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Capability of detection —

Part 8: Guidance for the implementation of the ISO 11843 series

Capacité de détection —

Partie 8: Recommandations pour la mise en œuvre de la série ISO 11843

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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This document was prepared by Technical Committee ISO/TC 69, *Applications of statistical methods*, Subcommittee SC 6, *Measurement methods and results*.

A list of all parts in the ISO 11843 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

0 Introduction

0.1 General

The purpose of this document is to facilitate the dissemination of the principles and methods of the ISO 11843 series on a global scale by providing a brief explanation of the background of its development, the significance of defining detection limits, the historical variation of the term detection limit, the modern concept of detection limit, and basic ideas of statistics and of each part of this series, intelligible to analytical chemists, biologists, operators, technicians, and others in various fields.

The series ISO 11843 provides statistical theories and some practical applications in a mathematically strict way. This guidance is put forth with the goal of guiding laymen in statistics in practicing the statistics of detection limits, not offering the in-depth knowledge of the relevant mathematics, but making them aware of some of the challenges of using statistical theory and the reasons for success and failure in using the formulae included in the series.

0.2 Background

The concept of detection limit was first described in 1949[1]; after that, a number of scientists submitted papers on the definition of detection limit[2][3]. Scientists in different countries have used detection limits with different definitions.

In order to avoid such global confusion, the International Union of Pure and Applied Chemistry (IUPAC) began considering the introduction of a modern detection limit using a new definition based on statistics. Representatives of the IUPAC and the International Organization for Standardization (ISO) met between 1993 and 1997 to begin efforts to develop a harmonized international chemical-metrological position on detection and quantification capabilities. The IUPAC nomenclature document was published in 1995 to help establish a uniform and meaningful approach to terminology, notation, and formulation for performance characteristics of the chemical measurement process, and in 1997 ISO published its standard (ISO 11843) for the international metrological community. IUPAC has incorporated the 1995 recommendations into its basic nomenclature volume, the Compendium on Analytical Nomenclature (IUPAC, 1998).

0.3 Parts of ISO 11843

The ISO 11843 series consists of the following published parts:

— ISO 11843-1, Capability of detection — Part 1: Terms and definitions;

— ISO 11843-2, Capability of detection — Part 2: Methodology in the linear calibration case;

— ISO 11843-3, Capability of detection — Part 3: Methodology for determination of the critical value for the response variable when no calibration data are used;

— ISO 11843-4, Capability of detection — Part 4: Methodology for comparing the minimum detectable value with a given value;

— ISO 11843-5, Capability of detection — Part 5: Methodology in the linear and non-linear calibration cases;

— ISO 11843-6, Capability of detection — Part 6: Methodology for the determination of the critical value and the minimum detectable value in Poisson distributed measurements by normal approximations;

— ISO 11843-7, Capability of detection — Part 7: Methodology based on stochastic properties of instrumental noise.

0.4 Social purposes

0.4.1 Significance of defining the minimum detectable value

The determination of the minimum detectable value is sometimes important in practical work. The value provides a criterion for deciding when “the signal is certainly not detected”, or when “the signal is significantly different from the background noise level". For example, it is valuable when measuring the presence of hazardous substances, the degree of calming of radioactive contamination, and surface contamination of semiconductor materials, as follows.

— RoHS (Restrictions on Hazardous Substances) sets limits on the use of six hazardous materials (hexavalent chromium, lead, mercury, cadmium and the flame retardant agents perbromobiphenyl, PBB, and perbromodiphenyl ether, PBDE) in the manufacturing of electronic components and related goods sold in the EU.

— Environmental pollution by radioactive materials due to accidents at nuclear power plants is a major problem. While it takes a considerable amount of time for the contaminated environment to return to its original state, it is important to monitor the state of contamination during that time.

— The condition of an analyser to be quantified when assessing the limiting performance of an instrument.

0.4.2 Trouble prevention with stakeholders

To avoid problems with stakeholders, concerning the presence or absence of hazardous substances, a kind of agreement or rule based on the scientific theory for judging the presence or absence of the hazardous substance is set up.

a) Health hazard trouble of hazardous substances.

b) Product quality assurance in commerce (non-inclusion of hazardous substances, product contamination).

0.4.3 Performance evaluation of measuring instruments

The series of ISO 11843 provides conditions for judgment on whether the detection capability of measuring instruments is adequate.

Capability of detection —

Part 8:
Guidance for the implementation of the ISO 11843 series

1 Scope

This document provides guidance for implementing the theories of the ISO 11843 series in various practical situation. As defined in this series, the term minimum detectable value corresponds to the limit of detection or detection limit defined by the IUPAC. The focus of interest is placed on the practical applications of statistics to quantitative analyses.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11843-1, *Capability of detection — Part 1: Terms and definitions*

3 Terms, definitions and symbols

3.1 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11843-1 apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

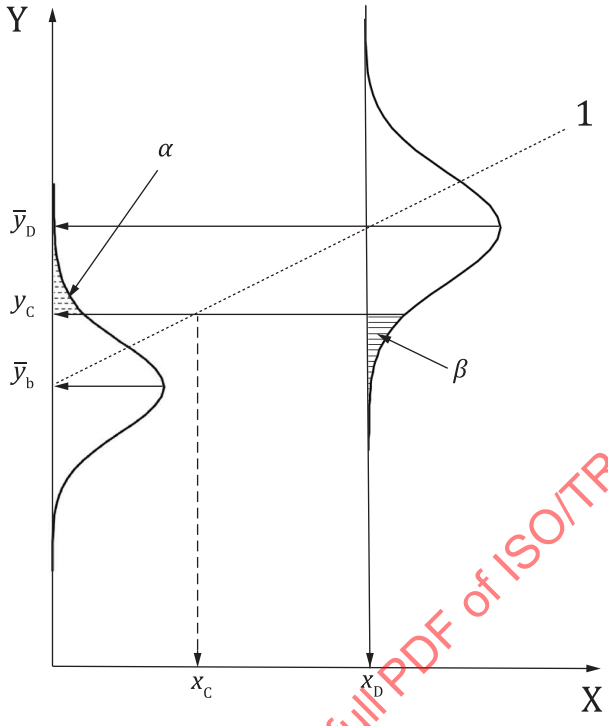
— IEC Electropedia: available at https://www.electropedia.org/

3.2 Symbols

X	state variable or probability density
Y	response variable
J	number of replications of measurements on the reference material representing the value of the basic state variable (blank sample)
k	constant for minimum detectable values and critical values, e.g. $x_D = k \times$ standard deviation
K	number of replications of measurements on the actual state (test sample)
N	number of replications of measurements of each reference material in assessment of the capability of detection
x	value of a state variable
y	value of a response variable

y_C	critical value of the response variable defined by ISO 11843-1 and ISO 11843-3
x_g	given value, tested to determine whether it is greater than the minimum detectable value
x_D	minimum detectable value of the state variable
σ_b	standard deviation under actual performance conditions for the response in the basic state
σ_g	standard deviation under actual performance conditions for the response in a sample with the state variable equal to x_g
η_b	expected value under the actual performance conditions for the response in the basic state
η_g	expected value under the actual performance conditions for the response in a sample with the state variable equal to x_g
$\bar{y}_b$	arithmetic mean of the actual measured response in the basic state
$\bar{y}_g$	arithmetic mean of the actual measured response in a sample with the state variable equal to x_g
y_D	minimum detectable response value with the state variable equal to x_d
λ	mean value corresponding to the expected number of events in Poisson distribution
α	probability of an error of the first kind
β	probability of an error of the second kind
$1-\alpha$	confidence level
$1-\beta$	confidence level
s_b	estimate of the standard deviation of responses for the basic state
s_g	estimate of the standard deviation of responses for a sample with the net state variable equal to x_g
$z_{1-\alpha}$	$(1-\alpha)$-quantile of the standard normal distribution NOTE Further information is provided in Annex A.
$z_{1-\beta}$	$(1-\beta)$-quantile of the standard normal distribution NOTE Further information is provided in Annex A.
$t_{1-\gamma}(\nu)$	$(1-\gamma)$-quantile of the t-distribution with ν degrees of freedom
T_0	lower confidence limit

4 Historical survey of terms



Key

X	net state variable or probability density	Y	response variable
x_D	minimum detectable value of the net state variable	x_C	critical value of the net state variable
$\bar{y}_b$	reference state the response variable	$\bar{y}_D$	minimum detectable value of the response variable
y_C	critical value of the response variable	α	probability of an error of the first kind
β	probability of an error of the second kind	1	calibration function

Figure 1 — Critical value of both the response variable and the net state variable, and minimum detectable value of both the response variable and the net state variable

In Figure 1, x_D is called the limit of identification by Boumans and the limit of guarantee by Kaiser[4]. As shown in Figure 1, when analysing a sample containing an x_D component, the probability that the value of the response variable (output) becomes smaller than y_C is as small as β. Indeed, x_D is the minimum detectable amount with a very low probability of being missed by analytical methods. Currie named it the detection limit[5].

In order to ensure consistency with ISO standards, IUPAC has defined detection limit as x_D since 1994, and minimum detectable quantity is also sometimes used[6]. This interpretation has not necessarily become widespread among analysts, but it is correct as long as detection limit is defined as the minimum amount that can be detected.

The term "detection limit," which is very familiar to most chemists, has been abolished in ISO 11843-1 because some chemists disagree with dividing the definition of "detection limit" into two interpretations, x_C and x_D. They feel that x_C alone is sufficient for the detection limit. Statistical interpretations of detection limits are given in 5.4 and Annex B.

Instead, the term “critical value of the response variable” was assigned to y_C, “critical value of the net state variable” to x_C, and “minimum detectable value of the net state variable” to x_D. In addition, the term “sensitivity” or “detection sensitivity” has often been used to express the detection capability of the measuring method.

Detection sensitivity, which is most frequently used on a daily basis, can represent the change rate of a response variable (equivalent to the slope of a calibration curve) with respect to the change per unit of a state variable[7]. In consideration of this situation, neither detection limit nor sensitivity has been used in this document as a term representing detection capability. The terms used in ISO 11843-1 and the terms the IUPAC recommended in 1994[6] are summarized in Table 1. The association of the IUPAC recommended detection limit with the ISO 11843 series is also described in Annex F.

Table 1 — Terms used in ISO 11843-1 and IUPAC

	ISO 11843-1	IUPAC
y_C	Critical value of the response variable	Minimum significant signal (critical level)
x_D	Minimum detectable value of the net state variable	Minimum detective quantity (detection limit)

5 Fundamental concepts of detection limit (minimum detectable value in ISO 11843)

5.1 General

Widely, and for many years, detection limits (DLs) have been recognized as a figure of merit of vital importance and utilized in every discipline of analytical chemistry to ensure statistical reliability and practical suitability of analytical systems. A fundamental quantity underlying DLs is the standard deviation (SD) of response variables or measurements. ISO 11843-1 provides general definitions of DLs on the basis of theoretical SDs (population SDs), while the other Parts of the ISO 11843 series are all devoted to the externalization of DLs with SD estimates (sample SDs), i.e. how to obtain SD estimates in practice. This clause shares a brief but comprehensive explanation of DLs in terms of population SDs. Estimation methods of sample SDs are given in detail in Clause 7.

In the ISO 11843 series, the definition of detection limits, referred to there as minimum detectable values, is founded on probabilities, α and β, of errors of the first and second kind, respectively. However, a DL with probability α alone has also played an important role in some fields of industry. This clause clarifies the theoretical backgrounds and similarities and differences of these DL definitions, which are recommended to be noted in practical applications.

5.2 General definition of detection limit

Detection limits are defined in *X*- and *Y*-axes that are spanned by a calibration function, $y = f(x)$. The X-axis denotes objective quantities of analyses, e.g. concentration or weight, and the Y-axis instrumental responses or measurements such as absorbance or electric current. However, the definitions in the different scales seem ostensible, because they come from a traditional understanding that a DL has necessarily been specified in the X-scale, whereas stochastic uncertainty of measurements is directly observable in the Y-scale. The ISO 11843 series takes the following approaches to interpreting the lingua franca expressed in the different dimensions.

Y-axis DL, y_D, is estimated from an observable distribution of measurements or responses, *y*. Then, y_D is transformed into its corresponding quantity, x_D, through the calibration function: $x_D = f^{-1}(y_D)$. In this clause, uncertainty of calibration functions is not taken into consideration. Therefore, errors of the final quantity, *x*, are totally attributable to those of *y*.

X-axis DL, x_D, is straightforwardly evaluated in the X-axis. As such, this treatment requires a distribution of the quantity, *x*, which is to be transformed from a distribution of observable *y* through the mathematical relationship between *x* and *y*. An example is given in ISO 11843-5.

As is well-known in probability theory, a function of a random variable is a random variable. For example, under the simplest calibration function, $y = ax$ where a is a constant, a normal distribution of *y* produces a normal distribution of x ($= y/a$) (called reproducibility in probability theory).

5.3 Detection limit with probability α

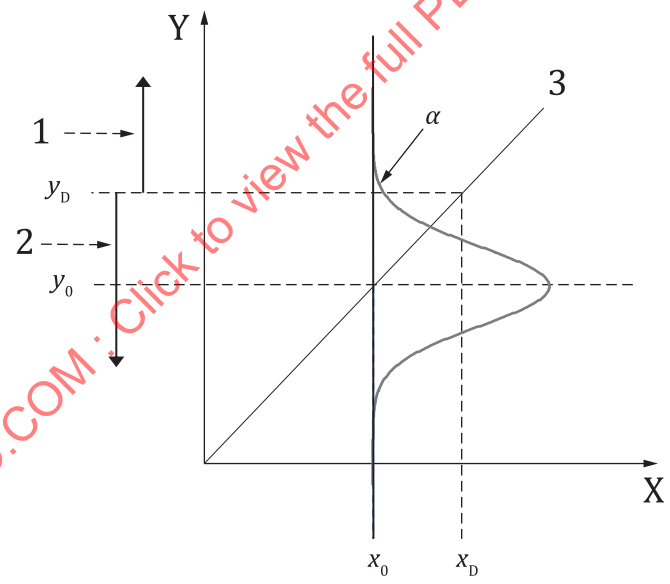
Let the normal distributions along the Y-axis of Figure 2 and the X-axis of Figure 3 be population distributions of observable y and estimable x (= $f^{1}(y)$), respectively, the averages of which are y_0 and x_0 (= $f^{1}(y_0)$) and the SDs of which are $\sigma(y_0)$ and $\sigma(x_0)$. With probability α, detection limits, y_D and x_D, are defined as k times the SDs for blank samples, respectively,

$$y_D = y_0 + z_{1-\alpha}\,\sigma(y_0) \tag{1}$$

$$x_D = x_0 + z_{1-\alpha}\,\sigma(x_0) \tag{2}$$

where blank samples mean $x_0 = 0$ and $z_{1-\alpha}$ is a constant. Lowercase k is often used in Formulae (1) and (2) in analytical chemistry, but $z_{1-\alpha}$ (and $z_{1-\beta}$) is preferred throughout this document. The DL value, y_D, is first determined in the Y-axis and then transformed into the final quantity, x_D, through $y = f(x)$ (Figure 2), whereas the DL, x_D, is directly evaluated in the X-axis (Figure 3). The DL definitions of Formulae (1) and (2) correspond to the decision limits or critical values defined in the following subclause.

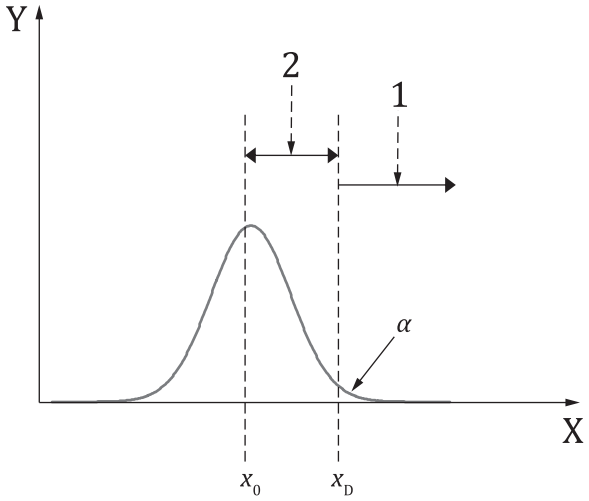
Symbol α denotes the probability of observable y or estimable x (= $f^{1}(y)$) exceeding the DL, y_D or x_D, when blank samples at a concentration of x_0 (= 0) are measured repeatedly under exactly the same experimental conditions. If $z_{1-\alpha} = 3$ and the distribution of y or x is normal, α is 0,14 %.



Key

X	net state variable or probability density	Y	response variable
1	detected	2	not detected
3	$y = f(x)$	X_D	$x_D = f^{-1}(y_D)$

Figure 2 — Definition of detection limit in Y-axis with probability α



Key

X	state variable	Y	probability density
1	detected	2	not detected

Figure 3 — Definition of detection limit in X-axis with probability α

For a sample of an unknown concentration, it can safely be said that with a risk of at most 0,14 %,

— if $y < y_D$ or $x < x_D$, nothing is detected;

— if $y \geq y_D$ or $x \geq x_D$, something is detected.

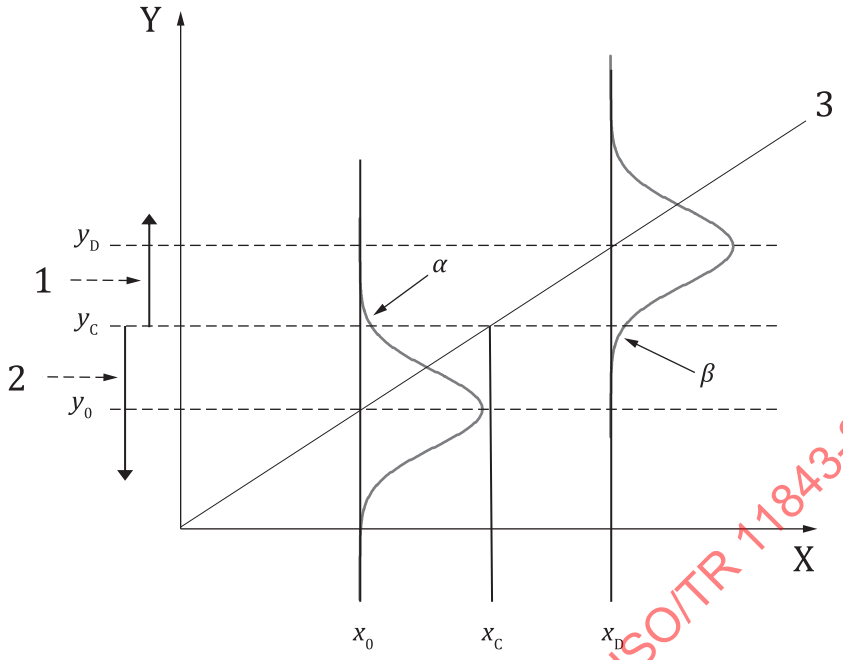
These judgments are confirmed by the assumption that the blank samples have a 99,86 % probability of measurement, y, (or concentration estimates, x) falling below the DL and have a 0,14 % probability of being above the DL.

In the above definitions, comments on concentration are too speculative to make. Only distributions for blank samples are drawn in Figures 2 and 3, whereas distributions for blank samples and samples of the DL concentration, x_D, called DL samples, are referred to in Figures 4 and 5 (see the following subclause). If DL samples, instead of blank samples, are measured repeatedly, the probability of observable y (or estimable x) rising above the DL is equal to that of being below the DL. As long as a decision is made by comparing y or x with y_D or x_D, the probability of detecting a target material in DL samples is 50 %. To achieve a higher probability of detection, e.g. 95 %, another criterion needs be introduced for judging detection that is less than y_D or x_D.

5.4 Detection limit with probabilities α and β

In this subclause, a detection limit is regarded as a target quantity of detection, but not a criterion for judging whether or not a target material is detected in an analytical system. The presence of a material in a sample is judged by a decision limit or critical value.

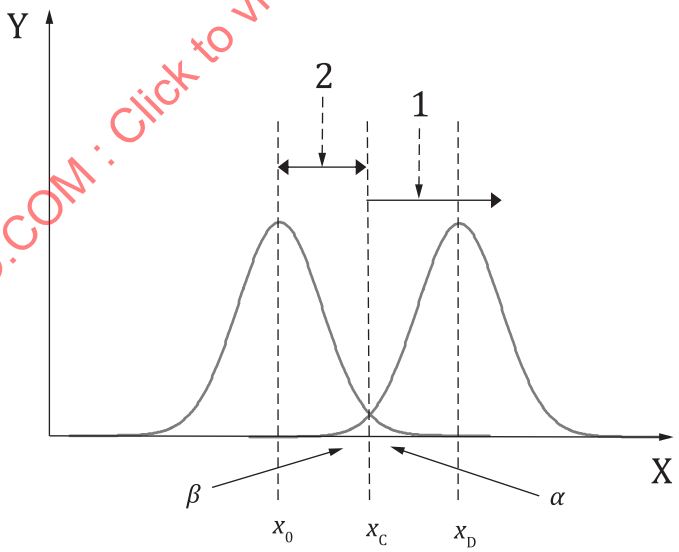
Figures 4 and 5 illustrate not only the distributions for blank samples shown in Figures 2 and 3, but also those for DL samples. Probability β appends a new limit referred to as a critical value, y_C or x_C (= $f^1(y_C)$), in the ISO 11843 terminology, which is also known as a decision limit in the fields of analytical chemistry. If blank samples at a concentration of x_0 (= 0) are measured repeatedly, the probability of a measurement running over the decision limit, y_C, is α, which is called the probability of an error of the first kind (false positive). The error and decision limit, α and x_C, in the X-axis can be interpreted in the same manner. As for DL samples of concentration x_D, the probability of a measurable y or estimable x failing to reach y_C or x_C is β, which is called the probability of an error of the second kind (false negative).



Key

X	net state variable or probability density	Y	response variable
1	detected	2	not detected
3	$y = f(x)$	X_D	$x_D = f^{-1}(y_D)$

Figure 4 — Definition of detection limit in Y-axis with α and β



Key

X	state variable	Y	probability density
1	detected	2	not detected

Figure 5 — Definition of detection limit in X-axis with α and β

Let α and β be both 5 %. It can safely be said that with a risk of at most 5 % (see Figures 4 and 5),

— if $y < y_C$ or $x < x_C$, the analyte of the concentration x_D is not detected;

— if $y \geq y_C$ or $x \geq x_C$, the analyte of the concentration x_D is detected.

If an analytical result is slightly more than the decision limit, y_C (or x_C), a material of the DL concentration can be regarded as being detected under the assumptions that the probability of a response being attributed to a blank sample is at most 5 % and that the probability of missing the presence of the analyte is at most 5 %. If a result falls slightly below the decision limit, the probability of the wrong decision (false negative) is less than 5 %. There is a possibility of detection, even if a measurement is less than the detection limit (see Figures 4 and 5).

The detection limit is a target quantity for detection, and the decision limit is a criterion for judging detection. The meaning of the term detection limit in this subclause is different from that of the previous subclause, 5.3, in which a decision is made at y_D (or x_D), i.e. the detection limit takes the same role as the decision limit.

The definitions of detection limits, y_D and x_D, with α and β are written as

$$y_D = y_0 + z_{1-\alpha}\,\sigma(y_0) + z_{1-\beta}\,\sigma(y_D) \tag{3}$$

$$x_D = x_0 + z_{1-\alpha}\,\sigma(x_0) + z_{1-\beta}\,\sigma(x_D) \tag{4}$$

where $\sigma(y_D)$ and $\sigma(x_D)$ denote the standard deviations of measurements and their concentration estimates, respectively, for DL samples of concentration x_D, and the other symbols are the same as those of Formulae (1) and (2). If the distributions with SDs of $\sigma(y_0)$ and $\sigma(y_D)$ ($\sigma(x_0)$ and $\sigma(x_D)$) are normal, $z_{1-\alpha} = 1{,}645$ and $z_{1-\beta} = 1{,}645$, the probabilities, α and β, are 5 %.

In general, $\sigma(y_0)$ and $\sigma(y_D)$ ($\sigma(x_0)$ and $\sigma(x_D)$) are not necessarily the same (heteroscedastic), but in many real situations, they may not substantially be dissimilar (homoscedastic). In homoscedastic situations, if $z = z_{1-\alpha} = z_{1-\beta}$, Formulae (3) and (4) take the simple forms

$$y_D - y_0 = 2z\sigma(y_0) = 2z\sigma(y_D) \tag{5}$$

$$x_D - x_0 = 2z\sigma(x_0) = 2z\sigma(x_D) \tag{6}$$

respectively. If $z = 1{,}645$, $\sigma_y = \sigma(y_0) = \sigma(y_D)$ and $\sigma_x = \sigma(x_0) = \sigma(x_D)$, the DLs are written as

$$y_D - y_0 = 3{,}290\sigma_y \approx 3{,}3\sigma_y \tag{7}$$

$$x_D - x_0 = 3{,}290\sigma_x \approx 3{,}3\sigma_x \tag{8}$$

Neglecting the blank measurement, y_0, and taking into account $x_0 = 0$, the following useful expressions are obtained:

$$\sigma_y / y_D = 1 / 3{,}290 \approx 30\ \% \tag{9}$$

$$\sigma_x / x_D = 1 / 3{,}290 \approx 30\ \% \tag{10}$$

where the left sides of Formulae (9) and (10) represent the relative standard deviations (RSD) or coefficients of variation (CV) of measurements, y, and concentration estimates, x, respectively. The above formulae are another indicator for detection: the DL samples are characterized by 30 % RSD or CV.

A sample of an unknown concentration is usually handled for the purpose of DLs. When its measurement, y, is obtained, consideration of its corresponding concentration is feasible with a calibration function, but makes no sense from the viewpoints of DLs. The question is which state an analytical system characterized by a measurement, y, belongs to, basic (blank) or reference (detection limit). Other concentrations than the blank or DL are outside the purview of the definitions of DLs.

In the above definitions of detection limits (Formulae (1)-(4)), the distributions of measurements and concentration estimates are assumed to be population distributions. In practice, however, the population SDs of Formulae (1)-(4) need to be replaced by sample SDs. Parts 2 to 7 of the ISO 11843 series focus on methodologies for estimating sample SDs in real situations.

6 Pragmatic view of α and β

6.1 Statistical definitions of α and β

In the ISO 11843 series, α is defined as the probability of erroneously detecting that a system is not in the basic state when really it is in that state, and β is the probability of erroneously detecting that a system is in the basic state when the value of the state variable is equal to the minimum detectable value.

More simply stated, a type I error corresponding to α is to falsely infer the existence of unacceptable hazardous substances that are not there, while a type II error corresponding to β is to falsely infer the absence of unacceptable hazardous substances that are present.

In other words, since α is the probability at which it is judged that an unacceptable hazardous substance is present, it is necessary to decide what numerical values that prioritize the producer's interests should be selected on the producer's side; the default value is set to 5 %.

Since β is the probability at which it is judged that an unacceptable hazardous substance is not present even though one actually is, it is a risk factor considered on the basis of the user's side of goods such as food and home electric appliances. As with α and β, 5 % is used in the ISO 11843 series as default value; however, if there is an appropriate reason, the use of other values is permitted, and in the past 10 % was widely used for α.

6.2 Actual examples of α and β values

The minimum detectable value defined by ISO 11843-4 is actually obtained in the most simplified conditions shown as $\alpha = \beta$, $J = 1$, $K = \infty$ in Formulae (11) and (12).

Supposing that α is 0,10 and β is 0,05, the corresponding $Z_{1-\alpha}$ and $Z_{1-\beta}$ values are 1,282 and 1,645, respectively, the minimum detectable value is written as follows:

minimum detectable value = background value + 1,282 σ_α + 1,645 σ_β.

Assuming $\sigma_\alpha = \sigma_\beta$, the minimum detectable value = background value + 2,927σ_α. When the background value is 0, it is approximately the minimum detectable value = 3σ_α.

Increasing the probability of α and β lowers the minimum detectable value, and it becomes easier to detect even a smaller measurement value or a smaller measurement peak. At the same time, the probability that the target substance is present when it is not present increase. In this way, the user of the ISO 11843 series can understand the meaning of α and β and then select appropriate numerical values for them.

7 In-depth explanations and examples of the Parts in the ISO 11843 series

7.1 General

The ISO 11843 series consists of Standards from Part 1 to Part 7. This Clause provides helpful commentaries on ISO 11843-3, ISO 11843-4, ISO 11843-6 and ISO 11843-7.

7.2 ISO 11843-3 and ISO 11843-4

7.2.1 General

ISO 11843-3 defines how to determine the critical value. The critical value itself is not used alone but is used in combination as a reference value when determining the minimum detectable value. Therefore, the exposition of ISO 11843-3 together with ISO 11843-4 is appropriate.

7.2.2 Number of repeated measurements, *J* and *K*

When determining the critical value, not only *J* blank measurements but *K* actual sample measurements are carried out in order to define a value calculated closer to the measurement result of the actual sample. In the actual measurement of the sample, it is defined on the assumption that the measured value is almost equal to the blank value.

As shown in ISO 11843-3 the critical value is defined by Formula (11).

$$y_C = \bar{y}_b \pm z_{1-\alpha}\sigma_b\sqrt{\frac{1}{J}+\frac{1}{K}} \tag{11}$$

where

J is the number of measurements on the reference material representing the value of the basic state variable (blank sample); the basic state is defined as a state in which the target material to be measured does not exist in the sample;

K is the number of measurements on the actual state (test sample); for measurement of an actual sample in which $x = 0$, see ISO 11843-3:2003, Annex A and Annex B.

The number of repeated measurements *K* is applied to an actual sample (test sample), but it is equivalent to a blank sample with the concentration of the target component set to 0 (zero). Two types of blank samples are measured *J* times and *K* times independently. The reliability of measurement is improved by measuring the variation of blank samples for two types.

On the other hand, in ISO 11843-4, when the minimum detectable value is examined, the numbers of repeated measurements *J* and *K* are used. The same variables *J* and *K* as those for obtaining the critical value y_c are used. Originally, different variables are supposed to be used, and this can mislead the user. However, when the critical value and the minimum detectable value are actually determined, it can be seen that the definition formula is simplified by unifying the conditions such as $J = K$. The process is shown below.

The minimum detectable value described in ISO 11843-4 is defined as the estimated value of the response variable y_g by Formula (12) in the measurement of the actual sample

$$\eta_g \geqq y_C + z_{1-\beta}\sqrt{\frac{1}{J}\sigma_b^2+\frac{1}{K}\sigma_g^2} \tag{12}$$

where

η_g is the expected value under actual performance conditions for responses of a sample with the net state variable equal to x_g;

J is the number of measurements on the reference material representing the value of the basic state variable (blank sample);

K is the number of measurements on the actual state (test sample).

By replacing y_c with $y_C = \eta_b + z_{1-\alpha}\sigma_b\sqrt{\frac{1}{J}+\frac{1}{K}}$, Formula (13) is obtained,

$$\eta_g - \eta_b \geqq z_{1-\alpha}\sigma_b\sqrt{\frac{1}{J}+\frac{1}{K}} + z_{1-\beta}\sqrt{\frac{1}{J}\sigma_b^2+\frac{1}{K}\sigma_g^2} \tag{13}$$

The formula $\sqrt{\frac{1}{J}\sigma_b^2+\frac{1}{K}\sigma_g^2}$ is adopted. Since the left-hand side is expressed as a difference of two kinds of mean, the additivity of variance, $\sigma^2 = \sigma_b^2 + \sigma_g^2$, is applied.

For Formula (13), the formula is simplified by finally unifying the conditions. Specifically, by setting $\alpha = \beta$ and $K = J$, even if K is adopted as another variable, the criterion is ultimately simplified and the measurement is performed as shown in Formula (14). The number of repeated measurements can be unified by J.

$$\eta_g - \eta_b \geqq z_{1-\alpha}\sqrt{\frac{1}{J}}\left(\sqrt{2\sigma_b^2}+\sqrt{\sigma_b^2+\sigma_g^2}\right) \tag{14}$$

7.2.3 Determination of the minimum detectable value

When analogue measurements are used, such as in spectrophotometry, it is possible to approximate with $\sigma_g \geqq \sigma_b$, so that Formula (14) is modified to Formula (15),

$$\eta_g - \eta_b \geqq \frac{2z_{1-\alpha}}{\sqrt{J}}\left(\sqrt{\sigma_b^2+\sigma_g^2}\right) \tag{15}$$

or modified to Formula (16),

$$\frac{\eta_g - \eta_b}{\sqrt{\sigma_b^2+\sigma_g^2}} \geqq \frac{2z_{1-\alpha}}{\sqrt{J}} \tag{16}$$

Furthermore, in analogue measurement such as spectrophotometry, since it can be assumed that $\sigma_b = \sigma_g, \eta_b = 0$ depending on the measurement conditions, Formula (16) can be simplified as shown in Formula (17),

$$\eta_g \geq 2z_{1-\alpha}\sigma_b\sqrt{\frac{2}{J}} \tag{17}$$

As described in the definitions of the critical value and the minimum detectable value, expressing the definition formula using the number of repeated measurements, J and K, it is necessary to understand the theoretical background, but in reality, those formulae are greatly simplified by various assumptions so that this makes those calculations easier.

When obtaining the minimum detectable value, $J = 1$ is set in Formula (17) in order to set a state in which a larger value cannot be taken because overly severe criteria can lead to a false result: that the target substance is present when it is not. If α is 5 %, $Z_{1-\alpha}$ becomes 1,645, so Formula (17) can be simplified to η_g (the minimum detectable value) = $4{,}65\sigma_b$. Alternatively, when 10 % is adopted for α, $Z_{1-\alpha}$ is 1,282, so it can be simplified to η_g (the minimum detectable value) = $3{,}625\sigma_b$.

7.2.4 Confirmation of the minimum detectable value for an obtained experimental value with the number of repeated measurements, N

In practice, the obtained value is often compared with the minimum detectable value. For this purpose, it is consistent to use a formula representing a confidence interval of the difference in mean. This is because the definition of the minimum detectable value adopts the form of the difference in mean for simplification.

The number of measurements N is adopted to derive the confidence limit T_0 for $\eta_g - \eta_b$ in ISO 11843-4:2003, 5.4 (Confirmation of the criterion for sufficient capability of detection). In both the measurement of the basic state and the measurement of the actual state (test sample), the adoption of the same number of N as the number of repeated measurements is recommended for simpler calculation.

As for the confidence interval on a difference in mean, $\bar{y}_g$ and $\bar{y}_b$, a confidence interval of $\eta_g - \eta_b$ is shown by Formula (18),

$$(\bar{y}_g - \bar{y}_b) - Z_{(1-\alpha/2)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \le \eta_g - \eta_b \le (\bar{y}_g - \bar{y}_b) + Z_{(1-\alpha/2)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \quad (18)$$

where

N is the number of measurements of each reference material in assessment of the capability of detection;

$\bar{y}_g$ is the observed mean response of a sample with the state variable equal to x_g;

η_b is the expected value under the actual performance conditions for the responses of the basic state;

η_g is the expected value under the actual performance conditions for the responses of a sample with the state variable equal to x_g.

To confirm the sufficient capability of detection criterion, a one-sided test is used. With α and β, $100(1-\alpha)$ % of the one-sided lower confidence bound on $\eta_g - \eta_b$ is shown in Formula (19),

$$\eta_g - \eta_b \ge (\bar{y}_g - \bar{y}_b) - Z_{(1-\alpha)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \quad (19)$$

The one-sided lower confidence bound on $\eta_g - \eta_b$ of Formula (19) is compared to the right-hand side of Formula (13), giving Formula (20),

$$(\eta_g - \eta_b) \ge (\bar{y}_g - \bar{y}_b) - Z_{(1-\alpha)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \ge Z_{1-\alpha}\alpha_b\sqrt{\frac{1}{J} + \frac{1}{K}} + Z_{1-\beta}\sqrt{\frac{1}{J}\sigma_b^2 + \frac{1}{K}\sigma_g^2} \quad (20)$$

The $100(1-\alpha)$ % value of the confidence limit T_0 with respect to $\eta_g - \eta_b$ can be calculated by Formula (21).

$$T_0 = (\bar{y}_g - \bar{y}_b) - \frac{z_{(1-\alpha)}}{\sqrt{N}}\sqrt{\sigma_b^2 + \sigma_g^2} \quad (21)$$

When using the standard deviation of the sample, the t-distribution with the degree of freedom v is used to calculate the value using Formula (22),

$$T_0 = (\bar{y}_g - \bar{y}_b) - \frac{t_{(1-\gamma^{(v)})}}{\sqrt{N}}\sqrt{s_b^2 + s_g^2} \quad (22)$$

or Formula (23),

$$T_0' = \frac{(\bar{y}_g - \bar{y}_b)}{\sqrt{s_b^2 + s_g^2}} - \frac{t_{(1-\gamma^{(v)})}}{\sqrt{N}} \quad (23)$$

If the left side of the equality satisfies Formulae (14) or (15), it can be concluded that the minimum detectable response value y_g is more than or equal to the minimum detectable response value y_D and that x_g is therefore more than or equal to x_D.

An actual calculation example described in ISO 11843-4:2003, Annex B is shown in Annex C to help understanding.

7.2.5 Number of repeated measurements, *J* and *K*, in ISO 11843-5 and ISO 11843-7

In ISO 11843-5 and ISO 11843-7, the number of repeated measurements such as *J* and *K* is not applied, since these Parts are based on the theory of obtaining "result" from "cause." The "cause" is noise, and the "result" means a set of measured values. A general statistical method for obtaining standard deviation (SD) by the number of repeated measurements estimates the property (SD) of a population from a set of measurement values (sample, sample space). On the other hand, in ISO 11843-5 and ISO 11843-7, firstly the formula describing the property of the population (SD of the measured value) is derived from the stochastic property (stationary stochastic process) of the noise, and secondly the probability parameters of this formula are estimated from the actual property of noise. In other words, the SD of the population is not estimated from the set of measured values; rather, it is directly derived from the cause of the variation (noise). Thus, ISO 11843-5 and ISO 11843-7 are independent of the number of repeated measurements

7.3 ISO 11843-6

7.3.1 Overview of ISO 11843-6

In recent years, the pulse measurement technique, which is a highly sensitive measurement method, has been widely used in the field of analytical chemistry. It is known that variations in measured values in pulse measurements follow a Poisson distribution. Therefore, the statistical treatment of measured values differs from analogue measurements in which measured values follow a normal distribution, such as the spectrophotometric method.

Normally, statistical processing of numerical values is performed using the Poisson distribution, but handling numerical values according to the Poisson distribution requires advanced knowledge, and the calculations are difficult to do with a personal computer. In such a situation, instead of obtaining the minimum detectable value by the Poisson distribution itself, a method of approximating the Poisson distribution with a normal distribution is used[8]. The introduction of ISO 11843-6 describes the necessity for a new International Standard that defines the minimum detectable value by an approximation. Examples of instruments to which the pulse measurement method is applied are also shown.

The X-ray photoelectron spectrometer (XPS), Auger electron spectrometer (AES), secondary ion mass spectrometer (SIMS), and gas chromatograph mass spectrometer (GCMS) are designed to measure pulses to detect particles such as electrons and ions. X-rays are not particles but electromagnetic waves; however, X-ray diffractometers (XRD) and X-ray fluorescence analysers (XRF) are classified as pulse measurement instruments since the detector of X-ray functions as a pulse count detector.

7.3.2 Features of pulse count measurement

7.3.2.1 General features of pulse count measurement

7.3.2.1.1 General

In order to clarify the difference from ISO 11843-2, ISO 11843-3 and ISO 11843-4: those were created for analogue measurements such as chemical analysis, and to promote understanding of ISO 11843-6, created for pulse measurement, various differences between analogue measurement and pulse measurement are summarized.

The conditions under which Poisson distribution measurement is made are usually specified by the experimental set-up. The number of pulses that are detected increases with both time and the width of the region over which the spectrum is being observed. These two parameters are noted and cannot be changed during the course of the measurement. The following conditions are essential for determining the minimum detectable value.

7.3.2.1.2 Measurement time vs. output

In the case of measurements using absorptiometry or emission spectroscopy in chemical analysis, it is necessary to wait until the absorbance or emission intensity becomes constant; then the indicated value when it does not change is adopted. This means the value to be measured does not increase with time. On the other hand, in the case of pulse measurement such as electron spectroscopy, the measured value is usually displayed as a count number, and the total count number increases during measurement. Therefore, it is desirable for accuracy to measure until sufficiently large counts are obtained. The approximation of the Poisson distribution by the normal distribution is more reliable with higher measured values. A measurement over a longer period of time is preferable to several shorter measurements. Also, the background measurement time and the sample measurement time must be the same.

When the measurement time is 1 ms and 10 counts, it is desirable for accuracy to continue the measurement to obtain 100 counts with 10 ms rather than 10 times. The average value of the measurement in the former case is 10 counts, so that the standard deviation is 3,16 counts, which is the square root of 10 counts. On the other hand, since the measured value in the latter case is 100 counts, the standard deviation is 10 counts. The variation of the former is expressed as 3,16/10, but the latter is 10/100, and as a result the variation is small.

7.3.2.1.3 Numerical values to be treated

The reading of the measured value is 87,6 % for example as a transmittance for the absorption spectrometry, and there is no particular unit for this measurement, but it is expressed as a real number. On the other hand, in pulse measurement, since particles are measured, it is expressed as an integer such as 20 counts or 2 345 counts.

7.3.2.1.4 Number of channels of detector

In pulse measurement, in order to measure the kinetic energy of particles with good resolution in electron spectroscopy, for example, many detectors corresponding to the magnitude of each energy are arranged. One detector corresponds to one channel, and for that purpose, a large number of channels, corresponding to the distribution of particle energy magnitudes, is required. Since the kinetic energy of an electron corresponding to a specific component is usually measured as one peak, the number of channels covering the entire peak is required. When the target measurement value is a peak top count value, the number of channels covering the entire peak is necessary to determine the peak top position. When the target measurement value is not the peak intensity but corresponds to the full width at half maximum or the peak area corresponding to the full value full width, the number of channels in the background measurement is adjusted to the same number as the sample measurement.

7.3.2.1.5 Repeated measurement

In analogue measurement or pulse measurement, it is necessary to make repeated measurements while changing the sample. It is desirable to measure multiple times even when it is possible to determine the minimum detectable value with sufficient measurement time and with one measurement, since only mean values are used in the approximations presented here.

7.3.2.1.6 Standard deviation

As shown in Table 2, the standard deviation is obtained by a well-known method in analogue measurement, whereas in pulse measurement, the square root of the measured value (average value) is the standard deviation. Therefore, the variance is the average value itself. In the definition of the critical value and the minimum detectable value, the distribution of measured values can be approximated to a normal distribution when the measured value (average value) is sufficiently large. The value obtained from the normal distribution table is adopted as the Z value.

7.3.2.2 Differences between analogue measurement and pulse measurement

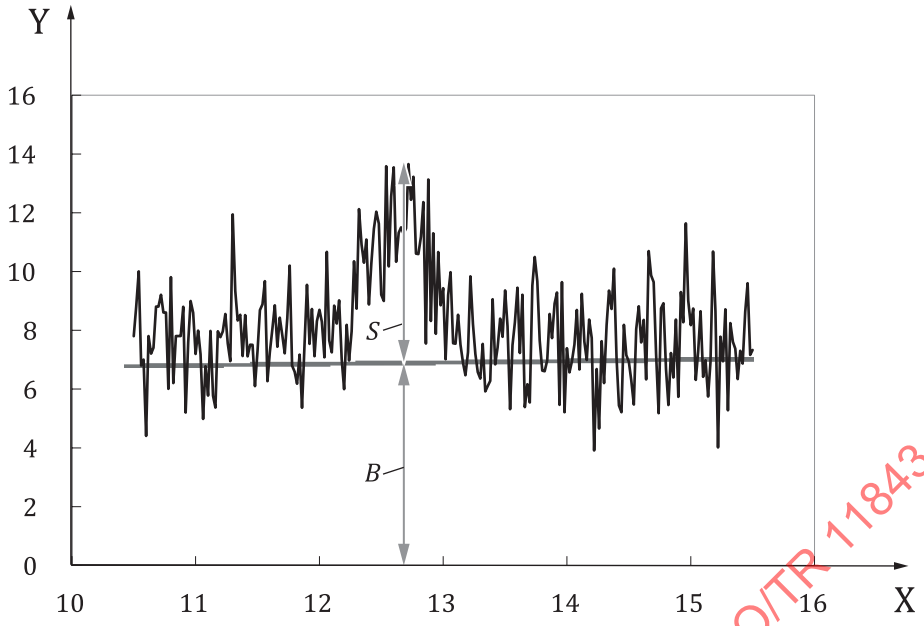
Table 2 shows the differences between analogue measurement and pulse measurement.

Table 2 — Differences between pulse measurement and analogue measurement

		Analogue	Pulse
a)	Output vs measuring time	Constant	Increase with time
b)	Target number	Real number	Integer
c)	Measurement time	Any time is applicable	Specify
d)	Number of channels (detector)	—	Specify
e)	Repeated measurement	Multiple times	When measurement takes time, a single measurement can be acceptable. Multiple measurements are preferable.
f)	Standard deviation	$\sqrt{\frac{\sum_{i=1}^{n}(y_i-\bar{y})^2}{n-1}}$ or $\sqrt{\frac{\sum_{i=1}^{n}(y_i-\bar{y})^2}{n}}$	$\sqrt{\bar{y}}$
g)	Statistical distribution of measured values	Normal distribution	Poisson distribution

7.3.2.3 Applying gross count

The signal is treated as the mean value of gross count. The "total measurement value (gross count)" is used when treating the measurement value in the pulse measurement. When describing the signal corresponding to the target component, that is, the magnitude of the peak on the spectrum, the total measured value ($S + B$) must be used (see Figure 6). The net measurement value S obtained by subtracting the background B from the measurement value must not be adopted. In pulse measurement, the standard deviation of the measured value can be expressed as the square root of the total measured value ($S + B$) shown in Figure 6.



Key

X	arbitrary unit such as wavelength, energy, etc.	Y	intensity (counts)
S	signal (counts)	*B*	blank (counts)

Figure 6 — Total measurement value (gross count)

7.3.2.4 Data treatment

The spectra under consideration must not have received any data treatment, such as smoothing. If data processing such as smoothing is performed on the total measured value, the value changes depending on the kinds of processing used. In particular, since the spectrum for obtaining the minimum detectable value is noisy, the shape of the spectrum peak is greatly changed by the smoothing process. Even though the strongest peak intensity value or large value as an area corresponding to the full width at half maximum is obtained, the numerical value changes if data processing such as smoothing is applied.

7.3.2.5 Simplification of formula

7.3.2.5.1 Calculation of the minimum detectable value

In ISO 11843-6:2019, 6.3 (Sufficient capability of the detection criterion), the definition of the minimum detectable value in pulse count measurement is described as shown in Formula (13),

$$\eta_g - \eta_b \geqq z_{1-\alpha}\sigma_b\sqrt{\frac{1}{J}+\frac{1}{K}} + z_{1-\beta}\sqrt{\frac{1}{J}\sigma_b^2+\frac{1}{K}\sigma_g^2} \tag{13}$$

where

η_b is the expected value under the actual performance conditions for the responses of the basic state;

η_g is the expected value under the actual performance conditions for the responses of a sample with the state variable equal to x_g.

This inequality is simplified by unifying the conditions as outlined in ISO 11843-4. Specifically, by setting $\alpha = \beta$ and $K = J$, the criterion is ultimately simplified to Formula (14),

$$\eta_g - \eta_b \geqq z_{1-\alpha}\sqrt{\frac{1}{J}}\left(\sqrt{2}\sigma_b + \sqrt{\sigma_b^2 + \sigma_g^2}\right) \tag{14}$$

Furthermore, $J = 1$ is set to have the minimum detectable value taken as the biggest value, so that Formula (14) is simplified to Formula (24). In this case, η_g corresponds to the minimum detectable value.

$$\eta_g - \eta_b \geq z_{1-\alpha}\left(\sqrt{2}\sigma_b + \sqrt{\sigma_b^2 + \sigma_g^2}\right) \tag{24}$$

The criterion gives Formula (24) by replacing σ_b and σ_g with $\bar{y}_b$ and $\bar{y}_g$, respectively, to give Formula (25),

$$\eta_g - \eta_b \geq z_{1-\alpha}\left(\sqrt{2\bar{y}_b} + \sqrt{\bar{y}_b + \bar{y}_g}\right) \tag{25}$$

The expected values of the responses of the sample given are usually unknown, and an assessment using criterion Formula (25) has to be made for the experimental data, whereas that on the right-hand side is known. If η_b can be replaced with $\bar{y}_b$, then η_g is supposed to be the minimum detectable value. Actually, η_g, the minimum detectable value, can be obtained by solving the transformed Formula (25) itself, that is, by finally solving the quadratic equation.

7.3.2.5.2 Confirmation of the minimum detectable value for an obtained experimental value

As described in 7.2, in practice, the obtained value is often compared with the minimum detectable value. For this purpose, it is consistent to use a formula representing a confidence interval of the difference in mean. A confidence interval of $\eta_g - \eta_b$ has to be treated to validate with N repeated measurements of the basic state and N repeated measurements of a sample. A $100(1-\alpha/2)$ % confidence interval for $\eta_g - \eta_b$ is

$$\left(\bar{y}_g - \bar{y}_b\right) - z_{(1-\alpha/2)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \leqq \eta_g - \eta_b \leqq \left(\bar{y}_g - \bar{y}_b\right) + z_{(1-\alpha/2)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \tag{18}$$

Formula (18) shows the range in which the difference between the mean values can be taken, but since the value to be adopted is to determine the minimum detectable value, the left side of the inequality, which is the smallest value, is adopted. Only one-sided confidence interval is considered.

Next, Formula (19) is obtained by comparing the left side of Formula (18) with Formula (14), which is the definition of the minimum detectable value.

$$\eta_g - \eta_b = \left(\bar{y}_g - \bar{y}_b\right) - z_{(1-\alpha)}\sqrt{\frac{1}{N}\sigma_b^2 + \frac{1}{N}\sigma_g^2} \geqq z_{(1-\alpha)}\sqrt{\frac{1}{J}}\left(\sqrt{2}\sigma_b + \sqrt{\sigma_b^2 + \sigma_g^2}\right) \tag{19}$$

An approximate $100(1-\alpha)$ % lower confidence limit (CL) for $\eta_g - \eta_b$ is given by replacing σ_b and σ_g with $\bar{y}_b$ and $\bar{y}_g$, respectively, as shown in Formula (26),

$$\mathrm{CL} = \left(\bar{y}_g - \bar{y}_b\right) - z_{(1-\alpha)}\sqrt{\frac{1}{N}}\sqrt{\bar{y}_b + \bar{y}_g} \tag{26}$$

If the lower confidence limit satisfies the criterion of Formula (25), it can be concluded that the minimum detectable response value, $\bar{y}_g$, is more than or equal to the minimum detectable response value, $\bar{y}_D$, and therefore it can be concluded that x_D is less than or equal to x_g. For relatively large values of N, the lower confidence limit of Formulae (14), (24) and (25) suffice.

7.3.2.6 Accuracy of approximation

ISO 11843-6 does not define the minimum value that can be measured by the Poisson distribution itself, but it defines the minimum detectable value that can be measured by approximating the Poisson distribution with a normal distribution. Therefore, the degree of difference in the minimum detectable value, in other words the accuracy of the approximation method, is analysed as follows. The minimum detectable value is given by Formula (25),

$$\eta_g - \eta_b \geq z_{1-\alpha}\left(\sqrt{2\bar{y}_b} + \sqrt{\bar{y}_b + \bar{y}_g}\right) \tag{25}$$

Also, the 100 (1-α) % value of the confidence limit CL for $\eta_g - \eta_b$ can be calculated by Formula (27),

$$\mathrm{CL} = \left(\bar{y}_g - \bar{y}_b\right) - z_{(1-\alpha)}\sqrt{\frac{1}{N}}\sqrt{\bar{y}_b + \bar{y}_g} \tag{27}$$

In actual measurement, the magnitude relationship between Formulae (25) and (27) can be compared. When N is set to infinity (∞) in Formula (27), substituting CL for the left side of Formula (14) yields the following Formula (28).

$$\bar{y}_g - \bar{y}_b \geqq z_{1-\alpha}\sqrt{\frac{1}{J}}\left(\sqrt{2\bar{y}_b} + \sqrt{\bar{y}_b + \bar{y}_g}\right) \tag{28}$$

Similar to ISO 11843-4, the minimum detectable value can be obtained as a solution when $\alpha = (\beta) = 0{,}05$ and $J = 1$ in Formula (28). In this case, $\bar{y}_g$ corresponds to the minimum detectable value.

Table E.1 in Annex E shows minimum detectable values when parameter y_b corresponding to basic state value is from 1 to 200 together with the differences from Poisson exact arithmetic[9].

In this table, the numerical value corresponding to "normal approximation" is a value obtained by using Formula (25) as a solution of the quadratic inequality. Table E.1 shows that the difference between the two methods is less than one count. Some data can show one count, which is the result of rounding up by rounding off the second decimal place. The difference between the two methods is extremely small and stable over a wide range of background values. It can be seen that the method of obtaining the Poisson distribution by approximating it with a normal distribution is sufficiently accurate and practically poses no problem.

The comparison between Poisson exact arithmetic and the approximations gives a fairly good coincidence within one count difference over a wide range of background count more than several counts.

7.3.2.7 Difference in treating standard deviations of analogue measurement and of pulse measurement

There is a difference in the application of standard deviations to analogue and to pulse measurement. ISO 11843-4:2003, 5.3 (Probability of detecting a given value of a net state variable) describes the definition of minimum detectable value in analogue measurement,

$$\eta_g - \eta_b \geqq z_{1-\alpha}\sigma_b\sqrt{\frac{1}{J} + \frac{1}{K}} + z_{1-\beta}\sqrt{\frac{1}{J}\sigma_b^2 + \frac{1}{K}\sigma_g^2} \tag{13}$$

Assuming that $\beta = \alpha$, $K = J$, and $\sigma_g \geqq \sigma_b$, the criterion can be simplified as shown in Formula (16),

$$\frac{\eta_g - \eta_b}{\sqrt{\sigma_b^2 + \sigma_g^2}} \geqq \frac{2z_{1-\alpha}}{\sqrt{J}} \tag{16}$$

That is, Formula (14) is simplified on the assumption that the standard deviation σ_b of the ground state response value and the standard deviation σ_g of the sample response value can be regarded as the same. In a situation where the conditions for determining the minimum detectable value are examined,

the concentration of the target component is extremely low, so that the standard deviation of both the measured value in the ground state and the actual state (sample) can be regarded as almost the same. For example, in the absorptiometry or emission spectroscopy, there can be a situation where the variation between the two is almost the same, so the assumption that $\sigma_g \geqq \sigma_b$ holds.

On the other hand, the above assumptions made in analogue measurement could not be applied to pulse measurement, and the reason for this is described below using specific measurement values.

Suppose that the mean response value in the ground state is 200 counts. Since the standard deviation σ_b of this measured value is the square root of 200 counts, it becomes 14,14 counts. Next, assuming that the response variable of the actual sample corresponding to this background value is the same as the minimum detectable value, as can be seen from Table E.1, its value is 296 counts. The standard deviation σ_g of this response value is 16,40 counts.

As can be seen from the results above, when σ_b = 14,14 and σ_g = 16,40, obviously there is a big difference of 2,26 counts. Therefore, the assumptions for simplification mut be limited to only $\beta = \alpha$ and $K = J$, and then Formula (13) is simplified to Formula (14).

$$\eta_g - \eta_b \geqq z_{1-\alpha}\sqrt{\frac{1}{J}}\left(\sqrt{2}\sigma_b + \sqrt{\sigma_b^2 + \sigma_g^2}\right) \tag{14}$$

An actual calculation example of pulse count measurement described in ISO 11843-6:2019, Annex E, is shown in Annex D to help in understanding.

7.4 Example from ISO 11843-7

ISO 11843-7 aims at describing detection limits (DLs) in instrumental analyses on the common understanding that when sample concentrations are low at or near a DL, the most predominant source of measurement errors is background noise in instrumental output. The process of ISO 11843-7 to evaluate DLs consists of the following assumptions and principles:

— error of an area measurement is assumed to be the area created by noise itself over the edge-to-edge domain of a signal;

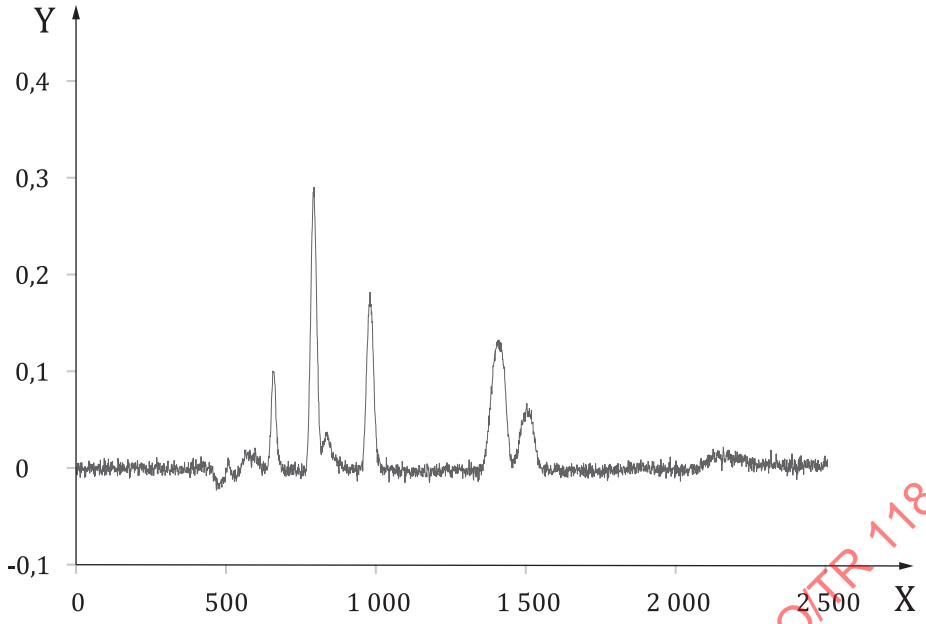
— the noise is modelled on mixed random processes of white noise and the first order autoregressive process, AR(1) (one of the Markov processes);

— the SD, $\sigma(k)$, of area measurements is mathematically formulated as a function of a width, k, of a target signal and noise parameters included in the mixed random processes.

Therefore, major procedures to estimate the SD, $\sigma(k)$, are to extract the noise parameters from instrumental output, called parametrization. Finally, a DL is calculated as a constant multiplication of the SD, e.g. 3,3 × SD as mentioned in Clause 5.

The parametrization is made up of some complicated mathematical techniques such as the Fourier transform and non-linear least squares fitting, and actually cannot be performed as easily as with spreadsheet software. This subclause uses software as a technical tool for DLs. Figures 7 to 10 show examples of software exports.

Figure 7 illustrates a chromatogram of organic acids in an HPLC system with a UV absorption detector. The target for analysis is the third peak (acetic acid) appearing at the 1 000 data point.



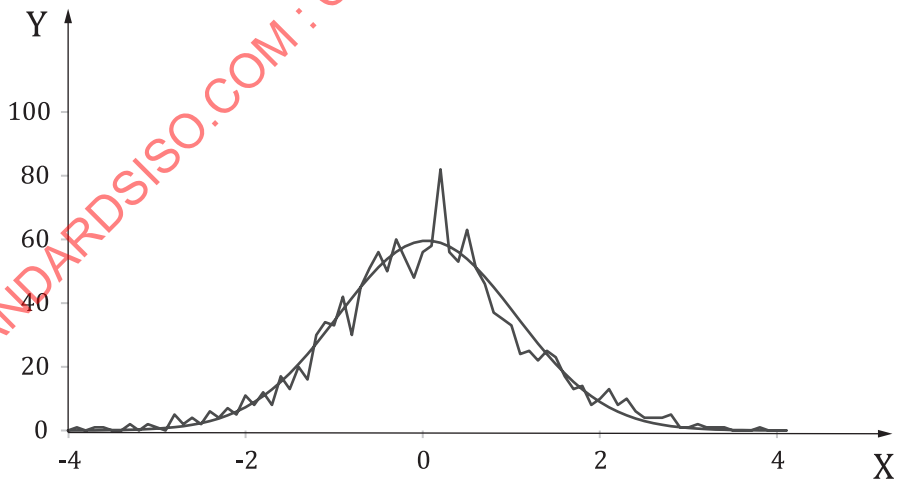
Key

X data point (0,2 s) Y absorbance (mAU)

NOTE The peaks are (from left) system, malic acid, acetic acid, citric acid and succinic acid (10 mg/l each). The wavelength of the monitor is 220 nm.

Figure 7 — Chromatogram of organic acids in an HPLC system equipped with a UV absorption detector

Figure 8 shows a histogram of the noise-created areas, $A(k')$, in the noise regions of Figure 7. The zig-zag line denotes the frequencies of the observed noise areas and the smooth line is the least-squares fitting of a normal distribution to the observed frequencies. The excellent agreement of theory and practice as shown in the figure is a necessary condition for the success of SD prediction.



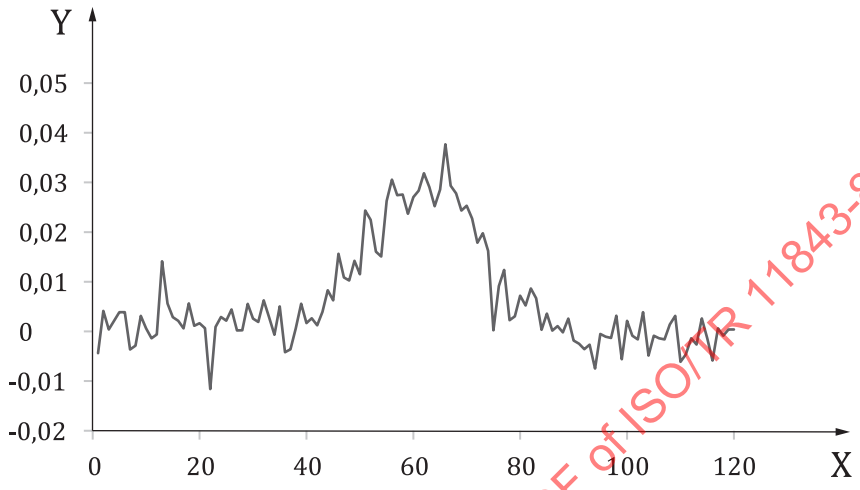
Key

X $A(k')/\sigma(k')$ Y frequency

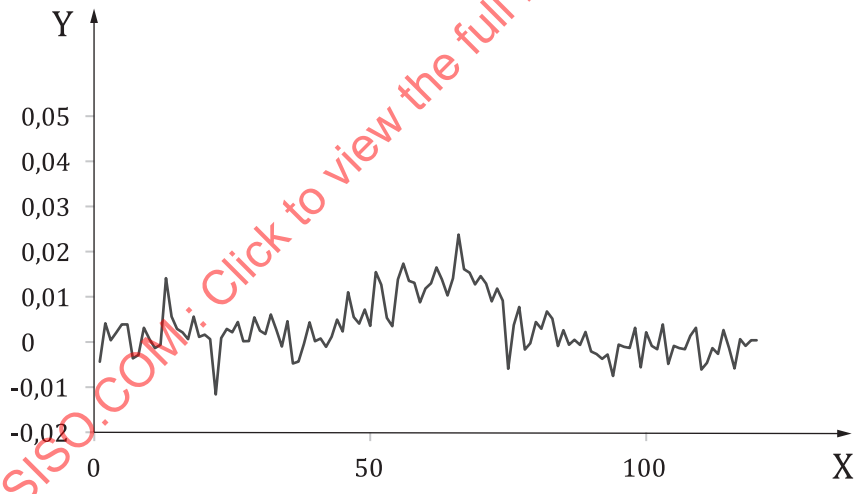
NOTE The peak width (k') is assumed to be 300 data points.

Figure 8 — Histogram of noise-created areas

Once the parameters of the model noise are determined by the parametrization (Figure 8) and a width, k, of a target signal is determined from the chromatogram of Figure 7, the DL, decision limit (critical value) and precision profile can be provided by the software. The concentration of acetic acid in Figure 7 is 10 mg/l and the DL (= 3,3σ(k)) is predicted to be 1,28 mg/l. Figure 9 a) illustrates a DL signal superimposed on the actual noise of Figure 7. The DL signal looks noisy. As is well-known, a signal-to-noise ratio (S/N) is a convenient indicator for DLs. The S/N in Figure 9 a) is close to the widely adopted value (= 3). It is quite interesting for the distinct methods to achieve the comparable results.



a) Simulated signal (normal distribution) at the detection limit (1,28 mg/l acetic acid)



b) Simulated signal (normal distribution) at the decision limit (0,64 mg/l acetic acid)

Key

X data point (0,2 s) Y absorbance (mAU)

NOTE The noise comes from Figure 8. The peak width is 60 data points.

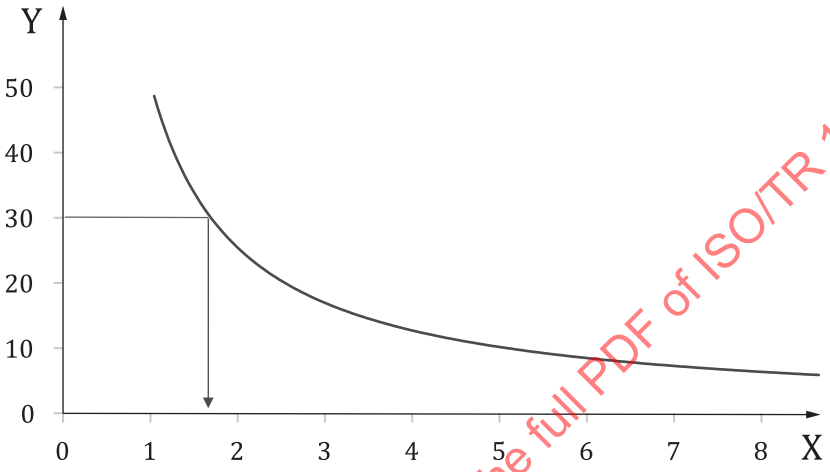
Figure 9 — Signals of acetic acid superimposed on observed noise

As mentioned in Clause 5, the definitions of DLs in the ISO 11843 series are based on the probabilities, α and β, of errors of the first and second kinds, and not the S/N. This ISO 11843 definition leads to the probabilistic interpretations of DLs and decision limits. A judgment of whether or not a target material is contained in a sample is made by comparing a measurement with the decision limit, and not with the detection limit. The detection limit is a target quantity for detection and the decision limit is a criterion for judging detection. For details, see Clause 5.

Figure 9 b) illustrates the signal on noise at the decision limit, which is half of the DL signal, see Figure 9 a). In this case, if blank samples are measured, the probability of a measurement exceeding the

signal area of Figure 9 b) (decision limit) is 5 % (false positive). With the DL samples, the probability of a measurement falling below the signal area of Figure 9 b) is also 5 % (false negative). Note that a signal equal to or more than Figure 9 b) can be observed once in 20 times and is not rare.

Precision profiles are a mathematical relationship between sample concentrations and relative standard deviations (RSDs) of measurements (see Figure 10) and provide an entire survey of uncertainty in an analytical system. In general, the RSD of measurements decreases with increasing sample concentrations, and at higher concentrations, the RSD converges to a value attributed to other error factors than noise, e.g. volume errors of sample injection into an analytical instrument. The predominant factor near a DL is assumed to be background noise. Thirty percent RSD is an indicator for DLs as mentioned in Clause 5. In the precision profile of Figure 10, the DL (= 1,28 mg/l) can be spotted at the concentration that corresponds to 30 % RSD of measurements.



Key

X concentration (mg/l) Y RSD (%)

NOTE The arrow indicates the DL of acetic acid.

Figure 10 — Precision profile of the acetic acid peak of Figure 8

The software used (TOCO19[1)]) is based on the same noise model as ISO 11843-7, but adopts an improved parametrization method for the automation of practical operations[10]. A close statistical correlation between the ISO standard and the TOCO19 algorithm has been proved with HPLC experiments[10].

1) TOCO19 is an example of a suitable product available commercially. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of this product.

Annex A
(informative)

Standard normal random variable

A normal random variable with

$$\mu = 0 \text{ and } \sigma^2 = 1$$

is called a standard normal variable[11] and is denoted as Z. The cumulative distribution function of a standard normal random variable is denoted as

$$\varnothing(z) = P(Z \leq z) \tag{A.1}$$

The value z such that $P(Z > z) = 0{,}05$ is found in the Table of cumulative standard normal distribution.

This probability expression can be written as $P(Z \leq z) = 0{,}95$. The value that corresponds to 0,95 is 1,645.

If X is a normal random variable with $E(X) = \mu$ and $V(X) = \sigma^2$, the random variable

$$Z = \frac{X - \mu}{\sigma} \tag{A.2}$$

is a normal random variable with $E(Z) = 0$ and $V(Z) = 1$, where

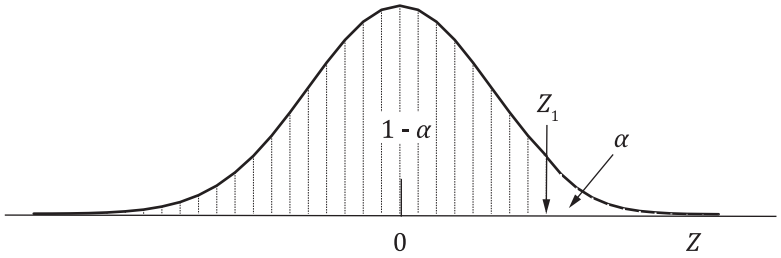
$E(X)$ is mean; suppose X is a continuous random variable;

the mean or expected value of X, denoted as μ or $E(X)$, is $\mu = E(X)$;

$V(X)$ is variance; the variance of X, denoted as $V(X)$ or σ^2, $\sigma^2 = V(X)$.

NOTE $P(Z < 1{,}65) = 0{,}950\,529$, which is the rounded value of $P(Z < 1{,}645) = 0{,}950\,015$, is occasionally used for simplicity, as for example in ISO 11843-5 and ISO 11843-7. This does not significantly affect the results, as the difference between the rounded and unrounded values is quite small.

See Figure A.1.



Key

Z	normal random variable	0	mean
Z_1	1,645	α	probability 0,05
1- α	probability 0,95		

Figure A.1 — Standard normal probability density function

Annex B
(informative)

Difference between the power of test and the minimum detectable value

Interpreting the difference between the power and the minimum detectable value leads to a good understanding of the ISO 11843 series.

The power of a hypothesis test is the probability of making the correct decision if the alternative hypothesis is true. That is, the power of a hypothesis test is the probability of rejecting the null hypothesis when the alternative hypothesis is the hypothesis that is true.

The power of a statistical test gives the likelihood of rejecting the null hypothesis when the null hypothesis is false. Just as the significance level (α) of a test gives the probability that the null hypothesis is rejected when it is actually true (a wrong decision), power quantifies the chance that the null hypothesis is rejected when it is actually false (a correct decision). Thus, power is the ability of a test to correctly reject the null hypothesis. As shown in Figure B.1, the power is the probability and is denoted as $1-\beta$.

A hypothesis test of the observed mean response y_C, $\bar{y}_g$ of a sample with the net state variable equal to x_g and the observed mean response $\bar{y}_b$ of the basic state is considered. In the definition of the power, y_C can be a significance level that can neglect the null hypothesis with a certain probability, α. However y_C is not the minimum detectable value from the definition of the ISO 11843 series. The critical value of the response variable, y_C, in Figure B.1 is defined by Formula (B.1) as described in ISO 11843-3,

$$y_C = \bar{y}_b + z_{1-\alpha}\sigma_b\sqrt{\frac{1}{J}+\frac{1}{K}} \tag{B.1}$$

where

$z_{1-\alpha}$ is the $(1-\alpha)$ quantile of the standard normal distribution;

σ_b is the standard deviation under actual performance conditions for responses of the basic state;

J is the number of replications of measurements on the reference material representing the value zero of the net state variable (blank sample) in an application of the method;

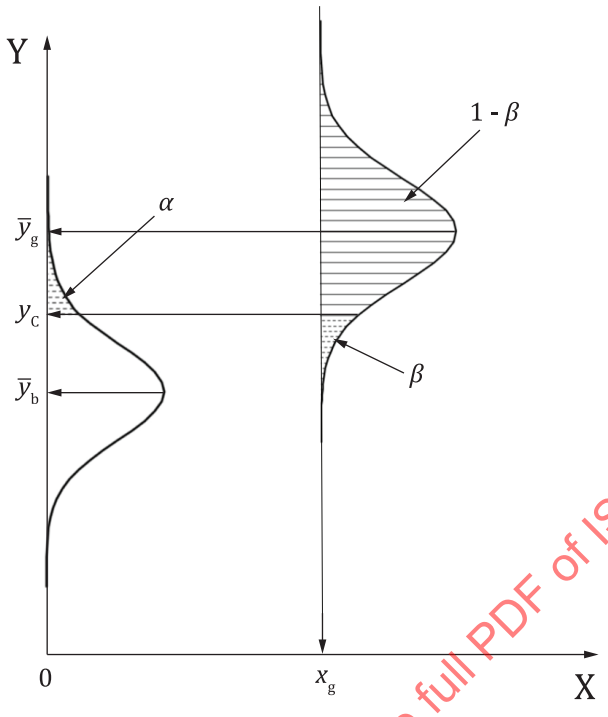
K is the number of replications of measurements on the actual state (test sample in which the net state variable is deemed to be zero) in an application of the method.

This is the case of a comparison of the responses of the test sample, $\bar{y}_g$, and a sample in the basic state, $\bar{y}_b$. The minimum detectable value of the response variable, $\bar{y}_g\,(\bar{y}_D)$ is defined by Formula (B.2) as described in ISO 11843-4,

$$\bar{y}_g \geq y_C + z_{1-\beta}\sqrt{\frac{1}{J}\sigma_b^2+\frac{1}{K}\sigma_g^2} \tag{B.2}$$

where σ_g is the standard deviation under actual performance conditions for responses of a sample with the net state variable equal to x_g. This means the minimum detectable value of the response

variable, $\bar{y}_g$ ($\bar{y}_D$), is the particular value and lies in the area of probability corresponding to the power $1-\beta$.



Key

X	state variable
Y	response variable
y_C	critical value
α	probability of an error of the first kind
β	probability of an error of the second kind
$1-\beta$	power, or probability of correctly rejecting a false null hypothesis

Figure B.1 — Conceptual diagram showing the relative position of the critical value, the power, the measured values of the active and basic states

Annex C
(informative)

Calculation example from ISO 11843-4

Low levels of "quickly reacting aluminium" in natural waters, expressed as mass concentration in micrograms per litre, were measured by connecting a continuous flow system to a graphite furnace atomic absorption spectrometer. The absorbance values for five measurements of two samples representing the blank concentration $x_b = 0$ and the net concentration $x_g = 0{,}5$ µg/l are given in Table C.1. Thus, in the assessment of the method N= 5. The capability of detection is to be calculated for $J = K = 1$ and $\alpha = \beta = 0{,}05$.

Table C.1 — Absorbance values for the blank concentration $x_b = 0$ and the net concentration $x_g = 0{,}5$ µg/l

Net concentration of aluminium x	Absorbance y
0	0,074 0,081 0,075 0,076 0,074
0,5	0,126 0,126 0,125 0,108 0,130

The statistical analysis yields $\bar{y}_b = 0{,}0760$, $\bar{y}_g = 0{,}1230$, $s_b = 0{,}0029$, $s_g = 0{,}0086$.

These values give $\dfrac{(\bar{y}_g - \bar{y}_b)}{\sqrt{s_b^2 + s_g^2}} = 5{,}17$

The hypothesis $\sigma_b = \sigma_g$ is not rejected with an F-test at the 5 % significance level.

For, $\gamma = 0{,}05$ and the number of degrees of freedom $\nu = 8$, then

$t_{1-\gamma}(8) = 1{,}86$, and for $\alpha = 0{,}05$ then $z_{1-\alpha} = 1{,}645$.

A 95 % lower confidence limit of $(\eta_g - \eta_b)/\sqrt{\sigma_b^2 + \sigma_g^2}$ calculated according to Formula (24) is 4,34, which is greater than $2z_{1-\alpha}/\sqrt{J} = 3{,}29$ in Formula (17). Thus, the evaluation shows that the minimum detectable value is less than $x_g = 0{,}5$ µg/l.

Here, the minimum detectable value in this measurement system is obtained by Formula (16). The minimum detectable value of response variable is 0,098 in terms of absorbance, and that of state variable corresponding to aluminium concentration is 0,231 µg/l.

Annex D
(informative)

Calculation example from ISO 11843-6:2019, Annex E (Measurement of hazardous substances by X-ray diffractometer)

D.1 Experimental data

The hazardous substance chrysotile asbestos is analysed by X-ray diffractometer. 0,10 mg of chrysotile was weighed accurately, dispersed in pure water, trapped on filter paper and analysed. The quantity weighed was equivalent to regulation value (0,10 %, 0,10 mg/100 mg) in building material products. Five repeated measurements for the blank $x_b = 0$ and the unknown concentration x_g were conducted.

A powder XRD scan of chrysotile asbestos, presented as a plot of relative intensity against the Bragg angle, 2θ, is given in Figure D.1. Using five repetitions, the capability of detection was calculated for $K = J = 1$ and $\alpha = \beta = 0{,}05$.

Conditions of measurements:

instrument: X-ray diffractometer;

X-ray source: X-ray tubes include Cu with corresponding wavelengths of 0,154 nm K-alpha monochromatic X-ray;

output power of X-ray: 40 kV, 40 mA;

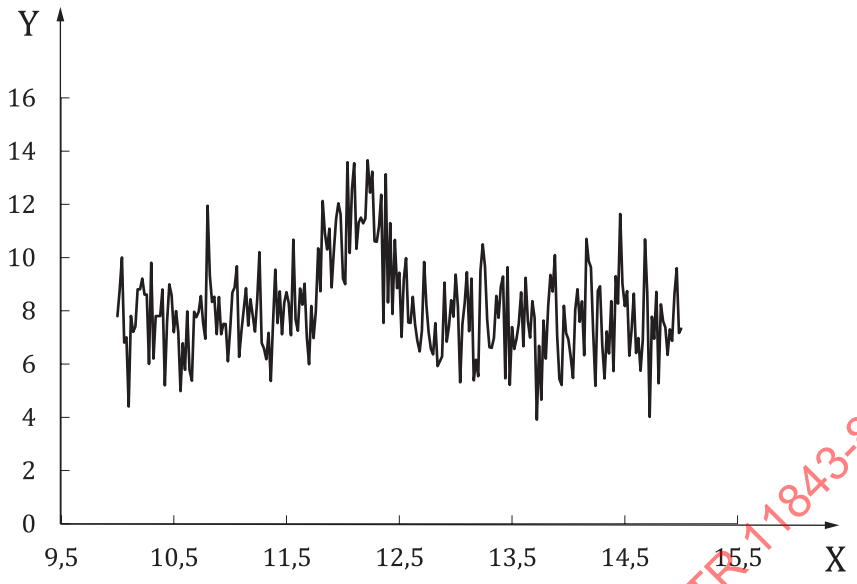
width of channel: 0,02 degree as scattering angle 2θ;

number of channels: 23 (for both background noise and peak area);

number of measurements: 5;

accumulation time of each channel: 0,2 s;

full width at half maximum (FWHM): 0,46 degree as scattering angle 2θ.



Key

X Bragg angle (2θ) Y intensity (counts)

Figure D.1 — Powder XRD scan from chrysotile asbestos as a plot of scattering intensity vs. scattering angle (2θ)

D.2 Statistical analysis

The experiment gave counts for $\bar{y}_b$ and $\bar{y}_g$ of 174 and 261, respectively. Using these values, a 95 % lower confidence limit of $(\bar{y}_g - \bar{y}_b) - z_{(1-\alpha)}\sqrt{\frac{1}{N}}\sqrt{\bar{y}_b + \bar{y}_g}$, calculated according to Formula (26) gave:

$$(\bar{y}_g - \bar{y}_b) - z_{(1-\alpha)}\sqrt{\frac{1}{N}}\sqrt{\bar{y}_b + \bar{y}_g} = (261-174) - 1{,}645\sqrt{\frac{1}{5}} \times \sqrt{174+261} = 71{,}7,$$

which is greater than $z_{1-\alpha}\left(\sqrt{2}\sigma_b + \sqrt{\sigma_b^2 + \sigma_g^2}\right) = 1{,}645\left(\sqrt{2} \times \sqrt{174} + \sqrt{174+261}\right) = 65{,}00$ in Formula (25).

It can be concluded, with better than 95 % confidence, that the 0,1 % of chrysotile asbestos is detected.

D.3 Estimation of the minimum detectable concentration of asbestos

The minimum detectable concentration of asbestos in construction materials can be estimated under the present conditions. The minimum detectable concentration can be lowered by increasing the number of measurements, and the marginal minimum detectable concentration can be obtained by increasing the number of measurements to an infinity level by the following calculations.

$$(\bar{y}_D - \bar{y}_b) - z_{(1-\alpha)}\sqrt{\frac{1}{N}}\sqrt{\bar{y}_b + \bar{y}_d} = z_{1-\alpha}\left(\sqrt{2}\sigma_b + \sqrt{\sigma_b^2 + \sigma_g^2}\right)$$

$$(\bar{y}_D - \bar{y}_b) - z_{(1-\alpha)}\sqrt{\frac{1}{\infty}}\sqrt{\bar{y}_b + \bar{y}_d} = z_{1-\alpha}\left(\sqrt{2\bar{y}_b} + \sqrt{\bar{y}_b + \bar{y}_d}\right)$$

$$\bar{y}_D - 174 = 1{,}645 \times \left(\sqrt{2 \times 174} + \sqrt{174 + \bar{y}_d}\right)$$

238 counts is obtained for the minimum detectable response variable, $\bar{y}_D$, from which the concentration of asbestos by percentage per count is estimated.

0,10 %/(261-174) counts = $1{,}15\times10^{-3}$ %/count.

The marginal minimum detectable concentration of chrysotile asbestos is obtained by the following calculation:

$1{,}15\times10^{-3}$ %× (238-174) counts = 0,074 %.

The estimated minimum detection limit of chrysotile asbestos is 0,074 %.