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Traceability of Chemical Measurement Results

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Abstract: Traceability to recognised references, ultimately to the SI units, is an indispensable prerequisite for measurement results to be comparable and trustworthy and hence accepted worldwide. This holds also for chemical measurement results, particularly as these are often used as a basis for important decisions and agreements, for example in health care and environmental protection. The concept of traceability and the special problems associated with its application to chemical analysis as compared to metrology in general are described. Current approaches to establish traceability of chemical measurement results are reported. The most important development in the last two decades was the establishment of the Consultative Committee for Metrology in Chemistry under the Metre Convention, which provided the basis for an international reference framework for chemical measurements. In order to link up laboratory results anywhere in the world with this international reference framework, traceability structures on the national level are required. It is shown, using the demand for traceable chemical measurements in Germany as an example, how such structures can be established and efficiently used.

Keywords: CCQM · Metrology in chemistry · Quality assurance · Traceability

1. Introduction

With the continuing globalisation of trade and economy, reliability of measurement results of any kind is of increasing importance. Measurement results are directly and indirectly involved in almost every aspect of daily life and play an essential role in cross-border exchanges of goods and services. This holds also for chemical measurements. Particularly in this field decisions and agreements on life and well being of each individual often critically depend on analytical results, for example in such important areas as health care, food safety, environmental protection and international trade. Such chemical measurement results must therefore be trustworthy. It is the central aim of current activities in metrology in chemistry to build confidence in the reliability of chemical measurements so that they are accepted without doubt and without the necessity for costly duplication, thus also minimising technical barriers to trade. An important prerequisite for confidence in the reliability of measurement results is comparability of the results across space and time, based on traceability to common references which in turn are traceable to the SI units of measurement. Traceability is therefore besides other requirements of quality assurance a key issue for all kinds of measurement results.

In the new 'Vocabulary of Metrology – Basic and General Concepts and Associated Terms' (VIM), 3rd edition, metrological traceability is defined as:[1]
"Property of a measurement result whereby the result can be related to stated references through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty."

The practical realisation of this definition requires efforts to provide references, *e.g.* measurement standards which are widely accepted, preferably in an international framework, and mechanisms which link up laboratory results with these references. The specific question here is: how can these requirements be met in the field of chemical analysis?

2. Special Problems Associated with Traceability in Chemical Analysis

Metrology in chemistry developed from 'classical' metrology, *e.g.* metrology of mechanical and electrical quantities, where traceability of measurement results to the SI units has been established for a long time and is usually taken for granted. The references at the top of the traceability chain are national measurement standards which are usually realisations of the corresponding SI units. Field level measurement results are related to the national standards through a chain of calibrations *via* intermediate measurement standards. International comparisons of the national standards (so-called key comparisons) carried out by the relevant Consultative Committees of the International Committee of Weights and Measures (CIPM) under the Metre Convention ensure their equivalence and thus traceability to the SI units of measurement results obtained worldwide.

Due to the great variety and complexity of chemical measurement tasks, establishing traceability of chemical measurement results is more difficult and more laborious than in most other fields of metrology. A peculiarity of traceability in chemical analysis is that the references at the top of the traceability chain must meet two requirements, one with respect to the identity of the chemical entity (analyte) to be determined which is represented by the analyte in high purity, and another with respect to the corresponding amount (value of the quantity, *e.g.* amount of substance, mass concentration, *etc.*). This corresponds to the qualitative and quantitative aspect of every chemical analysis. In addition to traceability to the SI units as in metrology in general, 'qualitative traceability' is also required in chemical measurement. High-purity substances are therefore very important at the reference level.

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A consequence of the qualitative aspect of chemical analysis is that the number of references which would be necessary corresponds to the number of analytes to be determined. Since concentration measurements of the same analyte in different matrices are different measurement tasks due to the matrix dependence of the results, the number of references required increases even more. This consideration shows that establishing traceability of chemical measurement results requires additional efforts compared to metrology in most other areas and will probably not reach a degree of 'completeness' as we take it for granted in other fields.

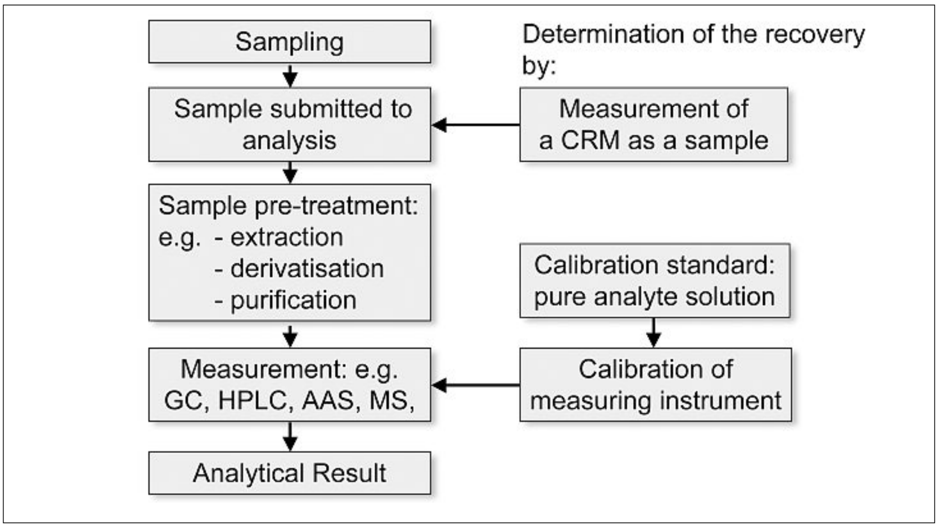

Fig. 1. Typical analytical procedure.

3. How Can Traceability in Chemical Analysis Be Established?

In everyday laboratory work reference materials are mostly used as measurement standards to establish traceability. This is mainly done in two ways:

i) In order to transfer the signal of an analytical measuring device (*e.g.* gas chromatograph) into a meaningful result in the form of the value of a measurand (*e.g.* mass concentration) the device is calibrated, usually with an in-house reference material like a solution of a pure analyte. With this value assignment traceability of the result to the SI unit, *e.g.* g/L of the target analyte (the unit 'litre' is accepted for use with the SI by the CIPM), is established within the uncertainty of the value of the in-house reference material and its application. The largest contribution to the uncertainty often comes from the uncertainty of identity of the analyte material used, *i.e.* uncertainty of its purity.

ii) It is quite common in analytical practice that the signal and thus the result depend on the matrix in which the analyte is to be determined. In this case matrix reference materials closely matching the composition of the sample are submitted to the analytical method in order to validate it, *i.e.* to determine, among other features, the recovery (ratio of the value of the measurand found to that present in the reference material) which is usually less than one due to analyte loss, *e.g.* in extraction. In this way traceability is established with an uncertainty which is composed of the uncertainty of the correction for recovery and of the observed precision.

Both kinds of application of reference materials are usually involved in a complete chemical measurement and are necessary to obtain traceable results. Fig. 1 illustrates the situation.

An important prerequisite for establishing traceability *via* reference materials is that these are themselves traceable to the SI units. According to their definition, certified reference materials (CRM) should meet this requirement.[2] In practice, however, for many reference materials provided under this label, traceability cannot be demonstrated. At present, reliable (traceable, homogeneous, stable, small uncertainty) reference materials are lacking for many analytical tasks. This holds, in particular, for matrix reference materials, although great efforts have been made and are still going on to develop reliable reference materials in accordance with the ISO Guides 30, 34 and 35.[3,4]

In some cases in practice comparability of results is only required for agreements between different parties within a given area or analytical sector. Reference materials supporting measurements for this purpose need not be traceable to the SI units but just to a common reference in such an area or sector. These requirements are easier to meet but are insufficient at the global level.

4. International Reference Framework for Chemical Measurements

With the establishment of the Consultative Committee for Metrology in Chemistry (CCQM) in 1993 by the International Committee for Weights and Measures (CIPM), the executive committee of the Inter-Governmental Treaty of the Metre Convention, work towards a traceability system for chemical measurements was started at the international level.[5,6] Other organisations such as Eurachem, CITAC and the regional metrology organisations also contributed to the process of building up an international infrastructure in metrology in chemistry and continue to do so. Eurachem and CITAC have jointly prepared an important guide on traceability in chemical measurement.[7] Additional impetus came from the CIPM Mutual Recognition Arrangement (CIPM-MRA) for national measurement standards and for calibration and measurement certificates issued by national metrology institutes, which was drawn up by the CIPM in 1999 in order to raise the confidence in measurement results of any kind and hence their acceptance.[8] The MRA has now been signed by 74 institutes from 46 Member States and 26 Associates of the General Conference of Weights and Measures (CGPM). As a result, the national references and the measurement capabilities of the national institutes have reached a higher level of mutual recognition and trustworthiness. Whereas this process was mainly an extension and consolidation of mutual recognition already existing in metrology in general, it was the first attempt to establish a globally recognised reference framework for chemical measurements.

Confidence in and hence mutual recognition of chemical measurement results is based on the degree of equivalence of national measurement standards which in turn is based on key comparisons, as mentioned above, carried out under the CCQM. The analytical measurement tasks for which key comparisons of the national references are performed are selected according to the actual demand for traceability. Areas of high priority are health care, food safety and environmental protection. The measurement programme is under permanent review by a special CCQM working group.

As result of a key comparison a reference value adopted by the CCQM after an assessment process and the deviations of the participating institutes from this reference value, as well as the mutual deviations of the participants are obtained, together with their uncertainties. The key comparisons are carried out by the national metrology institutes (NMIs) and designated national chemical institutes.

Besides the mutual recognition of the national measurement standards, the mutual recognition of calibration and measurement certificates issued by national institutes is an important measure for increasing confidence in the reliability of chemical measurement results in an international framework under the MRA. Recognition of these certificates is based on the calibration and measurement capabilities (CMCs) of the national institutes. The capabilities of the national institutes are underpinned by the results of the key comparisons and assessed on a continuous basis by a special working group under CCQM. Additional evidence of competence is provided by an obligatory quality assurance system in accordance with ISO/IEC standard 17025.[9]

The results of all key comparisons are collected in Appendix B to the MRA and are publicly accessible *via* the Internet in the key comparison database (KCDB) maintained at the Bureau International des Poids et Mesures (BIPM) on its website *www.bipm.org*. Appendix C to the MRA contains the CMCs of the national institutes. To ensure the trustworthiness of these entries, which are submitted by the national institutes, the Joint Committee of the Regional Metrology Organisations and the BIPM (JCRB) assesses the CMC claims of the institutes before approval for inclusion in Appendix C. This part of the database is also accessible on the BIPM website.

The appendices B and C to the MRA constitute a transparent system which reflects the metrological capabilities of national institutes and degrees of equivalence of their measurement standards. It can be used by all interested parties, *e.g.* accreditation bodies, regulatory authorities or trade partners that want to check the credibility of traceability claims for measurement results which are important to judge the quality of goods and services. The MRA thus provides an international reference framework which contains the reference points of traceability of chemical measurements in the form of mutually recognised national chemical measurement standards, *e.g.* certified reference materials, and mutually recognised calibration and measurement certificates, provided by the national institutes. The mutual recognition is based on the demonstrated and assessed calibration and measurement capabilities (CMCs) of the national institutes and underpinned by the results of the key comparisons. At present, the final results of about 80 key comparisons and 4300 assessed CMC claims form the basis of traceability of chemical measurement results produced worldwide.

The results of the work of the CCQM are of growing interest to other international organisations which by their activities either represent specific areas of chemical analysis or are more generally involved in chemical measurements. These are at present the International Atomic Energy Agency (IAEA), the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), the Committee on Reference Materials of the International Organisation for Standardisation (ISO REMCO), the International Union of Pure and Applied Chemistry (IUPAC), the World Health Organisation (WHO), the World Meteorological Organisation (WMO) and the International Laboratory Accreditation Cooperation (ILAC). IAEA, IFCC, ISO REMCO and IUPAC have become members of the CCQM.

As regards IFCC, clinical chemists have for a long time taken a leading position in applying the concept of traceability. In laboratory medicine the need for reliable and traceable measurement results is particularly obvious. An additional driver in this field is the *In Vitro* Diagnostic Medical Devices Directive (IVD Directive, 98/79/EC) of the European Union, which requires traceability of values assigned to calibrate and control materials to reference materials of higher order. In response to this requirement, the CIPM together with the BIPM created the Joint Committee for Traceability in Laboratory Medicine (JCTLM), supported by the IFCC and ILAC. As a result of the work of the JCTLM, reference materials and reference methods for clinical chemistry are now available which constitute the reference framework for traceability in laboratory medicine. Two categories of references exist: CRMs of well-defined chemical entities which are traceable to the SI and CRMs which have been agreed on by international convention and are not yet traceable to the SI. This reference system is under permanent review and is updated as required.

The other organisations mentioned above are also involved in developing traceability mechanisms in close cooperation with the CCQM.

5. Establishing Traceability of Laboratory Results to the International Reference Framework

In order to link up working level results with this international reference framework, or, expressed in other words, to disseminate the units of measurement down to the field laboratories, traceability infrastructures are required also at the national level. This is necessary because the large number of field laboratories (this may be more than a thousand in a single application field like clinical chemistry) cannot interact directly with the NMIs. In the following the national traceability infrastructure for chemical measurements in Germany is described as an example of how the results of chemical testing laboratories can be made traceable to the international reference framework *via* national measurement standards. Such measurement standards can be reference materials as well as reference methods of high metrological quality.[10] Primary methods are used if available for realising the national standards.[11]

The infrastructure consists of three levels, as shown in Fig. 2. At the top of the structure a network of national laboratories provides the national chemical measurement standards and ensures that these are linked up with the international reference framework for chemical measurements. An intermediate level consisting of accredited chemical calibration laboratories, in the field of laboratory medicine also referred to as reference measurement laboratories, is connected to the national standards level *via* transfer standards and comparison measurements. The accreditation is granted by the German Calibra-

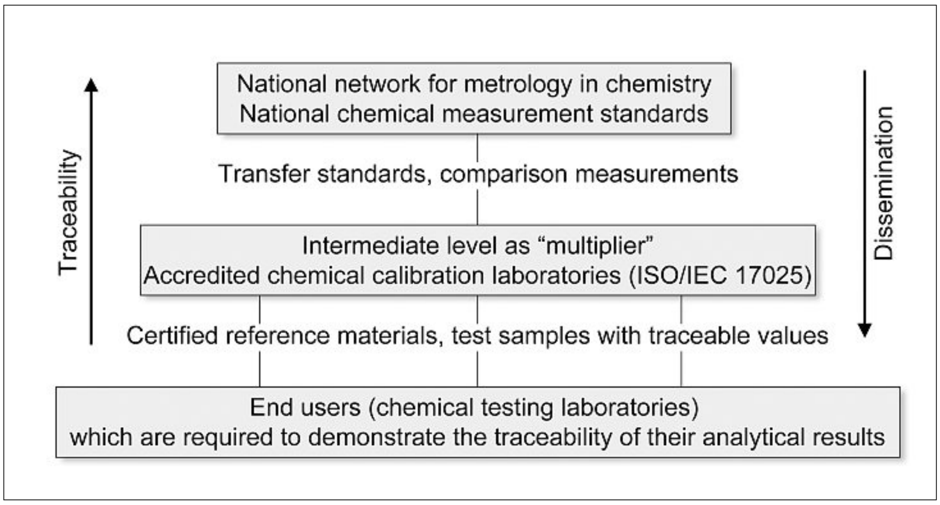

Fig. 2. Structure of the traceability system for chemical measurements in Germany.

tion Service (DKD) according to ISO/IEC 17025 as a calibration laboratory, in laboratory medicine also according to ISO 15195.[12] In the regulated area verification authorities are at the corresponding position in the traceability chain. This intermediate level has an important 'multiplier' function. It is firmly linked to the national standards and provides traceable calibration means (mainly certified reference materials) to the workshop level, which consists essentially of chemical testing laboratories which are required to give evidence to their customers that their measurement results are traceable to recognised references.

This multiplier function is of growing importance because it will not be possible for the national laboratories at the top of this traceability chain to serve the users directly, due the growing demand for traceability in the field of chemistry. It was the growing demand for traceability in metrology in general that led to the establishment of the calibration services some thirty years ago after the workload of calibration had become unbearable for the national metrology institutes. Now we are facing a similar situation in metrology in chemistry, although here other paths of dissemination exist also.

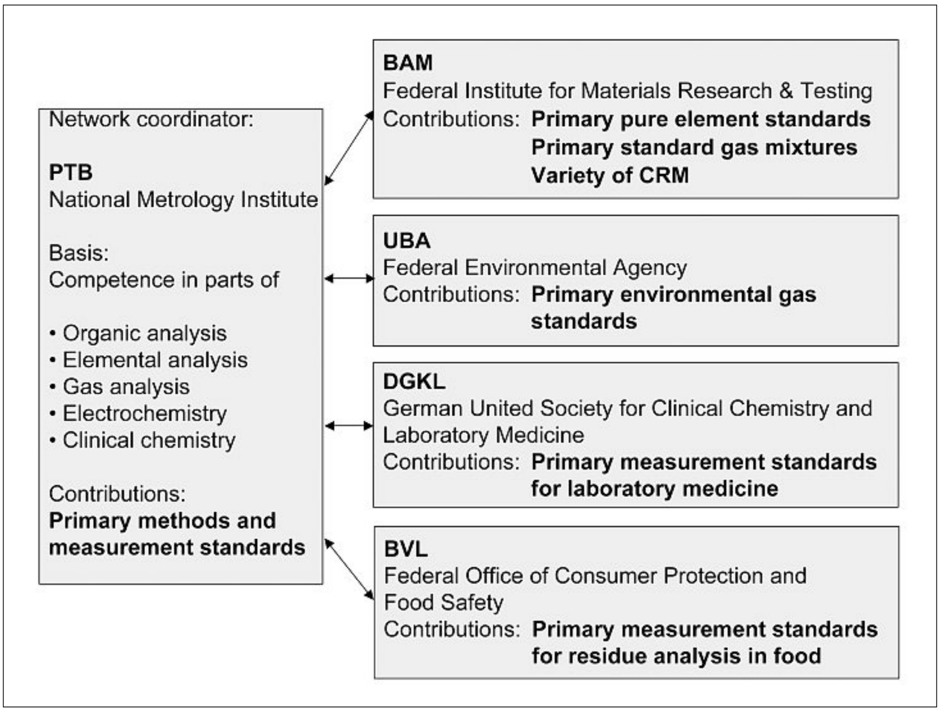

Fig. 3. Structure of the national standards network for chemical measurements. The double arrows indicate formal agreements between PTB and the network partners, in which parts of PTB's responsibility for the national measurement standards is devolved to the partners.

6. National Network for Chemical Measurement Standards

The network at the top of the traceability system providing the national standards for chemical measurements in Germany consists at present of five institutes as shown in Fig. 3.

The Physikalisch-Technische Bundesanstalt (PTB), the national metrology institute of Germany, which is responsible for the realisation and dissemination of the units of measurement, coordinates the network on the basis of its legal mandate and its own competence in metrology in chemistry. Partner institutes in the network are at present: Bundesanstalt für Materialforschung und -prüfung, BAM (Federal Institute for Materials Research & Testing), Umweltbundesamt, UBA (Federal Environmental Agency), Deutsche Vereinte Gesellschaft für klinische Chemie und Laboratoriumsmedizin, DGKL (German United Society for Clinical Chemistry and Laboratory Medicine), Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, BVL (Federal Office of Consumer Protection and Food Safety). These institutes, together with PTB, constitute the national reference system for traceability of chemical measurements to the SI units. An essential aim of this network is to ensure that the national references are firmly linked up with the international reference framework. For this purpose, the network members take part in CCQM comparisons and submit calibration and measurement capabilities (CMC) to the international evaluation procedure for entry into the KCDB in their own responsibility.

To have a network of laboratories at the top of a traceability system for chemical measurements instead of just the national metrology institute is quite typical for metrology in chemistry and is under development in many countries because, traditionally, competence for chemical analysis is largely outside of the metrology institutes, in most countries. The National Institute of Standards and Technology (NIST) USA, is an exception.

Traceability is realised in different ways in the different fields covered by the network, depending on the specific technical, legal and social requirements. A common feature of the dissemination paths is that accredited calibration laboratories (reference measurement laboratories in laboratory medicine) are used as 'multipliers' as shown in Fig. 2.

At present the state of accreditation of chemical calibration laboratories in Germany under DKD according to ISO/EC 17025, in laboratory medicine also to ISO 15195, is as follows:

– four calibration/reference measurement laboratories for measurands of clinical chemistry,
– four calibration laboratories for gas analysis,
– three calibration laboratories for pH and electrolytic conductivity measurement,
– one calibration laboratory for production of calibration solutions for elemental analysis.

The experience so far gained with this approach to an efficient traceability system for chemical measurements, as shown here as an example, is encouraging, although the system and particularly the dissemination mechanisms are still under development. In this stage of development, traceability of chemical measurement results obtained at the working level, up to the international reference framework can be provided for such important fields as laboratory medicine, food safety, environmental protection and forensics.

7. Example of a Traceability Chain

Clinical chemistry may serve as an example for a dissemination path in Germany. The primary references are disseminated to the medical laboratories at the working level mainly *via* interlaboratory tests on well characterised samples which are traceable to the primary references. Measurements are conducted within the framework of the so-called external quality assurance as required by the guidelines of the Federal Chamber of Physicians (Bundesärztekammer, BÄK). The calibration laboratory is connected to the national standards level *via* comparison measurements on laboratory samples taken from the calibration laboratory. It is the advantage of this way of transferring standards over the transfer of reference materials from the shelf that these standards perfectly match the matrices occurring in the calibration laboratory. The samples are analysed by the national standards laboratory and the calibration laboratory to be accredited or re-evaluated in regular intervals. Agreement within predefined limits is required as a proof of the competence of the calibration laboratory.

Samples with a known value undisclosed to the participants are then used by the calibration laboratory as measurement standard for the quality control of the large number of medical laboratories; again, agreement within predefined limits is required. In case of non-compliant results a medical laboratory has to discontinue its service until evidence for improved results is provided. The procedure is repeated at quarterly intervals. Many thousand interlaboratory test measurements are performed in this way every year by several thousand medical laboratories.

Because of the large number of analytes with clinical relevance traceability can only be provided for a selected group of measurands. Priority lists were established by the BÄK for this reason. On this basis traceability can be established for a large majority of all measurements in clinical chemistry. The list is continually updated. This process of selecting priorities is a typical feature of metrology in chemistry and is also applied in other areas like environmental protection or food safety.

8. Conclusions

The introduction of metrological concepts, particularly the concept of traceability, to analytical chemistry allows comparability of measurement results in chemistry on a global scale over space and time. Examples in the most relevant areas of public services such as health care or environmental measurements, which have shown to work in practise, demonstrate the feasibility of the approach. Although metrology in chemistry sometimes requires special adaptations, such as a selection process for priority measurands, its application is growing on a large scale and it is more and more introduced into the most important areas of public welfare and international trade.

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