with ν degrees of freedom. The parameter $\delta_{\alpha,\beta,\nu}$ is such that

$$t'_{\beta}(\nu, \delta_{\alpha,\beta,\nu}) = t_{1-\alpha}(\nu) \quad (20.63)$$

where $t'_{\beta}(\nu, \delta_{\alpha,\beta,\nu})$ denotes the β -quantile of the noncentral t -distribution. The noncentrality parameter $\delta_{\alpha,\beta,\nu}$ may be approximated by

$$\delta_{\alpha,\beta,\nu} \approx t_{1-\alpha}(\nu) \times \left(1 - \frac{1}{4\nu} \right) + z_{1-\beta} \sqrt{1 + \frac{t_{1-\alpha}(\nu)^2}{2\nu}} \quad (20.64)$$

which is based on an approximation for the noncentral t distribution function (NBS, 1964). When $\alpha = \beta = 0.05$ and $\nu \geq 4$, the noncentrality parameter is also approximated adequately by $t_{0.95}(\nu) \times 8\nu / (4\nu + 1)$ (Currie, 1997).

Conceptually the standard deviation $\hat{\sigma}_0$ used to calculate the critical value, S_C , is only an estimate and therefore can be considered a random variable. If it were the true standard deviation, the correct multiplier used to calculate S_C would be $z_{1-\alpha}$, not $t_{1-\alpha}(\nu)$. However, the standard deviation used to calculate S_D is, conceptually at least, the true standard deviation σ_0 , even if its value is not known exactly. The true standard deviation may be estimated by $\hat{\sigma}_0$, but since the estimator $\hat{\sigma}_0$ is

biased, a correction factor should be used for ν less than about 20.¹⁷ An unbiased estimator for σ_0 is $\hat{\sigma}_0 / c_4$, where

$$c_4 = \frac{\Gamma\left(\frac{\nu+1}{2}\right)}{\Gamma\left(\frac{\nu}{2}\right)} \sqrt{\frac{2}{\nu}} \quad (20.65)$$

and where Γ denotes the *gamma function* (NBS, 1964). The gamma function is easily computed in software (Press et al., 1992), but c_4 is also approximated well by $4\nu / (4\nu + 1)$, and values of c_4 are commonly tabulated in references for statistical quality control (whence the notation c_4 is borrowed). Then S_D is estimated by

$$S_D = \delta_{\alpha,\beta,\nu} \frac{\hat{\sigma}_0}{c_4} \quad (20.66)$$

which is approximately $2 t_{0.95}(\nu) \hat{\sigma}_0$, or $2 S_C$, when $\alpha = \beta = 0.05$ and $\nu \geq 4$. Values of c_4 for $\nu = 1$ to 40 are listed in Table 20.2.

TABLE 20.2 — Bias factor for the experimental standard deviation

ν	c_4	ν	c_4	ν	c_4	ν	c_4
1	0.79788	11	0.97756	21	0.98817	31	0.99197
2	0.88623	12	0.97941	22	0.98870	32	0.99222
3	0.92132	13	0.98097	23	0.98919	33	0.99245
4	0.93999	14	0.98232	24	0.98964	34	0.99268
5	0.95153	15	0.98348	25	0.99005	35	0.99288
6	0.95937	16	0.98451	26	0.99043	36	0.99308
7	0.96503	17	0.98541	27	0.99079	37	0.99327
8	0.96931	18	0.98621	28	0.99111	38	0.99344
9	0.97266	19	0.98693	29	0.99142	39	0.99361
10	0.97535	20	0.98758	30	0.99170	40	0.99377

EXAMPLE 20.12

Problem: Use the blank data from Example 20.10 to calculate the minimum detectable net signal, S_D . Assume the variance of the net signal, $\hat{S}$, is approximately constant at low analyte concentrations.

¹⁷ Although $\hat{\sigma}_0^2$ is assumed here to be an unbiased estimator for the variance, its square root, $\hat{\sigma}_0$, is a biased estimator for the standard deviation (see Section 19.4.5.2 in Chapter 19).

Solution: In Example 20.9 the standard deviation of the blank, s_B , based on seven replicate measurements was found to be 8.5912. The estimated standard deviation of the net signal therefore is

$$\hat{\sigma}_0 = (8.5912) \sqrt{1 + \frac{1}{7}} = 9.1844$$

The number of degrees of freedom, ν , equals $7 - 1 = 6$. So, the value of the noncentrality parameter, $\delta_{\alpha, \beta, \nu}$, may be approximated as follows.

$$\begin{aligned} t_{1-\alpha}(\nu) &= t_{0.95}(6) = 1.943 \\ \delta_{\alpha, \beta, \nu} &= t_{1-\alpha}(\nu) \times \left(1 - \frac{1}{4\nu}\right) + z_{1-\alpha} \sqrt{1 + \frac{t_{1-\alpha}(\nu)^2}{2\nu}} \\ &= 1.943 \times \left(1 - \frac{1}{(4)(6)}\right) + 1.645 \sqrt{1 + \frac{1.943^2}{(2)(6)}} \\ &= 3.748 \end{aligned}$$

The value of c_4 for 6 degrees of freedom is 0.95937. So,

$$S_D = \delta_{\alpha, \beta, \nu} \frac{\hat{\sigma}_0}{c_4} = (3.748) \frac{9.1844}{0.95937} = 35.88.$$

If the variance of $\hat{S}$ is not constant but increases with the mean signal S , the minimum detectable net signal is determined implicitly by the equation

$$t_{\beta}'\left(\nu, \frac{S_D}{\sigma_D}\right) = t_{1-\alpha}(\nu) \times \frac{\sigma_0}{\sigma_D} \quad (20.67)$$

where σ_D denotes the standard deviation of $\hat{S}$ when $S = S_D$. An iterative algorithm, such as the one shown below, may be needed to solve the equation for S_D .

1. Set $\sigma_0 = \sqrt{\sigma^2(\hat{S} | S = 0)}$
 2. Initially calculate $S_D = t_{1-\alpha}(\nu) \times \sigma_0$
 3. **repeat loop (Lines 4–7)**
 4. Set $\sigma_D = \sqrt{\sigma^2(\hat{S} | S = S_D)}$
-

5. Find the value of δ such that $t_{\beta}'(v, \delta) = t_{1-\alpha}(v) \times \sigma_0 / \sigma_D$
6. Set $h = S_D$
7. Recalculate $S_D = \delta \sigma_D$
8. **until** $|S_D - h|$ is sufficiently small
9. **output** the solution S_D

The value of the noncentrality parameter δ in Step 5 may be approximated by

$$\delta \approx \left(t_{1-\alpha}(v) \times \frac{\sigma_0}{\sigma_D} \right) \left(1 - \frac{1}{4v} \right) + z_{1-\beta} \sqrt{1 + \frac{(t_{1-\alpha}(v) \times \sigma_0 / \sigma_D)^2}{2v}} \quad (20.68)$$

When $\hat{\sigma}_0$ is determined by any means other than a statistical evaluation, S_D must be calculated differently.

EXAMPLE 20.13

Problem: Assume the signal, $\hat{S}$, is the net count for a radioactivity measurement, and its variance is given by an expression of the form

$$aS^2 + bS + c$$

The coefficient b is assumed to be 1, because the term bS represents the Poisson counting variance due to activity in the sample (see Section 20.4.2.2). The term c is estimated by $\hat{\sigma}_0^2$, the variance of the net signal observed when analyte-free samples are analyzed. The coefficient a is estimated to be 0.05^2 , and represents a 5 % coefficient of variation, which is observed at high analyte concentrations. Assume $\hat{\sigma}_0$ is evaluated from 7 replicate blank measurements and is found to be 9.1844, as in the preceding example. Use the iterative algorithm described above to approximate the minimum detectable net signal, S_D .

Solution: The first two steps are performed as follows.

$$\begin{aligned} \sigma_0 &= 9.1844 \\ S_D &= 1.943 \times 9.1844 = 17.85 \end{aligned}$$

Then the first iteration of the loop is performed as follows.

$$\begin{aligned}\sigma_D &= \sqrt{(0.05)^2(17.85)^2 + 17.85 + (9.1844)^2} = 10.149 \\ t_{1-\alpha}(v) \times \frac{\sigma_0}{\sigma_D} &= 1.943 \times \frac{9.1844}{10.149} = 1.7584 \\ \delta &= 1.7584 \times \left(1 - \frac{1}{(4)(6)}\right) + 1.645 \sqrt{1 + \frac{1.7584^2}{(2)(6)}} = 3.5298 \\ S_D &= (3.5298)(10.149) = 35.822\end{aligned}$$

Subsequent iterations produce the sequence of approximations

$$37.242 \quad 37.354 \quad 37.363 \quad 37.364 \quad 37.364 \quad \dots$$

The sequence converges to 37.364, which is the approximate value of the minimum detectable net signal.

20A.3.2 Poisson Counting

Another equation for S_D , which was described in Section 20.4.2.2, is

$$S_D = S_C + z_{1-\beta} \sqrt{\sigma^2(\hat{S} | S = S_D)} \quad (20.69)$$

where $S_C = z_{1-\alpha} \sigma_0$ and $\sigma^2(\hat{S} | S = S_D)$ denotes the variance of the measured signal, $\hat{S}$, when the true mean signal, S , equals S_D . This equation is the basis for formulas that are commonly used for S_D when the Poisson-normal approximation is assumed. Regardless of whether the signal follows the pure Poisson model or has non-Poisson variance, the variance of $\hat{S}$ can usually be expressed in the form

$$\sigma^2(\hat{S}) = aS^2 + bS + c \quad (20.70)$$

as in Example 20.13, where S denotes the true mean net signal and the constants a , b , and c do not depend on S . In this case, the minimum detectable net signal is given by

$$S_D = \frac{1}{I_\beta} \left(S_C + \frac{z_{1-\beta}^2 b}{2} + z_{1-\beta} \sqrt{bS_C + \frac{z_{1-\beta}^2 b^2}{4} + aS_C^2 + I_\beta c} \right) \quad (20.71)$$

where $I_\beta = 1 - z_{1-\beta}^2 a$.

Equation 20.69 is often used even when S_C is calculated using one of the formulas presented above for low-background Poisson counting, with $R_B t_B$ substituted for the blank count N_B , but in this case S_D may be underestimated because of the fact that the calculated value of S_C varies from measurement to measurement. One option for obtaining a more conservative estimate of S_D is to substitute a conservative value of S_C , which will be denoted here by $[S_C]$. For Poisson counting, one method of obtaining $[S_C]$ is to use the value of S_C calculated from the largest blank count N_B likely to be observed, given the assumed mean blank count rate R_B (e.g., use Table 20.1 with $R_B t_B$ replacing $R_B t_S$ and N_B replacing y_C in the column headings). To calculate S_D , one may substitute $[S_C]$ for S_C in Equation 20.71.

Note that $[S_C]$ is not used to make detection decisions. It is used only to calculate S_D .

For example, suppose $\alpha = \beta = 0.05$, the assumed mean blank count rate is $R_B = 8 \times 10^{-4} \text{ s}^{-1}$, and the blank count time is $t_B = 6000 \text{ s}$. Then $R_B t_B = 4.8$ counts. Using Table 20.1, one finds 4.8 in the first column between 4.695 and 5.425, and reads the value 9 from the second column. So, 9 is the largest value of N_B likely to be observed when measuring a blank. Now, if Stapleton's approximation is used to calculate S_C when making a detection decision, the value of $[S_C]$ used to calculate S_D is given by the following equation.

$$[S_C] = 0.4 \left(\frac{t_S}{t_B} - 1 \right) + \frac{1.645^2}{4} \left(1 + \frac{t_S}{t_B} \right) + 1.645 \sqrt{(9 + 0.4) \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B} \right)} \quad (20.72)$$

So, if $t_S = t_B$, then $[S_C] = 8.49$ counts.

PURE POISSON COUNTING

As previously noted, counting data never follow the Poisson model exactly, but the model can be used to calculate S_D if the variance of the blank signal is approximately Poisson and a conservative value of the sensitivity factor is used to convert S_D to x_D . Equation 20.28, which is repeated below as Equation 20.73, shows how to calculate S_D using the pure Poisson model.

$$S_D = S_C + \frac{z_{1-\beta}^2}{2} + z_{1-\beta} \sqrt{\frac{z_{1-\beta}^2}{4} + S_C + R_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.73)$$

When Formula A is used for the critical net count, and $\alpha = \beta$, this expression for S_D simplifies to $z_{1-\beta}^2 + 2S_C$. Example 20.5 in Section 20.4.2.3 illustrates the use of the latter expression.

DETECTION LIMITS FOR THE STAPLETON APPROXIMATION

When the Stapleton approximation is used for S_C , the minimum detectable net count S_D may be calculated using Equation 20.73, but when the pure Poisson model is assumed, a better estimate is given by the formula

$$S_D = \frac{(z_{1-\alpha} + z_{1-\beta})^2}{4} \left(1 + \frac{t_S}{t_B} \right) + (z_{1-\alpha} + z_{1-\beta}) \sqrt{R_B t_S \left(1 + \frac{t_S}{t_B} \right)} \quad (20.74)$$

Equation 20.74 also gives a better approximation of S_D even when Formula C is used for the critical value as long as the ratio of count times t_B / t_S is not too far from 1 (see Table 20.3). It is recommended by ISO 11929-1 in a slightly different but equivalent form.

When $\alpha = \beta = 0.05$ and $t_B = t_S$, the preceding equation becomes

$$S_D = 5.41 + 4.65 \sqrt{R_B t_S} \quad (20.75)$$

PRECISE CALCULATION OF S_D

When the pure Poisson model is assumed, with no other sources of variance, the mean blank count rate R_B and the analyte detection criteria completely determine S_D . So, in principle, a computer program can be written to calculate S_D precisely. The calculation is most easily described when the critical net count is expressed in terms of N_B but not N_S (e.g., S_C as defined by Formulas A–C, the Stapleton approximation, and the exact test). Then, at any specified value S of the mean net signal, the power of the detection test can be computed using either of the following expressions:

$$\begin{aligned} \text{Power} &= 1 - \sum_{n=0}^{\infty} \frac{(R_B t_B)^n e^{-R_B t_B}}{n!} \sum_{k=0}^{[y_C(n)]} \frac{(R_B t_S + S)^k e^{-(R_B t_S + S)}}{k!} \\ &= 1 - \exp(-R_B(t_S + t_B) - S) \sum_{n=0}^{\infty} \frac{(R_B t_B)^n}{n!} \sum_{k=0}^{[y_C(n)]} \frac{(R_B t_S + S)^k}{k!} \end{aligned} \quad (20.76)$$

where $y_C(n)$ denotes the value of y_C (or $S_C + N_B t_S / t_B$) when $N_B = n$. Terms of the infinite sum must be accumulated only until the cumulative Poisson probability, $e^{-R_B t_B} \sum_{m=0}^n (R_B t_B)^m / m!$, approaches 1. Given a software procedure to compute Equation 20.76, the value of S_D may be determined using an iterative algorithm, such as Newton's method or bisection, which calculates

the power at trial values of S until the correct value is found where the power equals $1 - \beta$ (e.g. see Burden and Faires, 1993).

Since no sources of variance except Poisson counting statistics are being considered here, a conservative value of the sensitivity factor should be used when converting S_D to the minimum detectable concentration, x_D .

A procedure of the type described above generated the true values of S_D for Table 20.3, which shows both the estimated and true values of S_D obtained when Formulas A and C and the Stapleton approximation are used for the critical value. The estimated values of S_D in this table are based on values of S_C calculated using the true mean blank count, not the upper bound $[N_B]$. The use of $[N_B]$ would produce larger estimates.

If one can assume that the sensitivity, A , has a particular distribution, such as a rectangular or triangular distribution, then it is still possible to calculate S_D precisely in software, although the mathematics is less straightforward than that needed when only Poisson variance is considered. At any specified value, S , of the mean net signal, the detection power equals

$$Power = 1 - e^{-R_B t_B} \sum_{n=0}^{\infty} \frac{(R_B t_B)^n}{n!} \sum_{k=0}^{[y_C(n)]} f(k; S) \quad (20.77)$$

where $f(k; S)$ is the probability that the gross count will equal k when the mean net signal is S . Given an assumed distribution for A , the value of $f(k; S)$ can be calculated in software. For example, if the sensitivity has a rectangular distribution with mean μ_A and half-width δ , then

$$f(k; S) = \frac{1}{2\delta x} \left(P\left(k+1, R_B t_S + S\left(1 + \frac{\delta}{\mu_A}\right)\right) - P\left(k+1, R_B t_S + S\left(1 - \frac{\delta}{\mu_A}\right)\right) \right) \quad (20.78)$$

where $P(\cdot, \cdot)$ denotes the incomplete gamma function. Other combinations of the incomplete gamma function appear when different polygonal distributions are assumed (e.g., triangular).

To the extent that this approach accounts for the variance of the sensitivity, A , it becomes unnecessary to assume a conservative value of A when converting S_D to x_D . Instead, one uses the best available estimates of the actual distribution parameters (e.g., μ_A and δ above).

TABLE 20.3 — Estimated and true values of S_D ($t_B = t_S$)

Mean Blank Count	Formula A		Formula C		Stapleton	
	Estimated by Eq. 20.73	True	Estimated by Eq. 20.73	True	Estimated by Eq. 20.74	True
0	2.706	2.996	7.083	6.296	5.411	6.296
1	7.358	8.351	9.660	10.095	10.063	10.095
2	9.285	10.344	11.355	12.010	11.991	12.010
3	10.764	11.793	12.719	13.551	13.469	13.551
4	12.010	13.021	13.894	14.826	14.716	14.826
5	13.109	14.091	14.942	15.930	15.814	15.930
6	14.101	15.076	15.897	16.902	16.807	16.902
7	15.015	16.028	16.780	17.785	17.720	17.785
8	15.864	16.945	17.605	18.614	18.570	18.614
9	16.663	17.804	18.383	19.406	19.368	19.406
10	17.418	18.595	19.120	20.170	20.123	20.170
11	18.136	19.324	19.823	20.903	20.841	20.903
12	18.822	20.002	20.496	21.602	21.527	21.602
13	19.480	20.642	21.142	22.267	22.185	22.267
14	20.113	21.257	21.764	22.900	22.819	22.900
15	20.724	21.854	22.366	23.506	23.430	23.506
16	21.315	22.438	22.948	24.091	24.020	24.091
17	21.888	23.010	23.513	24.657	24.593	24.657
18	22.444	23.569	24.062	25.206	25.149	25.206
19	22.985	24.116	24.596	25.738	25.690	25.738
20	23.511	24.649	25.116	26.252	26.217	26.252

20A.4 References

Altshuler, Bernard, and Bernard Pasternack. 1963. Statistical Measures of the Lower Limit of Detection of a Radioactivity Counter. *Health Physics* 9: 293–298.

Brodsky, Allen. 1992. Exact Calculation of Probabilities of False Positives and False Negatives for Low Background Counting. *Health Physics* 63(2): 198–204.

Burden, Richard L., and J. Douglas Faires. 1993. *Numerical Analysis*, 5th ed. PWS Publishing Company, Boston, MA.

- Currie, Lloyd A. 1968. Limits for Qualitative Detection and Quantitative Determination: Application to Radiochemistry. *Analytical Chemistry* 40(3): 586–593.
- Currie, L.A. 1997. Detection: International Update, and Some Emerging Di-lemmas Involving Calibration, the Blank, and Multiple Detection Decisions. *Chemometrics and Intelligent Laboratory Systems* 37: 151–181.
- International Organization for Standardization (ISO). 1997. *Capability of Detection – Part 1: Terms and Definitions*. ISO 11843-1. ISO, Geneva, Switzerland.
- International Organization for Standardization (ISO). 2000. *Determination of the Detection Limit and Decision Threshold for Ionizing Radiation Measurements – Part 1: Fundamentals and Application to Counting Measurements without the Influence of Sample Treatment*. ISO 11929-1. ISO, Geneva, Switzerland.
- International Organization for Standardization (ISO). 2000. *Determination of the Detection Limit and Decision Threshold for Ionizing Radiation Measurements – Part 2: Fundamentals and Application to Counting Measurements with the Influence of Sample Treatment*. ISO 11929-2. ISO, Geneva, Switzerland.
- International Union of Pure and Applied Chemistry (IUPAC). 1995. Nomenclature in Evaluation of Analytical Methods Including Detection and Quantification Capabilities. *Pure and Applied Chemistry* 67(10): 1699–1723.
- Lochamy, Joseph C. 1976. *The Minimum Detectable Activity Concept*. NBS Report No. NBS-SP456, National Bureau of Standards, Gaithersburg, MD.
- National Bureau of Standards (NBS). 1964. *Handbook of Mathematical Functions*. Applied Mathematics Series 55, National Bureau of Standards, Gaithersburg, MD.
- Nicholson, W.L. 1963. *Fixed Time Estimation of Counting Rates with Background Corrections*. AEC Research and Development Report HW-76279.
- Nicholson, W.L. 1966. Statistics of Net-counting-rate Estimation with Dominant Background Corrections. *Nucleonics* 24(8): 118–121.
- Nuclear Regulatory Commission (NRC). 1984. *Lower Limit of Detection: Definition and Elaboration of a Proposed Position for Radiological Effluent and Environmental Measurements*. NUREG/CR-4007. NRC, Washington, DC.
- Press, William H., et al. 1992. *Numerical Recipes in C: The Art of Scientific Computing*, 2nd ed. Cambridge University Press, New York, NY.

Stapleton, James H. 1999. Personal correspondence. Department of Statistics and Probability, Michigan State University.

Strom, Daniel J., and Jay A. MacLellan. 2001. Evaluation of Eight Decision Rules for Low-Level Radioactivity Counting. *Health Physics* 81(1): 27–34.

Strom, Daniel J., and Paul S. Stansbury. 1992. Minimum Detectable Activity When Background Is Counted Longer than the Sample. *Health Physics* 63(3): 360–361.

Turner, James E. 1995. *Atoms, Radiation, and Radiation Protection*, 2nd ed. John Wiley and Sons, New York, NY.