INTERNATIONAL
STANDARD

ISO
11843-2

First edition
2000-05-01

Capability of detection —

Part 2:
Methodology in the linear calibration case

Capacité de détection —

Partie 2: Méthodologie de l'étalonnage linéaire

Reference number
ISO 11843-2:2000(E)

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 3.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this part of ISO 11843 may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 11843-2 was prepared by Technical Committee ISO/TC 69, *Applications of statistical methods*, Subcommittee SC 6, *Measurement methods and results*.

ISO 11843 consists of the following parts, under the general title *Capability of detection*:

- *Part 1: Terms and definitions*
- *Part 2: Methodology in the linear calibration case*

Annex A forms a normative part of this part of ISO 11843. Annexes B and C are for information only.

Introduction

An ideal requirement for the capability of detection with respect to a selected state variable would be that the actual state of every observed system can be classified with certainty as either equal to or different from its basic state. However, due to systematic and random distortions, this ideal requirement cannot be satisfied because:

— in reality all reference states, including the basic state, are never known in terms of the state variable. Hence, all states can only be correctly characterized in terms of differences from basic state, i.e. in terms of the net state variable.

In practice, reference states are very often assumed to be known with respect to the state variable. In other words, the value of the state variable for the basic state is set to zero; for instance in analytical chemistry, the unknown concentration or the amount of analyte in the blank material usually is assumed to be zero and values of the net concentration or amount are reported in terms of supposed concentrations or amounts. In chemical trace analysis especially, it is only possible to estimate concentration or amount differences with respect to available blank material. In order to prevent erroneous decisions, it is generally recommended to report differences from the basic state only, i.e. data in terms of the net state variable;

NOTE In the ISO Guide 30 and in ISO 11095 no distinction is made between the state variable and the net state variable. As a consequence, in these two documents reference states are, without justification, assumed to be known with respect to the state variable.

— the calibration and the processes of sampling and preparation add random variation to the measurement results.

In this part of ISO 11843, the following two requirements were chosen:

— the probability is α of detecting (erroneously) that a system is not in the basic state when it is in the basic state;

— the probability is β of (erroneously) not detecting that a system, for which the value of the net state variable is equal to the minimum detectable value (x_d), is not in the basic state.

INTERNATIONAL STANDARD **ISO 11843-2:2000(E)**

Capability of detection —

Part 2:
Methodology in the linear calibration case

1 Scope

This part of ISO 11843 specifies basic methods to:

- design experiments for the estimation of the critical value of the net state variable, the critical value of the response variable and the minimum detectable value of the net state variable,
- estimate these characteristics from experimental data for the cases in which the calibration function is linear and the standard deviation is either constant or linearly related to the net state variable.

The methods described in this part of ISO 11843 are applicable to various situations such as checking the existence of a certain substance in a material, the emission of energy from samples or plants, or the geometric change in static systems under distortion.

Critical values can be derived from an actual measurement series so as to assess the unknown states of systems included in the series, whereas the minimum detectable value of the net state variable as a characteristic of the measurement method serves for the selection of appropriate measurement processes. In order to characterize a measurement process, a laboratory or the measurement method, the minimum detectable value can be stated if appropriate data are available for each relevant level, i.e. a measurement series, a measurement process, a laboratory or a measurement method. The minimum detectable values may be different for a measurement series, a measurement process, a laboratory or the measurement method.

ISO 11843 is applicable to quantities measured on scales that are fundamentally continuous. It is applicable to measurement processes and types of measurement equipment where the functional relationship between the expected value of the response variable and the value of the state variable is described by a calibration function. If the response variable or the state variable is a vectorial quantity the methods of ISO 11843 are applicable separately to the components of the vectors or functions of the components.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this part of ISO 11843. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this part of ISO 11843 are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 3534-1:1993, *Statistics — Vocabulary and symbols — Part 1: Probability and general statistical terms.*

ISO 3534-2:1993, *Statistics — Vocabulary and symbols — Part 2: Statistical quality control.*

ISO 3534-3:1999, *Statistics — Vocabulary and symbols — Part 3: Design of experiments.*

ISO 11095:1996, *Linear calibration using reference materials.*

ISO 11843-1:1997, *Capability of detection — Part 1: Terms and definitions.*

ISO Guide 30:1992, *Terms and definitions used in connection with reference materials.*

3 Terms and definitions

For the purposes of this part of ISO 11843, the terms and definitions of ISO 3534 (all parts), ISO Guide 30, ISO 11095 and ISO 11843-1 apply.

4 Experimental design

4.1 General

The procedure for determining values of an unknown actual state includes sampling, preparation and the measurement itself. As every step of this procedure may produce distortion, it is essential to apply the same procedure for characterizing, for use in the preparation and determination of the values of the unknown actual state, for all reference states and for the basic state used for calibration.

For the purpose of determining differences between the values characterizing one or more unknown actual states and the basic state, it is necessary to choose an experimental design suited for comparison. The experimental units of such an experiment are obtained from the actual states to be measured and all reference states used for calibration. An ideal design would keep constant all factors known to influence the outcome and control of unknown factors by providing a randomized order to prepare and perform the measurements.

In reality it may be difficult to proceed in such a way, as the preparations and determination of the values of the states involved are performed consecutively over a period of time. However, in order to detect major biases changing with time, it is strongly recommended to perform one half of the calibration before and one half after the measurement of the unknown states. However, this is only possible if the size of the measurement series is known in advance and if there is sufficient time to follow this approach. If it is not possible to control all influencing factors, conditional statements containing all unproven assumptions shall be presented.

Many measurement methods require a chemical or physical treatment of the sample prior to the measurement itself. Both of these steps of the measurement procedure add variation to the measurement results. If it is required to repeat measurements the repetition consists in a full repetition of the preparation and the measurement. However, in many situations the measurement procedure is not repeated fully, in particular not all of the preparational steps are repeated for each measurement; see note in 5.2.1.

4.2 Choice of reference states

The range of values of the net state variable spanned by the reference states should include

- the value zero of the net state variable, i.e. in analytical chemistry a sample of the blank material, and
- at least one value close to that suggested by a priori information on the minimum detectable value; if this requirement is not fulfilled, the calibration experiment should be repeated with other values of the net state variable, as appropriate.

The reference states should be chosen so that the values of the net state variable (including log-scaled values) are approximately equidistant in the range between the smallest and largest value.

In cases in which the reference states are represented by preparations of reference materials their composition should be as close as possible to the composition of the material to be measured.

4.3 Choice of the number of reference states, I, and the (numbers of) replications of procedure, J, K and L

The choice of reference states, number of preparations and replicate measurements shall be as follows:

- the number of reference states I used in the calibration experiment shall be at least 3; however, $I = 5$ is recommended;
- the number of preparations for each reference state J (including the basic state) should be identical; at least two preparations ($J = 2$) are recommended;
- the number of preparations for the actual state K should be identical to the number J of preparations for each reference state;
- the number of repeated measurements performed per preparation L shall be identical; at least two repeated measurements ($L = 2$) are recommended.

NOTE The formulae for the critical values and the minimum detectable value in clause 5 are only valid under the assumption that the number of repeated measurements per preparation is identical for all measurements of reference states and actual states.

As the variations and cost due to the preparation usually will be much higher than those due to the measurement, the optimal choice of J, K and L may be derived from an optimization of constraints regarding variation and costs.

5 The critical values y_c and x_c and the minimum detectable value x_d of a measurement series

5.1 Basic assumptions

The following procedures for the computation of the critical values and the minimum detectable value are based on the assumptions of ISO 11095. The methods of ISO 11095 are used with one generalization; see 5.3.

Basic assumptions of ISO 11095 are that

- the calibration function is linear,
- measurements of the response variable of all preparations and reference states are assumed to be independent and normally distributed with standard deviation referred to as "residual standard deviation",
- the residual standard deviation is either a constant, i.e. it does not depend on the values of the net state variable [case 1], or it forms a linear function of the values of the net state variable [case 2].

The decision regarding the applicability of this part of ISO 11843 and the choice of one of these two cases should be based on prior knowledge and a visual examination of the data.

5.2 Case 1 — Constant standard deviation

5.2.1 Model

The following model is based on assumptions of linearity of the calibration function and of constant standard deviation and is given by:

$$Y_{ij} = a + bx_i + \varepsilon_{ij} \tag{1}$$

where

x_i is the symbol for the net state variable in state i;

ε_{ij} are random variables which describe the random component of sampling, preparation and measurement error.

It is assumed that the ε_{ij} are independent and normally distributed with expectation zero and the theoretical residual standard deviation $\sigma : \varepsilon_{ij} \sim N\left(0; \sigma^2\right)$. Therefore, values Y_{ij} of the response variable are random variables with the expectation $E\left(Y_{ij}\right) = a + bx_i$ and the variance $V\left(Y_{ij}\right) = \sigma^2$, not depending on x_i.

NOTE In the cases in which J samples are prepared for measurement and each of them is measured L times so that $J{\cdot}L$ measurements are performed altogether for reference state i, then Y_{ij} refers to the average of the L measurements obtained on the prepared sample.

5.2.2 Estimation of the calibration function and the residual standard deviation

In accordance with ISO 11095, estimates (see note) for a, b and σ^2 are given by:

$$\hat{b} = \frac{\sum_{i=1}^{I} \sum_{j-1}^{J} (x_i - \bar{x})(\bar{y}_{ij} - \bar{y})}{s_{xx}} \tag{2}$$

$$\hat{a} = \bar{y} - \hat{b}\bar{x} \tag{3}$$

$$\hat{\sigma}^2 = \frac{1}{I \cdot J - 2} \sum_{i=1}^{I} \sum_{j=1}^{J} \left(\bar{y}_{ij} - \hat{a} - \hat{b}x_i\right)^2 \tag{4}$$

The symbols used here and elsewhere in this part of ISO 11843 are defined in annex A.

NOTE Estimates are denoted by a symbol ^ to differentiate them from the parameters themselves which are unknown.

5.2.3 Computation of critical values

The critical value of the response variable is given by:

$$y_{\mathrm{c}} = \hat{a} + t_{0,95}(\nu)\hat{\sigma}\sqrt{\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}}} \tag{5}$$

The critical value of the net state variable is given by:

$$x_{\mathrm{c}} = t_{0,95}(\nu)\frac{\hat{\sigma}}{\hat{b}}\sqrt{\frac{1}{K}+\frac{1}{I \cdot J}+\frac{\overline{x}^2}{s_{xx}}} \tag{6}$$

$t_{0,95}(\nu)$ is the 95 %-quantile of the t-distribution with $\nu = I \cdot J - 2$ degrees of freedom.

The derivation of these formulae is given in annex B.

5.2.4 Computation of the minimum detectable value

The minimum detectable value is given by:

$$x_{\mathrm{d}} = \delta\frac{\hat{\sigma}}{\hat{b}}\sqrt{\frac{1}{K}+\frac{1}{I \cdot J}+\frac{\overline{x}^2}{s_{xx}}} \tag{7}$$

where

$\delta = (\nu;\alpha;\beta)$ is the value of the noncentrality parameter determined in such a way that a random variable following the noncentral t-distribution with $\nu = I \cdot J - 2$ degrees of freedom and the noncentrality parameter δ, $T(\nu;\delta)$, satisfies the equation:

$$P\left[T(\nu;\delta) \leqslant t_{1-\alpha}(\nu)\right] = \beta$$

where $t_{1-\alpha}(\nu)$ is the $(1-\alpha)$-quantile of the t-distribution with ν degrees of freedom.

The derivation of this formula is given in annex B.

For $\alpha = \beta$ and $\nu > 3$, a good approximation for δ is given by

$$\delta(\nu;\alpha;\beta) \approx 2t_{1-\alpha}(\nu) \tag{8}$$

if $\nu = 4$ and $\alpha = \beta = 0{,}05$, the relative error of this approximation is 5 %; $t_{1-\alpha}(\nu)$ is the $(1-\alpha)$-quantile of the t-distribution with $\nu = I{\cdot}J - 2$ degrees of freedom.

Table 1 presents $\delta(\nu;\ \alpha;\ \beta)$ for $\alpha = \beta = 0{,}05$ and various values of ν.

For $\alpha = \beta$ and $\nu > 3$, x_{d} is approximated by

$$x_{\mathrm{d}} \approx 2t_{0,95}(\nu)\frac{\hat{\sigma}}{\hat{b}}\sqrt{\frac{1}{K}+\frac{1}{I \cdot J}+\frac{\overline{x}^2}{s_{xx}}} = 2x_{\mathrm{c}} \tag{9}$$

Table 1 — Values of the noncentrality parameter for $\alpha = \beta = 0{,}05$ and ν degrees of freedom

ν	$\delta(\nu; \alpha; \beta)$	ν	$\delta(\nu; \alpha; \beta)$	ν	$\delta(\nu; \alpha; \beta)$
2	5,516	19	3,415	36	3,354
3	4,456	20	3,408	37	3,352
4	4,067	21	3,402	38	3,350
5	3,870	22	3,397	39	3,349
6	3,752	23	3,392	40	3,347
7	3,673	24	3,387	41	3,346
8	3,617	25	3,383	42	3,344
9	3,575	26	3,380	43	3,343
10	3,543	27	3,376	44	3,342
11	3,517	28	3,373	45	3,341
12	3,496	29	3,370	46	3,339
13	3,479	30	3,367	47	3,338
14	3,464	31	3,365	48	3,337
15	3,451	32	3,362	49	3,336
16	3,440	33	3,360	50	3,335
17	3,431	34	3,358		
18	3,422	35	3,356		

5.3 Case 2 — Standard deviation linearly dependent on the net state variable

5.3.1 Model

The following model is based on the assumptions that the calibration function is linear and that the standard deviation is linearly dependent on the net state variable and is given by:

$$Y_{ij} = a + bx_i + \varepsilon_{ij} \tag{10}$$

where

x_i, a, b and Y_{ij} are as defined in 5.2.1 and the ε_{ij} are independent and normally distributed with expectation $E(\varepsilon_{ij}) = 0$ and variance:

$$V(\varepsilon_{ij}) = \sigma^2(x_i) = \left(c + dx_i\right)^2 \tag{11}$$

i.e., the residual standard deviation is linearly dependent on x

$$\sigma(x_i) = c + dx_i \tag{12}$$

The parameters of the model, a, b, c and d are estimated in a two part procedure as given in 5.3.2 and 5.3.3.

5.3.2 Estimation of the linear relationship between the residual standard deviation and the net state variable

The parameters c and d are estimated by a linear regression analysis with the standard deviations:

$$s_i = \sqrt{\frac{1}{J-1}\sum_{j=1}^{J}\left(\overline{y}_{ij} - \overline{y}_i\right)^2} \tag{13}$$

as values of the dependent variable S and with the net state variable x as the independent variable. Since the variance $V(S)$ is proportional to σ^2, a weighted regression analysis (see references [1] and [2] of the Bibliography) has to be performed with the weights:

$$w_i = \frac{1}{\sigma^2(x_i)} = \frac{1}{(c + dx_i)^2} \tag{14}$$

However, the variances $\sigma^2(x_i)$ depend on the unknown parameters c and d that have yet to be estimated. Therefore, the following iteration procedure with weights:

$$\hat{w}_{qi} = \frac{1}{(\hat{\sigma}_{qi})^2} \tag{15}$$

is proposed. At the first iteration, (q = 0), $\hat{\sigma}_{0i} = s_i$, where the s_i values are the empirical standard deviations. For successive iterations q = 1,2, ...

$$\hat{\sigma}_{qi} = \hat{c}_q + \hat{d}_q x_i \tag{16}$$

calculate with the auxiliary values:

$$\begin{aligned}
T_{q+1,1} &= \sum_{i=1}^{I} \hat{w}_{qi}\,; \\
T_{q+1,2} &= \sum_{i=1}^{I} \hat{w}_{qi} x_i\,; \\
T_{q+1,3} &= \sum_{i=1}^{I} \hat{w}_{qi} x_i^2\,; \\
T_{q+1,4} &= \sum_{i=1}^{I} \hat{w}_{qi} s_i\,; \\
T_{q+1,5} &= \sum_{i=1}^{I} \hat{w}_{qi} x_i s_i
\end{aligned} \tag{17}$$

and

$$\hat{c}_{q+1} = \frac{T_{q+1,3}T_{q+1,4} - T_{q+1,2}T_{q+1,5}}{T_{q+1,1}T_{q+1,3} - T_{q+1,2}^2} \tag{18}$$

and

$$\hat{d}_{q+1} = \frac{T_{q+1,1}T_{q+1,5} - T_{q+1,2}T_{q+1,4}}{T_{q+1,1}T_{q+1,3} - T_{q+1,2}^2} \tag{19}$$

This procedures converges rapidly so that the result for q = 3;

$$\hat{\sigma}_3 = \hat{c}_3 + \hat{d}_3 x\,;$$

can be considered, with $\hat{\sigma}_3 = \hat{\sigma}(x)$, $\hat{c}_3 = \hat{\sigma}_0$ and $\hat{d}_3 = \hat{d}$, as the final result:

$$\hat{\sigma}(x) = \hat{\sigma}_0 + \hat{d}(x) \tag{20}$$

5.3.3 Estimation of the calibration function

The parameters a and b are estimated by a weighted linear regression analysis (see references [1] and [2] in the Bibliography) with the $\bar{y}_{ij}$ as values of the dependent variable, x_i as values of the independent variable and weights:

$$w_i = \frac{1}{\hat{\sigma}^2(x_i)};$$

where

$\hat{\sigma}^2(x_i)$ is the predicted value of the variance at x_i according to equation (20)

with:

$$T_1 = J\sum_{i=1}^{I} w_i\,;$$

$$T_2 = J\sum_{i=1}^{I} w_i x_i\,;$$

$$T_3 = J\sum_{i=1}^{I} w_i x_i^2;$$

$$T_4 = J\sum_{i=1}^{I}\sum_{j=l}^{J} w_i \bar{y}_{ij}\,; \tag{21}$$

$$T_5 = J\sum_{i=1}^{I}\sum_{j=l}^{J} w_i x_i \bar{y}_{ij}$$

the estimates for a and b are:

$$\hat{a} = \frac{T_3 T_4 - T_2 T_5}{T_1 T_3 - T_2^2} \tag{22}$$

$$\hat{b} = \frac{T_1 T_5 - T_2 T_4}{T_1 T_3 - T_2^2} \tag{23}$$

5.3.4 Computation of critical values

The critical value of the response variable is given by:

$$y_{\mathrm{c}} = \hat{a} + t_{0,95}(\nu)\sqrt{\frac{\hat{\sigma}_0^2}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}}\right)\hat{\sigma}^2} \tag{24}$$

and the critical value of the net state variable is given by:

$$x_\mathrm{c} = \frac{t_{0,95}(\nu)}{\hat{b}}\sqrt{\frac{\hat{\sigma}_0^2}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}}\right)\hat{\sigma}^2} \tag{25}$$

where

$$\bar{x}_w = T_2 / T_1 \tag{26}$$

$$s_{xxw} = T_3 - T_2^2 / T_1 \tag{27}$$

$$\hat{\sigma}^2 = \frac{1}{I \cdot J - 2}\sum_{i=1}^{I}\sum_{j=1}^{J} w_i\left(\bar{y}_{ij} - \hat{a} - \hat{b}x_i\right)^2 \tag{28}$$

and $t_{0,95}(\nu)$ is the 95 %-quantile of the t-distribution with $\nu = I{\cdot}J - 2$ degrees of freedom; s_{xxw} is defined in annex A.

5.3.5 Computation of the minimum detectable value

The minimum detectable value is given by:

$$x_\mathrm{d} = \frac{\delta}{\hat{b}}\sqrt{\frac{\hat{\sigma}^2(x_\mathrm{d})}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}}\right)\hat{\sigma}^2} \tag{29}$$

where

$\delta = \delta(\nu;\ \alpha;\ \beta)$ is the value of the noncentrality parameter as defined in 5.2.4.

Since $\hat{\sigma}^2(x_\mathrm{d})$ depends on the value of x_d yet to be calculated, x_d has to be calculated iteratively.

The iteration starts with $\hat{\sigma}(x_\mathrm{d})_0 = \hat{\sigma}_0$ and results in $x_{\mathrm{d}0}$; for the next iteration step $\hat{\sigma}(x_\mathrm{d})_1 = \hat{\sigma}(x_{\mathrm{d}0})$ is computed and used in the formula for x_d, resulting in $x_{\mathrm{d}1}$,... In many cases even the first iteration step does not change the value of x_d appreciably; an acceptable value for x_d is obtained at the third iteration step.

6 Minimum detectable value of the measurement method

The minimum detectable value obtained from a particular calibration shows the capability of the calibrated measurement process for the respective measurement series to detect the value of the net state variable of an observed actual state to be different from zero, i.e. it is the smallest value of the net state variable which can be detected with a probability of $1 - \beta$ as different from zero. This minimum detectable value differs for different calibrations. The minimum detectable values of different measurement series for

- a particular measurement process based on the same type of measurement process,
- a type of measurement process based on the same measurement method, or
- a measurement method

can be interpreted as realizations of a random variable for which the parameters of the probability distribution can be considered characteristics of the measurement process, the type of measurement process or of the measurement method, respectively.

If, for a particular measurement process, m consecutive calibrations have been carried out in order to determine the minimum detectable value of the net state variable x_d, the m minimum detectable values x_d1, x_d2, ... $x_{\mathrm{d}m}$, can be used to determine a minimum detectable value of the measurement process under the following conditions:

a) the measurement process is not changed;

b) the distribution of the values x_d is unimodal and there are no outlying values x_d;

c) the experimental design (including the number of reference states, I, and the numbers of replications of procedure, J, K and L) was identical for each of the calibrations.

Under these conditions the median of the values $x_{\mathrm{d}i}$, for i = 1, ..., m, is recommended as the minimum detectable value of the measurement process; if another summary statistic of the values $x_{\mathrm{d}i}$ is used instead of the median, the statistic used shall be reported.

If any of these conditions are violated, the minimum detectable value of the measurement process is not sufficiently well-defined and the determination of a common value shall not be attempted.

If the same measurement method is applied in p laboratories and for each of them a minimum detectable value of the measurement process within the laboratory were to be determined, then under the same conditions as for the determination of the minimum detectable value of the measurement process, the median of the p minimum detectable values of the laboratories is recommended as the minimum detectable value of the measurement method; if another summary statistic of the minimum detectable values of the laboratories is used instead of the median, the statistic used shall be reported.

7 Reporting and use of results

NOTE Examples of the determination of critical and minimal detectable values are given in annex C.

7.1 Critical values

For decisions regarding the investigation of actual states only the critical value of the net state variable or of the response variable is to be applied. These values derived from a calibration of the measurement process are decision limits to be used to assess the unknown states of systems included in this series. Looking at consecutive calibrations of the same measurement process, the critical values may vary from one calibration to another. However, since each of the critical values is a decision limit belonging to a particular measurement series, it is meaningless to calculate overall critical values across calibrations and logically inappropriate to use these as critical values.

If a value of the net state variable or of the response variable is not greater than the critical value, it can be stated that no difference can be shown between the observed actual state and the basic state. However, due to the possibility of committing an error of the second kind, this value should not be construed as demonstrating that the observed system definitely is in its basic state. Therefore, reporting such a result as “zero” or as “smaller than the minimum detectable value” is not permissible. The value (and its uncertainty) should always be reported; if it does not exceed the critical value, the comment “not detected” should be added.

7.2 Minimum detectable values

The minimum detectable value derived from a particular calibration shows whether the capability of detection of the actual measurement process is sufficient for the intended purpose. If it is not, the number J, K or L may be modified.

A minimum detectable value derived from a set of calibrations following the conditions mentioned in clause 6 may serve for the comparison, the choice or the judgement of different laboratories or methods, respectively.

Annex A
(normative)

Symbols and abbreviations

a	intercept in the expression $y = a + bx + \varepsilon$
$\hat{a}$	estimate of the intercept a
b	slope in the expression $y = a + bx + \varepsilon$
$\hat{b}$	estimate of the slope b
c	intercept in the expression $\sigma(x) = c + dx$ for the residual standard deviation
$\hat{c}$	estimate of the intercept c
d	slope in the expression $\sigma(x) = c + dx$ for the residual standard deviation
$\hat{d}$	estimate of the slope d
$E(\ )$	expectation (of the random variable given in the brackets)
I	number of reference states used in the calibration experiment
$i = 1, ..., I$	identifying variable of the reference states
J	number of preparations for each reference state
$j = 1, ..., J$	identifying variable of preparations for the reference- and basic state
K	number of preparations for the actual state
$k = 1, ..., K$	identifying variable of preparations for the actual state
L	number of repeated measurements for each preparation
$l = 1,..., L$	identifying variable of the repeated measurements per preparation
M	multiplying factor
m	number of consecutive calibrations
N	number of preparations in the calibration experiment; if the number of preparations for each reference state is identical, then $N = I{\cdot}J$, and the total number of measurements in the calibration experiment is $N{\cdot}L$
$q = 0,1,2, ...$	number of the iteration step
s	empirical standard deviation

$s_{xx} = J\sum_{i=1}^{I}(x_i - \bar{x})^2$	sum of squared deviations of the chosen values of the net state variable for the reference states (including the basic state) from the average
$s_{xxw} = J\sum_{i=1}^{I} w_i(x_i - \bar{x}_w)^2$	weighted sum of squared deviations of the chosen values of the net state variable for the reference states (including the basic state) from the weighted average
T	auxiliary value for the weighted linear regression analysis
$V(\;)$	variance (of the random variable given in the brackets)
w_i	weight at x_i
$\hat{w}_{qi}$	weight at x_i in the q^{th} iteration step
X	net state variable, $X = Z - z_0$
x	a particular value of the net state variable
$x_1, ..., x_I$	chosen values of the net state variable X for the reference states including the basic state
x_c	critical value of the net state variable
x_d	minimum detectable value of the net state variable
$\bar{x} = \frac{1}{I}\sum_{i=1}^{I} x_i$	average of the chosen values of the net state variable for the reference states (including the basic state)
$\hat{x} = \frac{\bar{y}_a - \hat{a}}{\hat{b}}$	estimated value of the net state variable for a specific actual state
$\bar{x}_w = \sum_{i=1}^{I} w_i x_i \Big/ \sum_{i=1}^{I} w_i$	weighted average of the chosen values of the net state variable for the reference states (including the basic state)
Y	response variable
y_c	critical value of the response variable
y_{ijl}	l^{th} measurement of the j^{th} preparation of the i^{th} reference state
$y_{k1}, ..., y_{kl}$	obtained values of the response variable for the k^{th} preparation of a specific actual state in the measurement series
$\bar{y}_a = \frac{1}{K \cdot L}\sum_{k=1}^{K}\sum_{l=1}^{L} y_{kl}$	average of the observed values for a specific actual state
$\bar{y} = \frac{1}{I \cdot J \cdot L}\sum_{i=1}^{I}\sum_{j=1}^{J}\sum_{l=1}^{L} y_{ijl}$	average of the measurement values y_{ijl}
$\bar{y}_{ij} = \frac{1}{L}\sum_{l=1}^{L} y_{ijl}$	average of the measurement values of the j^{th} preparation of the i^{th} reference state

$\bar{y}_i = \frac{1}{J \cdot L}\sum_{j=1}^{J}\sum_{l=1}^{L} y_{ijl}$	average of the measurement values of the i^{th} reference state
$\bar{y}_0$	average of the $K \cdot L$ measurement values at $x = 0$
Z	state variable
z_0	value of the state variable in the basic state
α	probability of erroneously rejecting the null hypothesis "the state under consideration is not different from the basic state with respect to the state variable" for each of the observed actual states in the measurement series for which this null hypothesis is true (probability of the error of the first kind) in the absence of specific recommendations the value α should be fixed at $\alpha = 0{,}05$
β	probability of erroneously accepting the null hypothesis “the state under consideration is not different from the basic state with respect to the state variable” for each of the observed actual states in the measurement series for which the net state variable is equal to the minimum detectable value to be determined (probability of the error of the second kind) in the absence of specific recommendations the value β should be fixed at $\beta = 0{,}05$
δ	non-centrality parameter of the non-central t-distribution
ε	component of the response variable measurement representing the random component of sampling, preparation and measurement errors
ν	degrees of freedom
σ_{diff}	standard deviation of the difference between the average, $\bar{y}$, and the estimated intercept, $\hat{a}$
$\hat{\sigma}$	estimate of the residual standard deviation
$\hat{\sigma}_{qi}$	standard deviation at x_i in the q^{th} iteration step
$\hat{\sigma}_0$	estimate of the residual standard deviation, $x = 0$

Annex B
(informative)

Derivation of formulae

B.1 Case 1 — Constant standard deviation

Under the assumptions of 5.1 and in the case of constant standard deviation, estimations of the regression coefficients, $\hat{a}$ and $\hat{b}$, are normally distributed with expectations

$$E(\hat{a}) = a \quad ; \quad E(\hat{b}) = b$$

and variances:

$$V(\hat{a}) = \left(\frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}} \right) \sigma^2 \;;\; V(\hat{b}) = \frac{\sigma^2}{s_{xx}}$$

where

σ^2 is the variance of the residuals of the averages of the L repeated measurements for each preparation.

If the response variable is measured $K \cdot L$ times at the basic state $(z = z_0, x = 0)$, the difference between the average $\bar{y}_0$ of the $K \cdot L$ values and the estimated intercept $\hat{a}$ follows a normal distribution with expectation:

$$E(\bar{y}_0 - \hat{a}) = E(\bar{y}_0) - E(\hat{a}) = a - a = 0$$

and variance:

$$V(\bar{y}_0 - \hat{a}) = V(\bar{y}_0) + V(\hat{a}) = \frac{\sigma^2}{K} + \left(\frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}} \right) \sigma^2 = \left(\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}} \right) \sigma^2$$

Since $(\bar{y}_0 - \hat{a})$ is normally distributed, the random variable

$$U = \frac{\bar{y}_0 - \hat{a}}{\sigma_{\text{diff}}}$$

follows the standardized normal distribution, and the inequality:

$$\frac{\bar{y}_0 - \hat{a}}{\sigma_{\text{diff}}} \leqslant u_{0,95}$$

holds with probability 0,95. Since σ_{diff}^2 is unknown it can be estimated as:

$$\hat{\sigma}_{\text{diff}}^2 = \left(\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}} \right) \hat{\sigma}^2$$

where

$\hat{\sigma}^2$ is the estimated residual variance of the regression analysis that shall be used instead. The random variable

$$T(\nu) = \frac{\bar{y}_0 - \hat{a}}{\hat{\sigma}_{\text{diff}}}$$

follows the t-distribution with $\nu = I \cdot J - 2$ degrees of freedom, and the inequality:

$$\frac{\bar{y}_0 - \hat{a}}{\hat{\sigma}_{\text{diff}}} \leqslant t_{0,95}(\nu)$$

or

$$\bar{y}_0 \leqslant \hat{a} + t_{0,95}(\nu)\hat{\sigma}_{\text{diff}} = \hat{a} + t_{0,95}(\nu)\hat{\sigma}\sqrt{\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}}}$$

where

$t_{0,95}(\nu)$ is the 95 %-quantile of the t-distribution with ν degrees of freedom, holds with probability 0,95.

The right hand side of this inequality is the critical value of the response variable.

$$y_{\text{c}} = \hat{a} + t_{0,95}(\nu)\hat{\sigma}\sqrt{\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}}}$$

and the critical value of the net state variable is

$$x_{\text{c}} = \frac{y_{\text{c}} - \hat{a}}{\hat{b}} = t_{0,95}(\nu)\frac{\hat{\sigma}}{\hat{b}}\sqrt{\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}}}$$

Similar expressions describe these values when other quantiles of the t-distribution are appropriate.

In order to determine the minimum detectable value x_{d} of the net state variable, it is necessary to examine the distribution of $(\bar{y} - \hat{a})/\hat{\sigma}_{\text{diff}}$ in the case where the true value x of the net state variable is identical to the minimum detectable value x_{d} of the net state variable, $x = x_{\text{d}}$. It is required to detect this state with probability $1-\beta$, i.e:

$$P\left[\frac{\bar{y} - \hat{a}}{\hat{\sigma}_{\text{diff}}} > t_{0,95}(\nu) \,\middle|\, x = x_{\text{d}}\right] = 1 - \beta$$

or

$$P\left[\frac{\bar{y} - \hat{a}}{\hat{\sigma}_{\text{diff}}} \leqslant t_{0,95}(\nu) \,\middle|\, x = x_{\text{d}}\right] = \beta$$

If $x = x_{\text{d}}$, the expectation of $\bar{y}$ is:

$$E(\bar{y}) = a + bx_{\text{d}}$$

and therefore:

$$E(\bar{y}-\hat{a})=bx_\mathrm{d}$$

whereas:

$$V(\bar{y}-\hat{a})=\sigma_\mathrm{diff}^2$$

as for $x = 0$.

$$P\left[\frac{\bar{y}-\hat{a}}{\hat{\sigma}_\mathrm{diff}}\leqslant t_{0,95}(\nu)\,\middle|\; x=x_\mathrm{d}\right]$$

$$=P\left[\frac{(\bar{y}-\hat{a})-bx_\mathrm{d}+bx_\mathrm{d}}{\hat{\sigma}_\mathrm{diff}}\leqslant t_{0,95}(\nu)\,\middle|\; x=x_\mathrm{d}\right]$$

$$=P\left[\frac{\dfrac{\bar{y}-\hat{a}-bx_\mathrm{d}}{\sigma_\mathrm{diff}}+\dfrac{bx_\mathrm{d}}{\sigma_\mathrm{diff}}}{\hat{\sigma}_\mathrm{diff}\big/\sigma_\mathrm{diff}}\leqslant t_{0,95}(\nu)\right]$$

$$=P\left[\frac{U+\delta}{\sqrt{\chi^2(\nu)\big/\nu}}\leqslant t_{0,95}(\nu)\right]$$

$$=P\left[T(\nu;\delta)\leqslant t_{0,95}(\nu)\right]\ ;$$

since $U=(\bar{y}-\hat{a}-bx_\mathrm{d})\,/\,\sigma_\mathrm{diff}$ follows the standardized normal distribution and $\hat{\sigma}_\mathrm{diff}\big/\sigma_\mathrm{diff}$ independent of U follows the distribution of $\sqrt{\chi^2(\nu)\big/\nu}$, the random variable $T(\nu,\delta)$ follows the noncentral *t*-distribution with ν degrees of freedom and noncentrality parameter δ; $\delta=\delta(\nu;\alpha;\beta)$ for $\alpha=0{,}05$ or other appropriate value, if required is determined as the value of the noncentrality parameter of the noncentral *t*-distribution with ν degrees of freedom that satisfies:

$$P\left[T(\nu,\delta)\leqslant t_{1-\alpha}(\nu)\right]=\beta$$

From:

$$\delta=\frac{bx_\mathrm{d}}{\sigma_\mathrm{diff}}$$

the expression:

$$x_\mathrm{d}=\delta\frac{\sigma_\mathrm{diff}}{b}=\delta\frac{\sigma}{b}\sqrt{\frac{1}{K}+\frac{1}{I\cdot J}+\frac{\bar{x}^2}{s_{xx}}}$$

for the minimum detectable value of the net state variable follows.

For a prognosis, the estimates of b and σ are inserted into the formula so that the minimum detectable value is given by:

$$\hat{x}_\mathrm{d} = \delta \frac{\hat{\sigma}}{\hat{b}} \sqrt{\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}}}$$

The critical value of the response variable y_c is the sum of $\hat{a}$ and a multiple of $\hat{\sigma}$, and the critical value of the net state variable is a multiple of $\hat{\sigma}/\hat{b}$. If, according to the recommendations, the values of the net state variable of the reference states are equidistantly spaced with the smallest value zero, $\alpha = 0{,}05$ and either

— $K = 1$ (one preparation for the measurement of the actual state) or;

— $K = J$ (number of preparations for the measurement of the actual state equal to this for the reference states);

the multiplier:

$$M = t_{0,95}(\nu) \sqrt{\frac{1}{K} + \frac{1}{I \cdot J} + \frac{\bar{x}^2}{s_{xx}}}$$

in the expressions for the critical values is a function of the number of reference states, I, and the number of preparations of each reference state, J, only. For some cases M is given in Table B.1.

Table B.1 — Determination of the multiplier factor, M

For $K = 1$					
I	J	$I \cdot J$	$\sqrt{1+\frac{1}{I \cdot J}+\frac{\bar{x}^2}{s_{xx}}}$	$t_{0,95}(\nu)$	M
3	1	3	1,35	6,31	8,52
3	2	6	1,19	2,13	2,54
5	1	5	1,26	2,35	2,97
5	2	10	1,14	1,86	2,12
5	4	20	1,07	1,73	1,86
For $K = J$					
I	J	$I \cdot J$	$\sqrt{\frac{I+1}{I \cdot J}+\frac{\bar{x}^2}{s_{xx}}}$	$t_{0,95}(\nu)$	M
3	1	3	1,35	6,31	8,54
3	2	6	0,96	2,13	2,04
5	1	5	1,26	2,35	2,97
5	2	10	0,89	1,86	1,66
5	4	20	0,63	1,73	1,09

B.2 Case 2 — Standard deviation linearly dependent on the net state variable

Under the assumptions of 5.1 and in the case of the standard deviation being linearly dependent on the net state variable, the estimations of the regression coefficients, $\hat{a}$ and $\hat{b}$, are normally distributed with expectations:

$$E(\hat{a}) = a \quad ; \quad E(\hat{b}) = b$$

and variances:

$$V(\hat{a}) = \left(\frac{T_3}{T_1 T_3 - T_2^2} \right) \sigma^2 = \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}} \right) \sigma^2$$

$$V(\hat{b}) = \left(\frac{T_1}{T_1 T_3 - T_2^2} \right) \sigma^2 = \frac{\sigma^2}{s_{xxw}}$$

where

σ^2 is defined so that $w_i \sigma^2$ is the variance of the residuals of the averages of the L repeated measurements for preparation i.

If the response variable is measured $K \cdot L$ times at the basic state $(Z = z_0,\ X = 0)$, the difference between the average $\bar{y}$ of the $K \cdot L$ values and the estimated intercept $\hat{a}$ follows a normal distribution with expectation:

$$E(\bar{y} - \hat{a}) = E(\bar{y}) - E(\hat{a}) = a - a = 0$$

and variance:

$$V(\bar{y} - \hat{a}) = V(\bar{y}) + V(\hat{a}) = \frac{\sigma_0^2}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}} \right) \sigma^2 = \sigma_{\text{diff}}^2$$

σ_{diff}^2 is unknown, but can be estimated as follows:

$$\hat{\sigma}_{\text{diff}}^2 = \frac{\hat{\sigma}_0^2}{K} + \hat{V}(\hat{a}) = \frac{\hat{\sigma}_0^2}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}} \right) \hat{\sigma}^2$$

where

$\hat{\sigma}_0^2$ is taken from equation (20) and $\hat{\sigma}^2$ is the estimated residual variance of the weighted regression analysis, which shall be used instead.

In analogy to case 1 the critical value of the response variable is:

$$y_{\text{c}} = \hat{a} + t_{0,95}(\nu) \hat{\sigma}_{\text{diff}} = \hat{a} + t_{0,95}(\nu) \sqrt{\frac{\hat{\sigma}_0^2}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}} \right) \hat{\sigma}^2}$$

and the critical value of the net state variable is:

$$x_{\text{c}} = t_{0,95}(\nu) \frac{\hat{\sigma}_{\text{diff}}}{\hat{b}} = \frac{t_{0,95}(\nu)}{\hat{b}} \sqrt{\frac{\hat{\sigma}_0^2}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}} \right) \hat{\sigma}^2}$$

Similar expressions describe these values when other quantiles of the t-distribution are appropriate.

These formulae include the case of constant standard deviation for which all the weights are equal to one, $w_i = 1$ for $i = 1,\dots,I$ so that $T_1 = I \cdot J$, $\bar{x}_w = \bar{x}$, $s_{xxw} = s_{xx}$ and $\hat{\sigma}_0^2 = \hat{\sigma}^2$.

The minimum detectable value of the net state variable is:

$$x_\text{d} = \delta \frac{\sigma_\text{diff}}{b}$$

where, for $x = x_\text{d}$,

$$\sigma^2_{\text{diff},x_\text{d}} = V\left(\bar{y} - \hat{a} \middle| x = x_\text{d}\right) = V\left(\bar{y} \middle| x = x_\text{d}\right) + V(\hat{a})$$

For a prognosis, the estimates of b and $\sigma^2_{\text{diff},x_\text{d}}$, $\hat{b}$ and:

$$\hat{\sigma}^2_{\text{diff},x_\text{d}} = \hat{V}\left(\bar{y} \middle| x = x_\text{d}\right) + \hat{V}(\hat{a}) = \frac{\hat{\sigma}^2(x_\text{d})}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}}\right)\hat{\sigma}^2$$

are inserted into the formula so that the minimum detectable value of the net state variable is given by:

$$x_\text{d} = \frac{\delta}{\hat{b}} \sqrt{\frac{\hat{\sigma}^2(x_\text{d})}{K} + \left(\frac{1}{T_1} + \frac{\bar{x}_w^2}{s_{xxw}}\right)\hat{\sigma}^2}$$

Since $\hat{\sigma}^2(x_\text{d})$ depends on the value of x_d yet to be calculated the iterative procedure of 5.3.5 has to be used.

Annex C
(informative)

Examples

C.1 Example 1

The mercury content, expressed in ng/g[1] of plant materials, was measured by atomic absorption spectroscopy. Each sample was decomposed using a microwave (MLS-1200) technique and taken up in nitric acid / potassium dichromate solution. These solutions were examined through a Varian VGA-76 cold vapour reduction system leading to a gold-plated foil concentration system (MCA-90) prior to replicated atomic absorption measurements. In order to estimate the calibration function and to determine the capability of detection, each of six reference samples representing the blank concentration ($x = 0$) and the net concentrations x = 0,2 ng/g; 0,5 ng/g; 1,0 ng/g; 2,0 ng/g; 3,0 ng/g was prepared three times and each prepared sample measured once. Hence, I = 6; J = 3; L = 1.

It was assumed that the assumptions of linearity of the calibration function, constant standard deviation and normal distribution of the response variable hold; α and β had been fixed in advance at $\alpha = \beta = 0{,}05$. For the determination of the concentration of mercury in the material to be analysed, two different approaches were taken into consideration:

a) one measurement would be carried out (K = L = 1); or

b) three samples would be prepared for measurement and each of them measured once (K = 3; L = 1) and the average $\bar{y}_a$ of the observed values used as the measurement result.

The results of the calibration experiment are given in Table C.1.

Table C.1 — Results of the calibration experiment for the determination of mercury content in food or drugs

Reference sample i	**Net concentration of mercury** x_i ng/g	**Absorbance** y_{ij}		
1	0	0,003	− 0,001	0,002
2	0,2	0,004	0,005	0,005
3	0,5	0,011	0,011	0,012
4	1,0	0,023	0,023	0,023
5	2,0	0,048	0,047	0,048
6	3,0	0,071	0,072	0,072

---

[1] 1 part per billion (ppb) = 10^{-9} g/g = 1 ng/g. The use of ppb is deprecated.

The statistical analysis yields:

$\bar{x} = 1{,}116\ 7\ \text{ng/g}$

$s_{xx} = 20{,}425$

$\hat{a} = 9{,}995\ 9 \times 10^{-5}$

$\hat{b} = 0{,}023\ 74$

$\hat{\sigma} = 1{,}109\ 9 \times 10^{-3}$

Since $\nu = N - 2 = 16$;

$t_{0,95}(\nu) = t_{0,95}(16) = 1{,}746$;

$\delta(\nu; \alpha; \beta) = \delta(16; 0{,}05; 0{,}05) = 3{,}440$;

$\left(2t_{0,95}(\nu) = 3{,}492\right)$

The results for the approach a) are

critical value of the response variable [see equation (5)] $y_\text{c} = 0{,}003\ 05$

critical value of the net concentration [see equation (6)] $x_\text{c} = 0{,}086\ \text{ng/g}$

minimum detectable net concentration [see equation (7)] $x_\text{d} = 0{,}173\ \text{ng/g}$

- the smallest absorbance value which can be interpreted as coming from a sample with a net mercury concentration larger than the blank concentration is $y_\text{c} = 0{,}003\ 05$, the critical value of the response variable;
- the smallest net concentration of mercury in a sample which can be distinguished (with a probability of $1 - \beta = 0{,}95$) from the blank concentration is $x_\text{d} = 0{,}173\ \text{ng/g}$, the minimum detectable value of the net concentration.

The results for approach b) are:

critical value of the response variable [see equation (5)] $y_\text{c} = 0{,}002\ 30$

critical value of the net concentration [see equation (6)] $x_\text{c} = 0{,}055\ \text{ng / g}$

minimum detectable net concentration [see equation (7)] $x_\text{d} = 0{,}110\ \text{ng / g}$

C.2 Example 2[2)]

The amount of toluene in 100 µl of extracts was measured using gas chromatography interfaced with a mass spectrometric detector (GC/MS). 100 µl samples were injected into the GC/MS system. Six reference samples were used and contained toluene in known amounts in the range 4,6 pg/100 µl to 15 000 pg/100 µl. Each sample was injected and measured four times ($I = 6$, $J = 4$, $L = 1$, $N = 24$). The measurement results are given in Table C.2.

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2) D.M. Rocke and S. Lorenzato. A Two-Component Model for Measurement Error in Analytical Chemistry. *Technometrics*, 1995, **37**, pp. 181-182.

A look at the graphical representation of the measurement results shows that the relationship between the toluene amount and the response variable (peak area) is satisfactorily linear; the standard deviation of the peak area is linearly dependent on the amount of toluene. Under the additional assumption of normal distribution of the response variable the capability of detection can be determined according to 5.3.

Table C.2 — Results of the calibration experiment for the toluene amount in 100 µl extract

(1)	(2)	(3)				(4)	(5)	(6)	(7)
Reference sample	**Net amount of toluene**	**Peak area**				**Empirical standard deviation**	**Predicted standard deviation of iteration**		
							1	**2**	**3**
i	x_i pg/100 µl	y_{ij}				s_i	$\hat{\sigma}_{1i}$	$\hat{\sigma}_{2i}$	$\hat{\sigma}_{3i}$
1	4,6	29,80	16,85	16,68	19,52	6,20	4,56	5,17	5,15
2	23	44,60	48,13	42,27	34,78	5,65	7,07	7,93	7,92
3	116	207,70	222,40	172,88	207,51	21,02	19,73	21,87	21,88
4	580	894,67	821,30	773,40	936,93	73,19	82,91	91,43	91,57
5	3 000	5 350,65	4 942,63	4 315,79	3 879,28	652,98	412,46	454,22	455,02
6	15 000	20 718,14	24 781,61	22 405,76	24 863,91	2 005,02	2 046,54	2 253,14	2 257,23

In the estimation procedure for c and d an iteratively reweighted linear regression analysis according to 5.3.2 is carried out which produces the following estimated linear regression functions:

iteration 1: $\hat{\sigma}_{1i} = 3{,}933\ 23 + 0{,}136\ 174\ x_i$

iteration 2: $\hat{\sigma}_{2i} = 4{,}482\ 84 + 0{,}149\ 911\ x_i$

iteration 3: $\hat{\sigma}_{3i} = 4{,}462\ 28 + 0{,}150\ 185\ x_i$

The corresponding predicted standard deviations are given in columns (5) to (7) of Table C.2. After the third iteration the results are stable so that the equation of iteration 3 can be used as the final result of part 1 of the estimation procedure, i.e.:

$$\hat{\sigma}(x) = 4{,}462\ 28\ + 0{,}150\ 185\ x$$

$$\hat{\sigma}_0 = 4{,}462\ 28$$

The parameters a and b of the calibration function are estimated by a weighted linear regression analysis according to clause 5.3.3 with the y_{ij} of column (3) as values of the dependent variable, x_i of column (2) as values of the independent variable and weights:

$$w_i = \frac{1}{\hat{\sigma}^2(x_i)} = \frac{1}{(4{,}462\ 28 + 0{,}150\ 185\ x_i)^2}$$

This regression analysis yields:

$$T_1 = J\sum_{i=1}^{I} w_i \quad = 0{,}223\ 306$$

$$\bar{x}_w \quad = 15{,}566\ 9$$

s_{xxw} = 606,224

$\hat{a}$ = 12,218 5

$\hat{b}$ = 1,527 27

$\hat{\sigma}^2$ = 1,059 54

ν = $N - 2 = 22$

$t_{0,95}(\nu)$ = $t_{0,95}(22) = 1{,}717$

Therefore for $K = 1$, the following are obtained:

critical value of the response variable [see equation (24)] $y_{\text{c}} = 20{,}82$

the critical value of the net toluene amount in 100 µl of extract [see equation (25)] $x_{\text{c}} = 5{,}63$ pg.

The minimum detectable value is calculated iteratively:

For $\alpha = \beta = 0{,}05$, $\delta(\nu; \alpha; \beta) = \delta(22; 0{,}05; 0{,}05) = 3{,}397$ (see Table 1) and with $\hat{\sigma}(x_{\text{d}})_0 = \hat{\sigma}_0$ the first value for x_{d} [see equation (29)] is $x_{\text{d0}} = 11{,}139$; it follows $\hat{\sigma}(x_{\text{d}})_1 = 6{,}135\ 2$ and $x_{\text{d1}} = 14{,}553$;

with $\hat{\sigma}(x_{\text{d}})_2 = 6{,}647\ 9$ iteration 2 leads $x_{\text{d2}} = 15{,}627$ pg/100 µl and

with $\hat{\sigma}(x_{\text{d}})_3 = 6{,}809\ 2$ we get finally $x_{\text{d}} = x_{\text{d3}} = 15{,}967$ pg/100 µl.

The smallest peak area which can be interpreted as coming from a sample with a net toluene concentration larger than the blank concentration is $y_{\text{c}} = 20{,}82$, the critical value of the response variable.

The smallest net amount of toluene in a sample of 100 µl extract which can be distinguished (with a probability of $1 - \beta = 0{,}95$) from the blank concentration is $x_{\text{d}} = 15{,}97$ pg/100 µl, the minimum detectable value of the net toluene concentration.

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ICS 03.120.30; 17.020

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