IUPAC/CITAC Guide: Evaluation of risks of false decisions in conformity assessment of a multicomponent material or object due to measurement uncertainty (IUPAC Technical

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Ilya Kuselman*, Francesca R. Pennecchi, Ricardo J. N. B. da Silva and David Brynn Hibbert

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Abstract: Risks of a false decision on conformity of the chemical composition of a multicomponent material or object due to measurement uncertainty are defined using the Bayesian approach. Even if the conformity assessment for each particular component of a material is successful, the total probability of a false decision (total consumer's risk or producer's risk) concerning the material as a whole might still be significant. This is related to the specific batch, lot, sample, environmental compartment, or other item of material or object (specific consumer's and producer's risks), or to a population of these items (global consumer's and producer's risks). A model of the total probability of such false decisions for cases of independent actual ('true') concentrations or contents of the components and the corresponding measurement results is formulated based on the law of total probability. It is shown that the total risk can be evaluated as a combination of the particular risks in the conformity assessment of components of the item. For a more complicated task, *i.e.* for a larger number of components under control, the total risk is greater. When the actual values of the components' concentrations or contents, as well as the measurement results, are correlated, they are modelled by multivariate distributions. Then, a total global risk of a false decision on the material conformity is evaluated by the calculation of integrals of corresponding joint probability density function. A total specific risk can be evaluated as the joint posterior cumulative function of actual property values of a specific item lying outside the multivariate specification (tolerance) domain when the vector of measured values obtained for the item is inside this domain. The effect of correlation on the risk is not easily predictable. Examples of the evaluation of risks are provided for conformity assessment of denatured alcohols, total suspended particulate matter in ambient air, a cold/flu medication, and a PtRh alloy.

Keywords: Chemical composition; conformity assessment; correlation; measurement uncertainty; multicomponent material; risk of a false decision.

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***Corresponding author: Ilya Kuselman**, Independent Consultant on Metrology, 4/6 Yarehim St., 7176419 Modiin, Israel, E-mail: ilya.kuselman@bezeqint.net. https://orcid.org/0000-0002-5813-9051
Francesca R. Pennecchi, Istituto Nazionale di Ricerca Metrologica (INRIM), Strada delle Cacce 91, 10135 Turin, Italy, E-mail: f.pennecchi@finrim.it. https://orcid.org/0000-0003-1328-3858
Ricardo J. N. B. da Silva, Centro de Química Estrutural, Faculdade de Ciências da Universidade de Lisboa, Edifício C8, Campo Grande, 1749-016 Lisbon, Portugal, E-mail: rjsilva@fc.ul.pt. https://orcid.org/0000-0001-6378-0479
David Brynn Hibbert, School of Chemistry, UNSW Sydney, Sydney NSW 2052, Australia, E-mail: b.hibbert@unsw.edu.au. https://orcid.org/0000-0001-9210-2941

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1 Introduction

The Joint Committee for Guides in Metrology (JCGM) provides guidance and procedures JCGM 106 [1] for assessing the conformity of an item (entity, object, or system) with specified requirements. The approach of this document is to treat knowledge about an item property (the measurand) as a random variable, expressed in terms of a probability density function (pdf). According to Bayes' theorem, a prior knowledge of the measurand and new information acquired during the measurement are combined in a posterior pdf [2, 3]. Such a posterior pdf accumulates what is known about the measurand in the items and allows for the evaluation of the risks of false decisions in their conformity assessment caused by measurement uncertainty [4–6]. The probability of accepting the item, when it should have been rejected, is called the 'consumer's risk', whereas the probability of falsely rejecting the item is called the 'producer's risk'. These risk terms are taken from the field of product manufacturing and process control, but they are also applicable in other fields [7].

Guidelines for risk management [8–10] define risk as the product of the probability of an event and its severity (impact). The severity is expressed for each case in a different way, and not always quantitatively: examples include financial loss, safety and/or security changes, quality loss, and aesthetic and taste worsening in a product. In this Guide, severity is not discussed. The Guide's main task is to estimate the probabilities of false decisions in conformity assessment due to measurement uncertainty and so 'risk' will be considered solely in terms of these probabilities.

Besides the tolerance interval, which is related to the actual values of the measurand, a narrower (more stringent) acceptance interval for the measured values can be applied with the purpose of decreasing the consumer's risks by taking into account measurement uncertainty. In such a case, the decision rules (*i.e.* does the test item conform or not?) are based on a comparison of the measured property values with the acceptance limits [1].

Similar procedures are also described in the earlier Eurachem/CITAC guide [11] for chemical analytical testing laboratories, where the items of interest are samples for material analysis, customs control, environmental, food or clinical analysis, *etc.* The tolerance limits for a sample composition are established specifications in the pharmaceutical industry and other industries and fields, in regulatory and/or legislative limits, as well as in agreed requirements for a non-regulated product under chemical analysis/testing. In general, they are limits within which a product, material, or object would be expected to perform its stated and intended function for customer use [12, 13] or be acceptable from a medical, forensic, or other point of view [14–16].

In current practice, decision rules are often based on direct comparisons of measured property values with the specification, regulatory, or legislative limits. In such cases, the limits have already been set by taking into account the measurement uncertainty. Thus, the tolerance and the acceptance limits coincide. The measurement uncertainty is constrained for this purpose by a requirement to use a specific standardized or fit-for-purpose [17] validated chemical analytical/measurement method.

Guidance documents [1] and [11] are widely used, for example, for the conformity assessment of an analytical instrument [18], investigation of out-of-specification test results of chemical composition [19], forensic decisions on blood alcohol content [20], interpretation of test results of spectral analysis of materials [21], immunochemical screening of blood donors for infectious diseases [22], in legal metrology [23], and in numerous calibration and testing laboratories serving industry and trade. These procedures can be applied where the item is characterized by a single scalar quantity (a single measurable property). In other words, the conformity assessment is performed separately for each item property under testing.

The JCGM 106 approach was recently extended for conformity assessment in the presence of a systematic measurement error [24] and for qualitative human-based binary nominal and ordinal properties [25, 26]. A multivariate data analysis is described in the EURAMET guide to decision-making and conformity assessment [27] using bivariate examples of the 'post office parcel problem' (limitations of a parcel length and girth) and a healthcare study (skin cream friction and adhesion).

Multivariate conformity assessment is especially important in testing the chemical composition of multicomponent materials or objects where measurement uncertainties are not negligible. When conformity assessments for particular components are successful and particular consumer's risks or producer's risks are acceptable, the total probability of a false decision (total consumer's risk or producer's risk) on the conformity of the material or object as a whole might still be significant.

In this Guide, modelling and evaluating the total risks in the conformity assessment of a multicomponent material or object caused by measurement uncertainties are discussed in detail. Examples of the risk evaluation are provided for the conformity assessment of denatured alcohols, total suspended particulate matter (TSPM) in ambient air, a cold/flu medication, and a PtRh alloy.

1.1 Scope and field of application

This Guide is developed for the study of the total risks in the conformity assessment of a multicomponent material or object caused by measurement uncertainties. It will also be helpful for correct risk management, for example, in a factory producing multicomponent materials, for the environmental monitoring of several substances, and for similar tasks.

The document is intended for quality control, measurement and testing (chemical analytical) laboratories, metrologists and analytical chemists (analysts), specialists involved in laboratory accreditation activity, laboratory customers, quality managers, and regulators.

1.2 Terms and definitions

Terms and definitions used in this Guide correspond to JCGM 100 (GUM) [5], JCGM 106 [1], JCGM 200 (VIM) [28], ISO/IEC 17000 [29], ISO 9000 [30], ISO 3534 [31], and IUPAC recommended terms that may be found in the IUPAC Gold Book [32]. The following conventions are adopted:

1. The term '**concentration**' is used for a *quantity of a component of an item subject to conformity assessment* (amount of substance, mass, volume, number of entities) expressed per unit volume of the *item* [32], http://goldbook.iupac.org/html/C/C01222.html, [33].
2. The term '**content**' is used for a *quantity of a component of an item subject to conformity assessment* (amount of substance, mass, volume, number of entities) expressed per unit mass of the *item* [32], https://goldbook.iupac.org/html/S/S06073.html, [34, 35].

The most relevant definitions relating to risks in the conformity assessment of a multicomponent material or object due to measurement uncertainty are given below. The structure of definitions and terms follows ISO 10241 [36], and cross references are given in italic font.

1.2.1 item subject to conformity assessment
item

material or object (chemical entity or species) whose property values can be measured for *conformity assessment*

Note 1: The item can be a batch, lot, sample, or environmental compartment, in chemical or pharmaceutical industries, materials production, clinical testing, and forensic investigations.
Note 2: The property value may be an extensive quantity (amount) or intensive quantity (concentration or content).

1.2.2 component of an item subject to conformity assessment
component

part of an *item subject to conformity assessment* with one or more property values that can vary in *specification intervals*

Adapted from ref. [32], https://goldbook.iupac.org/html/C/C01209.html.

Note: The number of components of a given item is the minimum number of its parts necessary for a *conformity assessment* of the item.

1.2.3 actual value of a component property value
actual property value
actual value

best estimate of a *component* property value (concentration or content), considered the true quantity value when the definitional (intrinsic) uncertainty associated with the component concentration or content is negligible

Adapted from JCGM 200 [28], clauses 2.11 and 2.27, and JCGM 100 [5], Annex D.

Note 1: Definitional (intrinsic) uncertainty may be caused by inhomogeneity of the item, and/or its instability.
Note 2: True value is unknown, it is an idealized concept.

1.2.4 tolerance interval

interval of permissible property values of a *component*

Adapted from JCGM 106 [1], clause 3.3.5.

Note 1: Tolerance interval can be set as a specification, regulatory, or legislative interval.
Note 2: For a multicomponent material or object, the permissible property values of the components form a multivariate region called the 'tolerance domain'.

1.2.5 tolerance limit

upper or lower bound of a *tolerance interval*

Adapted from JCGM 106 [1], clause 3.3.4, and ref. [12, 13].

Note 1: When tolerance interval is set as a specification, regulatory, or legislative interval, there are specification, regulatory, or legislative limits, respectively.

Note 2: When only an upper or lower limit is specified, the tolerance interval is considered to extend from the minimal feasible value (*e.g.* mass fraction 0 %) to the upper limit, or from the lower limit to the maximal feasible value (*e.g.* mass fraction 100 %), respectively.

1.2.6 acceptance interval

interval of the permissible measured values of a *component* property

Adapted from JCGM 106 [1], clause 3.3.9.

Note 1: Acceptance interval is narrower than the corresponding *tolerance interval* when applied for decreasing the consumer's risks, taking into account the measurement uncertainty.
Note 2: For a multicomponent material or object, the permissible measured values of the components' property form a multivariate region called 'acceptance domain'.

1.2.7 acceptance limit

upper or lower bound of an *acceptance interval*

Adapted from JCGM 106 [1], clause 3.3.8.

Note: Acceptance limits and *tolerance limits* coincide when the tolerance limits have already taken the measurement uncertainty into account.

1.2.8 conformity assessment

activity to determine whether specified requirements relating to an *item* are fulfilled

Note: In chemical testing, the activity is measurement of the property values (concentrations or contents) of the item *components*, and comparison of the obtained results with the *specification or other limits* on these values.

Adapted from ISO/IEC 17000 [29], clause 2.1.

1.2.9 particular specific consumer's risk

probability that an *item*, accepted as a result of a *conformity assessment* of a particular *component* property (concentration or content), does not conform

Adapted from JCGM 106 [1], clause 3.3.13.

Note 1: It is the probability of failure to reject the null hypothesis 'the component concentration or content is in its *tolerance interval*', when in fact the null hypothesis is not true, a Type II error according to ISO/IEC 3534 [31], clause 1.47.
Note 2: When the conformity assessment is related to the upper limit of the tolerance interval of a component concentration or content, for example, the specific consumer's risk is the risk of underestimating the true property value.

1.2.10 particular specific producer's risk

probability that an *item*, rejected as a result of a *conformity assessment* of a particular *component* property (concentration or content), does conform

Adapted from JCGM 106 [1], clause 3.3.14.

Note 1: It is the probability of rejection of the null hypothesis 'the component concentration or content is in its *tolerance interval*', when in fact the null hypothesis is true, a Type I error according to ISO/IEC 3534 [31], clause 1.46.

Note 2: When the conformity assessment is related to the upper limit of the tolerance interval of a component concentration, for example, the producer's risk is the risk of overestimating the true concentration or content.

1.2.11 particular global consumer's risk

probability that a non-conforming property value of a particular *component* will be assessed as conforming based on a statistical analysis of earlier performed measurement (chemical analytical test) results

Adapted from JCGM 106 [1], clause 3.3.15.

Note: The particular global consumer's risk corresponds to the consumer's risk of incorrect assessment of a particular component concentration or content in an *item* randomly drawn from a statistical population of such items. Thus, this consumer's risk characterizes the material production (or objects) globally.

1.2.12 particular global producer's risk

probability that a conforming property value of a particular *component* will be assessed as non-conforming based on a statistical analysis of earlier performed measurement (chemical analytical test) results

Adapted from JCGM 106 [1], clause 3.3.16.

Note: The particular global producer's risk corresponds to the producer's risk of incorrect assessment of a particular component concentration or content in an *item* randomly drawn from a statistical population of such items. This producer's risk characterizes the material production (or objects) globally, as the consumer's risk in clause 1.2.11.

1.2.13 total specific consumer's risk

probability that a specific accepted *item* does not conform, as a whole, when *conformity assessment* is related to property values of two or more *components*

Note: The term 'total risk' is derived from the law of total probability, a fundamental rule [37–39] that expresses the total probability of an outcome realized *via* several distinct events.

1.2.14 total specific producer's risk

probability that property values of all *components* in a specific rejected *item* are conforming

1.2.15 total global consumer's risk

probability that an *item* with non-conforming property values of one or more *components* will be accepted based on a statistical analysis of earlier performed measurement (chemical analytical test) results

1.2.16 total global producer's risk

probability that an *item* with conforming property values of all the *components* will be rejected based on a statistical analysis of earlier performed measurement (chemical analytical test) results

1.2.17 prior distribution
prior

pre-measurement knowledge about the distribution of property values of a *component*

Adapted from JCGM 106 [1], clause 6.1.

Note 1: The knowledge is usually expressed as a probability density function (pdf).
Note 2: When the property values of the components' concentrations or contents are correlated, a joint multivariate prior pdf should be considered.

1.2.18 likelihood function
likelihood

knowledge about the distribution of measured values for a given *actual value* of a *component* property

Adapted from JCGM 106 [1], clause 6.2.

Note 1: The knowledge is usually expressed as a pdf.
Note 2: When the measured values of the components' concentrations or contents are correlated, a joint multivariate pdf should be considered.

1.2.19 posterior distribution
posterior

post-measurement knowledge about the distribution of property values of a *component*

Adapted from JCGM 106 [1], clause 6.2.

Note 1: The knowledge is usually expressed as a pdf.
Note 2: When either the *prior* pdf or the *likelihood function* is multivariate, the posterior pdf is also multivariate.

1.3 Symbols

A_i	acceptance interval of measured values $c_{i\mathrm{m}}$ of i-th component concentration or content
$A_{\mathrm{L}i}$	lower limit of the acceptance interval of $c_{i\mathrm{m}}$
$A_{\mathrm{U}i}$	upper limit of the acceptance interval of $c_{i\mathrm{m}}$
B	event, when true concentration or content c_i of one or more components are not within their tolerance interval T_i
$\overline{\mathrm{B}}$	event, when c_i for any i are within their tolerance intervals T_i
$\mathrm{B_i}$	event, when c_i is not within its tolerance interval T_i
$\overline{\mathrm{B}}_i$	event, when c_i is within its tolerance interval T_i
C_i	event, when measured value $c_{i\mathrm{m}}$ is within its acceptance interval A_i
$\overline{\mathrm{C}}_i$	event, when $c_{i\mathrm{m}}$ is not within its A_i
C	event, when $c_{i\mathrm{m}}$ for any i are within their A_i
C	normalizing constant
$\overline{\mathrm{C}}$	event, when one or more $c_{i\mathrm{m}}$ are not within their A_i
$\boldsymbol{c}_n$	vector of c_i, $i = 1, 2, \ldots, n$
C	superscript 'complementary'
$\boldsymbol{c}$	vector of the prior mean values μ_i, $i = 1, 2, \ldots, n$
$\boldsymbol{c}_{\mathbf{post}}$	vector of the posterior means
$\overline{\boldsymbol{c}}_{\mathrm{m}}$	vector of the arithmetic means of replicated measured values
c_i	actual (true) concentration or content of i-th component in an item
$c_{i\mathrm{m}}$	measured value of concentration or content of i-th component
$\boldsymbol{c}_{\mathrm{m}}$	vector of $c_{i\mathrm{m}}$, $i = 1, 2, \ldots, n$
cov_{ij}	covariance of concentrations or contents of components $i \neq j$
$\exp[\ldots]$	exponential function $e^{[\ldots]}$

g	posterior pdf
g_0	prior pdf
h	likelihood function
i, j, k, l, and q	subscripts of the components in the range from 1 to n
l_i	labeled amount of component i in a medication tablet
m_i	experimental (sampling) mean of i-th component concentration or content
μ_i	theoretical (population) mean of i-th component concentration or content
n	number of components
n_{rep}	number of replicated measured values
Ω	scenario (set of conditions)
P	probability
R^*_{ci}	particular specific risk
$R^*_{ci(\text{c})}$	particular specific consumer's risk
$R^*_{ci(\text{p})}$	particular specific producer's risk
R_{ci}	particular global risk
$R_{ci(\text{c})}$	particular global consumer's risk
$R_{ci(\text{p})}$	particular global producer's risk
R^*_{total}	total specific risk
$R^*_{\text{total}\,(\text{c})}$	total specific consumer's risk
$R^*_{\text{total}\,(\text{p})}$	total specific producer's risk
R_{total}	total global risk
$R_{\text{total(c)}}$	total global consumer's risk
$R_{\text{total(p)}}$	total global producer's risk
r_{ij}	correlation coefficient of concentrations or contents of components $i \neq j$
S_{c}	prior covariance matrix
S_{cm}	likelihood covariance matrix
S_{post}	posterior covariance matrix
s_i^2	experimental (sampling) variance of i-th component concentration or content
σ_i^2	theoretical (population) variance of i-th component concentration or content
T_i	tolerance interval of i-th component concentration or content
$T_{\text{L}i}$	lower limit of the tolerance interval of i-th component concentration or content
$T_{\text{U}i}$	upper limit of the tolerance interval of i-th component concentration or content
u_i	measurement uncertainty of i-th component concentration or content
v	number of components, for which the measured values are out of their acceptance intervals

1.4 Abbreviations

CITAC	Cooperation on International Traceability in Analytical Chemistry
CDA	completely denaturing alcohol
DB	denatonium benzoate
EtOH	ethyl alcohol
Eurachem	A Focus for Analytical Chemistry in Europe
HPLC	high performance liquid chromatography
IEC	International Electrotechnical Commission
IPA	isopropyl alcohol
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JCGM	Joint Committee for Guides in Metrology
MC	Monte Carlo method
MCMC	Markov Chain Monte Carlo method
MEK	methyl ethyl ketone
PCA	principal component analysis
pdf	probability density function
TSPM	total suspended particulate matter (in ambient air)

2 Classification of risks

The chemical composition of a multicomponent material or object is considered to conform when the true concentration or content, c_i, of each i-th *component* under control in the *item*, $i = 1, 2, \ldots, n$, is within its *tolerance interval*, $T_i = [T_{Li}, T_{Ui}]$, where T_{Li} and T_{Ui} are the lower and upper *tolerance limits* of the interval, respectively. To decide whether or not the material or object conforms, the measured value, c_{im}, is compared with the limits of the *acceptance interval*, $A_i = [A_{Li}, A_{Ui}]$, where A_{Li} and A_{Ui} are the lower and upper limits of the interval, respectively, taking into account the measurement uncertainty associated with c_{im}. Note that the acceptance interval may be narrower than the tolerance interval when defending the interests of a consumer, and wider than the tolerance interval when defending the interests of a producer. The tolerance and acceptance intervals may also coincide, as discussed in the Introduction to this Guide.

2.1 Particular risks

A *component-by-component* conformity assessment of an *item* includes the comparison of each measured value, c_{im}, with the corresponding *acceptance interval*, A_i, for component $i = 1, \ldots, n$. The risks of false decisions on conformity related to the particular i-th component (of n) are the 'particular risks.' The evaluation of such univariate risks is described in JCGM 106 [1].

2.1.1 Consumer's risk and producer's risk

The probability of a false decision that a component concentration or content does not exceed the upper *tolerance limit*, for example, based on the measured value $c_{im} \le A_{Ui}$, when the true concentration or content exceeds the upper tolerance limit ($c_i > T_{Ui}$), is the '*particular consumer's risk*'.

The probability of falsely rejecting conformity ($c_{im} > A_{Ui}$, when in fact $c_i \le T_{Ui}$, in the considered example) is the '*particular producer's risk*'.

2.1.2 Specific risk and global risk

For a specified item, the particular risks, related to i-th component concentration or content, are referred to as the '*particular specific consumer's risk*' $R^*_{ci(c)}$ and the '*particular specific producer's risk*' $R^*_{ci(p)}$, respectively.

The particular risks of the incorrect *conformity assessment* of i-th component concentration or content in an item randomly drawn from a statistical population of such items are the '*particular global consumer's risk*' $R_{ci(c)}$ and the '*particular global producer's risk*' $R_{ci(p)}$, respectively.

2.2 Total risks

A multicomponent material or object is not simply a mixture of n *components* or their sum. When the *conformity assessment* for each i-th component concentration or content in an *item* is successful (*i.e.* the particular risks are small enough), the total probabilities of a false decision concerning the conformity of the item as a whole—the total risks—might still be significant [40–43]. The evaluation of the multivariate total risks is detailed in this Guide.

2.2.1 Consumer's specific and global risks

The probability of a false decision that an item is conforming, based on the measured values not exceeding their upper acceptance limits, for example, $c_{im} \le A_{Ui}$ for all $i = 1, \ldots, n$, while as minimum one true component concentration or content exceeds its upper tolerance limit ($c_j > T_{Uj}$), is the '*total consumer's risk*'.

If the conformity of a specific item is assessed, this risk is the '*total specific consumer's risk*' $R^*_{\text{total (c)}}$. When an item is randomly drawn from a statistical population of such items, this is the '*total global consumer's risk*' $R_{\text{total(c)}}$.

2.2.2 Producer's specific and global risks

The probability of falsely rejecting conformity of an item is the '*total producer's risk*' when, at minimum, one measured value exceeds its upper *acceptance limit* ($c_{jm} > A_{Uj}$), for example, while all true values satisfy their upper *tolerance limits*, *i.e.* $c_i \le T_{Ui}$ for all $i = 1, \ldots, n$.

It is the '*total specific producer's risk*', $R^*_{\text{total (p)}}$, when the conformity of a specific item is assessed, and the '*total global producer's risk*', $R_{\text{total(p)}}$, if an item is randomly drawn from a statistical population of such items.

2.3 A map of the risks

A scheme summarizing the classification of the risks of false decisions on the conformity of a multicomponent material or object, represented as a map of the relationships among the different kinds of these risks, is shown in Fig. 1.

There are four kinds of particular risks for each *i*-th *component* of the material and four kinds of total risks in Fig. 1. Therefore, for $n > 1$ components under control, one can distinguish $4(n+1)$ kinds of risks of false decisions. For example, for two, three, and four components, this means 12, 16, and 20 kinds of risks, respectively: the complexity of *conformity assessment* increases with the number of components under control [44].

3 Modelling total risks for independent variables

Bayes' theorem regarding the concentration c_i of a particular *component i* is formulated as

$$g(c_i|c_{im}) = C\, g_0(c_i) h(c_{im}|c_i), \tag{1}$$

where g is the univariate posterior pdf, C is a normalizing constant, g_0 is the univariate *prior* pdf, and h is the

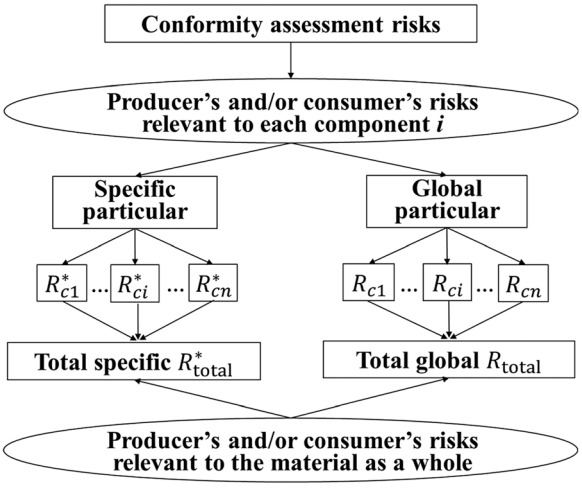

Fig. 1: A map of the risks of false decisions on the conformity of a multicomponent material or object. Specific risks refer to a given *item* and global risks to the population of the items. Particular risks (specific R^*_{ci} or global R_{ci}) refer to the *i*-th *component* of the material under control, $i = 1, \ldots, n$; total risks (specific R^*_{total} or global R_{total}) refer to the material as a whole. These risks are relevant for both the material producer and for its consumer.

univariate *likelihood function*. The product $g_0(c_i)h(c_{im}|c_i)$ is the joint pdf of actual ('true') values, c_i, and measured values, c_{im}. Based on this theorem, the *particular global consumer's risk* and *particular global producer's risk* are formulated in JCGM 106 [1] as integrals of the joint pdf, using Eqs. (2) and (3), respectively:

$$R_{ci(c)} = \int_{T_i^c} \int_{A_i} g_0(c_i)h(c_{im}|c_i)\mathrm{d}c_{im}\mathrm{d}c_i \text{ and} \tag{2}$$

$$R_{ci(p)} = \int_{T_i} \int_{A_i^c} g_0(c_i)h(c_{im}|c_i)\mathrm{d}c_{im}\mathrm{d}c_i, \tag{3}$$

where superscript 'c' indicates the integration intervals 'complementary' to the corresponding *tolerance limits* or *acceptance limits*. Thus, the consumer's risk by Eq. (2) is for measured values c_{im} within *acceptance interval* A_i, when true values c_i are outside *tolerance interval* T_i. The producer's risk by Eq. (3) is for c_{im} outside A_i, when c_i values are within T_i.

The *particular specific consumer's risk* and *particular specific producer's risk*, for a given measured value c_{im}, are the respective integrals of the *posterior* pdf:

$$R^*_{ci(c)} = \int_{T_i^c} g(c_i|c_{im})\mathrm{d}c_i \text{ and} \tag{4}$$

$$R^*_{ci(p)} = \int_{T_i} g(c_i|c_{im})\mathrm{d}c_i, \tag{5}$$

where c_{im} is within acceptance interval A_i in Eq. (4) and outside A_i in Eq. (5).

The following modelling of the total risks in this Guide is a combination of the particular risks according to the law of total probability [37–39]. The law is applicable when any pair of measured values c_{im} and c_{jm}, $i \neq j$, as well as any pair of the true component concentrations or contents c_i and c_j, $i \neq j$, are mutually independent in the same item.

3.1 Combination of particular consumer's risks

3.1.1 Events and probabilities

For simplicity, consider the measurement of just two *component* concentrations or contents and define the following events that may occur:

- C_1: the measured value c_{1m} for component 1 is in its acceptance interval A_1; probability of this event is $P(C_1)$.
- C_2: the measured value c_{2m} for component 2 is in its acceptance interval A_2; probability of this event is $P(C_2)$.
- C: the item as a whole is assessed as conforming, since both the measured values c_{1m} and c_{2m} are in their acceptance intervals simultaneously, hence $C = C_1 \cap C_2$; probability of this event $P(C) = P(C_1)\,P(C_2)$, when C_1 and C_2 are mutually independent.
- B_1: the true concentration or content c_1 of component 1 is not within its tolerance interval T_1; probability of this event is $P(B_1)$.
- B_2: the true concentration or content c_2 of component 2 is not within its tolerance interval T_2; probability of this event is $P(B_2)$.
- B: the item of the material or object as a whole is not conforming, since the true concentrations or contents of one or both of components are not within their tolerance intervals, hence $B = B_1 \cup B_2$; probability of this event is $P(B) = P(B_1) + P(B_2) - P(B_1 \cap B_2) = P(B_1) + P(B_2) - P(B_1)P(B_2)$. The last equality is valid if B_1 and B_2 are mutually independent.

Events C_1 and C_2, as well as B_1 and B_2, are shown schematically in Fig. 2 by ellipses of a Venn diagram. Other events of interest are indicated as intersections of these ellipses.

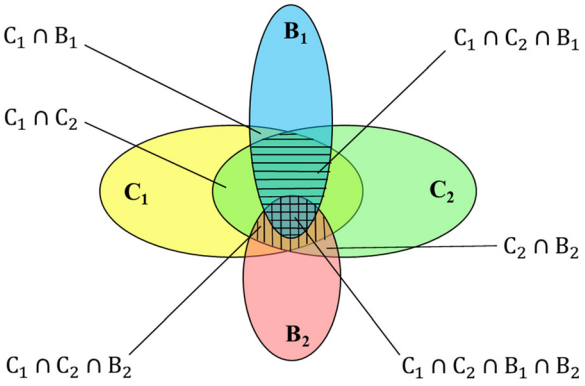

Fig. 2: Venn diagram of the considered events. Events C_1 and C_2, when measured values c_{im} for components $i = 1$ and 2, respectively, are in their acceptance intervals, and events B_1 and B_2, when the true concentrations or contents c_i are not within their tolerance intervals, are shown by ellipses. Other events of interest are indicated as intersections of these ellipses: $C_1 \cap C_2$ – c_{im} for both components 1 and 2 being within their acceptance intervals simultaneously; $C_1 \cap B_1$ and $C_2 \cap B_2$ – c_{im} for component 1 or 2, respectively, being within their acceptance intervals, while corresponding c_i are not within their tolerance intervals; $C_1 \cap C_2 \cap B_1$ and $C_1 \cap C_2 \cap B_2$ – c_{im} for both components 1 and 2 being within their acceptance intervals simultaneously, when c_i are not within their tolerance intervals; $C_1 \cap C_2 \cap B_1 \cap B_2$ – c_{im} for both components 1 and 2 being within their acceptance intervals, when none of the c_i are within their tolerance intervals.

3.1.2 Total global consumer's risk

Particular global consumer's risk $R_{ci(c)}$ for i-th component ($i = 1, 2$) is the probability of false conformance when the corresponding measured value c_{im} falls within its acceptance interval A_i, while the true value c_i is outside the tolerance interval T_i :

$$R_{c1(c)} = P(C_1 \cap B_1), \tag{6}$$

$$R_{c2(c)} = P(C_2 \cap B_2). \tag{7}$$

At the same time, the *total global consumer's risk* $R_{total(c)}$ is the risk of having c_{im} of both the components within their acceptance intervals (which are the two-dimensional domain $A_1 \times A_2$) when at least one of c_i is outside its tolerance intervals T_1 and/or T_2, *i.e.* $R_{total(c)} = C \cap B$, where

$$C \cap B = C_1 \cap C_2 \cap (B_1 \cup B_2) = (C_1 \cap C_2 \cap B_1) \cup (C_1 \cap C_2 \cap B_2). \tag{8}$$

In Fig. 2, event $(C_1 \cap C_2 \cap B_1)$ corresponds to the area shaded by horizontal lines, whereas event $(C_1 \cap C_2 \cap B_2)$ corresponds to the area shaded by vertical lines. The total global consumer's risk is thus:

$$R_{total(c)} = P(C_1 \cap C_2 \cap B_1) + P(C_1 \cap C_2 \cap B_2) - P(C_1 \cap C_2 \cap B_1 \cap B_2). \tag{9}$$

Event $(C_1 \cap C_2 \cap B_1 \cap B_2)$ is marked in Fig. 2 as a net. Whenever C_1 and C_2, as well as B_1 and B_2, are mutually independent, events $C_1 \cap B_1$ and $C_2 \cap B_2$ are also independent and Eq. (9) can be rewritten using notations (6) and (7) in the following way:

$$\begin{aligned} R_{total(c)} &= P(C_2)P(C_1 \cap B_1) + P(C_1)P(C_2 \cap B_2) - P(C_1 \cap B_1)P(C_2 \cap B_2) \\ &= P(C_2)R_{c1(c)} + P(C_1)R_{c2(c)} - R_{c1(c)}R_{c2(c)}. \end{aligned} \tag{10}$$

For example, for particular risks $R_{ci(c)} = 0.05$ and probabilities $P(C_i) = 0.90$, $i = 1, 2$; Eq. (10) gives $R_{total(c)} = 2 \times (0.90 \times 0.05) - 0.05^2 = 0.09$. Here and further in this Guide, numerical values are rounded.

For three components, under the same assumption of independent true values of each component's concentration or content and independent corresponding test results, the total global consumer's risk is:

$$R_{\text{total(c)}} = P(\text{C}_2)P(\text{C}_3)R_{c1(\text{c})} + P(\text{C}_1)P(\text{C}_3)R_{c2(\text{c})} + P(\text{C}_1)P(\text{C}_2)R_{c3(\text{c})} - P(\text{C}_3)R_{c1(\text{c})}R_{c2(\text{c})} - P(\text{C}_2)R_{c1(\text{c})}R_{c3(\text{c})} - P(\text{C}_1)R_{c2(\text{c})}R_{c3(\text{c})} + R_{c1(\text{c})}R_{c2(\text{c})}R_{c3(\text{c})}. \quad (11)$$

For example, for particular risks $R_{ci(\text{c})} = 0.05$ and probabilities $P(\text{C}_i) = 0.90$, $i = 1, 2, 3$; Eq. (11) gives $R_{\text{total(c)}} = 3 \times (0.90^2 \times 0.05) - 3 \times (0.90 \times 0.05^2) + 0.05^3 = 0.12$.

For four components, the total global risk is:

$$\begin{aligned} R_{\text{total(c)}} = {} & P(\text{C}_2)P(\text{C}_3)P(\text{C}_4)R_{c1(\text{c})} + P(\text{C}_1)P(\text{C}_3)P(\text{C}_4)R_{c2(\text{c})} + P(\text{C}_1)P(\text{C}_2)P(\text{C}_3)R_{c4(\text{c})} - P(\text{C}_3)P(\text{C}_4)R_{c1(\text{c})}R_{c2(\text{c})} \\ & - P(\text{C}_2)P(\text{C}_4)R_{c1(\text{c})}R_{c3(\text{c})} - P(\text{C}_2)P(\text{C}_3)R_{c1(\text{c})}R_{c4(\text{c})} - P(\text{C}_1)P(\text{C}_4)R_{c2(\text{c})}R_{c3(\text{c})} - P(\text{C}_1)P(\text{C}_3)R_{c2(\text{c})}R_{c4(\text{c})} \\ & - P(\text{C}_1)P(\text{C}_2)R_{c3(\text{c})}R_{c4(\text{c})} + P(\text{C}_4)R_{c1(\text{c})}R_{c2(\text{c})}R_{c3(\text{c})} + P(\text{C}_3)R_{c1(\text{c})}R_{c2(\text{c})}R_{c4(\text{c})} + P(\text{C}_2)R_{c1(\text{c})}R_{c3(\text{c})}R_{c4(\text{c})} \\ & + P(\text{C}_1)R_{c2(\text{c})}R_{c3(\text{c})}R_{c4} - R_{c1(\text{c})}R_{c2(\text{c})}R_{c3(\text{c})}R_{c4(\text{c})}. \end{aligned} \quad (12)$$

For particular risks $R_{ci(\text{c})} = 0.05$ and probabilities $P(\text{C}_i) = 0.90$, $i = 1, 2, 3, 4$; by Eq. (12) one obtains $R_{\text{total(c)}} = 4 \times (0.90^3 \times 0.05) - 6 \times (0.90^2 \times 0.05^2) + 4 \times (0.90 \times 0.05^3) - 0.05^4 = 0.13$. Comparing this result with the total global risk values for the previous cases of two and three components, it is easy to see that the risk is greater for a larger number of the components under control.

In general, the expression for the total global consumer's risk for a number n of components under control is:

$$\begin{aligned} R_{\text{total(c)}} = {} & \sum_{i=1}^{n}\left(\prod_{l\neq i}P(\text{C}_l)\right)R_{ci(\text{c})} - \sum_{i=1}^{n}\sum_{j>i}\left(\prod_{l\neq i,j}P(\text{C}_l)\right)\left(\prod_{q=i,j}R_{cq(\text{c})}\right) \\ & + \sum_{i=1}^{n}\sum_{j>i}\sum_{k>j}\left(\prod_{l\neq i,j,k}P(\text{C}_l)\right)\left(\prod_{q=i,j,k}R_{cq(\text{c})}\right) + \ldots + (-1)^{n-2}\sum_{i=1}^{n}P(\text{C}_i)\left(\prod_{q\neq i}R_{cq(\text{c})}\right) + (-1)^{n-1}\prod_{q=1}^{n}R_{cq(\text{c})}, \end{aligned} \quad (13)$$

where i, j, k, l and q are indices of the components in the range 1 to n. Thus, the total global consumer's risk can be evaluated as a combination of n particular global risks of conformity assessment of any material or object in which n component concentrations or contents are measured.

3.1.3 Total specific consumer's risk

When a specific item is tested for the content of two components, the *total specific consumer's risk* $R^*_{\text{total(c)}}$ is the probability $P(\text{B}|c_{1\text{m}}, c_{2\text{m}})$ that the true concentration or content of one or both the components in this item are not within the corresponding tolerance interval ($\text{B} = \text{B}_1 \cup \text{B}_2$), when the measured values $c_{1\text{m}}$ and $c_{2\text{m}}$ are within their acceptance intervals. If the events B_1 and B_2 are conditionally independent [39, p. 57], *i.e.* independent one from each other at the given measured values $c_{1\text{m}}$ and $c_{2\text{m}}$, the total specific risk is

$$\begin{aligned} R^*_{\text{total(c)}} &= P(\text{B}|c_{1\text{m}}, c_{2\text{m}}) = P(\text{B}_1 \cup \text{B}_2|c_{1\text{m}}, c_{2\text{m}}) = P(\text{B}_1|c_{1\text{m}}, c_{2\text{m}}) + P(\text{B}_2|c_{1\text{m}}, c_{2\text{m}}) - P(\text{B}_1 \cap \text{B}_2|c_{1\text{m}}, c_{2\text{m}}) \\ &= P(\text{B}_1|c_{1\text{m}}) + P(\text{B}_2|c_{2\text{m}}) - P(\text{B}_1|c_{1\text{m}})P(\text{B}_2|c_{2\text{m}}). \end{aligned} \quad (14)$$

Since *particular specific consumer's risk* $R^*_{ci(\text{c})}$ for the i-th component, $i = 1, 2$, are:

$$R^*_{c1(\text{c})} = P(\text{B}_1|c_{1\text{m}}), \quad (15)$$

$$R^*_{c2(\text{c})} = P(\text{B}_2|c_{2\text{m}}), \quad (16)$$

substituting Eqs. (15) and (16) into Eq. (14) gives the following:

$$R^*_{\text{total(c)}} = R^*_{c1(\text{c})} + R^*_{c2(\text{c})} - R^*_{c1(\text{c})}R^*_{c2(\text{c})}. \quad (17)$$

For example, for particular specific risks $R^*_{ci(\text{c})} = 0.05$, the total risk by Eq. (17) is $R^*_{\text{total(c)}} = 2 \times 0.05 - 0.05^2 = 0.10$. Total specific consumer's risk for three components is:

$$R^*_{\text{total(c)}} = R^*_{c1(\text{c})} + R^*_{c2(\text{c})} + R^*_{c3(\text{c})} - R^*_{c1(\text{c})}R^*_{c2(\text{c})} - R^*_{c1(\text{c})}R^*_{c3(\text{c})} - R^*_{c2(\text{c})}R^*_{c3(\text{c})} + R^*_{c1(\text{c})}R^*_{c2(\text{c})}R^*_{c3(\text{c})}. \quad (18)$$

For example, when the particular specific risks are $R^*_{ci\,(c)} = 0.05$, $i = 1, 2, 3$; the total risk by Eq. (18) is $R^*_{\text{total}\,(c)} = 3 \times 0.05 - 3 \times 0.05^2 + 0.05^3 = 0.14$.

When four components are under control, the total specific risk is:

$$R^*_{\text{total}\,(c)} = R^*_{c1} + R^*_{c2} + R^*_{c3} + R^*_{c4} - R^*_{c1}R^*_{c2} - R^*_{c1}R^*_{c3} - R^*_{c1}R^*_{c4} - R^*_{c2}R^*_{c3} - R^*_{c2}R^*_{c4} - R^*_{c3}R^*_{c4} + R^*_{c1}R^*_{c2}R^*_{c3} + R^*_{c1}R^*_{c2}R^*_{c4} + R^*_{c1}R^*_{c3}R^*_{c4} + R^*_{c2}R^*_{c3}R^*_{c4} - R^*_{c1}R^*_{c2}R^*_{c3}R^*_{c4}\,. \tag{19}$$

For example, when the particular risks are again $R^*_{ci\,(c)} = 0.05$, $i = 1, 2, 3, 4$; Eq. (19) gives $R^*_{\text{total}\,(c)} = 4 \times 0.05 - 6 \times 0.05^2 + 4 \times 0.05^3 - 0.05^4 = 0.19$. Thus, as for the total global risk values, the total specific risk value is greater for a larger number of the components under control.

In general, the total specific consumer's risk for a number n of components is:

$$R^*_{\text{total}\,(c)} = \sum_{i=1}^{n} R^*_{ci\,(c)} - \sum_{i=1}^{n}\sum_{j>i}\left(\prod_{q=i,j} R^*_{cq\,(c)}\right) + \sum_{i=1}^{n}\sum_{j>i}\sum_{k>j}\left(\prod_{q=i,j,k} R^*_{cq\,(c)}\right) + \cdots + (-1)^{n-2}\sum_{i=1}^{n}\left(\prod_{q\neq i} R^*_{cq\,(c)}\right) + (-1)^{n-1}\prod_{q=1}^{n} R^*_{cq\,(c)}, \tag{20}$$

where i, j, k, l and q are subscripts of the components in the range from 1 to n.

Note: Eqs. (10), (11), (12) and (13) for calculation of total global risk can be simplified to similar combinations of the particular global risks, as for specific risks in Eqs. (17), (18), (19) and (20) for 2, 3, 4 and n components, respectively, when each probability $P(C_i)$ of acceptance of the measured values for component $i = 1, 2, \ldots, n$ is equal to 1.

Examples of the evaluation of the total consumer's risks according to the discussed modelling for the conformity assessment of denatured alcohols are available in Annex A, Example 1, and for the assessment of TSPM in ambient air in Annex A, Example 2.

3.2 Combination of particular producer's risks

3.2.1 Events and probabilities

Define the following additional events for two and more *components*, necessary for understanding the producer's risks:

- $\overline{B}_i$: the true component concentration or content c_i is within its tolerance interval T_i; probability of this event is $P(\overline{B}_i) = 1 - P(B_i)$.
- $\overline{B}$: the true values c_i for any i are within their tolerance intervals T_i, $\overline{B} = \overline{B}_1 \cap \overline{B}_2 \cap \ldots \cap \overline{B}_n$; probability of this event is $P(\overline{B}) = \prod_{i=1}^{n} P(\overline{B}_i)$ if $\overline{B}_i$ are mutually independent.
- B: the item of the material or object as a whole is not conforming, since the true concentrations or contents c_i of one or more components are not within their T_i, $B = B_1 \cup B_2 \cup \ldots \cup B_n$; probability of this event is $P(B) = 1 - P(\overline{B}) = 1 - \prod_{i=1}^{n} P(\overline{B}_i)$.
- $\overline{C}_i$: the measured value c_{im} is not within its acceptance interval A_i; probability of this event is $P(\overline{C}_i) = 1 - P(C_i)$.
- $\overline{C}$: one or more measured values c_{im} are not within their A_i, $\overline{C} = \overline{C}_1 \cup \overline{C}_2 \cup \ldots \cup \overline{C}_n$; probability of this event is $P(\overline{C}) = 1 - P(C) = 1 - \prod_{i=1}^{n} P(C_i)$.
- C: the item of the material or object as a whole is assessed as conforming, since the measured values c_{im} for any i are within their acceptance intervals A_i simultaneously, $C = C_1 \cap C_2 \cap \ldots \cap C_n$; probability of this event is $P(C) = \prod_{i=1}^{n} P(C_i)$ if C_i are mutually independent.

3.2.2 Total global producer's risk

Particular global producer's risk $R_{ci(p)}$ is

$$R_{ci(\mathrm{p})} = P\left(\overline{\mathrm{B}}_i \cap \overline{\mathrm{C}}_i\right), \tag{21}$$

while the *total global producer's risk* is $R_{\mathrm{total(p)}} = P(\overline{\mathrm{B}} \cap \overline{\mathrm{C}})$. For $n = 3$ components, for example,

$$\overline{\mathrm{B}} \cap \overline{\mathrm{C}} = \overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \left(\overline{\mathrm{C}}_1 \cup \overline{\mathrm{C}}_2 \cup \overline{\mathrm{C}}_3\right) = \left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_1\right) \cup \left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_2\right) \cup \left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_3\right). \tag{22}$$

Thus, the total global producer's risk is

$$\begin{aligned} R_{\mathrm{total(p)}} = {} & P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_1\right) + P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_2\right) + P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_3\right) - P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_1 \cap \overline{\mathrm{C}}_2\right) \\ & - P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_1 \cap \overline{\mathrm{C}}_3\right) - P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_2 \cap \overline{\mathrm{C}}_3\right) + P\left(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_1 \cap \overline{\mathrm{C}}_2 \cap \overline{\mathrm{C}}_3\right). \end{aligned} \tag{23}$$

Whenever $\overline{\mathrm{B}}_1$, $\overline{\mathrm{B}}_2$, and $\overline{\mathrm{B}}_3$, as well as $\overline{\mathrm{C}}_1$, $\overline{\mathrm{C}}_2$, and $\overline{\mathrm{C}}_3$, are mutually independent, events $\overline{\mathrm{B}}_1 \cap \overline{\mathrm{C}}_1$, $\overline{\mathrm{B}}_2 \cap \overline{\mathrm{C}}_2$ and $\overline{\mathrm{B}}_3 \cap \overline{\mathrm{C}}_3$ are also independent and Eq. (23) can be rewritten using notation (21) in the following way:

$$\begin{aligned} R_{\mathrm{total(p)}} = {} & P\left(\overline{\mathrm{B}}_2\right)P\left(\overline{\mathrm{B}}_3\right)R_{c1(\mathrm{p})} + P\left(\overline{\mathrm{B}}_1\right)P\left(\overline{\mathrm{B}}_3\right)R_{c2(\mathrm{p})} + P\left(\overline{\mathrm{B}}_1\right)P\left(\overline{\mathrm{B}}_2\right)R_{c3(\mathrm{p})} - P\left(\overline{\mathrm{B}}_3\right)R_{c1(\mathrm{p})}R_{c2(\mathrm{p})} \\ & - P\left(\overline{\mathrm{B}}_2\right)R_{c1(\mathrm{p})}R_{c3(\mathrm{p})} - P\left(\overline{\mathrm{B}}_1\right)R_{c2(\mathrm{p})}R_{c3(\mathrm{p})} + R_{c1(\mathrm{p})}R_{c2(\mathrm{p})}R_{c3(\mathrm{p})}. \end{aligned} \tag{24}$$

Note that Eq. (24) is similar to Eq. (11) for the total global consumer's risk. However, it involves probabilities of different events and different particular risks.

In general, for any number n of components

$$\begin{aligned} R_{\mathrm{total(p)}} = {} & \sum_{i=1}^{n}\left(\prod_{l\neq i} P(\overline{\mathrm{B}}_l)\right)R_{ci(\mathrm{p})} - \sum_{i=1}^{n}\sum_{j>i}\left(\prod_{l\neq i,j} P(\overline{\mathrm{B}}_l)\right)\left(\prod_{q=i,j} R_{cq(\mathrm{p})}\right) \\ & + \sum_{i=1}^{n}\sum_{j>i}\sum_{k>j}\left(\prod_{l\neq i,j,k} P(\overline{\mathrm{B}}_l)\right)\left(\prod_{q=i,j,k} R_{cq(\mathrm{p})}\right) + \ldots + (-1)^{n-2}\sum_{i=1}^{n} P(\overline{\mathrm{B}}_i)\left(\prod_{q\neq i} R_{cq(\mathrm{p})}\right) + (-1)^{n-1}\prod_{q=1}^{n} R_{cq(\mathrm{p})}, \end{aligned} \tag{25}$$

where i, j, k, l and q are subscripts of the components in the range from 1 to n.

3.2.3 Total specific producer's risk

The *total specific producer's risk* $R^*_{\mathrm{total(p)}}$ is the probability that the true concentrations or contents of all the components are within their tolerance interval, when one or more measured values are found outside their acceptance intervals. For example, when an item of a material or object is tested for concentrations or contents of three components, $R^*_{\mathrm{total(p)}}$ is the probability that the true concentrations or contents of the components are within their tolerance interval ($\overline{\mathrm{B}} = \overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3$), while one or more of $c_{1\mathrm{m}}$, $c_{2\mathrm{m}}$, and/or $c_{3\mathrm{m}}$ are not within their acceptance intervals. This event can occur when:

a) Just one measured value out of the three, for example $c_{1\mathrm{m}}$ without losing generality, is not within its acceptance interval, while the true concentration or content c_1 is within its tolerance interval. Hence, the total risk that the item is falsely considered as not conforming is equal to the *particular specific producer's risk* concerning the first component: $R^*_{\mathrm{total(p)}} = P(\overline{\mathrm{B}}_1|c_{1\mathrm{m}})$.
b) Two measured values, *e.g.* $c_{1\mathrm{m}}$ and $c_{2\mathrm{m}}$, are not within their acceptance intervals. The total risk is $R^*_{\mathrm{total(p)}} = P(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2|c_{1\mathrm{m}}, c_{2\mathrm{m}})$.
c) All three measured values are not within their acceptance intervals. The total risk is $R^*_{\mathrm{total(p)}} = P(\overline{\mathrm{B}}|c_{1\mathrm{m}}, c_{2\mathrm{m}}, c_{3\mathrm{m}}) = P(\overline{\mathrm{B}}_1 \cap \overline{\mathrm{B}}_2 \cap \overline{\mathrm{B}}_3|c_{1\mathrm{m}}, c_{2\mathrm{m}}, c_{3\mathrm{m}})$.

If the events $\overline{\mathrm{B}}_i$ are conditionally independent, *i.e.* each is independent from the others at the given measured values $c_{i\mathrm{m}}$, the total specific risk in each of the three considered situations is, respectively:

a) $R^*_{\mathrm{total(p)}} = P(\overline{\mathrm{B}}_1|c_{1\mathrm{m}})$,
b) $R^*_{\mathrm{total(p)}} = \prod_{i=1}^{2} P(\overline{\mathrm{B}}_i|c_{i\mathrm{m}})$,
c) $R^*_{\mathrm{total(p)}} = \prod_{i=1}^{3} P(\overline{\mathrm{B}}_i|c_{i\mathrm{m}})$,

where $(\overline{\mathrm{B}}_i|c_{i\mathrm{m}}) = R^*_{ci(\mathrm{p})}$.

For any number n of components, v of which are characterized by the measured values exceeding their acceptance limits ($v \le n$), the total specific producer's risk is

$$R^*_{\text{total (p)}} = \prod_{i=1}^{v} R^*_{ci\,(\text{p})}. \tag{26}$$

From Eq. (26), it follows that any one of v particular specific producer's risk $R^*_{ci\,(\text{p})}$ equal to zero will lead to $R^*_{\text{total (p)}} = 0$. That occurs when the true concentration or content of the i-th component, c_i, can never be within its tolerance interval at a given measured value, $c_{i\text{m}}$, which is also out of the acceptance interval for this component. In such a case, regardless of the measured values of the concentrations or contents of the other components, the item as a whole certainly does not conform. Therefore, the producer should take action to change the i-th component concentration or content, to reduce the i-th measurement uncertainty, and/or to pay a fine or a specified compensation.

The opposite case of a particular specific producer's risk $R^*_{ci\,(\text{p})} = 1$ is also possible when, for a measured value $c_{i\text{m}}$ outside its acceptance interval, the true concentration or content c_i certainly does conform, as it is known from another source of information. Such $R^*_{ci\,(\text{p})}$ would not influence the total specific risk $R^*_{\text{total (p)}}$ by Eq. (26). In this case, the number n of components concentrations or contents under control is *de facto* decreased by one.

Another property of Eq. (26) is the reduction of $R^*_{\text{total (p)}}$ with the increasing number v of components for which the measured values are not within their acceptance intervals. The logic is that the more such measurement results, the smaller the total probability of a false decision on conformity of the tested item, and the greater the probability that this item, as a whole, does not actually conform.

Note also that the model used in the work [45] and later adopted in the EURAMET guide [27] leads to an expression equivalent to Eq. (26) when the variables are independent.

An example of the calculation of the total producer's risks according to the discussed modelling is available in Annex A, Example 2 (assessment of TSPM in ambient air).

4 Modelling total risks for correlated variables

4.1 Interdependence of events

It is not always possible to assert the independence of C_i and C_j, as well as of B_i and B_j. A number of chemical analytical techniques are used to overcome possible correlations between measurement results. There are extractions of analytes from a sample, *e.g.* the extraction of organic mercury from fish samples with concentrated HBr followed by extraction into toluene and back-extraction with aqueous cysteine solution for distinguishing total and organic mercury concentrations [46]; the chromatographic separation of an analyte from other *components*, *etc.* Chemometrics software is applied for the separation of spectral signals [47]. Sample digestion and standard additions of an analyte to a sample are used for the calibration of a measurement system overcoming the multiplicative matrix effects of a sample, and so on. There are also requirements in validation guidelines, *e.g.* [17, 48, 49], for evaluating the method selectivity and/or specificity and trueness (systematic errors possible at extraction, separation, and other steps of the analytical procedure). An experimental proof is necessary to show that the response of the measurement system is caused by the analyte/component proper, not by another component or the sample matrix. Something may still happen in practice, but in general this kind of correlation should be negligible.

The correlation of actual values of concentrations or contents of different components of an item may be caused by the stoichiometry of native compounds (in geological, environmental, and other samples). The law of conservation of mass also applies here, requiring the interdependence of the true concentration or content values of the components in an item (their sum must be 100 %). Technological reasons in the production of materials (alloys, drugs, *etc.*) lead to such correlations as well.

Metrologically-independent measurements/test results for two or more components are, however, inevitably correlated when their actual values are correlated. In other words, when B_i and B_j are interdependent, for example, C_i and C_j must also be, though the correlation between measured values may be weaker because of random measurement errors.

4.2 Multivariate modelling total risks

Bayes' theorem for a multicomponent material or object as a whole is expressed by the following equation:

$$g(\boldsymbol{c}_n|\boldsymbol{c}_\mathrm{m}) = Cg_0(\boldsymbol{c}_n)h(\boldsymbol{c}_\mathrm{m}|\boldsymbol{c}_n), \tag{27}$$

where $\boldsymbol{c}_n = [c_1, c_2, \ldots, c_n]$ and $\boldsymbol{c}_\mathrm{m} = [c_{1\mathrm{m}}, c_{2\mathrm{m}}, \ldots, c_{n\mathrm{m}}]$ are vectors of the actual values and measured values, respectively, and so g, g_0 as well as h are multivariate functions. The product $g_0(\boldsymbol{c}_n)h(\boldsymbol{c}_\mathrm{m}|\boldsymbol{c}_n)$ is the multivariate joint pdf of the actual values $\boldsymbol{c}_n$ and the measured values $\boldsymbol{c}_\mathrm{m}$. Bayes' theorem in this form takes into account the possible correlation between actual values of the concentrations or contents of the *components* and/or between their measured values.

4.2.1 Total global consumer's and producer's risks

We discuss again, for simplicity, the case of two components under control ($n = 2$). The *total global consumer's risk* can be expressed as the following probability:

$$R_{\mathrm{total(c)}} = P(\mathrm{C} \cap \mathrm{B}) = P[(\mathrm{C} \cap \mathrm{B}_1) \cup (\mathrm{C} \cap \mathrm{B}_2)] = P(\mathrm{C} \cap \mathrm{B}_1) + P(\mathrm{C} \cap \mathrm{B}_2) - P(C \cap B_1 \cap B_2) \tag{28}$$

The terms in Eq. (28) involve integrals of the joint pdf of the actual values $\boldsymbol{c}_n$ and the measured values $\boldsymbol{c}_\mathrm{m}$, taking into account the possible correlation between c_1 and c_2, as well as between $c_{1\mathrm{m}}$ and $c_{2\mathrm{m}}$. Just as an example of how to calculate each term in Eq. (28), the last one is the following probability:

$$P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_2) = \int_{T_1^c}\int_{T_2^c}\int_{A_1}\int_{A_2} g_0(c_1, c_2)h(c_{1\mathrm{m}}, c_{2\mathrm{m}}|c_1, c_2)\mathrm{d}c_{1\mathrm{m}}\mathrm{d}c_{2\mathrm{m}}\mathrm{d}c_1\mathrm{d}c_2. \tag{29}$$

The *total global producer's risk* is:

$$R_{\mathrm{total(p)}} = P\left(\overline{\mathrm{C}} \cap \overline{\mathrm{B}}\right) = P\left[\left(\overline{\mathrm{B}} \cap \overline{\mathrm{C}}_1\right) \cup \left(\overline{\mathrm{B}} \cap \overline{\mathrm{C}}_2\right)\right] = P\left(\overline{\mathrm{B}} \cap \overline{\mathrm{C}}_1\right) + \left(\overline{\mathrm{B}} \cap \overline{\mathrm{C}}_2\right) - P\left(\overline{\mathrm{B}} \cap \overline{\mathrm{C}}_1 \cap \overline{\mathrm{C}}_2\right). \tag{30}$$

Like the probability in Eq. (29), the last term of Eq. (30) is the following integral of the joint pdf:

$$P\left(\overline{\mathrm{B}} \cap \overline{\mathrm{C}}_1 \cap \overline{\mathrm{C}}_2\right) = \int_{T_1}\int_{T_2}\int_{A_1^c}\int_{A_2^c} g_0(c_1, c_2)h(c_{1\mathrm{m}}, c_{2\mathrm{m}}|c_1, c_2)\mathrm{d}c_{1\mathrm{m}}\mathrm{d}c_{2\mathrm{m}}\mathrm{d}c_1\mathrm{d}c_2. \tag{31}$$

Similar expressions for total global risks in the *conformity assessment* of a material or object with more than two components under control can be formulated using the same multivariate modelling.

4.2.2 Total specific consumer's and producer's risks

The *total specific consumer's risk*, when measured values $\boldsymbol{c}_\mathrm{m}$ are within their acceptance intervals A_i, is

$$R^*_{\mathrm{total(c)}} = 1 - \int_{T_1} \ldots \int_{T_n} g(\boldsymbol{c}_n|\boldsymbol{c}_\mathrm{m})\mathrm{d}\boldsymbol{c}_n. \tag{32}$$

The *total specific producer's risk* for v (only) measured values that are outside their acceptance intervals A_i, is

$$R^*_{\mathrm{total(p)}} = \int_{T_1} \ldots \int_{T_v} \int_0^\infty \ldots \int_0^\infty g(\boldsymbol{c}_n|\boldsymbol{c}_\mathrm{m})\mathrm{d}\boldsymbol{c}_n, \tag{33}$$

where, without losing generality, the measured values that are outside their acceptance intervals are the first v.

Note: for independent c_i, Eq. (33) reduces to Eq. (26), since integration of the univariate posteriors g on the whole real axis gives 1 for each i.

Examples of the calculation of the total risks according to the discussed modelling for correlated variables are available in Annex A, in Example 3 on the conformity assessment of a cold/flu medication, and in Example 4 on the assessment of a PtRh alloy.

5 Implementation remarks

5.1 Tolerance domain

The *tolerance limits* of the concentrations or contents of the *components*, T_{Li} and T_{Ui}, form a multivariate tolerance domain of permissible compositions of the material or object $T_1 \times T_2 \times \ldots \times T_n$. However, there also might be constraints of the mass balance to be satisfied, and/or technological constraints. These constraints lead to a multivariate sub-domain of feasible compositions, which may influence the calculation of the risks, as shown in Annex A, Example 4.

5.2 Prior pdf

A large enough dataset of results from testing items of the same material produced at the same factory, as well as results of monitoring the same environmental compartment, can be used for the approximation of the *prior* pdf $g_0(\boldsymbol{c}_n)$. The assumption is that the actual concentration values are approximated by the test/measurement results adequately, since measurement uncertainty is negligible in comparison with item-to-item (batch-to-batch) variations caused by changes in the conditions of the material production, environmental conditions, *etc*. Known statistical goodness-of-fit criteria of experimental and theoretical distributions (normal in Annex A, Examples 3 and 4, and lognormal in Annex A, Example 2) are applied. A choice of the theoretical distribution may also be based on the chemical understanding of the material nature, as in Annex A, Example 1, related to denatured alcohols. If there is no detailed prior knowledge about the distribution of the *component* concentrations or contents in the tested item, the prior pdf is vague. In such cases, a uniform pdf may be used, limited by the least and the greatest possible values of the component concentrations or contents.

When the actual values of the concentrations or contents c_i are correlated, the prior covariance matrix S_c has variances σ_i^2 of prior distributions as diagonal elements and covariances $cov_{ij} = r_{ij}\,\sigma_i\,\sigma_j$ as off-diagonal elements, where r_{ij}, $i \neq j$, are the correlation coefficients.

5.3 Likelihood function

The *likelihood* $h(c_{im}|c_i)$ is a function describing the plausibility of the actual values of a *component* concentration or contents at a given measurement result. In practice, a distribution of measured values c_{im} at a given actual concentration or actual content c_i of component in a sample of a multicomponent material or object, caused by measurement uncertainty u_i, is available from the analytical method validation data. This distribution of the measured values, regarded as a function of c_i, is nothing else than the likelihood function itself.

When measured values c_{im} are correlated, the likelihood $h(\boldsymbol{c}_m|\boldsymbol{c}_n)$ is a multivariate pdf having covariance matrix S_{cm} with variances equal to the squared measurement uncertainties u_i^2 as diagonal elements, and covariances $cov_{ij} = r_{ij}\,u_i\,u_j$, $i \neq j$ as off-diagonal elements.

5.4 Posterior pdf

The *posterior distribution* $g(\boldsymbol{c}_n|\boldsymbol{c}_\mathrm{m})$ can be expressed as the posterior pdf of actual concentration values or actual content values at the same measured values of the *component's* concentrations or contents in an item. It is the normalized product of the *prior* and the *likelihood*. For example, for multivariate normal prior pdf and normal likelihood function, a multivariate normal posterior pdf has the following parameters [50]:

$$S_{\mathrm{post}(\omega)} = \left(S^{-1}_{\mathrm{c}(\omega)} + n_\mathrm{rep}\ \ S^{-1}_{\mathrm{cm}(\omega)}\right)^{-1} \text{and}\ \ \boldsymbol{c}_{\mathrm{post}(\omega)} = S_{\mathrm{post}(\omega)}\left(S^{-1}_{\mathrm{c}(\omega)}\boldsymbol{c} + n_\mathrm{rep}\ \ S^{-1}_{\mathrm{cm}(\omega)}\overline{\boldsymbol{c}}_\mathrm{m}\right), \tag{34}$$

where $S_{\mathrm{c}(\omega)}$ and $S_{\mathrm{cm}(\omega)}$ are the prior and likelihood covariance matrices, respectively, at the scenario (set of conditions) ω; $S_{\mathrm{post}(\omega)}$ and $\boldsymbol{c}_{\mathrm{post}(\omega)}$ are the posterior covariance matrix and the vector of the posterior means, respectively; $\boldsymbol{c}$ is the vector of the prior mean values $[\mu_1, \mu_2, \ldots, \mu_n]$; and $\overline{\boldsymbol{c}}_\mathrm{m}$ is the vector of the arithmetic means of n_rep-replicated measured values.

Examples of uncorrelated prior, likelihood, and posterior functions are in Annex A, Examples 1 and 2, correlated (multivariate) – in Annex A, Examples 3 and 4.

5.5 Computational details

Principal component analysis (PCA) of the observed multivariate data can be employed to handle the effects of covariance on conformance probabilities using the data transformation as shown in a study of skin cream friction and adhesion, described in Deliverable 3.2.4 of the EURAMET guide [27] and references therein.

When all *components* involved in the *conformity assessment* of a material or object are participants of the mass balance constraint (sum of their mass fractions is 100 %), the data-containing mass fractions of the components' contents are referred to as compositional. There is an extensive literature stressing how traditional statistical techniques may produce inadequate results if applied to raw compositional data without suitable transformation [51–53]. However, there might be no easy way to transform relevant estimates (calculation results) back to the original variable space for conformity assessment purposes. Regardless, in each chemical analytical and conformity assessment case the chosen mathematical statistical method should be fit-for-purpose.

In this Guide, the calculation of parameters of the *posterior* multivariate normal distributions by Eq. (34) and descending risk values were performed in the R programming environment described in Annex A, Examples 3 and 4. Simulation of the posterior distribution is also possible by Markov Chain Monte Carlo (MCMC) method, using the Metropolis–Hastings algorithm with MS Excel [54]. The analytical solution (34) for parameters of the posterior pdf and corresponding specific risk values is more accurate by definition than the MCMC solution, even when obtained by a large number of trials. On the other hand, an analytical solution is not always available, especially when *prior* pdf and *likelihood function* are more complicated than normal. For examples of Annex A, the analytical and the simulated MCMC results (parameters of the posterior pdf and specific risk values) practically coincided. Also, global risks evaluated using R, as well as Monte Carlo (MC) simulation and Cholesky decomposition of the covariance matrix with MS Excel [55, 56], produced satisfactorily close calculation results.

The core of the R codes [57], developed for calculations of the risks for uncorrelated and correlated data, are published in papers [41] and [43], respectively. User-friendly MS Excel spreadsheet programs for the same purposes are described in papers [54, 55]. Both the R codes and Excel spreadsheet programs can be sent by the corresponding author upon request.

5.6 Limitations

Any model is a simplified reflection of reality and can be useful if one remembers its limitations. There are some limitations that are relevant for this Guide.

The assumption of negligible definitional uncertainty of the actual *component* concentration or content c_i may influence the prior pdf. In particular, the inhomogeneity and/or instability of an item of the

multicomponent material or object may lead to an increase of the standard deviation (and variance) of the prior pdf and its skewness. The adequacy of a dataset of item-to-item (batch-to-batch) test/measurement results for use in modelling the prior pdf is a not simple question, including as it does the necessary volume of this dataset, the time of its accumulation, possible changes of raw materials for production during this time, *etc*. The goodness-of-fit of experimental and theoretical distributions must also be taken into account.

Measurement uncertainty evaluation is important for the formulation of the *likelihood function*. Note that the multivariate tolerance domain may be large enough for a doubt if the same measurement uncertainty can be applied in this domain, *e.g*. when the uncertainty value u_i depends on the measurand—the component concentration or content c_i.

As mentioned already above, a correct choice of the mathematical statistical method, with or without the raw data transformation, should be fit-for-purpose. This also requires the formulation of clear criteria.

Calculated total risk values can be used for setting multivariate acceptance limits for test/measurement results, as proposed in ref. [43]. However, according to risk management principles [9], setting acceptance limits requires a study of not only the producer's and consumer's risks, given as probabilities depending on measurement uncertainty, but also the economic, safety, and/or other impacts of related false decisions.

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Annex A. Examples

A-1. Example 1. Risks in customs control of denatured alcohols due to measurement uncertainty

A-1-1 Introduction

The guidelines of the World Customs Organization [58] and the European Commission [59, 60] define risk as the potential non-compliance with customs laws. When substances and/or materials are under customs control, one such risk is caused by the measurement uncertainty of chemical analytical test results. For example, alcohol (ethanol for human consumption) is subject to excise duties, while denatured alcohols (for industrial use) are not, and the task of the control is to distinguish between them. According to EU Regulation [61], a common procedure for the purpose of completely denaturing alcohol (CDA) consists of adding 3 L of propan-2-ol, *i.e.* isopropyl alcohol (IPA), 3 L of butan-2-one, called methyl ethyl ketone (MEK), and 1 g of denatonium benzoate (DB) to 100 L (1 hL) of absolute ethyl alcohol (EtOH). Similar regulations exist in Israel [62], Australia [63], and other countries.

A decision on conformity assessment can be made using IPA and MEK test results, rather than DB test results [64]. Therefore, an analysis of the customs' risks caused by the measurement uncertainties is discussed below for two scenarios: when only IPA and MEK concentrations are under control, and when concentrations of all the denaturants (IPA, MEK, and DB) are considered [40]. Since the customs authority dealing with CDA is the 'consumer' in this study, the customs' risks caused by the measurement uncertainties are the consumer's risks.

A-1-2 Experimental

Analytical procedures for testing CDA include the determination of EtOH, IPA, and MEK using gas chromatography with flame ionization detection and the determination of DB using high performance liquid chromatography with ultraviolet detection. The analytes are separated completely from other components of a sample at the chromatographic conditions of the methods. Relevant internal standards and calibration standards are used for the quantification of analyte concentrations. IPA and MEK concentrations are expressed in L per hL of EtOH (as measured) and DB concentrations in g per hL of EtOH. These procedures have been validated at the Institute for Reference Materials and Measurements with the participation of a number of customs laboratories [64]. There is no evidence of correlation between measurement results of the concentrations of the denaturants. The standard measurement uncertainties were evaluated in the validation process based on the interlaboratory study: u_1 = 0.05 L hL^{-1} for IPA, u_2 = 0.07 L hL^{-1} for MEK, and u_3 = 0.07 g hL^{-1} for DB.

As the measurand is the denaturant concentration in a batch of alcohol, the variation of test/measurement results is influenced by the inhomogeneity of the batch (shortly after DB dissolution) and 'batch-to-batch' differences [65]. The following relative standard deviations of measured values are set in the report [64] as acceptable: 5 %, or $s_{r1} = s_{r2} = 0.05$ in fractions of 1, for IPA and MEK; and 10 %, or $s_{r3} = 0.10$, for DB.

A-1-3 Tolerance domain

Because denaturing is the process of transformation of absolute ethanol into an undrinkable poisonous mixture of chemicals, the regulatory requirements to the actual ('true') concentrations c_1, c_2 and c_3 of the denaturants, IPA, MEK, and DB, respectively, are the lower regulatory limits T_{L1}, T_{L2}, and T_{L3} of their tolerance intervals. By regulation [61], IPA and MEK concentrations c_1 and c_2 in a CDA sample shall be not less than $T_{L1} = T_{L2} = 3$ L hL^{-1}, whereas DB concentration c_3 shall be not less than $T_{L3} = 1$ g hL^{-1}. Thus, any concentrations c_1, c_2, and c_3 of the denaturants larger than the corresponding T_{L1}, T_{L2} and T_{L3} are feasible, but not those lower than these limits.

Acceptance limits A_{Li} used here do not differ from T_{Li}, and measured values c_{im} should be compared directly with the regulatory limits, *i.e.* $A_{Li} = T_{Li}$.

A-1-4 Prior pdfs

There is no dataset for recovering the prior distributions of denaturant concentrations. The relative standard deviations s_{ri} are applied in this study for the estimation of the standard deviations of these distributions. For simplicity, the priors are approximated by the normal distributions:

$$g_0(c_i) = \frac{1}{s_{ri}\mu_i\sqrt{2\pi}}\exp\left[-\frac{(c_i-\mu_i)^2}{2(s_{ri}\mu_i)^2}\right], \tag{35}$$

where μ_i is the mean and $s_{ri}\mu_i$ is the standard deviation of the i-th denaturant concentration; exp[…] is exponential function $e^{[\ldots]}$.

It is impossible to test the hypothesis of goodness-of-fit of this approximation in the absence of experimental data. However, normal distributions are not only the simplest ones widely used, but also natural for batches produced by mixing the components without any reaction among them. The 'batch-to-batch' variations of the denaturant concentrations are caused by purity and errors in volume measurements of EtOH, IPA, and MEK, as well as errors in DB mass measurements. Hence, when the number of these batches is large enough, the distributions probably tend to be normal.

A-1-5 Likelihood functions

The distributions of measured values c_{im} at the same actual concentration value c_i (in the same sample)—likelihood functions—are also taken as normal based on the validation data [65]:

$$h(c_{im}|c_i) = \frac{1}{u_i\sqrt{2\pi}}\exp\left[-\frac{(c_{im}-c_i)^2}{2u_i^2}\right], \tag{36}$$

where the standard measurement uncertainties u_i are used as the standard deviations of the distributions.

Normal distributions truncated at zero should be used instead of 'regular' normal pdf in Eqs. (35) and (36), since the concentration of a denaturant is a non-negative property. However, for the example under consideration, the influence of the truncation was negligible.

A-1-6 Global risks

The i-th particular global customs risk, $i = 1, 2, 3$, is evaluated by the following equation derived from Eq. (2):

$$R_{ci(C)} = \int_0^{T_{Li}} \int_{A_{Li}}^{\infty} g_0(c_i)h(c_{im}|c_i)\mathrm{d}c_{im}\mathrm{d}c_i\,, \tag{37}$$

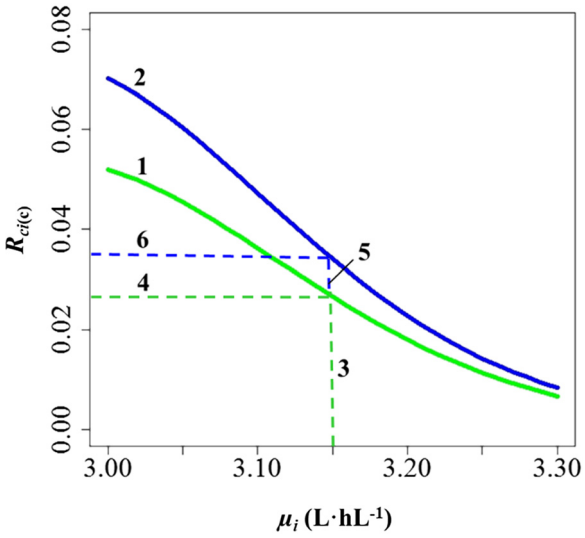

Fig. 3: Particular global customs risks $R_{ci(c)}$ at control of IPA and MEK concentrations. Curve 1 is for IPA ($i = 1$), and curve 2 – for MEK ($i = 2$); μ_i is the mean of the prior distribution of actual values of the denaturant concentrations c_1 and c_2 in CDA batches. The risk values at $\mu_1 = \mu_2 = 3.15$ L hL^{-1} are indicated by dotted lines 3 and 4 for IPA, and by dotted lines 5 and 6 for MEK.

The results of the calculations of the particular global risks R_{ci} in dependence on mean actual values μ_i when measured values are compared directly with the regulation limits ($A_{Li} = T_{Li}$) are presented in Fig. 3 for IPA and MEK, curves 1 and 2, respectively. In Fig. 3, one can notice how greater measurement uncertainty leads to greater risks.

For example, at $\mu_1 = \mu_2 = 3.15$ L hL^{-1} and $\mu_3 = 1.10$ g hL^{-1}, the following risks are observed: $R_{c1(c)} = 0.027$ for IPA, $R_{c2(c)} = 0.034$ for MEK (indicated in Fig. 3 by dotted lines 3 and 4 for IPA, and 5 and 6 for MEK), and $R_{c3(c)} = 0.046$ for DB.

The probability $P(C_i)$ of conforming measured values for i-th denaturant is calculated by marginalization of the corresponding joint pdf:

$$P(C_i) = \int_0^{\infty} \int_{A_{Li}}^{\infty} g_0(c_i) h(c_{im}|c_i) \mathrm{d}c_{im} \mathrm{d}c_i \,. \tag{38}$$

The following results were obtained (again at $A_{Li} = T_{Li}$) when $\mu_1 = \mu_2 = 3.15$ L hL^{-1} and $\mu_3 = 1.10$ g hL^{-1}: $P(C_1) = 0.818$ for IPA, $P(C_2) = 0.808$ for MEK, and $P(C_3) = 0.778$ for DB.

The total global customs risk, in the case of control of IPA and MEK at the above-mentioned conditions, is given by Eq. (10): $R_{total(c)} = 0.808 \times 0.027 + 0.818 \times 0.034 - 0.027 \times 0.034 = 0.048$. It is greater than each particular risk.

When all three denaturants (IPA, MEK and DB) are under control at the same conditions, the total global customs risk by Eq. (11) is $R_{total(c)} = 0.808 \times 0.778 \times 0.027 + 0.818 \times 0.778 \times 0.034 + 0.818 \times 0.808 \times 0.046 - 0.778 \times 0.027 \times 0.034 - 0.808 \times 0.027 \times 0.046 - 0.818 \times 0.034 \times 0.046 + 0.027 \times 0.034 \times 0.046 = 0.066$. This value is greater than that calculated in the case of control of just IPA and MEK.

A-1-7 Specific risks

When a specific CDA batch is under customs control, the particular specific customs risk value $R^*_{ci(c)}$ for the i-th denaturant can be evaluated according to Eq. (4):

$$R^*_{ci(c)} = \int_0^{T_{Li}} g(c_i|c_{im})\mathrm{d}c_i, \tag{39}$$

where

$$g(c_i|c_{im}) = \frac{1}{u_{ipost}\sqrt{2\pi}}\exp\left[-\frac{\left(c_i - \mu_{ipost}\right)^2}{2u^2_{ipost}}\right] \tag{40}$$

is the posterior pdf for the actual values of the i-th denaturant concentration $\boldsymbol{c_i}$, while the measured value $\boldsymbol{c_{im}}$ obtained at the batch testing is inside the tolerance limits. When both the prior and likelihood are normal distributions, the posterior pdf is also normal, with the following parameters:

$$\mu_{ipost} = \frac{\mu_i/(s_{ri}\mu_i)^2 + c_{im}/u_i^2}{1/(s_{ri}\mu_i)^2 + 1/u_i^2}, \tag{41}$$

$$u_{ipost} = \frac{1}{\sqrt{1/(s_{ri}\mu_i)^2 + 1/u_i^2}}. \tag{42}$$

The $R^*_{ci(c)}$ values calculated under the same conditions as previously ($\mu_1 = \mu_2 = 3.15$ L hL^{-1} and $\mu_3 = 1.10$ g hL^{-1}), in dependence on measured values c_{im} within their acceptance/tolerance interval, are shown in Fig. 4 by lines 1 and 2 for IPA and MEK, respectively.

For example, when a customs laboratory reports in a certificate of analysis of a CDA batch the measured values $c_{1m} = c_{2m} = 3.10$ L hL^{-1} for IPA and MEK, and $c_{3m} = 1.05$ g hL^{-1} for DB, the batch should be recognized as properly denatured according to the regulation [62]. However, there are still the following particular specific customs risks: $R^*_{c1(c)} = 0.014$, $R^*_{c2(c)} = 0.045$, and $R^*_{c3(c)} = 0.138$. They are shown in Fig. 4 by dotted lines 3 and 4 for IPA, 5 and 6 for MEK.

If only IPA and MEK influence the decision on the batch conformity, the total specific risk is $R^*_{total(c)} = 0.014 + 0.045 - 0.014 \times 0.045 = 0.059$, by Eq. (17). When all the denaturants are taken into account, the total specific risk is $R^*_{total(c)} = 0.014 + 0.045 + 0.138 - 0.014 \times 0.045 - 0.014 \times 0.138 - 0.045 \times 0.138 + 0.014 \times 0.045 \times 0.138 = 0.188$, by Eq. (18). This value is caused mostly by DB, since $R^*_{c3(c)}$ is significantly larger here than $R^*_{c1(c)}$ and $R^*_{c2(c)}$.

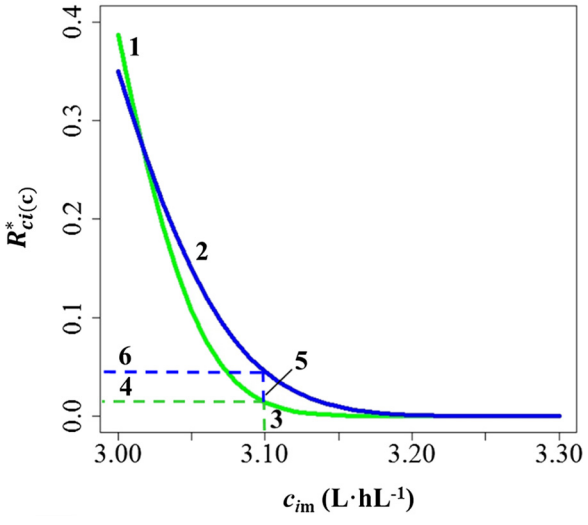

Fig. 4: Particular specific customs risk $R^*_{ci(c)}$ at control of IPA and MEK concentrations. Line 1 is for IPA ($i = 1$), and line 2 – for MEK ($i = 2$); c_{im} is the measured value. Dotted lines 3 and 4 mark an example for IPA, 5 and 6 – for MEK.

A-2. Example 2. Risks in monitoring total suspended particulate matter (TSPM) in ambient air

A-2-1 Introduction

The actual ('true') concentration c_i of the i-th pollutant, $i = 1, 2, \ldots, n$, in an environmental compartment, *e.g.* ambient air, should not exceed a regulation or legal tolerance upper limit T_{Ui}. A measured value c_{im} of the i-th pollutant concentration obtained during environmental monitoring (with the associated measurement uncertainty) is compared directly with the T_{Ui} value to decide whether the compartment conforms to the regulation or not.

In the present example, the total risks of underestimation of the pollutant concentration (consumer's/inhabitants' risks) and overestimation (producer's risks) are calculated for uncorrelated measured values of concentration of total suspended particulate matter (TSPM) in ambient air contributed by three independent stone quarries in Israel [41]. In this study, TSPM from the i-th quarry, $i = 1, 2, 3$, is considered as the i-th pollutant. While particular risk values of false decisions on conformity of the i-th TSPM concentration, evaluated earlier [66], were related to each i-th pollutant (i-th quarry) separately, the total risk values discussed below allow for the characterization of conformity of the TSPM concentration in the region of the quarries as a whole. That is important for the Regulator (the Ministry of Environmental Protection) protecting the inhabitants' quality of life in the area surrounding the quarries, as well as for the Manufacturers Association acting in the interests of the stone producers in the country.

A-2-2 Experimental

A measured TSPM concentration in ambient air c_{im}, mg m^{-3}, is an averaged mass of particles with aerodynamic diameters of 100 μm or less collected from the air drawn through a filter in a high-volume sampler over the sampling period of the test in proximity to the i-th stone quarry. The testing was organized at a distance of (1–3) km from each quarry during the quarry' work. Each test lasted 24 h, for the collection of particles from about 2000 m^3 of air [67].

The dataset of 496 test results obtained during a year and described in the work [66] is considered here also. On the basis of the analysis of variances (ANOVA), it was shown that the wind from the desert did not influence the test results significantly, whereas anthropogenic contributions to TSPM concentration were dominant. No correlation among test results for different quarries was observed.

A-2-3 Tolerance domain

There are national regulations of ambient air quality, including upper regulation limits T_{Ui} for TSPM concentration depending on the period of sampling. In Israel, the same limit value, $T_{Ui} = 0.200$ mg m^{-3} for 24 h, is valid for any location, including close to the i-th quarry.

Since the regulations require the direct comparison of monitoring measured values c_{im} with T_{Ui}, the acceptance limits A_i are taken as coincidental with the regulation limits.

A-2-4 Prior pdfs

The theoretical distributions of actual values of TSPM concentration c_i, fitting successfully the data collected close to quarry i, were lognormal distributions, used in the following as prior pdfs:

$$g_0(c_i) = \frac{1}{c_i \sigma_i \sqrt{2\pi}} \exp\left[-\frac{(\ln c_i - \mu_i)^2}{2\sigma_i^2} \right], \tag{43}$$

where standard deviations σ_i and means μ_i are for the first quarry ($i = 1$) 0.434 and −2.326, respectively, on the logarithmic scale; for the second quarry ($i = 2$), they are 0.280 and −2.031; and, for the third quarry, $\sigma_3 = 0.403$ and $\mu_3 = -2.338$.

A-2-5 Likelihood functions

The distribution of the measured values c_{im} at the same actual concentration value c_i (in the same location and practically at the same time) was found to be normal, with standard deviation equal to the standard measurement uncertainty $u_i = 0.07\, c_{im}$ and mean equal to c_i [66]. Corresponding likelihood functions $h(c_{im}|c_i)$ are normal pdfs as in Example 1, Eq. (36).

A-2-6 Global risks

The global risks of under- and overestimation related to the TSPM regulation limit T_{Ui}, are, respectively:

$$R_{ci(c)} = \int_{T_{Ui}}^{\infty} \int_{0}^{T_{Ui}} g_0(c_i) h(c_{im}|c_i) \mathrm{d}c_{im} \mathrm{d}c_i, \tag{44}$$

$$R_{ci(p)} = \int_{0}^{T_{Ui}} \int_{T_{Ui}}^{\infty} g_0(c_i) h(c_{im}|c_i) \mathrm{d}c_{im} \mathrm{d}c_i. \tag{45}$$

The probability $P(\mathrm{C}_i)$ of a conforming measured value for the i-th pollutant ($c_{im} \le A_i = T_{Ui}$) is calculated by the marginalization of the joint pdf of the measured values and the actual values of TSPM concentration:

$$P(\mathrm{C}_i) = \int_{0}^{\infty} \int_{0}^{T_{Ui}} g_0(c_i) h(c_{im}|c_i) \mathrm{d}c_{im} \mathrm{d}c_i. \tag{46}$$

The probability $P(\overline{\mathrm{B}}_i)$ that the actual concentration value for the i-th pollutant is conforming ($c_i \le T_{Ui}$) is calculated as:

$$P\left(\overline{\mathrm{B}}_i\right) = \int_{0}^{T_{Ui}} g_0(c_i) \mathrm{d}c_i. \tag{47}$$

Note that the probability $P(\overline{\mathrm{B}}_i)$ of a conforming actual ('true') value c_i in Eq. (47) does not depend on the measured value c_{im} by definition. However, the *vice versa* holds: the probability $P(\mathrm{C}_i)$ of a conforming measured value c_{im} by Eq. (46) does depend on the relevant actual value c_i.

The particular global risks of underestimation are $R_{c1(c)} = 0.006$, $R_{c2(c)} = 0.010$, and $R_{c3(c)} = 0.005$. The probabilities of conforming measured values are $P(\mathrm{C}_1) = 0.949$, $P(\mathrm{C}_2) = 0.929$, and $P(\mathrm{C}_3) = 0.963$. The total risk of underestimation is $R_{\mathrm{total(c)}} = 0.019$, greater than the particular risk contribution by each quarry.

The particular global risks of overestimation are $R_{c1(p)} = 0.007$, $R_{c2(p)} = 0.015$, and $R_{c3(p)} = 0.006$. The probabilities of conforming actual concentration values calculated are $P(\overline{\mathrm{B}}_1) = 0.951$, $P(\overline{\mathrm{B}}_2) = 0.934$, and $P(\overline{\mathrm{B}}_3) = 0.965$. The total risk of overestimation is $R_{\mathrm{total(p)}} = 0.026$, again greater than each $R_{ci(p)}$.

The total risk of overestimation $R_{\mathrm{total(p)}}$ exceeds the total risk of underestimation $R_{\mathrm{total(c)}}$, which implies that there is a reasonable balance between the requirements of an inhabitant's quality of life and the producer's expenditure on the environmental protection.

A-2-7 Specific risks

The particular specific risks of the pollutant concentration under- and overestimation are, respectively:

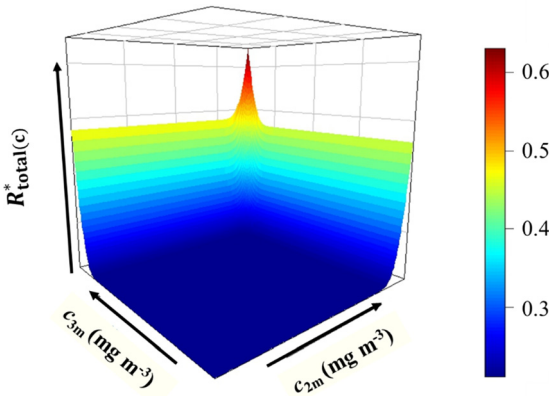

Fig. 5: Dependence of the total specific risks of underestimation $R^*_{total\,(c)}$ of TSPM concentration in air on the measured values c_{im}. It is a case when all the three quarries are active and $R^*_{total\,(c)}$ – the color surface - is depending on c_{2m} and c_{3m} in the range [0.010, 0.200] mg m^{-3}, while c_{1m} = 0.194 mg m^{-3}. The meaning of the color is the total risk value according to the color scale of the bar on the right side of the plot.

$$R^*_{ci(c)} = \int_{T_{Ui}}^{\infty} g(c_i|c_{im})\mathrm{d}c_i, \quad \text{for } c_{im} \le T_{Ui}, \text{and} \tag{48}$$

$$R^*_{ci(\mathrm{p})} = \int_{0}^{T_{\mathrm{Ui}}} g(c_i|c_{im})\mathrm{d}c_i, \quad \text{for } c_{\mathrm{im}} > T_{Ui}\,, \tag{49}$$

where $g(c_i|c_{im})$ is the posterior pdf for the actual value of the TSPM concentration c_i contributed by the i-th quarry, given the measured value c_{im} near the quarry. The posterior pdf is here:

$$g(c_i|c_{im}) = g_0(c_i)h(c_{\mathrm{im}}|c_i) \Big/ \int_{-\infty}^{\infty} g_0(c_i)h(c_{im}|c_i)\mathrm{d}c_i\,. \tag{50}$$

The dependence of the total specific risks of underestimation of TSPM concentration in air on the measured values $c_{i\mathrm{m}}$ is demonstrated in Fig. 5.

The surface lies mostly on the bottom of the three-dimensional region where $R^*_{total\,(c)}$ is close to zero, increasing with $c_{2\mathrm{m}}$ and $c_{3\mathrm{m}}$ approaching their tolerance limits $T_{\mathrm{U1}} = T_{\mathrm{U2}} = 0.200$ mg m^{-3}. When both $c_{2\mathrm{m}}$ and $c_{3\mathrm{m}}$ simultaneously approach 0.200 mg m^{-3}, this leads to a "protuberance" in the total risk surface.

The dependence of the total specific risks of overestimation $R^*_{total\,(p)}$ of the actual TSPM concentration in air on measured values, when they are out-of-specification ($c_{\mathrm{im}} > T_{Ui}$), is detailed in Fig. 6. The maximum $R^*_{total\,(p)}$ value at $c_{1\mathrm{m}}$ = 0.250 mg m^{-3} is observed when $c_{2\mathrm{m}}$ and $c_{3\mathrm{m}}$ are close to the tolerance limit simultaneously. In other words, if an out-of-specification measured value is significantly greater than the tolerance limit, the probability of an actual violation of the regulation is high and the particular risk of overestimation is low. Therefore, the total specific risk of overestimation is low here also.

A-3. Example 3. Risks in conformity assessment of a medication

A-3-1 Introduction

In this example, the 'producer' of a medication is a factory (pharmaceutical company), while the 'consumer' is fuzzy: people who may catch cold or get sick with the flu. Their interests are defended by regulatory authorities supported by official medicines control laboratories controlling the quality of marketed medicinal products [68, 69].

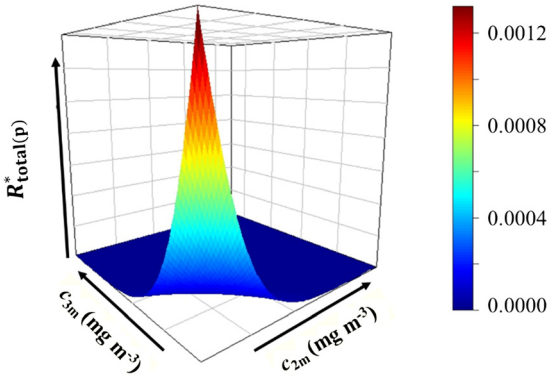

Fig. 6: Dependence of the total specific risks of overestimation $R^*_{total(p)}$ of the TSPM concentration in air on the measured values c_{im}. This is a case when all the three quarries are active simultaneously: $c_{1m} = 0.250$ mg m^{-3}, whereas c_{2m} and c_{3m} are in the range [0.210, 0.300] mg m^{-3}.

NyQuil tablets, being a cold/flu medication, contain four active components: 1) acetaminophen (APAP), as a pain reliever and fever reducer; 2) dextromethorphan hydrobromide (DEX), as a cough suppressant; 3) racemic doxylamine succinate (DOX), as an antihistamine and hypnotic; and 4) (R)-phenylephrine hydrochloride (PE), as a nasal decongestant [70]. However, there are publications which have claimed that the last component (PE) is no more effective than a placebo [71]. Therefore, this study is performed for both scenarios: when measurement uncertainties of the contents of four components contribute to the total consumer's risks, as well as when only three do so (*i.e.*, without PE) . To assess the influence of the correlation between the test results on the evaluated total risks, they are compared with those calculated for independent test results by Eqs. (11), (12), (18), and (19) of this Guide, as well as with the values obtained supposing a much stronger correlation than that observed [42].

A-3-2 Experimental

A sample of the tablets is weighed, dissolved in a solution of phosphoric acid and acetonitrile in water on a magnetic stirrer plate, and then centrifuged. An aliquot is transferred into an autosampler vial for the determination of the low-dose active components: DEX, DOX, and PE. Another diluted aliquot is used for determination of the high-dose active component: APAP.

The stock standard solution containing the four active components, in concentrations higher than those in the sample solutions, is prepared from the USP reference standards [72], which are also available from Merck [73]. The working standard solution is prepared from the stock standard solution by dilution to bring the analyte concentrations to the same values as in the sample solutions. Two independent working standards solutions are prepared according to the USP <621> chromatography requirements [74]: one for quantitation of the analyte content, and the second one for the system suitability control.

The separation and quantification of the analytes are performed using an HPLC system with diode-array ultra violet detector or a multichannel detector and column (C18) heater.

Measured values c_{im} are expressed in % of labeled amount l_i in a tablet: $l_1 = 325$ mg for APAP, $l_2 = 10$ mg for DEX, $l_3 = 6.25$ mg for DOX, and $l_4 = 5$ mg for PE, per tablet (a tablet's mass is 775 mg on average).

A-3-3 Tolerance domain

The assay test lower and upper specification (tolerance) limits, T_{Li} and T_{Ui}, for the product release for each active component $i = 1, \ldots, 4$ are 95.0 and 105.0 % of the labeled amount l_i, respectively. The acceptance limits of measured values coincide with the specification limits in this study, *i.e.* $A_{Li} = T_{Li}$ and $A_{Ui} = T_{Ui}$.

A-3-4 Prior pdfs

A total of 105 lots of the medication produced and released at the same factory during a year were tested in the same laboratory belonging to the factory. The theoretical distributions of actual component contents c_i in a tablet, fitting successfully the collected data, were normal distributions with means m_i and standard deviations s_i of the measured values presented in Table 1.

Linear correlation among the test results for different components was estimated by the Pearson's correlation coefficients r_{ij}, $i \neq j = 1, \ldots, 4$, reported in Table 2.

The two-sided critical values of the coefficient r_{crit} for 103 degrees of freedom are 0.195 for the level of confidence $P = 0.95$ and 0.254 for $P = 0.99$ [75, 76]. Therefore, only the test results for APAP are independent of the others, since $r_{1j} < r_{crit}$ for each j and for both the confidence levels. The test results for the low-dose active components—DEX, DOX and PE—are correlated significantly.

Note that the observed correlation coefficients were positive only. Negative correlation is also possible, for example when the sum of component concentrations cannot exceed 100 % mass. However, the treated quantities are expressed in % of labeled amount of the component in a tablet: there is no limitation of the sum of such values.

Thus, the prior covariance matrix is the following:

$$S_{c1} = \begin{pmatrix} 1.8769 & 0.1495 & 0.1798 & 0.2958 \\ 0.1495 & 1.0404 & 0.3331 & 0.5027 \\ 0.1798 & 0.3331 & 1.1025 & 0.6905 \\ 0.2958 & 0.5027 & 0.6905 & 1.4884 \end{pmatrix},$$

where the diagonal elements are variances $\sigma_i^2 = s_i^2$ (s_i, as in Table 1), while off-diagonal elements are covariances $cov_{ij} = r_{ij}\,\sigma_I\,\sigma_j$, $i \neq j$ (r_{ij}, as in Table 2). Both σ_i^2 and cov_{ij} are expressed in squared % of labeled amount.

For comparison with the case of uncorrelated data, the prior covariance matrix was transformed into corresponding diagonal ones, setting correlation coefficient values equal to zero ($r_{ij} = 0$):

$$S_{c2} = \begin{pmatrix} 1.8769 & 0.0000 & 0.0000 & 0.0000 \\ 0.0000 & 1.0404 & 0.0000 & 0.0000 \\ 0.0000 & 0.0000 & 1.1025 & 0.0000 \\ 0.0000 & 0.0000 & 0.0000 & 1.4884 \end{pmatrix}.$$

Table 1: Parameters of the prior distributions.

Component	Index	Parameters	
	i	m_i, %	s_i, %
APAP	1	99.18	1.37
DEX	2	97.70	1.02
DOX	3	99.33	1.05
PE	4	98.94	1.22

Table 2: Pearson's correlation coefficients of test results r_{ij}.

Component	Index $i \setminus j$	APAP 1	DEX 2	DOX 3	PE 4
APAP	1	1	0.107	0.125	0.177
DEX	2		1	0.311	0.404
DOX	3			1	0.539
PE	4				1

Another chosen point for comparison was the case of much stronger correlation than that observed, assuming correlation coefficients $r_{ij} = 0.7$:

$$S_{c3} = \begin{pmatrix} 1.8769 & 0.9782 & 1.0070 & 1.1700 \\ 0.9782 & 1.0404 & 0.7497 & 0.8711 \\ 1.0070 & 0.7497 & 1.1025 & 0.8967 \\ 1.1700 & 0.8711 & 0.8967 & 1.4884 \end{pmatrix}.$$

In this way, the three scenarios—three points ω on the correlation scale—are addressed: 1) r_{ij} as in Table 2; 2) $r_{ij} = 0$; and 3) $r_{ij} = 0.7$.

A-3-5 Likelihood functions

The evaluated relative measurement uncertainty was 2.8 % of the measured value c_{im}. This is typical for HPLC. No deviation from normal distribution was indicated [42]. Therefore, pdfs of normal distributions with c_i as mean and standard deviation $u_i = 0.028\, c_{im}$, % of labeled amount are used as the likelihood functions $h(c_{im}|c_i)$, similar to Example 1, Eq. (36).

Note that the s_i values in Table 1 are smaller than the measurement uncertainty $u_i = 0.028\, c_{im}$, % of the labeled amount, in spite of the fact that the lot-to-lot variation of test results is formed by variation in the production/technological factors and the measurement uncertainty. The reason is that each released lot has passed not only assay determination, but also tests of uniformity of dosage units by USP <905>, dissolution by USP <711> [74], and some other tests. Any out-of-specification and/or out-of-trend test result investigation, pointing out a production problem, prevents the lot release. As a result, s_i values are minimized in this way and the lot-to-lot (empirical) distributions of test results are truncated by the specification limits.

There is no indication of systematic errors that could cause correlation in the chemical analysis/testing/measurement discussed above in Section A-3-4. Random chemical analytical factors contributing to measurement uncertainty are only able to decrease the correlation as any numerical noise. Probably the root cause is in the technological conditions. However, the reason for the observed correlation is not important in the framework of this study, since correlation should be taken into account irrespective of its origin.

If the "noise" of the random chemical analytical factors contributing to measurement uncertainty in a control laboratory is negligible, the correlation among the test results is the same as shown in Table 2. Then, the likelihood covariance matrix for measured values c_{im} equal, for example, to the prior means $\mu_i = m_i$ (Table 1), is:

$$S_{cm1} = \begin{pmatrix} 7.7120 & 0.8129 & 0.9655 & 1.3617 \\ 0.8129 & 7.4835 & 2.3662 & 3.0617 \\ 0.9655 & 2.3662 & 7.7353 & 4.1530 \\ 1.3617 & 3.0617 & 4.1530 & 7.6747 \end{pmatrix},$$

where the diagonal elements are variances $u_i^2 = (0.028\, c_{im})^2$; and the covariances are $cov_{ijm} = r_{ij}\, u_i\, u_j$, $i \neq j$ (r_{ij} as in Table 2). The values u_i^2 and cov_{ijm} are expressed in the same squared % of labeled amount as elements of the prior covariance matrix S_{c1}.

For uncorrelated data ($r_{ij} = 0$), the covariance matrix transformed into corresponding diagonal one is:

$$S_{cm2} = \begin{pmatrix} 7.7120 & 0.0000 & 0.0000 & 0.0000 \\ 0.0000 & 7.4835 & 0.0000 & 0.0000 \\ 0.0000 & 0.0000 & 7.7353 & 0.0000 \\ 0.0000 & 0.0000 & 0.0000 & 7.6747 \end{pmatrix}.$$

When correlation coefficients $r_{ij} = 0.7$ are assumed, the matrix is:

$$S_{\mathrm{cm3}} = \begin{pmatrix} 7.7120 & 5.3178 & 5.4065 & 5.3853 \\ 5.3178 & 7.4835 & 5.3259 & 5.3049 \\ 5.4065 & 5.3259 & 7.7353 & 5.3934 \\ 5.3853 & 5.3049 & 5.3934 & 7.6747 \end{pmatrix}.$$

The last subscript in the matrix symbol $S_{\mathrm{cm}\omega}$ means the point ω on the correlation scale, exactly as the last subscript in the symbol of prior matrix $S_{\mathrm{c}\omega}$.

A-3-6 Global risks

Since the actual content values of the four components are jointly described by a multivariate prior normal pdf and the likelihood function of their test results is also modelled by a multivariate normal distribution, the joint posterior function is a multivariate normal pdf as well. No transformation of the raw data is required for its formulation. Hence, the joint posterior function was calculated as a multivariate normal pdf by Eq. (34).

According to the framework of this Guide, the total global consumer's risk $R_{\mathrm{total(c)}}$ is the probability of the event $\mathrm{C} \cap \mathrm{B} = (\mathrm{C} \cap \mathrm{B}_1) \cup (\mathrm{C} \cap \mathrm{B}_2) \cup (\mathrm{C} \cap \mathrm{B}_3) \cup (\mathrm{C} \cap \mathrm{B}_4)$. In general, the event $\mathrm{C} = \mathrm{C}_1 \cap \mathrm{C}_2 \cap \mathrm{C}_3 \cap \mathrm{C}_4$ occurs when all the measured values c_{im} are within their acceptance intervals simultaneously, and $\mathrm{B} = \mathrm{B}_1 \cup \mathrm{B}_2 \cup \mathrm{B}_3 \cup \mathrm{B}_4$ is the event occurring when at least one of the true values of the components' content c_i is outside its specification interval. Therefore, $R_{\mathrm{total(c)}}$ can be considered as the following:

$$\begin{aligned} R_{\mathrm{total\,(c)}} = P(\mathrm{C} \cap \mathrm{B}) &= P(\mathrm{C} \cap \mathrm{B}_1) + P(\mathrm{C} \cap \mathrm{B}_2) + P(\mathrm{C} \cap \mathrm{B}_3) + P(\mathrm{C} \cap \mathrm{B}_4) - P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_2) \\ &- P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_3) - P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_4) - P(\mathrm{C} \cap \mathrm{B}_2 \cap \mathrm{B}_3) - P(\mathrm{C} \cap \mathrm{B}_2 \cap \mathrm{B}_4) - P(\mathrm{C} \cap \mathrm{B}_3 \cap \mathrm{B}_4) \\ &+ P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_2 \cap \mathrm{B}_3) + P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_2 \cap \mathrm{B}_4) + P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_3 \cap \mathrm{B}_4) + P(\mathrm{C} \cap \mathrm{B}_2 \cap \mathrm{B}_3 \cap \mathrm{B}_4) \\ &- P(\mathrm{C} \cap \mathrm{B}_1 \cap \mathrm{B}_2 \cap \mathrm{B}_3 \cap \mathrm{B}_4). \end{aligned} \tag{51}$$

Each probability term in the expression (51) was calculated as a multiple integral of the product of the multivariate prior normal pdf (modelling events $\mathrm{B}_i \cap \mathrm{B}_j$, *etc.*) and the multivariate normal likelihood (modelling conditional event $\mathrm{C}|[c_1, c_2, c_3, c_4]$), *i.e.* as the integral of the joint distribution of actual values and measured values. Concerning the relevant integration limits, note that the measured values spread in their multivariate acceptance interval (coinciding in this study with the specification interval/domain $[T_{\mathrm{L}i}, T_{\mathrm{U}i}]$), whereas actual values are outside the specification domain if the probability of events B_i needed to be calculated. Otherwise, they spread on the whole range of real positive values leading to the marginalization of the joint distribution with respect to those quantities.

The integration was performed in an R programming environment by application of the 'adaptIntegrate' function from the R package 'cubature' [77].

For diagonal matrices $S_{\mathrm{c}2}$ and $S_{\mathrm{cm}2}$, defined in Sections A-3-4 and A-3-5 for uncorrelated variables, $R_{\mathrm{total(c)}} = 0.19 \times 10^{-2}$. This value is equal to that calculated by Eq. (12). The observed correlation did not visibly influence the total risk: it was again $R_{\mathrm{total(c)}} = 0.19 \times 10^{-2}$, whereas for the correlation coefficients $r_{ij} = 0.7$ $R_{\mathrm{total(c)}} = 0.10 \times 10^{-2}$.

Practically the same risk values were obtained at all levels of correlation when PE content was not taken into account, as well as by Eq. (11). That is apparently due to the minor contribution of the particular PE risk to the total probability.

A-3-7 Specific risks

The total specific risk R^*_{total} was evaluated as the probability that at least one of the true values c_i of a specific lot lies outside the multivariate specification domain when the vector of measured values c_{im}, obtained for the lot

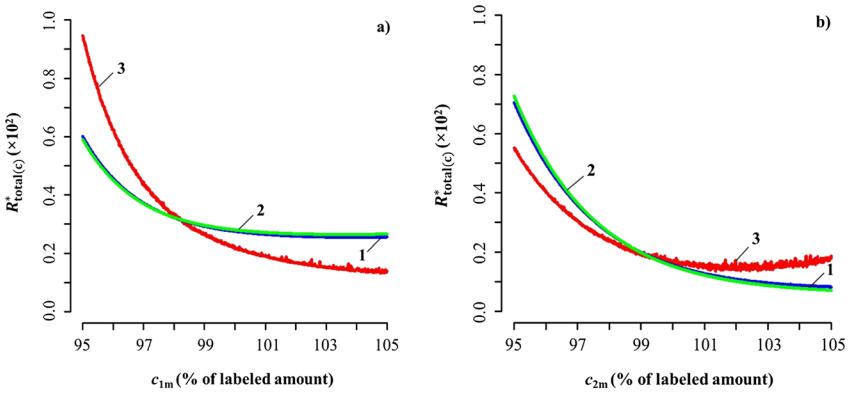

Fig. 7: Total specific risk in the specification interval. The dependence of the consumer's total specific risk $R^*_{total\,(c)}$ (×10²) on measured values c_{im} in the specification interval, 95 to 105 % of labeled amount, when measured values for other active components c_{jm}, $j \neq i$ are equal to their prior pdf mean (Table 1). The plots are for: a) APAP, c_{1m}; and b) DEX, c_{2m}. Line 1 is for the observed correlation among the test results (Table 2, correlation point $\omega = 1$), line 2 for the case when there is no correlation (correlation coefficients $r_{ij} = 0$, $\omega = 2$), and line 3 for a case when the correlation is much stronger than that observed ($r_{ij} = 0.7$, $\omega = 3$).

is completely inside this domain. For the estimation of this probability, the 'pmvnorm' function from the R package 'mvtnorm' [78] was used to calculate the joint posterior cumulative function.

The dependences of the total specific risk $R^*_{total\,(c)}$ (×10²) on measured values c_{im} in the specification interval, 95–105 % of labeled amount, when the measured values for other active components c_{jm}, $j \neq i$ are equal to their prior pdf means $\mu_j = m_j$ (Table 1) are shown in Fig. 7. The plots are for: a) APAP, c_{1m}; and b) DEX, c_{2m}. Line 1 is for the observed correlation among test results (Table 2), line 2 for the case when there is no correlation (correlation coefficients $r_{ij} = 0$), and line 3 for a case when the correlation is much stronger than that observed ($r_{ij} = 0.7$). The "noise" in line 3 is due to the intrinsic numerical inaccuracies in the 'pmvnorm' function when computing joint probability values for the strong correlation case. Fig. 7 shows that the correlation influence on the risk values is not easily predictable.

There is no significant difference between the risk values if the test results are independent or correlated as observed (lines 2 and 3, respectively). However, when the correlation among the test results is stronger (line 3), this may lead either to a decrease in the total risk or to an increase, depending on the actual values of the component contents.

Note that the results of calculations by Eq. (34) using the multivariate normal distributions for uncorrelated test results of the content of three and four components (diagonal covariance matrices) coincide with those obtained by Eqs. (18) and (19), respectively. If PE is not taken into account, while the independent c_{1m}, c_{2m} and c_{3m} values are equal to their prior pdf means μ_i (Table 1), the total risk is $R^*_{total\,(c)} = 0.27 \times 10^{-2}$. Considering any possible c_{4m} values for PE in the specification interval for the same conditions on the other components (independent test results and $c_{im} = \mu_i$, $i = 1, 2, 3$), it was found that the minimal value of the total risk for all the four components is, after rounding, also $R^*_{total\,(c)} = 0.27 \times 10^{-2}$. That is because of the minor contribution of the particular PE specific risk to $R^*_{total\,(c)}$, as for the total global risk above, due to the minimal amount of PE and its corresponding measurement uncertainty (at the same relative measurement uncertainty for all components). However, in general, $R^*_{total\,(c)}$ for the four components is greater than for only three components under control, *i.e.* it increases with the number of components under control, a fact also observed in Example 1 for denatured alcohols.

A-4. Example 4. Risks in conformity assessment of an alloy

A-4-1 Introduction

The aim of the present Example is the implementation of modelling and calculation of the total risks in the conformity assessment of an alloy as a multicomponent material with a complex nature of correlation among the contents of components. The risks in the conformity assessment of a PtRh alloy (CAS No. 11107-71-4) in relation to the standard [79] due to measurement uncertainty are quantified when four components of the alloy composition are under control ($n = 4$) and strong correlations among test/measurement results are observed [43]. The evaluation of these risks can be important for understanding the quality of such alloys, which are widely used in thermocouples for temperature measurements; oxidation catalysts, in particular, automobile catalytic converters; electronics; the glass industry; and optics; as well as in the manufacture of jewelry [80].

A-4-2 Experimental

Platinum ingots, rhodium powder, and PtRh alloy wastes are melted in a vacuum induction furnace, providing homogeneity in the alloy. The melt is cast into graphite molds. Samples are cut down from an alloy ingot as a strip for the preparation of two disks for wavelength dispersive X-ray fluorescence (XRF) analysis with an Axios spectrometer [81], measuring the Rh content. Samples in the form of a band from the same ingot are prepared for optical atomic emission spectrometry (AES) analysis with a Baird spectrometer [82] for measurement of the contents of impurities. Metrologically traceable in-house reference materials are used for the calibration of the spectrometers. Corresponding certified reference materials are described in the catalog [83].

Measured values are expressed as mass fractions, %. The sum c_{3m} of the measured values of mass fractions of the three precious impurities (Au, Ir, and Pd) and the sum c_{4m} of the measured values of mass fractions of the eight impurities, both precious, (Au, Ir, and Pd) and non-precious (Fe, Pb, Si, Sn, and Zn) are reported. A measured value of the Pt content c_{1m} is calculated as a difference between 100 % and the measured values of the Rh content c_{2m} and the content of the eight impurities c_{4m} according to the standard [84]: $c_{1m} = 100\ \% - c_{2m} - c_{4m}$.

A-4-3 Tolerance domain

The standard [79] sets the lower and upper specification limits (tolerance limits) T_{Li} and T_{Ui} of contents c_i of the four following components in PtRh 92.5-7.5 alloy:

$i = 1$) Pt content c_1 as mass fraction, $T_{L1} = 92.2\ \% \le c_1 \le 92.8\ \% = T_{U1}$;

$i = 2$) Rh content c_2 as mass fraction, $T_{L2} = 7.3\ \% \le c_2 \le 7.7\ \% = T_{U2}$;

$i = 3$) content c_3 of three precious impurities—Au, Ir and Pd—as the sum of mass fractions, $c_3 \le 0.12\ \% = T_{U3}$;

$i = 4$) content c_4 of eight impurities, both precious (Au, Ir, and Pd) and non-precious (Fe, Pb, Si, Sn, and Zn), as the sum of mass fractions, $c_4 \le 0.18\ \% = T_{U4}$.

The limitation of the impurities' contents, which assures the alloy purity, prevents a change of its microstructure, influencing high-temperature resistance, catalytic, and other alloy properties. By agreement with a consumer, the number of impurities under control (each with its separate upper specification limit) can be increased [79], but for simplicity, this is not discussed further in the discussed Example.

The specification limits T_{Li} and T_{Ui}, form a multivariate specification domain of permissible alloy compositions. However, there are also two mass constraints to be satisfied: 1) the sum of the contents of the main components and the eight impurities should be equal to 100 %, *i.e.* $c_1 + c_2 + c_4 = 100\ \%$, the mass balance constraint; and 2) the content of the three precious impurities cannot exceed the content of the eight precious and non-precious impurities in the same alloy, *i.e.* $c_3 \le c_4$. These constraints lead to a multivariate sub-domain

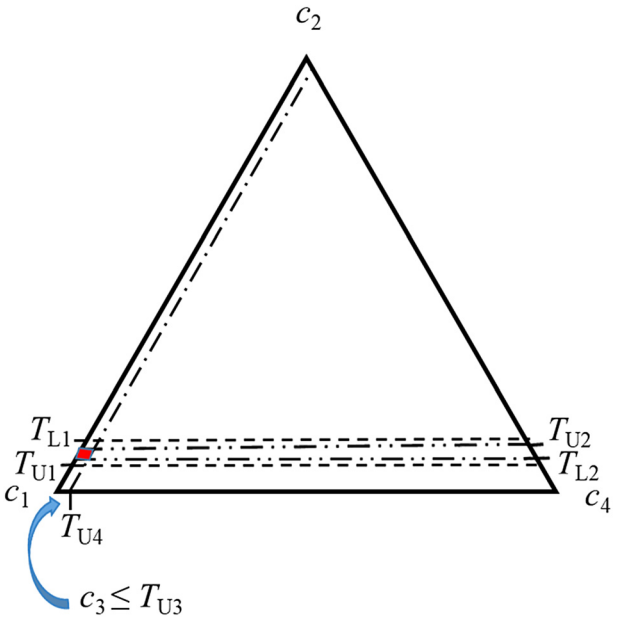

Fig. 8: A scheme of the four-dimensional sub-domain of feasible compositions of the PtRh alloy. This is a three-dimensional simplex (each vertex is $c_i = 100$ %, $i = 1, 2, 4$), where the parallelogram of feasible alloy compositions is shown in red, while the fourth dimension of c_3 is indicated by a blue curve-pointer. The dotted lines are the specification limits truncating the simplex.

of feasible alloy compositions. For example, at the Rh content $c_2 = T_{U2} = 7.7$ % and the content of the eight impurities $c_4 = T_{U4} = 0.18$ %, the Pt content is $c_1 = 92.12$ %, which is less than $T_{L1} = 92.2$ % and hence not permissible. On the other hand, compositions such as $c_1 = T_{L1}$, $c_2 = T_{U2}$, $c_3 \leq c_4$ and $c_4 = T_{U4}$ are within the specification domain, but cannot be realized in practice.

Therefore, in spite of the limitation $c_1 + c_2 + c_4 = 100$ %, typical for compositional data 'consisting of vectors of positive components subject to a unit-sum constraint' [85], the multivariate sub-domain of feasible alloy compositions is more complex than a simplex of compositional data [86]. This sub-domain, having four dimensions, can be imagined as a kind of three-dimensional simplex of c_1, c_2, and c_4, truncated by T_{Li} and T_{Ui} ($i = 1$, 2 and 4), while c_3 is the fourth dimension, limited by T_{U3} and influencing c_4 in the simplex, shown schematically in Fig. 8.

The acceptance limits in this study coincide with the specification limits.

A-4-4 Prior pdfs

Test results from a total of 100 batches of PtRh 92.5-7.5 alloy for catalytic systems, produced during about two years at the same plant, were used as a dataset for the quantification of the total risks. The testing was performed at the plant laboratory for conformity assessment of the alloy batches to the standard [80]. The mean m_i and standard deviation s_i of the measured values are presented in Table 3.

Linear correlations among the test results for different components were estimated by Pearson's correlation coefficients r_{ij}, $i \neq j = 1, \ldots, 4$, and reported in Table 4. The one-tailed critical values of the coefficient (when the correlation sign is known) for 98 degrees of freedom are 0.197 for level of confidence $P = 0.95$ and 0.256 for $P = 0.99$ [75, 76].

Test results for Rh are slightly correlated with mass fractions of impurities (statistically significant at $P = 0.95$, but insignificant at $P = 0.99$). This is possible because some part of the impurities came into the alloy with rhodium: the standard [87] permits up to 0.10 % and even 0.20 % of the impurities in different marks of Rh

Table 3: Parameters of the prior distributions.

Component	Index	Parameters	
	i	m_i, %	s_i, %
Pt	1	92.483	0.081
Rh	2	7.457	0.073
Three impurities	3	0.052	0.019
Eight impurities	4	0.059	0.021

Table 4: Pearson's correlation coefficients r_{ij} of the test results.

Component	Index $i \setminus j$	Pt 1	Rh 2	Three impurities 3	Eight impurities 4
Pt	1	1	−0.967	−0.469	−0.467
Rh	2		1	0.239	0.228
Three impurities	3			1	0.970
Eight impurities	4				1

powder. Contents of the three and the eight impurities, limited by the constraint $c_3 \le c_4$, have a correlation coefficient close to 1, as the content of the three impurities, especially of Pd, is the main contribution to the content of the eight impurities.

The contents of the main components of the alloy, Pt and Rh, have a high negative correlation: the greater the Rh content, the smaller the Pt content. This is mainly due to the constraint on the mass fractions where they must sum up to 100 %. Such a correlation, typical in compositional data, is referred to as 'spurious' [88–90]. The correlations of the Pt content with the impurities' contents are also negative, for the same reason. The corresponding coefficients are significant at both levels of confidence, in spite of the fact that the impurities' contents in different marks of Pt ingots, used as a raw material, may be up to 0.07 % and even 0.20 % [78]. As in the case of Rh content *vs*. contents of the impurities, this is the reason for positive correlation.

Note that the correlation coefficients estimated analytically from the constraint $c_1 + c_2 + c_4 = 100$ % are for Pt *vs*. Rh contents $(r_{12})_{an} = -s_2/\sqrt{s_2^2 + s_4^2} = -0.961$, and for Pt vs. the eight impurities' contents $(r_{14})_{an} = -s_4/\sqrt{s_2^2 + s_4^2} = -0.276$ (the standard deviations s_i are available in Table 3). The absolute values of $(r_{12})_{an}$ and $(r_{14})_{an}$ are even smaller than those of r_{12} and r_{14}, respectively, calculated directly from the experimental data, reported in Table 4. Thus, the observed correlations are caused as much by the natural chemical origin of the raw materials used in the alloy production, as by the mass balance constraints.

Taking into account the strong correlation between the contents of the three and of the eight impurities, as well as between the contents of Rh and Pt, it is worthwhile to analyze the following two scenarios: 1) when the measurement uncertainties of test results for all four components ($i = 1, \ldots, 4$) influence the probabilities of false decisions on the alloy conformity, and 2) when only two practically uncorrelated components, Rh and the eight impurities ($i = 2, 4$), are considered in this context, similar to 'principal components' in PCA [27, 91]. Note also that there is no reason for 'spurious' correlation in the second scenario.

In the present study, the effect of the mass balance constraints is embedded within the experimental correlation matrix (Table 4). This reflects a mixture of spurious correlation and the correlation caused by the native chemical properties of the raw materials used. This matrix influences all subsequent multivariate results.

Probability density functions (pdfs) of the theoretical normal distributions with means $\mu_i = m_i$ and standard deviations $\sigma_i = s_i$ are used as pdfs approximating the distributions of the actual content values c_i in the batches.

A multivariate normal distribution was considered as the joint prior pdf for the vector of actual components' contents [c_1, c_2, c_3, c_4] having the vector of mean values [m_1, m_2, m_3, m_4]. The prior covariance matrix is

$$S_{c1} = \begin{pmatrix} 0.0065 & -0.0057 & -0.0007 & -0.0008 \\ -0.0057 & 0.0054 & 0.0003 & 0.0004 \\ -0.0007 & 0.0003 & 0.0004 & 0.0004 \\ -0.0008 & 0.0004 & 0.0004 & 0.0004 \end{pmatrix},$$

where the diagonal elements are variances $\sigma_i^2 = s_i^2$, (s_i are in Table 3), and the off-diagonal elements are covariances $cov_{ij} = r_{ij}\,\sigma_i\,\sigma_j$, $i \neq j$ (r_{ij} are in Table 4). Both σ_i^2 and cov_{ij} are expressed in squared %, as in Example 3 above.

In the second scenario, where only two components—Rh and the eight impurities (i = 2, 4)—are taken into account, the prior covariance matrix is

$$S_{c2} = \begin{pmatrix} 0.0054 & 0.0004 \\ 0.0004 & 0.0004 \end{pmatrix}.$$

A-4-5 Likelihood functions

It was shown, based on the validation data, that (repeated) measured values c_{im} of the component contents in the same sample have normal distributions. No interference of the analytes, which could be interpreted as a cause of correlation of measured values and taken into account at the measurement uncertainty evaluation, was observed. Standard measurement uncertainty associated with measured values c_{2m} of Rh content in the specification interval (7.3–7.7) %, is u_2 = 0.04 %. For any measured value of content of the three and eight impurities, c_{3m} and c_{4m}, respectively, the standard uncertainties $u_3 = 0.18\,c_{3m}$ and $u_4 = 0.18\,c_{4m}$ were used in the following calculations. Then, the standard uncertainty of a measured Pt content c_{1m} is $u_1 = \sqrt{u_2^2 + u_4^2} = \sqrt{0.04^2 + (0.18\ \ c_{4m})^2}$.

Therefore, the vector [c_{1m}, c_{2m}, c_{3m}, c_{4m}] is modelled by a multivariate normal likelihood having a mean equal to the vector of actual components' contents [c_1, c_2, c_3, c_4] and covariance matrix defined on the base of measurement uncertainties u_i and correlation coefficients r_{ij}.

For measured values c_{im} equal, for example, to the prior means μ_i, = m_i (Table 3), the likelihood covariance matrix is:

$$S_{cm1} = \begin{pmatrix} 0.0017 & -0.0016 & -0.0002 & -0.0002 \\ -0.0016 & 0.0016 & 0.0001 & 0.0001 \\ -0.0002 & 0.0001 & 0.0001 & 0.0001 \\ -0.0002 & 0.0001 & 0.0001 & 0.0001 \end{pmatrix},$$

where the diagonal elements are variances ${u_1}^2 = 0.04^2 + (0.18\ \ c_{4m})^2$, ${u_2}^2 = 0.04^2$, ${u_3}^2 = (0.18\ c_{3m})^2$ and ${u_4}^2 = (0.18\ c_{4m})^2$. The covariances are $cov_{ijm} = r_{ij}\,u_i\,u_j$, $i \neq j$ (r_{ij} as in Table 4).

For the second scenario, with only Rh and the eight impurities (i = 2 and 4), the likelihood covariance matrix, in the case when the measured values c_{im} are equal to prior means μ_i, = m_i (Table 3), is:

$$S_{cm2} = \begin{pmatrix} 0.0016 & 0.0001 \\ 0.0001 & 0.0001 \end{pmatrix}.$$

A-4-6 Global risks

As in Example 3 above, the actual content values of the four components in the current study are jointly described by a multivariate prior normal pdf, and the likelihood of their measured values is also modelled by a multivariate normal pdf. Therefore, the joint posterior pdf is a multivariate normal pdf, as well, and parameters

of the posterior pdf can be calculated by Eq. (34). For example, for the vector of measured values c_m = [92.423, 7.457, 0.120, 0.120], the posterior covariance matrix is

$$S_{post1} = \begin{pmatrix} 7.6741 & -8.5547 & 0.6761 & 0.8088 \\ -8.5547 & 9.6566 & -0.9075 & -1.0709 \\ 0.6761 & -0.9075 & 0.4016 & 0.3144 \\ 0.8088 & -1.0709 & 0.3144 & 0.3510 \end{pmatrix} \times 10^{-4},$$

and the vector of the posterior means is $\boldsymbol{c}_{post1}$ = [92.405, 7.481, 0.104, 0.111].

Under scenario $\omega = 2$ with only two components ($i = 2$ and 4), for the vector of measured values $\boldsymbol{c}_m$ = [7.457, 0.120] corresponding to the example above, the posterior covariance matrix is:

$$S_{post2} = \begin{pmatrix} 0.0012 & 0.0001 \\ 0.0001 & 0.0002 \end{pmatrix},$$

and the vector of the posterior means is $\boldsymbol{c}_{post2}$ = [7.452, 0.088].

The calculated total global consumer's risk for the first scenario is $R_{total(c)} = 5.6 \times 10^{-7}$. This is an indication of a reliable quality assurance system.

To understand the influence of the correlation on $R_{total(c)}$, the risk was estimated for a simulated case of uncorrelated contents of the components. This simulation was carried out by setting all correlation coefficients $r_{ij} = 0$ ($i \neq j$), transforming $S_{c\omega}$ and $S_{cm\omega}$ into diagonal matrices. The resulting $R_{total(c)} = 6.2 \times 10^{-3}$ was four orders of magnitude greater than that for the correlated contents. In fact, the strong correlation between c_1 and c_2 and between c_3 and c_4 ties the variables together, dramatically decreasing the risk whenever all the measured quantities are within their acceptance intervals, while at least one of the actual components' content values is outside its specification interval. Thus, the total global consumer's risk for strongly correlated contents of the components is much smaller than for uncorrelated contents, a fact also observed in Example 3 above.

In the framework of the scenario ω = 2, when only c_2 and c_4 are taken into account, the risk is $R_{total(c)} = 5.1 \times 10^{-3}$ for correlated contents and $R_{total(c)} = 4.9 \times 10^{-3}$ for contents simulated as uncorrelated. It is seen that the risk is not practically affected by the observed (small) correlation between these two components' contents. The risk for two simulated uncorrelated contents (4.9×10^{-3}) is a little smaller than that for four uncorrelated ones (6.2×10^{-3}), as predicted in Example 1. Both these values, and also the risk for the scenario of two correlated contents (5.1×10^{-3}), are of the same order of magnitude. Therefore, reducing the number of components under control would lead to practically the same overestimation of the global risk as neglecting the strong correlation among the four components' contents.

Note that the total global consumer's risk $R_{total(c)} = 5.1 \times 10^{-3}$ for the case of control of Rh content and content of the eight impurities (scenario $\omega = 2$) means accepting one non-compliant alloy batch in 200 produced batches when it should have been rejected. Since 100 batches were produced during about two years at the plant, this false decision would be expected, on average, once every four years, assuming unchanged conditions. However, in practice each batch is tested according to the standards [79] and [84] for the contents of the four components (scenario $\omega = 1$). The greater amount of information available in this case decreases the risk of false decisions in spite of the complexity of the correlations among the test results. The risk value $R_{total} = 5.6 \times 10^{-7}$ means that there is no practical chance for a non-compliant alloy batch to find a way out of the plant to the market.

The counterpart models for the total producer's risks are easily obtainable.

A-4-7 Specific risks

For any vector of measured values [c_{1m}, c_{2m}, c_{3m}, c_{4m}] within the multivariate specification domain, the total specific consumer's risk $R^*_{total(c)}$ is calculated as one minus the integral of the posterior pdf on this domain. This represents the probability of at least one of the actual components' content lying outside its own specification interval. $R^*_{total(c)}$ values are dependent on the measured value of i-th component content c_{im}, as shown in Fig. 9 by line 1, where the c_{im} values are on their specification intervals, *i.e.* from T_{Li} to T_{Ui}.

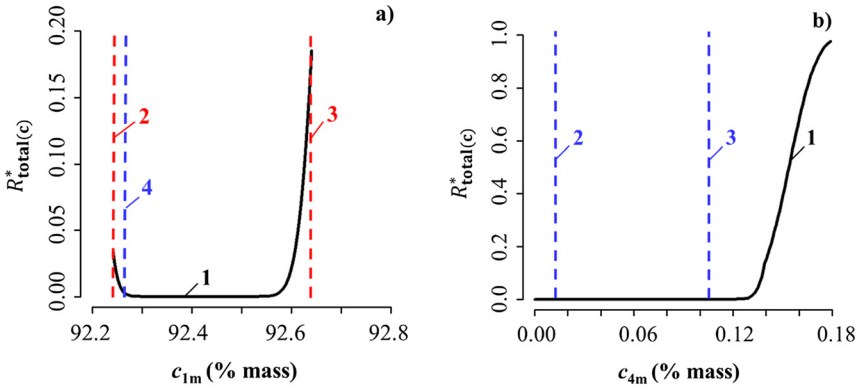

Fig. 9: Total specific consumer's risk $R^*_{total\,(c)}$ values in dependence on measured values of *i*-th component content c_{im}. The c_{im} values vary on their specification intervals from T_{Li} to T_{Ui}. The risk values are shown by line 1 versus: a) Pt content c_{1m} at the Rh content c_{2m} in the specification interval from 7.3 to 7.7 %, and the contents of the three and the eight impurities, c_{3m} = 0.052 % and c_{4m} = 0.059 %, respectively; lines 2 and 3 demonstrate the sub-domain of feasible alloy compositions; dotted line 4 is for the minimum observed c_{1m} value, whereas line 3 coincides with the maximum observed c_{1m} value; and b) content c_{4m} of the eight impurities at c_{1m} = 100 % − c_{2m} − c_{4m}, c_{2m} = 7.46 % and c_{3m} = c_{4m}/1.16 ≤ 0.12 %; lines 2 and 3 show the interval of observed c_{4m} values.

The risk values plotted against the measured values of Pt content c_{1m} are in Fig. 9a. The sub-domain spreads from c_{1m} = 100 % − T_{U2} − c_{4m} = 92.24 % (line 2) to c_{1m} = 100 % − T_{L2} − c_{4m} = 92.64 % (line 3). This is because the Rh upper and lower specification limits are T_{U2} = 7.7 % and T_{L2} = 7.3 %, respectively, and the assumed content of eight impurities in this case is equal to its prior mean, c_{4m} = 0.059 %. The assumed content of the three impurities is also equal to its prior mean: c_{3m} = 0.052 %. Line 4 indicates the minimum observed value c_{1m}, whereas line 3 coincides with the maximum observed value.

Figure 9b demonstrates the risk dependence on content c_{4m} of the eight impurities at c_{1m} = 100 % − c_{m2} − c_{4m}, the mean observed Rh content c_{2m} = 7.46 %, and the mean observed ratio c_{3m} = c_{4m}/1.16. Since the upper specification limit for c_{3m} is T_{U3} = 0.12 %, c_{3m} was required to be below 0.12 % at any c_{4m} value. Lines 2 and 3 are again the minimum and maximum observed c_{4m} values.

The values $R^*_{total\,(c)}$ vs. c_{im} in Fig. 9 are examples calculated at particular values of c_{jm}, $i \neq j$. More information can be provided using a three-dimensional representation, as in Fig. 10, where surfaces of $R^*_{total\,(c)}$ vs. c_{2m} and c_{4m} are shown.

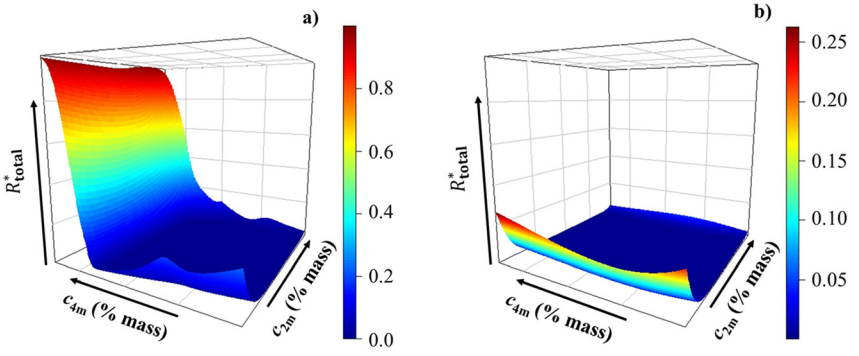

Fig. 10: Surface of $R^*_{total(c)}$ vs. measured values of Rh content c_{2m} and of the eight impurities c_{4m}. The plot in Fig. 10a is for the four-components scenario at c_{3m} = c_{4m}/1.16, but not exceeding 0.12 %, and 92.2 % ≤ c_{1m} = 100 % − c_{2m} − c_{4m} ≤ 92.8 %. The second plot, in Fig. 10b, shows the surface of the risks $R^*_{total(c)}$ for the two-components scenario, when c_{1m} and c_{3m} are not taken into account as strongly correlated with c_{2m} and c_{4m}, respectively. A color column bar gives indication of the risk values between the minimum and the maximum on the surface. The same scale of the risk axis from 0 to 1 is used in both Fig. 10 plots, but each color bar refers to its plot only.

The plot in Fig. 10a is for the four-components scenario at $c_{3m} = c_{4m}/1.16$, but not exceeding 0.12 %, and 92.2 % ≤ c_{1m} = 100 % − c_{2m} − c_{4m} ≤ 92.8 %. The color column bar gives indication of the risk between minimum 0 and maximum 1 on the surface. The risk increases slightly with c_{2m} near both the specification limits of the Rh content and, more significantly, at c_{4m} approaching its upper specification limit. This behavior corresponds to the two-dimensional dependences in Fig. 9, discussed above.

The plot in Fig. 10b shows the surface of the risks for the two-components scenario of the practically independent c_{2m} and c_{4m}. Note that the maximum risk value for this scenario is only 0.26, in contrast to nearly 1 when all four components are considered. One can see that the simplification of the conformity assessment task from a four- to a two-components scenario leads to the undervaluation of $R^*_{\text{total (c)}}$: its maximum value in Fig. 10b is four times smaller than in Fig. 10a. The form of the surfaces is also different. In particular, the surface in Fig. 10b is less sensitive to c_{4m} increasing in comparison to the four-components scenario in Fig. 10a. In other words, the simplification is not usable, since the observed strong correlation increases significantly and complicates the dependence of specific risks $R^*_{\text{total (c)}}$ on the measured values.

References

[1] JCGM 106. *Evaluation of Measurement Data – The Role of Measurement Uncertainty in Conformity Assessment* (2012), http://www.bipm.org/utils/common/documents/jcgm/JCGM_106_2012_E.pdf (accessed Apr 11, 2020).
[2] I. Lira. *Metrologia* **36**, 397 (1999).
[3] G. B. Rossi and F. Crenna. *Measurement* **39**, 101 (2006).
[4] A. B. Forbes. *Measurement* **39**, 808 (2006).
[5] JCGM 100. *Evaluation of Measurement Data – Guide to the Expression of Uncertainty in Measurement (GUM)*, 1st ed. (2008), https://www.bipm.org/utils/common/documents/jcgm/JCGM_100_2008_E.pdf (accessed Apr 11, 2020).
[6] S. L. R. Ellison and A. Williams (Eds.). *Eurachem/CITAC Guide: Quantifying Uncertainty in Analytical Measurement* (2012), https://www.eurachem.org/images/stories/Guides/pdf/QUAM2012_P1.pdf (accessed Apr 11, 2020).
[7] W. T. Estler and D. B. Hibbert. *OIML Bulletin* **LIV**, 14 (2013).
[8] ISO Guide 73. *Risk Management — Vocabulary* (2009).
[9] ISO 31000. *Risk Management — Principles and Guidelines* (2009).
[10] IEC/ISO 31010. *Risk Management — Risk Assessment Techniques* (2009).
[11] S. L. R. Ellison and A. Williams (eds). *EURACHEM/CITAC Guide: Use of Uncertainty Information in Compliance Assessment* (2007), https://www.eurachem.org/images/stories/Guides/pdf/Interpretation_with_expanded_uncertainty_2007_v1w.pdf (accessed Apr 11, 2020).
[12] M. Dobbert. *Measure* **5**, 68 (2010).
[13] J. L. Smith. *Quality Magazine* 1 (2017), https://www.qualitymag.com/articles/94158-the-role-of-specification-limits (accessed Apr 11, 2020).
[14] ILAC G8. *Guidance on Decision Rules and Conformity with Requirements* (draft 2019), https://ilac.org/publications-and-resources/ilac-guidance-series/ (accessed Apr 11, 2020).
[15] Eurolab Technical Report No. 01/2017. *Decision Rules Applied to Conformity Assessment* (2017), https://www.eurolab.org/pubs-techreports (accessed Apr 11, 2020).
[16] WADA Technical Document TD2019DL. *Decision Limits for Confirmatory Quantification of Threshold Substances* (2019), https://www.wada-ama.org/sites/default/files/td2019dl_final_eng_clean.pdf (accessed Apr 11, 2020).
[17] B. Magnusson and U. Örnemark (eds). *EURACHEM Guide: The Fitness for Purpose of Analytical Methods – A Laboratory Guide to Method Validation and Related Topics* (2014), www.eurachem.org/images/stories/Guides/pdf/MV_guide_2nd_ed_EN.pdf (accessed Apr 11, 2020).
[18] G. V. Hoyos and G. G. Horta. in *16th International Congress of Metrology* (2013), https://doi.org/10.1051/metrology/201305003, http://cfmetrologie.edpsciences.org/articles/metrology/pdf/2013/01/metrology_metr2013_05003.pdf (accessed Apr 11, 2020).
[19] I. Kuselman, F. Pennecchi, C. Burns, A. Fajgelj, P. de Zorzi. *Pure Appl. Chem.* **84**, 1939 (2012).
[20] L. Zamengo, G. Frison, G. Tedeschi, S. Frasson, F. Zancanaro, R. Sciarrone, *Drug Test. Anal.* **6**/**10**, 1028 (2014).
[21] Thermo Scientific. *Measurement Uncertainty and Material Conformance Probability*. Standard OXSAS software feature for Thermo SCIENTIFIC OES and XRF spectrometers (2012), https://tools.thermofisher.com/content/sfs/brochures/XO-PS41282-OXSAS-Measurement-Uncertainty-1112.pdf (accessed Apr 11, 2020).
[22] P. Pereira, B. Magnusson, E. Theodorsson, J. O. Westgard, P. Encarnação. *Accred. Qual. Assur.* **21**, 25 (2016).
[23] OIML Document G19. *The Role of Measurement Uncertainty in Conformity Assessment Decisions in Legal Metrology* (2017), https://www.oiml.org/en/files/pdf_g/g019-e17.pdf (accessed Apr 11, 2020).

[24] C. Carobbi and F. Pennecchi. *Metrologia* **53**, S74 (2016).
[25] L. Pendrill. *Metrologia* **51**, S206 (2014).
[26] L. Pendrill and N. Petersson. *Meas. Sci. Technol.* **27**/**9** (2016), https://doi.org/10.1088/0957-0233/27/9/094003.
[27] L. Pendrill, H. Karlson, N. Fischer, S. Demeyer, A. Allard. *EURAMET: A Guide to Decision-making and Conformity Assessment – A Report of the EMRP Joint Project NEW04 "Novel mathematical and statistical approaches to uncertainty evaluation"* (2015), http://publikationer.extweb.sp.se/ViewDocument.aspx?RapportId=29488 (accessed Apr 11, 2020).
[28] JCGM 200. *International Vocabulary of Metrology – Basic and General Concepts and Associated Terms* (VIM), 3rd ed. (2012), https://www.bipm.org/utils/common/documents/jcgm/JCGM_200_2012.pdf (accessed Apr 11, 2020).
[29] ISO/IEC 17000. *Conformity Assessment – Vocabulary and General Principles* (2004).
[30] ISO 9000. *Quality Management Systems – Fundamentals and Vocabulary* (2015).
[31] ISO/IEC 3534. *Statistics – Vocabulary and Symbols – Part 1: General Statistical Terms and Terms Used in Probability* (2006).
[32] IUPAC. *Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book"). Compiled by McNaught A.D. and Wilkinson A. Blackwell Scientific Publications, Oxford (1997).
[33] T. Cvitaš. *Metrologia* **33**, 35 (1996).
[34] T. J. Tolhurst, A. J. Underwood, R. G. Perkins, M. G. Chapman. *Estuar. Coast Shelf Sci.* **63**, 665 (2005).
[35] X. Fuentes-Arderiu. *Biochem. Med.* **23**, 141 (2013).
[36] ISO 10241-1. *Terminological Entries in Standards — Part 1: General Requirements and Examples of presentation* (2011).
[37] D. Rumsey. *Probability for Dummies*. Wiley, ISBN 978-0-471-75141-0, p. 58 (2006).
[38] K. Baclawski. *Introduction to Probability with R*. CRC Press, ISBN 978-1-4200-6521-3, p. 179 (2008).
[39] H. Pishro-Nik. *Introduction to Probability. Statistics and Random Processes*. Kappa Research LLC, ISBN 978-0-9906372-0-2, p. 51 (2014).
[40] I. Kuselman, F. R. Pennecchi, R. J. N. B. da Silva, D. B. Hibbert. *Talanta* **164**, 189 (2017).
[41] F. R. Pennecchi, I. Kuselman, R. J. N. B. da Silva, D. B. Hibbert. *Chemosphere* **202**, 165 (2018).
[42] I. Kuselman, F. R. Pennecchi, R. J. N. B. da Silva, D. B. Hibbert. *Talanta* **174**, 789 (2017).
[43] I. Kuselman, F. R. Pennecchi, R. J. N. B. da Silva, D. B. Hibbert, E. Anchutina. *Talanta* **189**, 666 (2018).
[44] I. Kuselman, F. R. Pennecchi, R. J. N. B. da Silva, D. B. Hibbert. *J. Phys.* **1420**, 012001 (2019).
[45] A. Subaric-Leitis. *TM Tech. Mess.* **77**, 662 (2010).
[46] V. Branco, J. Canario, C. Vale, J. Raimundo, C. Reis. *Mar. Pollut. Bull.* **49**, 871 (2004).
[47] J. Dubrovkin. *Mathematical Processing of Spectral Data in Analytical Chemistry: A Guide to Error Analysis*. Cambridge Scholars Publishing, ISBN: 978-1-5275-1152-1 (2018).
[48] ICH Harmonized Tripartite Guideline Q2(R1). *Validation of Analytical Procedures. Text and Methodology* (2005), http://www.gmp-compliance.org/guidemgr/files/Q2(R1).PDF (accessed Apr 11, 2020).
[49] A. Kruve, R. Rebane, K. Kipper, M. L. Oldekop, H. Evard, K. Herodes, P. Ravio, I. Leito. *Anal. Chim. Acta* **870**, 8–28 and 29–44 (2015).
[50] A. Gelman, J. B. Carlin, S. H. Stern, D. B. Dunson, A. Vehtari, D. B. Rubin. *Bayesian Data Analysis*, Charman & Hall/CRC, Boca Raton, 3rd ed. (2014).
[51] A. Buccianti. *Comput. Geosci.* **50**, 165 (2013).
[52] A. Buccianti, E. Grunsky. *J. Geochem. Explor.* **141**, 1 (2014).
[53] J. Bacon-Shone. in *Compositional Data Analysis. Theory and Applications* V. Pawlowsky-Glahn, A. Buccianti (Eds), pp. 3–11, Wiley, West Sussex, UK, 1st ed. (2011).
[54] R. J. N. B. da Silva, F. R. Pennecchi, D. B. Hibbert, I. Kuselman. *Chemometr. Intell. Lab. Syst.* **182**, 109 (2018).
[55] R. J. N. B. da Silva, F. R. Lourenço, F. R. Pennecchi, D. B. Hibbert, I. Kuselman. *Chemometr. Intell. Lab. Syst.* **188**, 1 (2019).
[56] C. Zaiontz, *Real Statistics using Excel. Cholesky Decomposition*; http://www.real-statistics.com/linear-algebra-matrix-topics/cholesky-decomposition/ (accessed Apr 11, 2020).
[57] *The R Project for Statistical Computing*; http://www.r-project.org (accessed Apr 11, 2020).
[58] World Customs Organization. *Risk Management Compendium* (2011), http://www.wcoomd.org/en/topics/enforcement-and-compliance/instruments-and-tools/compendiums/rmc.aspx (accessed Apr 11, 2020).
[59] European Commission, Customs Policy Committee, *A Guide to Risk Analysis and Customs Control* (1999), http://biblio.central.ucv.ro/bib_web/bib_pdf/EU_books/0070.pdf (accessed Apr 11, 2020).
[60] European Commission, Directorate General, Taxation and Customs Union, *Compliance Risk Management Guide for Tax Administrations* (2010), http://ec.europa.eu/taxation_customs/sites/taxation/files/resources/documents/common/publications/info_docs/taxation/risk_managt_guide_en.pdf (accessed Apr 11 2020).
[61] *Commission Implementing Regulation (EU) 162/2013 Amending the Annex to Regulation (EC) No. 3199/93 on the Mutual Recognition of Procedures for the Complete Denaturing of Alcohol for the Purposes of Exemption from Excise Duty*; http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:049:0055:0061:EN:PDF (accessed Apr 11, 2020).
[62] *Israel Regulations of Denatured Alcohols* (1932), http://www.nadel-law.co.il/Index.asp?ArticleID=642&CategoryID=231 (accessed Apr 11, 2020).
[63] Australian Government, Australian Taxation Office, *The Alcohol Industry – Excise Technical Guidelines* (2006), www.ato.gov.au/law/view/document?docid=SAV/ALCIND/00009&PiT=99991231235958 (accessed Apr 11, 2020).

[64] E. Aries, F. Cordeiro, A. Maquet, A. Boix, B. Slowikowski, C. Von Holst. Euro-denaturant project – Phase II, Administrative Arrangement TAXUD-2014-DE-317, Geel, Belgium, European Commission, Joint Research Centre – Institute for Reference Materials and Measurements, JRC101833 (2016), 70 p.
[65] M. H. Ramsey, S. L. R. Ellison and P. Postron (eds.), Eurachem/EUROLAB/CITAC/Nordtest/AMC Guide: *Measurement Uncertainty Arising from Sampling. A Guide to Methods and Approaches*, 2nd ed. (2019), https://www.eurachem.org/images/stories/Guides/pdf/UfS_2019_EN_P1.pdf (accessed Apr 11 2020).
[66] I. Kuselman, S. Shpitzer, F. Pennecchi, C. Burns. *Air Qual. Atmos. Health.* **5**, 269 (2012).
[67] EPA IO-2.1. *Sampling of Ambient Air for Total Suspended Particulate Matter (SPM) and PM10 using High Volume (HV) Sampler* (1999), http://www.epa.gov/ttnamti1/inorg.html (accessed Apr 11, 2020).
[68] OMCL – Official Medicines Control Laboratories; https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/international/partnerships/official-medicines-control-laboratories.html (accessed Apr 11, 2020).
[69] General European OMCL Network (GEON); https://www.edqm.eu/en/general-european-omcl-network-geon (accessed Apr 11, 2020).
[70] Drugs.com Overview: What is NyQuil Severe Cold & Flu (acetaminophen, dextromethorphan, doxylamine, and phenylephrine)? https://www.drugs.com/mtm/nyquil-severe-cold-flu.html (accessed Apr 11, 2020).
[71] L. Homewood, *UF Researchers Question Effectiveness of Decongestant*. University of Florida, news.ufl.edu, 07 (2006); http://news.ufl.edu/archive/2006/07/uf-researchers-question-effectiveness-of-decongestant.html (accessed Apr 11, 2020).
[72] The United States Pharmacopeial Convention. *United States Pharmacopeia (USP). Reference Standards Catalog*; http://www.usp.org/reference-standards/reference-standards-catalog (accessed Apr 11, 2020).
[73] Sigma-Aldrich/Merck Catalog. *Acetaminophen USP Reference Standard*; http://www.sigmaaldrich.com/catalog/product/usp/1003009?lang=en&region=IL (accessed Apr 11, 2020).
[74] The United States Pharmacopeial Convention. *United States Pharmacopeia (USP)* 39 (2016).
[75] D. B. Owen. *Handbook of Statistical Tables*. Addison-Wesley Publishing Company Inc, Massachusetts (1962).
[76] R. E. Odeh. *Commun. Stat. Simulat. Comput.* **11**, 1 (1982).
[77] B. Narasimhan, S. G. Johnson. *Package 'cubature'. Adaptive Multivariate Integration Over Hypercubes* (2016); https://cran.r-project.org/web/packages/cubature/cubature.pdf (accessed Apr 11, 2020).
[78] A. Genz, F. Bretz, T. Miwa, X. Mi, T. Hothorn. *Package 'mvtnorm'. Multivariate Normal and t Distributions* (2016); https://cran.r-project.org/web/packages/mvtnorm/mvtnorm.pdf (accessed Apr 11, 2020).
[79] GOST 13498. *Platinum and its Base Alloys. Marks*. Standardinform, Moscow (2010).
[80] *American Elements. Platinum Rhodium Alloy*; https://www.americanelements.com/platinum-rhodium-alloy-11107-71-4 (accessed Apr 11, 2020).
[81] *PANanalytial. Model Axious XRF-Spectrometers*; https://www.environmental-expert.com/products/model-axios-xrf-spectrometers-19076 (accessed Apr 11, 2020).
[82] Z. Zhou, K. Zhou, X. Hou and H. Luo. *Appl. Spectrosc. Rev.*, **40/2**, 165 (2005).
[83] *Ekaterinburg Non-Ferrous Metal Processing Plant*. Certified reference materials; https://en.ezocm.ru/services/analytical-services/reference-materials-production/ (accessed Apr 11 2020).
[84] GOST R 52599. *Precious Metals and Their Alloys. General Requirements for Methods of Analysis*. Standardinform, Moscow (2006).
[85] J. Aitchison. *The Statistical Analysis of Compositional Data*. Chapman & Hall, London (1986).
[86] J. Aitchison. in *Multivariate Analysis and its Applications*. IMS Lecture Notes – Monograph Series, T. W. Anderson, K. T. Fang, I. Olkin (Eds.), Vol. **24**, pp. 73–81, Institute of Mathematical Statistics, Hayward, CA (1994).
[87] GOST 13098. *Rhodium. Marks*. Standardinform, Moscow (2006).
[88] H. R. Rollinson. *Using Geochemical Data: Evaluation, Presentation, Interpretation*. Taylor & Francis, New York (1993).
[89] T. Vigen. *Spurious Correlations*. Hachette Books, New York – Boston (2015).
[90] P. Kynčlová, K. Hron, P. Filmoser. *Math. Geosci.* **49/6**, 777 (2017).
[91] I. T. Jolliffe. *Principal Component Analysis*, 2nd ed. Springer Series in Statistics. Springer, New York (2002).