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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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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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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

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 —

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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

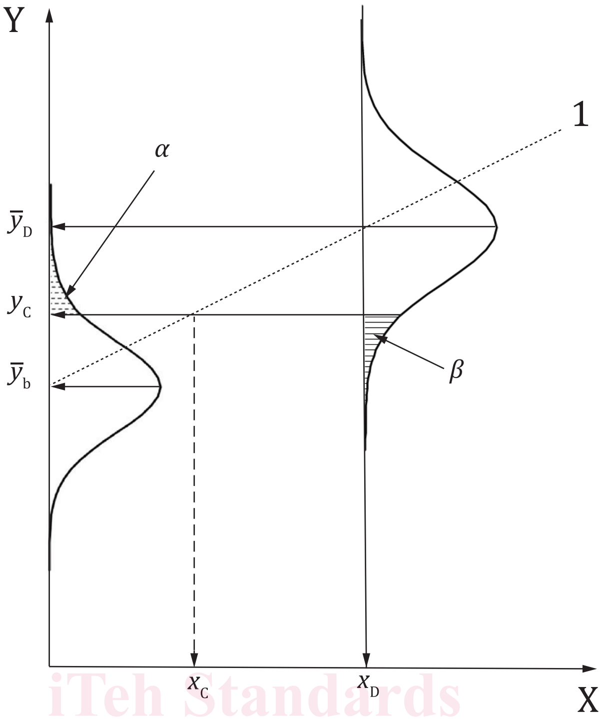
— IEC Electropedia: available at https://www.electropedia.org/

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

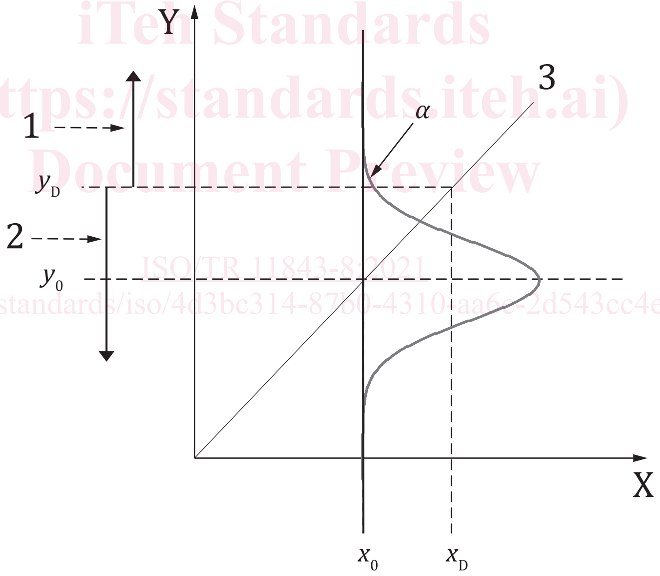
Let the normal distributions along the Y-axis of Figure 2 and the X-axis of Figure 3 be population distributions of observable y and estimable x (= $f^1(y)$), respectively, the averages of which are y_0 and x_0 (= $f^1(y_0)$) and the SDs of which are $\sigma(y_0)$ and $\sigma(x_0)$. With probability 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.

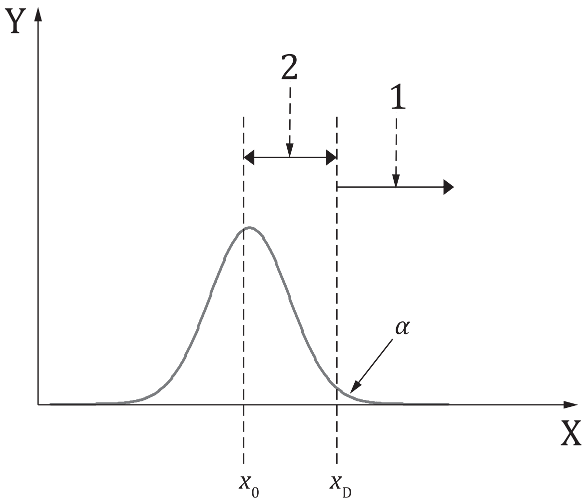
Symbol α denotes the probability of observable y or estimable x (= $f^1(y)$) exceeding the DL, y_D or x_D, when blank samples at a concentration of x_0 (= 0) are measured repeatedly under exactly the same experimental conditions. If $z_{1-\alpha}$ = 3 and the distribution of y or x is normal, α is 0,14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



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).