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Forum For Exchange Of
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Forum

Methodology for recommending analytical methods to check compliance with REACH Annex XVII restrictions

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Executive Summary

This document presents a methodology to recommend analytical methods for checking the compliance with REACH Annex XVII restrictions.

The basic steps of the methodology are:

1. To define what are the functional qualities (characteristics) of an analytical method that can be attributed to the method in order to know how it works. General principles applied in widely accepted international standards as well as in other legislation fields have been considered and a set of key characteristics have been identified for the purpose of assessing the suitability of an analytical method to check compliance with restrictions on chemicals under REACH Annex XVII. The characteristics identified are: applicability, limit of detection, recovery, reproducibility and measurement uncertainty.

2. For each of the selected characteristics, to agree upon generally acceptable performance requirements for analytical methods to be recommended. Widely accepted criteria have been applied to define the requirements for the considered characteristics of an analytical method to be suitable for checking compliance with REACH Annex XVII restrictions. Due to the broad ranges of products covered by REACH Annex XVII, and to the different limit values (including a total ban for certain substances) set forth in different entries, it is deemed necessary to foresee a case by case approach where appropriate.

The methodology is then implemented by the Forum WG Group on Enforceability of Restrictions to elaborate the Compendium of analytical methods recommended by the Forum to check compliance with REACH Annex XVII restrictions. A data gathering on the available analytical methods within MS public and private laboratories and within the ECHA Accredited stakeholders linked laboratories is conducted based on the present methodology.. A data analysis follows, where the performance of gathered methods is assessed according to the proposed requirements. Such requirements may be applied on a case-by-case basis in the light of the technical issues encountered and taking into consideration the available sample preparation and analysis protocols and techniques.

Once adopted by the Forum, the Compendium of recommended analytical methods to check compliance with REACH Annex XVII restrictions is published on the ECHA website and is revised at regular intervals to reflect changing technical standards, new available methods as well as modification of existing ones.

The Compendium of analytical methods recommended by the ECHA Forum for checking compliance with Annex XVII restrictions will include:

- Official methods (with references published in REACH legal text);
- Standard methods;
- Methods published by a recognized technical organisation, a national or EU reference laboratory (EPA, etc.);
- Internal methods, which have been considered fit for purpose according to the set of performance criteria.

Glossary

Accuracy: the closeness of agreement between a test result and the accepted reference value. It is determined by determining trueness and precision.

Analyte: the substance that has to be detected, identified and/or quantified and derivatives emerging during its analysis.

Applicability: the set of information about the identity of analyte(s), the concentration range and the kind of matrix/material/item of a specific analytical method for its intended application.

Bias: difference between the expectation of the test results and an accepted reference value.

Certified reference materials (CRM): a material that has had a specified analyte content assigned to it.

Collaborative study: analysis of the same sample by the same method in different laboratories to determine the performance characteristics of the method. The study covers random measurement error and laboratory bias.

Concentration range (working or measuring): the range in which the method gives an acceptable trueness and precision. The lowest limit of the working or measuring concentration range is the lowest limit of the calibration range. However the upper limit of the working range could be not only the highest point in the calibration curve, but a higher concentration at which acceptable accuracy(trueness and precision)can be proven.

Intermediate precision (or within-laboratory reproducibility): precision obtained in the same laboratory under stipulated (predetermined) conditions (concerning e.g. method, test materials, operators, environment) over justified long time intervals.

Interlaboratory study (comparison): organisation, performance and evaluation of tests on the same sample by two or more laboratories in accordance with predetermined conditions to determine testing performance. According to the purpose the study can be classified as collaborative study or proficiency study.

Limit of detection (LOD): the lowest concentration or mass of an analyte, which can be detected with acceptable certainty, even though it cannot be quantified with acceptable precision.

Limit of quantification (LOQ): the lowest concentration or mass of an analyte, which can be determined with an acceptable level of uncertainty.

Limit of restriction (LOR): the concentration or mass of an analyte, which exceedance leads to the sample being not in compliance with the legal requirements.

Measurement uncertainty: a non-negative parameter characterising the dispersion of the quantity values being attributed to a measure and based on the information used[1].

Qualitative methods: analytical methods which allow to identify the presence of a substance on the basis of its chemical, biological or physical properties. These methods do not enable a conclusive judgment for enforcement purpose and entail a confirmatory analysis.

Quantitative methods: analytical methods which determine the amount or mass fraction of a substance so that it may be expressed as a numerical value of appropriate units[2].

Performance characteristic: functional quality that can be attributed to an analytical

[1] JCGM 200:2012 "International vocabulary of metrology – Basic and general concepts and associated terms (VIM)" 3rd edition, point 2.26

[2] Commission Decision 2002/657/EC, of 12 August 2002 implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results.

method. This may be for instance accuracy, trueness, precision, repeatability, reproducibility, recovery, LOD and LOQ.

Performance requirements: requirements for a performance characteristic according to which it can be judged that the analytical method is fit for the purpose and generates reliable results.

Precision: the closeness of agreement between independent test results obtained under stipulated (predetermined) conditions. The measure of precision is expressed in terms of imprecision and computed as standard deviation of the test result. Less precision is determined by a larger standard deviation.

Proficiency study: analysis of the same sample allowing laboratories to choose their own methods, provided that these methods are used under routine conditions. The study can be used to assess the reproducibility of a method, when the same method is used by participants.

Proficiency testing: evaluation of participant performance against pre-established criteria by means of inter-laboratory comparisons.

Recovery: the fraction of the analyte that is recovered after addition of a known amount of the analyte, under defined conditions to the sample, when the test sample is analyzed using the entire method.

Relative standard deviation (RSD): Repeatability (or reproducibility) relative standard deviation RSDr[R] (coefficient of variation) is the repeatability (or reproducibility) standard deviation divided by the mean. The RSD is also known as coefficient variation.

Repeatability: precision under repeatability conditions, namely the closeness of agreement between mutually independent test results obtained under repeatability conditions.

Repeatability conditions: conditions where independent test results are obtained with the same method on identical test items in the same laboratory by the same operator using the same equipment.

Reproducibility: precision under reproducibility conditions, namely the distribution of measurement results obtained under reproducibility conditions.

Reproducibility conditions: conditions where test results are obtained with the same method on identical test items in different laboratories with different operators using different equipment.

Repeatability limit (r): the value less than or equal to which the absolute difference between two results, obtained under repeatability conditions, may be expected to be with a probability of 95%.

Reproducibility limit (R):the value less than or equal to which the absolute difference between two results, obtained under reproducibility conditions, may be expected to be with a probability of 95%.

Screening methods: analytical methods that are used to detect the presence of a substance or class of substances at the level of interest. These methods have the capability for a high sample throughput and are used to sift large numbers of samples for potential non-compliant results.

Trueness: the closeness of agreement between the average value obtained from a large series of test results and an accepted value. Trueness is usually expressed as bias.

Validation: the confirmation by examination and the provision of effective evidence that the particular requirements of a specific intended use are fulfilled.

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Preface

According to Article 77 (4) of REACH Regulation, the Forum shall undertake *inter alia* tasks regarding the spreading of good practice. A draft inventory of testing methods used at MS level was established by the Forum in 2010. That inventory indicated that the number and the variety of analytical methods used in different Member States were huge and the harmonised enforcement of Annex XVII restrictions could be jeopardized.

At its 7th meeting in June 2010, the Forum adopted advice with regards to the analytical methods inventory. Key conclusion was the following:

Not to include a harmonised analytical method in all entries of Annex XVII, but only to produce guidance for suitable analytical methods. The currently available methods contained in the cited inventory can be the basis for this guidance, but first the methods to be recommended have to be identified. As preliminary criteria for recommending methods, the Forum agreed the recommended methods should preferable be standardised ones. If such methods are not available, other methods can be used. The improved inventory can be published as a guide document.

With the above premise, the WG on enforceability of restrictions was tasked to develop a methodology for recommending analytical methods.

The main goal is to recommend analytical methods to check compliance with Annex XVII restrictions aiming at improving the reliability of controls.

This document presents the developed methodology for recommending analytical methods to be used in the verification of compliance with the restrictions set forth in Annex XVII of REACH Regulation.

Such methodology is applied to assess the suitability of both existing and new analytical methods for the enforcement of REACH Annex XVII. The final purpose is to compile a Compendium of recommended analytical methods and make it public. Such Compendium can be used for both control and self-control purpose concerning REACH Annex XVII restrictions.

1. Methodology for recommending analytical methods

For the purpose of this document a "characteristic" of an analytical method means a functional quality that can be attributed to that method in order to know how it works.

Accordingly, a "performance requirement" means a requirement for a characteristic according to which it can be judged that the analytical method is fit for the purpose and generates reliable results.

In order to develop the present methodology, generally accepted characteristics of analytical methods have been considered and among those, a set of functional qualities have been selected as essential to describe the performance of an analytical method and in particular to assess the adequateness of an analytical method. Performance requirements for each characteristic have been then proposed to assess the suitability of the methods to be recommended for checking the compliance with REACH Annex XVII restrictions. Finally, a testing exercise has been carried out to verify the initial assumptions and eventually refine the methodology before submitting it to the Forum for adoption.

1.1 Characteristics of analytical methods

The WG on enforceability of restrictions recognises the following five characteristics to be considered when assessing whether a method can be recommended for the purpose of checking the compliance with REACH Annex XVII provisions.

1. **Applicability**
2. **Limit of detection (LOD)**
3. **Recovery**
4. **Reproducibility**
5. **Measurement uncertainty**

Due to the broad range of products under the scope of REACH Annex XVII entries, and to different limit values set for a specific substance in a certain matrix, ranging from a total ban (no limit value-NLV) to a relatively high concentration limit, different methods are appropriate for control purpose and all the above characteristics might not necessarily need to be assessed. (For example for qualitative screening methods not all of the selected characteristics are expected to be pertinent, thus a case by case assessment is needed).

1.2 Performance requirements for analytical methods

For each of the agreed characteristics, a proposal of acceptable performance requirements for an analytical method to be recommended is given in the next sub-paragraphs.
The requirement values and ranges are based on criteria accepted in other legislation fields and on common knowledge in the analytical chemist community, taking into account different substance identities and different matrices.

1.2.1 Applicability

The applicability of an analytical method covers the information about the identity of analyte/s, the concentration range and the kind of matrix/material/item, as specified in the scope of an analytical method for its intended application. These criteria have to be assessed in order to verify the suitability of a certain analytical method to check compliance with a restriction set out in Annex XVII. A table listing the current entries of REACH Annex XVII with reference to the substance/s under the scope of the restriction and relative concentration limit and clear indication of the concerned matrix is reported in Annex 1.

1.2.2 Limit of detection

There are various methods to determine the limit of detection (LOD), depending on the particular characteristics of the analytical method (type of analyte, sample preparation, analytical technique, etc.).

The limit of quantification (LOQ) is always higher than the LOD and is often taken as a fixed multiple of the LOD. Accordingly, the LOQ of a method is calculated from the LOD, via the following simple equation[3]:

$$LOQ = 3^* LOD \quad (1)$$

The LOQ should always be verified by measuring a number of samples containing the analyte at a concentration equal or close to its value.

When selecting an analytical method it is desirable the relation between Limit of restriction (LOR), LOD and LOQ to be:

$$LOD \leq 0.1^* LOR \text{ or } LOQ \leq 0.3^* LOR \quad (2)$$

This in order to determine analyte concentrations near the LOR with the lowest possible uncertainty. The above relations are commonly agreed among the analytical chemists and are applied in some ISO standard methods (e.g. EN 71: Safety of toys)[4] and in some EC directives (e.g. 98/83/EC)[5]. Depending on the concentration of the LOR it might be also possible to encounter a different ratio between LOD/LOR and LOQ/LOR and consider this as still acceptable.

The justification of the relation (2) is reported in Annex 2, paragraph 1.

1.2.3 Recovery

Recovery means the fraction of the analyte that is recovered after addition of a known amount of the analyte, under defined conditions to the sample, when the test sample is analysed using the entire method. It is determined, instead of trueness, if no certified reference material or other sources of reference values (reference method, collaborative study, proficiency test results) are available.

In fact the trueness of a method is an expression of how close the mean of a set of results (produced by the method) is to an accepted reference value. Trueness is usually expressed in terms of bias, the difference between the accepted reference value (derived from a certified reference material) and the mean of the results. When certified reference materials, or other sources of reference values, are not available, trueness can be expressed in terms of recovery.

Due to the huge range of matrix-matched analytes encountered in the Annex XVII restrictions and, as a consequence, to the lack of certified reference materials, the recovery has been selected as one of the relevant characteristic for an analytical method to be recommended.

Expected recovery as a function of analyte concentration is reported in the following table 1[6].

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[3] Depending on the analytical method, some laboratories use the following equation: LOQ = ^{2}*LOD

[4] EN 71.03: Safety of toys – Part 3: Migration of certain elements (point 9).

[5] Directive 98/83/EC: On the quality of water intended for human consumption (Annex III).

[6] Table excerpted from "Guidelines for performance criteria and validation procedures of analytical methods used in controls of food contact materials" EUR 24105 EN - 1st edition 2009 European Commission-Joint Research Centre- Institute for Health and Consumer Protection.

Table 1

Concentration	Mean recovery (%)
≤ 0.01 ppm (≤10 ppb)	40-120
0.1-0.01 ppm (100-10 ppb)	60-110
≥ 0.1 ppm (≥ 100 ppb)	80-110

1.2.4 Reproducibility

The conditions under which precision can be evaluated are repeatability, intermediate precision and reproducibility condition of measurement.

In fact repeatability means precision under repeatability condition of measurement, namely the closeness of agreement between mutually independent test results obtained under repeatability conditions. Repeatability condition of measurement refers to measurements being made on the same material by a single analyst, using the same method and the same equipment, in the same laboratory over a short time period (often called short-term repeatability).

Intermediate precision condition of measurement refers to measurements being made on the same sample using the same method in the same laboratory, but over an extended time period and possibly by different analysts who may be using different equipment. Intermediate precision (also called within-laboratory reproducibility) is often used to provide an estimate of the between-batch variability of the results. It also provides a more realistic estimate of the long-term variability of measurement results in the laboratory.

Differently from the repeatability and intermediate precision, estimates of reproducibility are obtained only from measurement results produced by different laboratories. In fact reproducibility means precision under reproducibility conditions, namely the distribution of measurement results obtained under reproducibility conditions. Reproducibility condition of measurement refers to measurements being made on the same material by different analysts working in different locations. Reproducibility may be measured by means of collaborative studies (identical test materials, identical methods, different analysts, different equipment and different laboratories). Mathematically, reproducibility is the variability of the average values obtained by several analysts while measuring the same item and it represents the overall measure of variability, including the within laboratory component (repeatability and intermediate precision).

Precision (in terms of repeatability, intermediate precision and reproducibility) is expressed as standard deviation (SD) or relative standard deviation (RSD) or percentage coefficient of variation (%CV or %RSD).

From the reproducibility (and also repeatability) standard deviations it is useful to calculate the reproducibility limit R (or the repeatability limit r). It is the value below which the absolute difference between two single test results obtained under reproducibility (repeatability) conditions, may be expected to lie within a specific probability (typically 95 %). For a large number of degrees of freedom the Student-t value is commonly approximated to the value of 2, this leads to the following formula for the reproducibility (repeatability) limit:

$$R = 2.8 * S_R \quad (r = 2.8 * S_r) \qquad (3)$$

1.2.4.1 Assessment of reproducibility according to Horwitz

Horwitz established an empirical equation after examination of the results of several hundred food based collaborative studies conducted by the Association of Analytical Chemist (AOAC). The Horwitz curve is an empirically derived exponential equation that relates the percentage relative standard deviation among laboratories (RSD_R%) to concentration (C), expressed in mass/mass or volume units. The relation is more or less independent from the analyte, the matrix, the analytical method or sample preparation which are used. The Horwitz equation is:

$$RSD_R(\%) \text{ predicted} = 2^{(1-0.5\log C)} = 2*C^{(-0.5\log 2)} = 2*C^{-0.15} \qquad (4)$$

Or as a standard deviation:

$$S_{RH} = 2 * C^{0.8495} \qquad (5)$$

where C is the mass fraction expressed as a power (exponent) of 10 (e.g. 1 mg/g = 10^{-3}).

The subsequent table gives some examples of the standard deviation dependent on the analyte concentration:

Table 2

Analyte %	Analyte ratio	Unit	RSD_R (%)predicted
0.01	10^{-4}	100 ppm	8.0
0.001	10^{-5}	10 ppm	11.3
0.0001	10^{-6}	1 ppm	16.0
0.00001	10^{-7}	100 ppb	22.6

Thompson made an adjustment of the initial model, and as a result, there are three different equations, depending on the concentration range. Expressed as a standard deviation:

If $C < 1.2 * 10^{-7}$ → S_{RH} (%) predicted = $0.22 * C$ (6)
If $1.2 * 10^{-7} \leq C \leq 0.138$ → S_{RH} (%) predicted = $2 * C^{0.8495}$ (7)
If $C > 0.138$ → S_{RH} (%) predicted = $0.01 * C^{0.5}$ (8)

1.2.4.2 Common analytical practice in assessment of reproducibility

The values taken for the Horwitz equation are indicative of the precision that is achievable and acceptable of analytical methods by different laboratories. Although the Horwitz equation has been derived from food based studies its applicability to non-food based methods has been proposed and supported by the elevated number of variable factors (methods, matrices, analytes, laboratories) considered for its estimation.

Nevertheless the Horwitz equation enables only a rough estimation of mean values, due to its applicability to the various analytical methods. In practice reproducibility of a certain method is measured by means of collaborative studies (identical test materials, identical methods, different persons, different instruments and different laboratories).

The application of the Horwitz equation is limited to analytical methods that express measures as concentration of mass. It does not apply to empirical analytes, indefinite analytes or physical properties.

1.2.5 Measurement uncertainty

A measurement result is generally expressed as a single measured quantity value and a measurement uncertainty and it is usually reported in the form "x ± U", where x is the single measured quantity value and U is the associated uncertainty. This can be interpreted as a "set of quantity values", meaning that any value within the interval defined by the measurement uncertainty, is a possible value for the measured quantity.

The reporting of uncertainty is intended to provide a higher level of confidence in the validity of the reported result. This information provides the end-user with sufficient information on the reliability of the measurement result, to be taken into account when - for example - it is to be compared with a stated limit value in an Annex XVII restriction.

To obtain the uncertainty on the measured quantity value, the 3 options reported in Annex 2, paragraph 2, can be used.

1.2.5.1 Maximum measurement uncertainty

The Horwitz formula is a helpful tool to compare the estimated uncertainty against the expected value derived from published inter-laboratory studies and it can be used as a maximum acceptable uncertainty when no criteria for uncertainty have been established (Table 3).

The values reported below (Table 3) are derived from several hundred collaborative trials for food chemical analysis and represent the extent of the uncertainty that could be expected at different concentrations (expressed as mass fraction), derived from taking the Horwitz formula**.**

Table 3

Concentration (expressed as mass fraction)	**Uncertainty**	**Range of acceptable concentrations***
100g/100g	4%	96 to 104g/100g
10g/100g	5%	9.5 to 10.5g/100g
1g/100g	8%	0.92 to 1.08g/100g
1g/kg	11%	0.89 to 1.11g/kg
100mg/kg	16%	84 to 116mg/kg
10mg/kg	22%	7.8 to 12.2mg/kg
1mg/kg	32%	0.68 to 1.32mg/kg
< 100µg/kg	44%	56 to 144µg/kg

* this effectively means that values falling within these ranges may be regarded as being of the same analytical population.

Some of the current European legislation have specified alternative fitness for purpose approach, to evaluate the acceptability of methods of analysis, specifying the maximum level of measurement uncertainty regarded as fit for purpose.

2. Implementation of the methodology

In 2009 the MSs were invited to communicate the analytical methods as accepted by them for checking compliance with Annex XVII restrictions. A compilation of those replies is available at ECHA.

This inventory of analytical methods used by the National Enforcement Authorities in the Member States (version May 2010) presents several shortcomings. The inventory does not include all necessary information allowing to assess whether the method can be recommended or not and it is possible that it does not represent the complete list of available analytical methods to check compliance with Annex XVII restrictions in all circumstances covered.

The Forum agreed on the need for gathering the above additional information on the available analytical methods, taking into consideration the selected characteristics proposed in the present methodology, and then implementing the present methodology by applying the proposed criteria for performance to the gathered information, for each of the specific cases a restriction entry can cover.

2.1 Data gathering

2.1.1 Questionnaire

As first step of the implementation of the methodology a data gathering of the required data from the laboratories with capacity to carry out chemical analysis to check compliance with Annex XVII restrictions is set. For this purpose, a questionnaire including the necessary instructions has been developed by the WG on enforceability of restrictions (Annex 3), and after adoption by the Forum it is made available to the laboratories. In order to achieve the highest quality possible gathered data, conventions for the format to be used when reporting non-standard methods are established. It is deemed necessary to gather also contact details of the laboratory/ies applying the reported methods to retrieve additional information from the laboratories, if needed. The above details are regarded as confidential and stored only for internal use by the Member States.

2.1.2 Method

With the view to have the best possible quality Compendium of analytical methods, the project foresees that public and industry laboratories are invited to fill in the questionnaire.

The questionnaire is submitted to the Forum members and to the accredited stakeholders observers in the Forum (ECHA Forum ASOs). The Forum members and ECHA Forum ASOs liased with the relevant laboratories in the MS and within their networks inviting them to submit the information requested.

Forum members and accredited stakeholder organisations were requested to submit the filled in questionnaires to ECHA Forum Secretariat after 3 months.

The above data gathering scheme can be used for the future amendment of the Compendium of analytical methods.

2.2 Data analysis

The gathered information are assessed by the WG on enforceability of restrictions in relation to the defined performance requirements. Such requirements are applied on a case-by-case basis, in light of the technical issues encountered and taking into consideration the available sample preparation and analysis protocols and techniques.

The Forum decided to consider, as a short term solution for the methods relevant for restrictions without a limit value, only the applicability and the limit of detection. Only the methods considered applicable to the specific restriction and which show low LODs are recommended as the best available applicable method/s in terms of capability to detect low concentration of a certain analyte with acceptable certainty.

Those criteria (applicability and LOD) can be subject to expert judgment on a case by case basis.

Similarly, a deviation from the present methodology is applied for qualitative and screening methods. While recognizing that for enforcement purpose a qualitative or screening method cannot be conclusive and a confirmatory analysis is needed, these methods could be used as fast scan of potential non-compliant goods. For this reason, the Forum decided to include in the Compendium qualitative analytical methods or techniques, with relevant LOD value accompanied by a note to make explicit reference to the qualitative method.

In general, the WG contacts laboratories to request additional or missing information if needed to make a conclusion on the advisability of such methods.

The WG evaluates whether a given method satisfies the pre-established requirements and whether other practicability considerations need to be taken into account (e.g. the method doesn't satisfy all the requirements but it is the only method available).

2.3 Compendium of analytical methods recommended by the Forum to check compliance with REACH Annex XVII restrictions

The WG on enforceability of restrictions proposes to the Forum the compiled Compendium of analytical methods which are considered suitable for checking compliance with REACH Annex XVII restrictions.

The Forum acknowledges that the Compendium is based on information submitted by laboratories and has no legal validity. Usage of the information remains under the sole responsibility of the users. Furthermore, the information contained in the Compendium are subject to changes.

2.4 Process for the amendment of the Compendium of analytical methods

The first version of the Compendium is published with the aim to complete or to amend the information on this first version.

The Compendium will be revised at regular intervals to reflect changing technical standards, new available methods as well as modifications of existing ones. The revisions will be published on the ECHA website.

ECHA Forum invites interested parties to submit additional information to be incorporated in future updates of the Compendium. These can be submitted via forum@echa.europa.eu .

Annex 1 – Restriction matrices and concentration ranges covered by REACH Annex XVII entries

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
1	Polychlorinated terphenyls (PCTs)		Non-aqueous liquids	>50 mg/kg (0,005 % by weight).	Oils including waste oils
2	Chloroethene (vinyl chloride)	CAS No 75-01-4	gas	Banned from use	Aerosol propellants
3	Liquid substances or mixtures which are regarded as dangerous in accordance with Directive 1999/45/EC or are fulfilling the criteria for any of the following hazard classes or categories set out in Annex I to Regulation (EC) No 1272/2008:		Non-aqueous liquids	Banned from use	Oils
4	Tris (2,3 dibromopropyl) phosphate	CAS No 126-72-7	Textiles	Banned from use	Skin contact textiles

[7] The matrices listed in this annex are indicative only. Annex XVII to REACH is the only authoritative text.

[8] The limit values reported in this column are indicative and might not fully correspond to the actual restriction conditions as set out in Annex XVII to REACH.

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
5	Benzene	CAS No 71-43-2	Toys, substances and mixtures	>5 mg/kg (0,0005 %) in toys, >0,1 % by weight as constituent of other substances or in mixtures	
6	Asbestos fibres	CAS No 12001-28-4 CAS No 12172-73-5 CAS No 77536-67-5 CAS No 77536-66-4 CAS No 77536-68-6 CAS No 12001-29-5 CAS No 132207-32-0	Articles	Banned from use	
7	Tris(aziridinyl)phosphin oxide	CAS No 545-55-1	Textiles	Banned from use	Skin contact textiles
8	Polybrominatedbiphenyls (PBB)	CAS No 59536-65-1	Textiles	Banned from use	Skin contact textiles

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
9	(a) Soap bark powder (Quillaja saponaria) and its derivatives containing saponines, (b) Powder of the roots of Helleborus viridis and Helleborus niger (c) Powder of the roots of Veratrum album and Veratrum nigrum (d) Benzidine and/or its derivatives (e) o-Nitrobenzaldehyde	CAS No 68990-67-0, CAS No 92-87-5, CAS No 552-89	Liquids and solid powders	Banned from use	
10	(a) Ammonium sulphide (b) Ammonium hydrogen sulphide (c) Ammonium polysulphide	CAS No 12135-76-1, CAS No 12124-99-1, CAS No 9080-17-5	solid powders	Banned from use	
11	Volatile esters of bromoacetic acids: (a) Methyl bromoacetate (b) Ethyl bromoacetate (c) Propyl bromoacetate (d) Butyl bromoacetate	CAS No 96-32-2, CAS No 105-36-2, CAS No 35223-80-4, CAS No 18991-98-5	Non-aqueous liquids	Banned from use	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
12	2-Naphthylamine	CAS No 91-59-8	Solids and liquids	>0,1 % by weight	
13	Benzidine	CAS No 92-87-5	Solids and liquids	>0,1 % by weight	
14	4-Nitrobiphenyl	CAS No 92-93-3	Solids and liquids	>0,1 % by weight	
15	4-Aminobiphenyl xenylamine	CAS No 92-67-1	Solids and liquids	>0,1 % by weight	
16	Lead carbonates: (a) Neutral anhydrous carbonate (PbCO 3) (b) Trilead-bis(carbonate)-dihydroxide 2Pb CO 3 - Pb(OH) 2	CAS No 598-63-0, CAS No 1319-46-6	Non-aqueous liquids	Banned from use	Paint
17	Lead sulphates: (a) PbSO 4 (b) Pb x SO 4	CAS No 7446-14-2, CAS No 15739-80-7	Non-aqueous liquids	Banned from use	Paint
18	Mercury compounds		Paint, wood, textiles and aqueous liquids	Banned from use	Anti-fouling paint, heavy duty industrial textiles

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
18a	Mercury	CAS No 7439-97-6	Pure element	Banned in certain products	
19	Arsenic compounds		Paint, wood and aqueous liquids	Banned for certain uses	Anti-fouling paint
20	Organostannic compounds		Paint, textiles and aqueous liquids	Banned for certain uses, >0.1% by weight Sn in some mixtures and articles	Anti-fouling paint, free association paint, skin contact textiles and leather, wall and floor coverings,
21	Dibutyltin hydrogen borate C 8 H 19 BO 3 Sn (DBB)	CAS No 75113-37-0	Solids and liquids	>0.1 % by weight.	
22	Pentachlorophenol	CAS No 87-86-5	Solids, non-aqueous and aqueous liquids	>0.1 % by weight.	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
23	Cadmium	CAS No 7440-43-9	Plastic, paint, aqueous liquids, wood, leather, paper and metal	>0.01 % by weight of the plastic material. >0,1 % by weight of the paint on the painted article. For paints with a zinc content > 10 % by weight of the paint, the concentration of cadmium (as Cd) shall not be =>0,1 % by weight, Brazing fillers =>0,01 % by weight, =>0,01 % by weight as Cd in jewellery	Specified synthetic organic polymers, paints, brazing fillers and cadmium plated metal
24	Monomethyl — tetrachlorodiphenyl methane Trade name: Ugilec 141	CAS No 76253-60-6	Non-aqueous and aqueous liquids	Banned from use	
25	Monomethyl-dichloro-diphenyl methane Trade name: Ugilec 121		Non-aqueous and aqueous liquids	Banned from use	
26	Monomethyl-dibromo-diphenyl methane bromobenzylbromotoluene, mixture of isomers Trade name: DBBT	CAS No 99688-47-8	Non-aqueous liquid	Banned from use	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
27	Nickel and it's compounds	CAS No 7440-02-0	Synthetic sweat (release during contact with skin)	rate of nickel release from such post assemblies is <0.2 µg/ cm 2 /week (migration limit) - post assemblies, nickel release from the parts of these articles (jewellery,watch straps etc.) coming into direct and prolonged contact with the skin is >0.5 µg/cm 2 /week.	Jewellery, metals
28	Substances which appear in Part 3 of Annex VI to Regulation (EC) No 1272/2008 classified as carcinogen category 1A or 1B (Table 3.1) or carcinogen category 1 or 2 (Table 3.2) and listed as follows: etc		Solids and liquids	Banned from use - with derogations	
29	Substances which appear in Part 3 of Annex VI to Regulation (EC) No 1272/2008 classified as germ cell mutagen category 1A or 1B (Table 3.1) or mutagen category 1 or 2 (Table 3.2) and listed as follows: etc		Solids and liquids	Banned from use - with derogations	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
30	Substances which appear in Part 3 of Annex VI to Regulation (EC) No 1272/2008 classified as toxic to reproduction category 1A or 1B (Table 3.1) or toxic to reproduction category 1 or 2 (Table 3.2) and listed as follows:		Solids and liquids	Banned from use - with derogations	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
31	(a) Creosote; wash oil (b) Creosote oil; wash oil (c) Distillates (coal tar), naphthalene oils; naphthalene oil, (d) Creosote oil, acenaphthene fraction; wash oil (e) Distillates (coal tar), upper; heavy anthracene oil (f) Anthracene oil (g) Tar acids, coal, crude; crude phenols (h) Creosote, wood (i) Low temperature tar oil, alkaline; extract residues (coal), low temperature coal tar alkaline	CAS No 8001-58-9, CAS No 61789-28-4, CAS No 84650-04-4, CAS No 90640-84-9, CAS No 65996-91-0, CAS No 90640-80-5, CAS No 122384-78-5, CAS No 8021-39-4 CAS No 65996-85-2	Solids, non-aqueous, aqueous liquids and wood	Banned from use - with derogations	
32	Chloroform	CAS No 67-66-3	Non-aqueous and aqueous liquids	concentrations =>0.1 % by weight,	
34	1,1,2-Trichloroethane	CAS No 79-00-5	Non-aqueous and aqueous liquids	concentrations =>0.1 % by weight,	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
35	1,1,2,2-Tetrachloroethane	CAS No 79-34-5	Non-aqueous and aqueous liquids	concentrations =>0.1 % by weight,	
36	1,1,1,2-Tetrachloroethane	CAS No 630-20-6	Non-aqueous and aqueous liquids	concentrations =>0.1 % by weight,	
37	Pentachloroethane	CAS No 76-01-7	Non-aqueous and aqueous liquids	concentrations =>0.1 % by weight,	
38	1,1-Dichloroethene	CAS No 75-35-4	Non-aqueous and aqueous liquids	concentrations =>0.1 % by weight,	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
40	Substances classified as flammable gases category 1 or 2, flammable liquids categories 1, 2 or 3, flammable solids category 1 or 2, substances and mixtures which, in contact with water, emit flammable gases, category 1, 2 or 3, pyrophoric liquids category 1 or pyrophoric solids category 1, regardless of whether they appear in Part 3 of Annex VI to that Regulation or not.		Gases, liquids and solids	Banned from use	Aerosols
41	Hexachloroethane	CAS No 67-72-1	Solids and non-aqueous liquids	Banned from use	
43	Azocolourants and Azodyes		Solid compounds, textiles and leather	>30 mg/kg (0,003 % by weight) in the articles or in the dyed parts thereof, >0.1 % by weight, where the substance or the mixture is intended for colouring textile and leather articles	Dyes

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
45	Diphenylether, octabromo derivative C 12 H 2 Br 8 O		Solid compound, non-aqueous liquids, textiles and foams	>0.1 % by weight	
46	(a) Nonylphenol C 6 H4(OH)C 9 H 19 (b) Nonylphenol ethoxylates (C 2 H 4 O) n C 15 H 24 O	CAS 25154-52-3	Non-aqueous, aqueous liquids, textiles, leather and paper	concentrations =>0.1 % by weight	
47	Chromium VI compounds		Cement	when hydrated, >2 mg/kg (0,0002 %) soluble chromium VI of the total dry weight of the cement.	
48	Toluene	CAS No 108-88-3	Non-aqueous liquids	concentration => than 0.1 % by weight	Adhesives and spray paints
49	Trichlorobenzene	CAS No 120-82-1	Non-aqueous liquids	concentration => than 0.1 % by weight	
50	Polycyclic-aromatic hydrocarbons (PAH)		Non-aqueous liquids and rubber tyres	Extender oils - >1 mg/kg (0,0001 % by weight) BaP or >10 mg/kg (0,001 % by weight) of the sum of all listed PAHs. Tyres and treads - vulcanised rubber compounds do not exceed the limit of 0,35 % Bay protons as measured and calculated by ISO 21461	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
51	The following phthalates (or other CAS and EC numbers covering the substance): (a) Bis (2-ethylhexyl) phthalate (DEHP) (b) Dibutyl phthalate (DBP) (c) Benzyl butyl phthalate (BBP)	CAS No 117-81-7, CAS No 84-74-2, CAS No 85-68-7	Toys and childcare articles	>0.1 % by weight of the plasticised material	Plastic
52	The following phthalates (or other CAS- and EC numbers covering the substance): (a) Di-'isononyl' phthalate (DINP) (b) Di-'isodecyl' phthalate (DIDP) (c) Di-n-octyl phthalate (DNOP)	CAS No 28553-12-0 and 68515-48-0, CAS No 26761-40-0 and 68515-49-1, CAS No 117-84-0	Toys and childcare articles	>0.1 % by weight of the plasticised material in toys and childcare articles which can be placed in the mouth by children	Plastic
54	2-(2-methoxyethoxy)ethanol (DEGME)	CAS No 111-77-3	Non-aqueous liquids	concentrations =>0.1 % by weight.	paints, paint strippers, cleaning agents, self-shining emulsions and floor sealants

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
55	2-(2-butoxyethoxy)ethanol (DEGBE)	CAS No 112-34-5	Non-aqueous liquids	concentrations =>3 % by weight	spray paints or spray cleaners in aerosol dispensers
56	Methylenediphenyl diisocyanate (MDI)	CAS No 26447-40-5	Solid compound and foams	concentrations =>0.1 % by weight	
57	Cyclohexane	CAS No 110-82-7	Non-aqueous liquids	concentrations =>0.1 % by weight	neoprene-based contact adhesives
58	Ammonium nitrate (AN)	CAS No 6484-52-2	Solids and aqueous liquids	Solid fertilizer - >28 % by weight of nitrogen in relation to ammonium nitrate, Other uses - >16 % by weight of nitrogen in relation to ammonium nitrate	
59	Dichloromethane	CAS No 75-09-2	Non-aqueous liquids	concentration =<0.1 % by weight	Paint strippers
60	Acrylamide	CAS No 79-06-1	Solids and gels	concentration =>0.1 % by weight	Grout
61	Dimethylfumarate (DMF)	CAS No 624-49-7	Solid compound, leather and textiles	>0.1 mg/kg.	

Restriction No.	Compound covered	CAS No.	Matrices covered by restriction[7]	Limit value within the restriction[8]	Specific materials covered by the restriction
63	Lead and its compounds	CAS No 7439-92-1	Metals	Jewellery - =>0.05 % by weight.	Jewellery, watches

Annex 2- Additional technical information on analytical methods characteristics

2.5 Limit of detection

The typical methodology of determining the analyte concentration in a sample is to treat the sample in such a way as to get the analyte in a form (e.g. solution) that can be introduced in an analytical instrument and an instrumental response to be obtained. In order for the analyte concentration to be calculated, a calibration scheme, relating the analyte concentration to instrumental response is required. Fortunately in many cases, there is a significant range of concentrations where this relation is linear, having the form:

$$y = a + b * x \qquad (1)$$

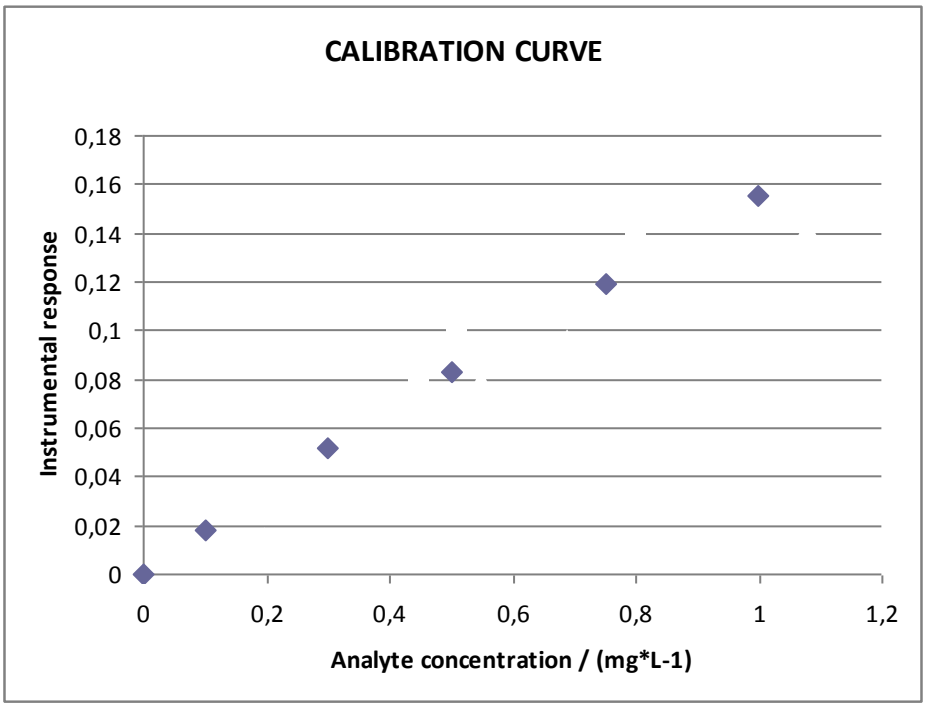
where y is the instrumental response and x is the analyte concentration.
The evaluation of the intercept "a" and the slope "b" of the above equation will lead to the calculation of the analyte concentration of any solution if its instrumental response is measured. To achieve this, a number of solutions (usually 5-7), called "calibration solutions", with known, different analyte concentrations are prepared and their instrumental response is measured. An arithmetic example is shown in the following table 1:

Table 1: Analyte concentration of calibration solutions along with the corresponding Instrumental response

Calibration solution	Analyte concentration ($mg*L^{-1}$)	Instrumental response
Blank	0.00	0.000
1	0.10	0.018
2	0.30	0.052
3	0.50	0.083
4	0.75	0.119
5	1.00	0.155

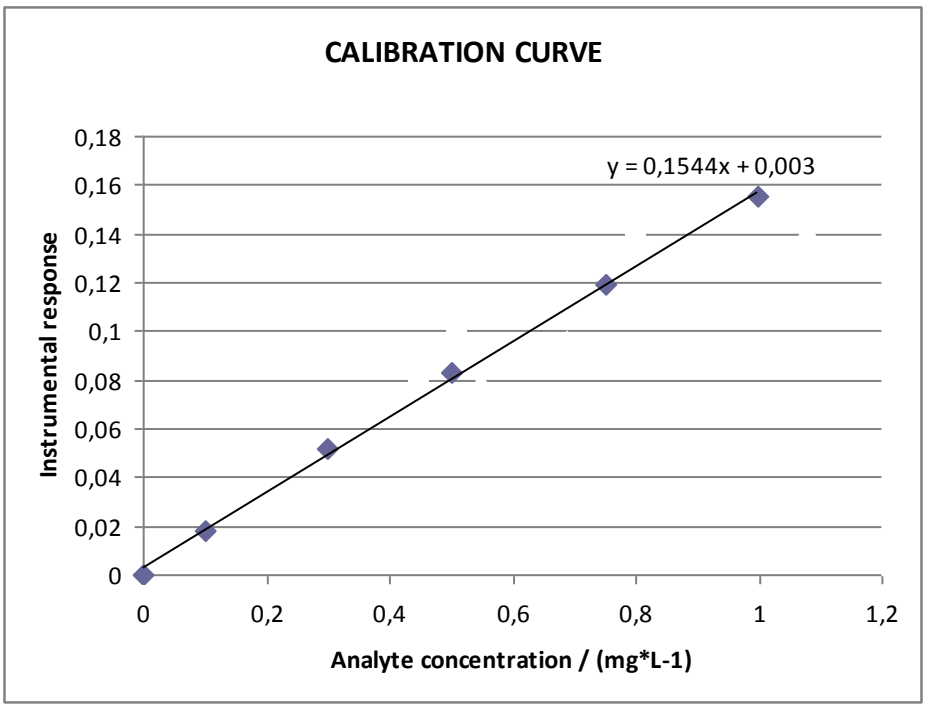
Then, the instrumental response "y" is plotted against the analyte concentration "x", as in the following figure 1:

Figure n.1.: Instrumental response versus analyte concentration



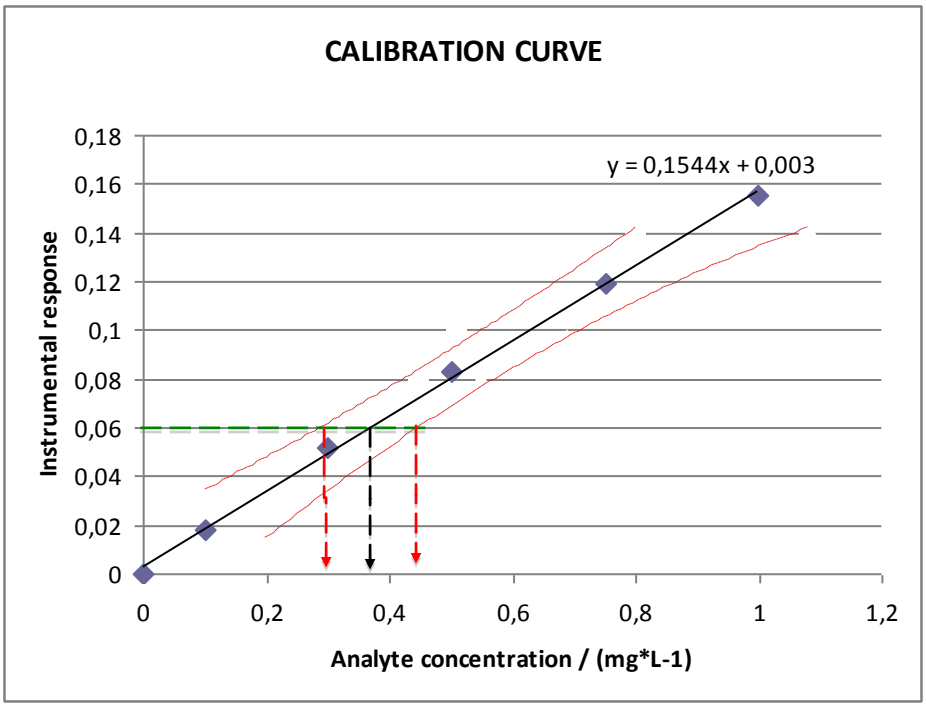
From the data of Table 1 and taking into account the visual verification of the linear relationship between instrumental response and analyte concentration, shown in Figure 1, the values of "a" and "b" are calculated, using the method of linear least squares. The result is given in the following Figure 2:

Figure n.2.: Instrumental response versus analyte concentration, along with the calculated calibration curve (continous black line)



The equation of the calibration curve is y=0.003+0.1544*x. Having this equation in hand, the analyte concentration in any unknown sample can be calculated. The uncertainty related to any determined concentration can be obtained by the mathematics accompanying the linear least squares method. What is important however, is the variation of uncertainty across the calibration curve. The 95% confidence intervals are shown schematically in Figure 3 (red dashed lines):

Figure n.3.: Instrumental response versus analyte concentration, along with the calculated calibration curve (continous black line) and the confidense intervals (red dashed lines)



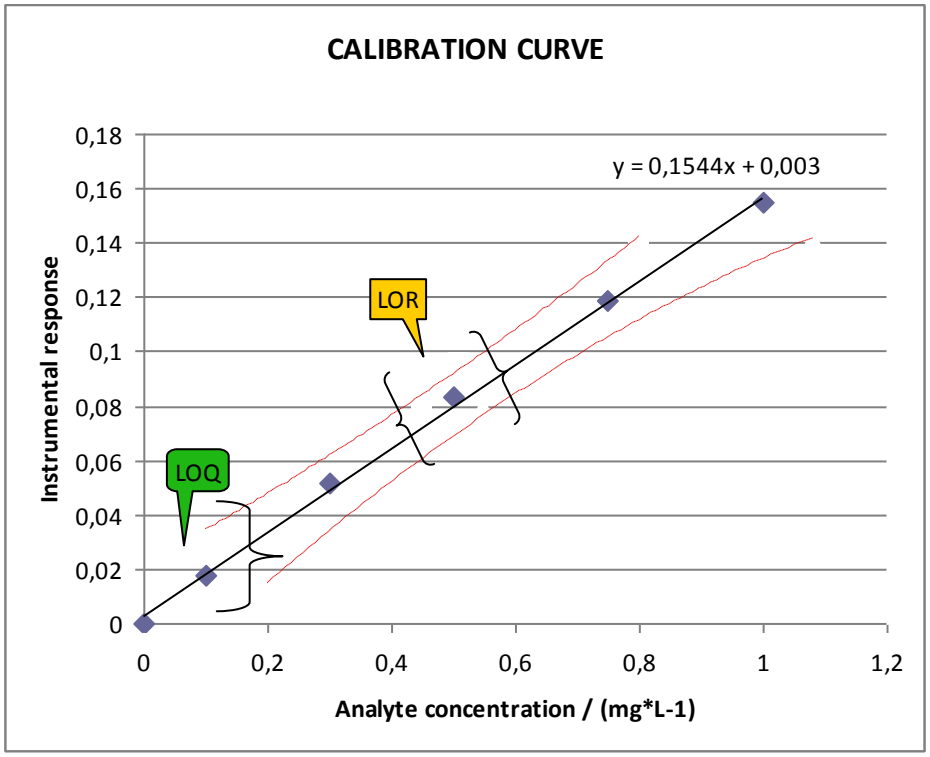
The importance of the confidence intervals is explained in the example depicted in the above Figure 3. Let's suppose that an unknown sample produces when measured, an instrumental response of 0.06. This according to the calibration curve corresponds to an analyte concentration of 0.37mg*L^{-1} (black arrow). In addition, the analyte concentration is estimated between 0.29mg*L^{-1} and 0.45mg*L^{-1} with 95% confidence (red arrows).
From the above Figure 3, it is important to notice that the narrowest confidence limits are calculated for concentrations close to the centre of the calibration curve. This is the reason why it is preferable to select the range of the calibration solutions, so as to have the LOR at the centre of the calibration curve. In this way, analyte concentrations near the LOR are determined with the lowest uncertainty. In addition, as shown in Figure 4, if the following relations

$$LOD \leq 0.1 * LOR \text{ or } LOQ \leq 0.3 * LOR \qquad (2)$$

hold, it is possible to construct the calibration curve with the first calibration solution containing the analyte at a concentration C ≈ LOQ and two other calibration solutions with concentrations between LOQ and LOR, thus determining the part of the calibration curve below LOR adequately.

Figure n.4.: Instrumental response versus analyte concentration, along with the

calculated calibration curve (continous black line) and the confidense intervals (red dashed lines). The preferable regions of LOQ and LOR are depicted in curly brackets.



2.6 Approaches for obtaining measurement uncertainty

The measurement uncertainty can be estimated by using the following approaches:

- The theoretical "bottom-up" approach (or the component-by-component approach) consists in the evaluation of all the relevant sources of uncertainty that can affect the result, quantifying those that are significant and combining them by using the law of propagation of uncertainty. This approach can be very laborious and requires a detailed knowledge of the whole analytical process, in fact all steps of the process have to be considered in order to avoid an underestimation of the measurement uncertainty. Nevertheless, the benefit to the analyst is that this approach provides a clear understanding of the analytical activities which contribute significantly to the measurement uncertainty and which therefore may be assigned as critical control points to reduce or manage measurement uncertainty in future applications of the method [1,2].

- The practical "top-down" approach (more suitable for analytical chemical activities) is based on method validation and long-term precision data derived from laboratory control samples, proficiency testing results, published literature data and/or inter-laboratory collaborative trials. For example, data obtained from inter-laboratory study carried out to validate a published method (collaborative study), according to the AOAC/IUPAC protocol or ISO 5725 standard [3,4,5], include estimate of standard deviation among laboratories (reproducibility) for several levels of response, and may include an estimate of bias based on Certified Reference Material (CRM) studies. These data can be utilized to estimate the measurement of uncertainty.

When the above experimental data are available, this approach provides a reliable information on measurement uncertainty requiring minor efforts by the analysts.

- The Horwitz approach is based on the Horwitz formula (applicable for water and food matrices) which relates the relative standard deviation to concentration, expressed as a mass fraction, and it is based on the results from a large number of food-based collaborative studies reported in the literature, primarily published in the Journal of AOAC INTERNATIONAL. The uncertainty is estimated by using the reproducibility obtained by the Horwitz formula at the concentration of interest.

  The Horwitz formula is also a helpful tool to compare the estimated uncertainty against the expected value derived from the published inter-laboratory studies and it can be used as a maximum acceptable uncertainty when no criteria for uncertainty have been established.

Annex 3 – Questionnaire on available analytical methods to check compliance with REACH Annex XVII restrictions and Legend to the questionnaire

For further information, check Annex 3.

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