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REVIEW PAPER

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REMCO, the ISO Council Committee on Reference Materials – its first 25 years

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Abstract The 25th Anniversary of the first meeting of REMCO presents an occasion to summarize the events preceding and leading up to the establishment of this Committee, the ever growing use of reference materials, the ISO Guides REMCO has prepared, the help for Technical Committees to achieve valid measurements, the help for Developing Countries in upgrading their laboratories, its structure and contact points.

Introduction

The aim of REMCO, the Committee on Reference Materials of the International Organization for Standardization, is to carry out and encourage a broad, international effort for the harmonization, production and application of CRMs.

25 years ago REMCO started with its first meeting. 14 delegates from 21 Member Bodies met at a round table in Geneva. The last couple of meetings have been attended by some 50 delegates from 62 Member Bodies and 15 international organisations, which indicates a steady growing interest in its activities.

In this first 25 years a series of ISO Guides on reference materials (RMs) has been developed. ISO Guide 30 was decided to harmonize the vocabulary used in connection with reference materials. Its basic definitions of the reference material and the certified reference material (CRM) have been included in the international vocabulary of basic and general terms in metrology (VIM). To ensure that users have sufficient information on a CRM, ISO Guide 31 deals with the contents of certificates and labels. Calibration of chemical analyses is the target of ISO Guide 32, ISO Guide 33 takes care of the uses of certified reference materials in widely diverse fields. As accreditation became more and more important to analytical laboratories involved in certification analysis and production of CRMs, quality system guidelines for the production of RMs, ISO Guide 34 has been developed in 1996, followed by a revised version in 2000 – General requirements for the competence of RM producers. Recently the first CRM producer received his accreditation based on ISO Guide 34. The general and statistical principles used for the certification of CRMs are covered by ISO Guide 35, which is currently under revision.

Besides of these "official" Guides, REMCO started publishing information booklets like "*The role of Reference materials in achieving Quality in Analytical Chemistry*". REMCO organised or supported different workshops and seminars in co-operation with other organizations, e.g. ISO/DEVCO, IUPAC and others. REMCO also supported the international database on CRMs COMAR to ensure information on their availability.

At its last meeting in Geneva REMCO decided to modify its structure and to develop a strategic plan to meet the future needs and to be prepared for the next 25 years.

Historical background

The modern history of RMs begins in 1906 when the first cast iron RMs (at that time called as "Standard Samples") were prepared in the United States by the National Bureau of Standards (NBS) in conjunction with the American Foundrymen's Association.

The history of **STANDARDS** and **REFERENCE MATERIALS** is closely connected and up until recently they were used somewhat interchangeably.[1] **Standards** were weights (or other measures) to which others conform, examples for following, samples of certain materials for reference. Physical measures (mass, length, volume, etc.) were also materialized.

Description of commodities (and the requirements of different quality grades) became "written standards", "standard specifications". The way of classification of grades, the way of inspection, the way of test methods has been written down and they are also "standards".

Later in the 19th and 20th centuries the description of the traded goods more and more replaced the actual material samples.

In the second half of the 20th century the instrumental methods of analysis, together with their "black box magic" required the calibration of the instruments using carefully analysed, homogeneous samples of the materials to be tested. So we have again samples of RMs.

There are, therefore, at least two main types of standards: 1)"Standard specifications", the written standards, and 2) "Standards *in bottle*", or "in solid disc form" the RMs. For the analytical chemists there is a third type: 3) "Standard solutions" that are also in bottle, and are related to the above type 2). They can be regarded as measuring solutions made of high purity materials, like: solution of KOH 0.1 mol/l for titration.

History of REMCO

The problem of quoting RMs was discussed at the Council meeting of the International Organization for Standardization (ISO) in 1973**. On the basis of an ad hoc group recommendation REMCO was established and it had its first meeting in January 1976.** REMCO is the short name of the REferece Material COmmittee of ISO.

Already at the first Round Table conference on RMs nine other international organizations had been represented:

- International Electrotechnical Commission – IEC
- World Health Organization – WHO (subsequently withdrawn)
- United Nations Educational, Scientific and Cultural Organization – UNESCO
- International Committee of Weights and Measures – CIPM
- International Organization of Legal Metrology – OIML
- International Bureau of Legal Metrology – BIPM
- International Federation of Clinical Chemistry – IFCC
- International Union of Immunological Societies
- Committee on World Standards – World Association of Societies of Pathology.

All the above international organizations agreed that ISO took the lead (OIML even stopped its work in this area in favour of REMCO being the world's central focus) and all co-operated with REMCO.

The interaction with other bodies was also fruitful. IUPAC had a section that dealt with CRMs. AOAC INTERNATIONAL has created a group to deal with specific CRMs of their interest. To deal with biological and environmental reference materials BERM has been established. All these cooperate with REMCO in a very efficient manner.

Documents mention for the first time the *"problem of reference materials"* referring to the 27th meeting of ISO Council held in Washington, on 5, 6 and 7 September 1973. Council adopted the following resolution:

> "Council establishes an ad hoc group to study further the proposal for the creation of a Council committee on standard reference materials...; Council appoints Mr. W. Andrus (USA) as Chairman of this group and invites him, in consultation with the Secretary-General, to nominate the members of this group..."

The group that was called "ad hoc working party on Reference Materials (REMPA)" discussed the situation and submitted its proposed scope, terms of reference and suggested liaisons for Council acceptance. Mr. W. Andrus became Chairman of REMPA and Mr. T. Földesi became its first Secretary. The first meeting of REMPA took place in Geneva, 9–11 April 1975. The need for a permanent committee was expressed by the delegates and by representatives of important international organizations in liaison.

At its meeting in September 1975

> "Council decides to transform the ad hoc working party on reference materials (REMPA) into a Council committee on reference materials (REMCO) under Article 7.4 of the Constitution, with the following terms of reference:
>
> – to establish definitions, categories, levels and classification of reference materials for use by ISO,
> – to determine the structure of related forms of reference materials,

[1] NIST markets its CRMs using the trade name "Standard Reference Materials" (SRMs).

– to formulate criteria to be applied for choice of sources for mention in ISO documents (covering also legal aspects),
– to prepare guidelines for technical committees for making reference to reference materials in ISO documents,
– to propose, as far as necessary, action to be taken on reference materials required for ISO work,
– to deal with matters within its competence arising in relation with other international organizations and to advise Council on action to be taken.

Membership of REMCO is open to all ISO member bodies"

"Council appoints Mr. W.E. Andrus (USA) as Chairman of REMCO for 1976–1978"

That was the beginning of a very important and vivid activity. **The first meeting of REMCO took place in Geneva, 19–20 January 1976 attended by 14 delegates.** The committee had 12 Participating (P) and 9 Observer (O) members. Already this meeting made progress drafting a document on definitions and another on the use of RMs in ISO standards. The meeting reached consensus on two basic definitions: reference material (RM) and certified reference material (CRM) (See below).

Chairmen of REMCO between 1976 and 2001:

– W.E. Andrus (USA) 1976–1978 and 1978–1981
– G.A. Uriano (USA) 1982–1984
– A. Marschal (France) 1985–1987 and 1988–1990
– S.D. Rasberry (USA) 1991–1993 and 1994–1996
– H. Klich **(**Germany) 1997–1999 and 2000–2002.

Secretaries of REMCO between 1976 and 2001:

– T. Földesi 1976–1977
– M. Parkany 1977–1996
– J-R Alessi 1996–1999
– A. J. Williams 1999-

Valid measurements

Good measurements cost money, bad ones cost more – sometimes even more than the original investment – and often more than money alone. They can cause wrong medical diagnosis and treatment. They can mean lost production time, waste of energy and materials, manufacturing rejects, and product liability problems. They can bring opposing parties to court over commercial, environmental issues. On the positive side, good measurement is a key to productivity. CRMs are a way of marrying economy and accuracy in the interest of everybody.

CRMs are tangible objects. In many cases they are prototypes, samples of a commercial material such as cement, glass or stainless steel, certified for chemical composition. Some are natural materials such as soil or plant tissue. The earliest developments and uses of CRMs were found in the field of industrial quality control – particularly in the metal industries. There are other reasons why CRMs are produced and used. In some instances they aid buyer-seller transactions, an example being in the sale of iron ore (in millions of tons) where the price of it is directly related to its iron content. In this case, a variation of 0.1% in the average iron content of the ore can increase or decrease the value of the contents of a large ore carrier by thousands of pounds, hence the use of high quality CRMs of iron ore are very important to laboratories analysing this material. Both the buyer and the seller require a fair analysis of the material – one where accuracy of analysis is assured by reference to an impartial standard.

Where enough CRMs of a given type are available, they can provide calibration points for industrial chemical analysis and other types of industrial measurements. For example, steel analysts employ NIST or BAS CRM series for low alloy steel X-ray fluorescence and Optical Emission analysis, relative analytical methods in which good calibration standards are crucial.

And this leads us to the new horizons for CRMs because of fundamental changes that have occurred in the way quality is defined and assessed. Formal systems of quality assessment and management have begun to replace informal ones and this affects CRMs in at least two important ways. First, and already realized to some extent, there are increases in demand for new types, larger quantities, and better quality CRMs. Secondly, more formal, systems will be needed to document quality "pedigree" of the CRMs, themselves. This second need has been partially met by the fact that in the past, a few top-level national metrology and specialist laboratories produced most CRMs; but now increased demands have led to many untested producers.

REMCO Task Group 4, *Accreditation* has prepared ISO Guide 34:2000 *General requirements for the competence of reference material producers.* Furthermore, REMCO examine possible options, including their pros and cons, for establishing some form of international recognition for RM producers.

By performing reliable chemical measurements, laboratories provide scientific evidence for important **decisions** such as:

– The fate of materials and products **(pass/fail)**

  Example: all production where the chemical compositions of the products are specified

– Health or illness of humans **(to operate/not to operate)**

  Examples: it is often vital to establish whether a woman is pregnant or not for pregnant women should not take certain medicines and the results of testing their urine compared to a RM urine serves as a basis for important decisions; professional illnesses, e.g.

workers in contact with lead or cadmium must be surveyed and their urine/blood analysed in comparison with RMs; the contents of pesticide residues (e.g. in food) need to be checked using RMs.

– Whether or not a law or regulation has been violated **(support for legal actions by police and court of law)**

  Examples: breath and blood analyses by the police are compared with CRMs; the exhaust gases of cars are compared against CRMs; airline pilots sometimes undergo tests based on RMs to ensure that they have not taken any drugs; sportsmen, horses at horse races are checked whether they are doped or not: RMs are the reference for the amounts of chemicals in urine.

– Whether or not a crime has been committed and how **(forensic evidence)**

  Examples: when traces of explosives are found on supposed criminals' hands, the analysis are made against CRMs; blood tests providing forensic evidence have to be used against the relevant CRMs.

The list of RMs is long: as of now, more than 12 000 items, and the figure is growing constantly. Some 3000 International Standards for test methods often need also to refer to RMs. Raw materials and finished products are equally concerned. In order to guarantee the reliability and validity of chemical measurements, such RMs are needed those have been certified by a procedure, which has established traceability against an accurate unit of measurement, in most cases the well-known basic SI units. These are the CRMs.

RMs and chemical standards

RMs provide essential traceability in chemical measurements and are used to demonstrate the accuracy of results, calibrate equipment and methods, monitor laboratory performance and validate methods, and enable comparison of methods by use as transfer standards. Their use is encouraged whenever possible.

Where matrix interferences exist, ideally a method should be validated using a matched matrix RM certified in a reliable manner. If such a material is not available it may be acceptable to use a sample spiked with a chemical standard.

It is important that the CRM has been produced and characterized in a technically valid manner. Users of CRMs should be aware that not all materials are validated to the same standard. Details of homogeneity trials, stability trials, and the methods used in certification, and the uncertainties and variations in the stated analyte values are usually available from the producer and should be used to judge the pedigree.

For many types of analysis, calibration may be carried out using standards prepared within the laboratory from chemicals of known purity and composition. Some chemicals may be purchased with manufacturers' certificates stating purity. Alternatively, uncertified chemical standards may be purchased from suppliers whose manufacturing processes are certified/registered to ISO 9001 (or EN 29001). Whatever the source, it is the users' responsibility to verify that the quality of such standards is satisfactory. Normally a new batch of a standard should be checked against the old. Ideally, all chemical standards should be purchased from producers with demonstrated quality assurance system such as ISO 9001. However, a quality assurance system such as ISO 9001 does not automatically guarantee the quality of the producer's products and laboratories should take all reasonable steps to confirm the quality of chemical standards.

The purity requirements of chemical standards may be considered in relation to the permitted tolerance of the method. For example, a tolerance of <0.1% of the target value will require a chemical standard to have a certainty of concentration significantly better than 99.9%.

RMs and chemical standards should be clearly labelled so that they are unambiguously identified and referenced against accompanying certificates or other documentation. Information should be available indicating shelf-life, storage conditions, applicability, and restrictions of use. Prepared standards should be treated as reagents for the purpose of labelling.

For trace analysis the control of impurities is essential. Due regard should be paid to the manufacturers recommendations on storage and shelf-life.

RMs and standards should be handled in order to safeguard against contamination or loss of determinand. Training procedures should reflect these requirements.

RM definitions

Reference material (RM)

Material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials. [1, 2].

Certified reference material (CRM)

RM, accompanied by a certificate, one or more of whose property values are certified by a procedure which establishes its traceability to an accurate realization of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence. [1, 2].

Proper use of RMs

RMs of any type must be appropriate in matrix and composition and of stable composition over the intended period of use. They must be sufficiently uniform in composition when sub-sampled (homogeneous) and available in sufficient quantity to be useful over a reasonable period of time. When appropriate to the application, consideration of additional characteristics may be needed, e.g. particle size distribution.

CRMs have the further requirement that they must be issued with a certificate in which the measured (critical) parameters and assigned values are fully documented. [2–6]

The user of an RM should be aware that he or she is responsible for selecting the most appropriate material. RM producers try to provide materials that best meet a broad need, which is not necessarily the best for a specific user application. [5]

From the user's point of view, the choice of CRM should depend on the required accuracy of the measurement results, i.e. it needs to be fit-for-purpose. However, as a result it is often difficult to know which is the most appropriate CRM for a given application or, indeed, whether such material exists at all.

Ideally the material should match the matrix of the routine test materials as closely as possible in order to avoid comparison of "apples" with "oranges". The user should also be aware of the certification parameters/criteria used by the producer. For example: stated application, method used, consensus value, uncertainty calculation, etc. The analytical method should conform to the requirements given in the certificate. [4]

Certified values and their associated uncertainties are not the only aspect of the material that the user needs to consider for quality assurance. The proper use of a RM includes correct storage, observation of expiration date, and relevant implementation and application of the material according to any instructions on its certificate of analysis. [9]

Availability of RMs

The development of any CRM is an expensive task; it requires deep technical knowledge and relevant experience, both carefully applied. For many of the various chemical analyses performed daily, reference materials have been, and continue to be, developed by (among others) metrology institutes. Properties and compositions can also be determined (certified) on the basis of interlaboratory tests of laboratories in a certain area. [7]

However, the great scope and variety of components, concentrations and matrices make it impossible to encompass the whole field of analytical chemistry; consequently the development of new CRMs is almost completely prioritized according to the strongest market and economical demands. Both nationally and internationally, considerable attention is given to the avoidance of duplication. This has, in turn, initiated international development programmes, in which end-users of CRMs play an important role.

It has been estimated that approximately 20000 CRMs exist worldwide. However, there is often some confusion among potential users about availability, applicability, position in a metrological hierarchy and the method of use for a given RM. [9]

Therefore several national bodies for RMs are responsible for developing and maintaining inventories of available CRMs. This information is used to serve trade and industry, and is also of benefit to activities in the governmental, educational and health sectors. These national bodies offer information concerning specifications, applicability, usage and worldwide availability of (certified) RMs and can, on request, assist in their supply. In addition, they maintain collections of catalogues from producers and suppliers of RMs and can also provide information about guidelines for the use and production of (certified) RMs. [5–7]

A computerized databank "Code of Reference Materials" (COMAR) contains information on approximately 10 000 RMs from 20 countries.

The database provides the following information: name and general description of the material, name and address of the producer, form of the material, the properties certified and their values and the field of application.

By means of a structured search of the database, sequentially indicating qualitative (e.g. components and matrix) and quantitative (concentration limits) criteria, a RM suitable for a user's application may be found. (See below for more information on COMAR).

COMAR

COMAR Coding Centers currently exist in Canada, China, France, Germany, Hungary, Japan, the Netherlands, Poland, Russian Federation, Slovakia, South Africa, Sweden, United Kingdom, and USA. For full contact information and any additional centres, please either visit the COMAR website (www.comar.bam.de) or apply to the COMAR Central Secretariat at:

CONTACTS

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New proposed structure of REMCO

With proposed chairpersons

Main Committee

Secretary
Andrew Williams

Chair
Harry Klich

Executive Committee

Chair, Vice Chair (Ron Walker),
Past chair (Stan Rasberry),

Secretary 3 Subcommittee Chairs
DEVCO (NN), CASCO (NN)
Strategic Planning Business plan Vice Chair

Subcommittee 1

International Coordination and Harmonization
Paul De Bièvre

Subcommittee 2

Technical Guidance
Aadrian van der Veen

Subcommittee 3

Classification Education
Henry Steger

WG

Revision ISO Guide 35
SC1 SC2 SC3
Aadrian van der Veen

WG

Inclusion GUM in ISO Guides
SC2
Jean Pauwels

WG

Categories of CRMs
SC1 SC3
Ales Fajgelj

WG

Transportation
SC1
Peter Jenks

WG

Pharmacopoeia
SC1 SC2
Nancy Trahey

WG

Information Booklets
SC3
Andy Williams

WG

Revision of VIM
SC1 SC3
Paul de Bièvre

ANNEX 1

ISO Guides developed by REMCO

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

The first edition of this Guide (1981) was the outcome of collaboration between REMCO and the organizations IEC, IAEA, OIML, IUPAC, IFCC and WHO. The revision leading to the second edition was undertaken because it had become apparent that some confusion existed as to what types of *measurement standards* or *etalons*

should legitimately be included within the definition of a reference *material.* Moreover, the recognition that CRMs are measurement standards made it desirable to examine the vocabulary of standards in metrology, as detailed in the International *vocabulary of basic and general terms in metrology (VIM), Second* edition (1993) with particular reference to CRMs.

ISO Guide 31:2000 *Reference materials- Contents of certificates and labels*

The certificate which accompanies a CRM should contain all the information which is essential to its use. Without the certificate, the material, however costly its production, is valueless. It follows, therefore, that producers of CRMs should pay very careful attention to the preparation of certificates. The ISO Committee on Reference Materials (ISO/REMCO) published the first edition of this Guide in 1981. During the past 16 years there has been considerable growth in the number and variety of RMs produced, and in their use. The increasing demand for reliability in the results obtained by analytical and metrological techniques, which has arisen especially from growing concern about pollution of the environment, has led to the demand for a widening range of CRMs of increasingly high quality for use in validation of measurement methods and as calibrants.

The definition of a CRM in ISO Guide 30 (see clause 2) requires all certified property values to be accompanied by an uncertainty at a stated level of confidence and for traceability to "an accurate realization of the unit in which the property value is expressed" to be demonstrated. These additional requirements must therefore be met in the certificate.

The *Guide* to *the expression of uncertainty in measurement,* published by ISO (see Bibliography), summarizes more recent international consideration of the subject of uncertainty in measurement and will require some modification of the definition of a CRM quoted above. Uncertainty should now be expressed as combined (type A + type B) standard uncertainty or as expanded uncertainty (with a coverage factor to be applied to the combined standard uncertainty). The concept of probability or level of confidence is now no longer central.

The first edition of this Guide discussed the difference between the information provided on the label, the certificate, and the certification report, and stressed the brief synoptic nature of the certificate. The past 16 years, however, have seen a general decline in the issuing of certification reports and an increase in the information provided in certificates. This decline in the publication of certification reports is not necessarily to be condemned, provided all the information appropriate to a full certification report can always be obtained on application to the producers of the CRM. Production of certification reports is expensive and it is clearly unnecessary for one to be supplied to the same user every time a fresh sample from the same batch of material is purchased. At the same time, the information required from a certificate is usually more than the certified property value. Details concerning the way in which the container should be opened, the minimum sample size that should be taken for a measurement, the stability of the material, the way in which it should be stored, and, in the case of CRMs where the certified value is method-dependent, the method used to determine the certified value are all essential information for the user.

ISO Guide 32:1997 *Calibration in analytical chemistry using certified reference materials*

This guide that has been prepared by Task Group 2 and to which M. Alain Marschal prepared the drafts and evaluated the comments received was accepted for publication.

ISO Guide 33:2000 *Uses of certified reference materials*

Today's world of modern technology requires a large number of CRMs in widely diverse fields and the demand for such materials is expected to increase. The preparation of a CRM is a time-consuming, meticulous and expensive endeavour and consequently it has not always been, and will continue not to be, possible to satisfy the demand for all types and quantities of CRMs. For this reason, CRMs must be used properly, i.e. effectively, efficiently and economically.

CRMs must be used on a regular basis to ensure reliable measurements. However, in doing so, the magnitude of the supply of that CRM, its relative cost, its availability (accessibility) and the measurement technique, be it destructive or non-destructive, must be considered. Also important to the user is the fact that the misuse of a CRM may not provide the intended information.

Misuse of CRMs differs from incorrect use. The user of a CRM is expected to be familiar with all information pertinent to the use of the CRM as specified in its certificate. He should comply with such factors as the period of validity of the CRM, the prescribed conditions for storage of the CRM, instructions for the use of the CRM, and specifications for validity of the certified properties of the CRM. A CRM should not be used for a purpose other than that for which it was intended. Nevertheless, from time to time, when a user must resort to applying a CRM in an incorrect manner because of the unavailability of a suitable CRM, he must be fully cognizant of the potential pitfalls and therefore assess his measurement output accordingly.

There are many measurement processes where CRMs are in general use but are replaceable by a host of working standards such as homogeneous materials, previously analysed materials, pure compounds, solutions of pure elements, etc. Some examples are where only a "rough" estimate of the trueness or precision of a method is

sought, where "blind" unknown check samples are used routinely in quality control programmes, and where only the variation in trueness or precision of a method with some parameter such as time, analyst, instrument, etc., is being evaluated. The first example illustrates the use of a CRM where the well-defined certified value and uncertainty of the CRM is under-utilized. The others illustrate the case where a series of "one-time" trueness and precision assessments are compared with one another. There is no need to base that comparison on a well-defined certified value and uncertainty of a CRM. The advantages in using CRMs are that the user has the means to assess the trueness and precision of his measurement method and establishes metrological traceability for his results.

Whether the use of CRMs in these procedures is in fact "misuse" depends largely on the availability and relative cost of the CRMs. Where CRMs are in short supply or very expensive, their use would indeed be misuse. However, for CRMs in ample supply or where similar CRMs are available from one or more sources, it is strongly recommended that CRMs always be used instead of in-house standards because of the resultant enhanced confidence in the measurement output.

It is important that users remain aware that the preparation of in-house standards for use instead of CRMs has an associated cost based on factors such as material cost, facility usage charges, personnel labour rates, etc. in which the material cost is in general the lowest. For some CRMs such as the complex compositional materials certified for chemical composition, the cost of preparing in-house standards to match the composition of real samples can exceed that of available CRMs. In these cases, the use of CRMs is recommended.

The user should be aware of the potential misuse of CRMs as "blind" unknown check samples in quality control programmes. Where there are only a few CRMs in an area of expertise, they are easily recognized and they may therefore not satisfy the intended purpose. Moreover, the same CRMs should never be used for both calibration purposes and as "blind" unknown check samples in a measurement process.

The misuse of CRMs can also occur when the user does not fully take into account the uncertainty in the certified property. The combined standard uncertainty of a certified property of a CRM can have contributions from the inhomogeneity of the material, the within-laboratory uncertainty and, where applicable, the between-laboratories uncertainty. The level of homogeneity defined for a CRM by the producer is dependent on both the statistical design used to evaluate it and the repeatability of the method of measurement. For certain CRMs, the level of homogeneity is valid for a test portion defined by mass, physical dimension, time of measurement, etc. The user must be aware that the use of a test portion that does not meet or exceed that specification could severely increase the contribution of the inhomogeneity of the CRM to the uncertainty of the certified property to the point where the statistical parameters of certification are no longer valid.

The variation in the repeatability of different methods has another implication for the user. Since the degree of inhomogeneity of a CRM is dependent on the repeatability of the method of measurement, it is possible that a user, in applying a method capable of better repeatability, could detect inhomogeneity in that CRM. In such cases, the observed inhomogeneity is already accounted for in the statistical parameters for the certified property and therefore the statistical tests presented in this Guide remain valid but the scientific basis for using that particular CRM to give a true assessment of the user's method must again be questioned.

It is well known that different methods of measurement of a property are not capable of equal repeatability. Accordingly there could arise instances where the user may wish to assess a method that has greater repeatability than that or those used in the certification of the CRM. In such cases, the statistical tests presented in this Guide remain valid but the scientific basis for using that particular CRM to give a true assessment of the precision (and possibly the trueness) normally expected from the user's method must be questioned. It is recommended that the user resorts to a CRM of lesser uncertainty, if available.

For CRMs certified by a primary method, the user should not assume that his method is capable of matching the precision and trueness reported for the CRM. It is unreasonable therefore to apply the statistical procedures in this Guide for assessing the trueness and precision of a method by application to a CRM using the certification parameters for a property reported in the certificate. The user, as a consequence, must either experimentally establish or make estimates based on available information for those parameters that are more appropriate. Similarly, where a user applies a method to a CRM that has been certified by a single different method, the user must not assume that the certification parameters for the certified property are applicable to his method except in cases where the trueness and precision capable by both methods are known to be comparable.

One of the important considerations in selecting a CRM for use either in assessing the trueness and precision of a method or in the calibration of instruments in a method is the level of uncertainty required by the end-use of the method. Obviously the user should not apply a CRM of greater uncertainty than permitted by the end-use.

The selection of CRMs must take into account not only the level of uncertainty required for the intended purpose but also their availability, cost, and chemical and physical suitability for the intended purpose. For example, the unavailability or high cost of one CRM could force a user to resort to using another CRM of greater uncertainty than the preferred one. Also, in chemical

analysis, a CRM of greater, but still acceptable, uncertainty in the certified property may be preferred over another CRM because of better matching with the composition of real samples. This could result in minimizing "matrix" or chemical effects in the measurement process which are capable of causing errors far greater than the difference between the uncertainties of the CRMs.

In conclusion, CRMs are meant to fulfil many purposes. Accordingly, a CRM used properly for one purpose in one laboratory may be misused for another purpose in another laboratory. It is recommended that the user consider the suitability of a CRM for his intended purpose on a case-by-case basis.

ISO Guide 34:2000 *General requirements for the competence of reference material producers*

The use of RMs makes possible the transfer of the values of measured or assigned quantities between testing, analytical and measurement laboratories. They are widely used for the calibration of measuring equipment and for the evaluation or validation of measurement procedures. In certain cases, they enable properties to be expressed conveniently in arbitrary units.

There is an increasing number of RM producers and a demonstration of their scientific and technical competence is now a basis requirement for ensuring the quality of reference materials. The demand for new RMs of higher quality is increasing as a consequence of both the increased precision of measuring equipment and the requirement for more accurate and reliable data in the scientific and technological disciplines. Some previously acceptable RMs may not meet these more stringent requirements. It is, therefore, not only necessary for RM producers to supply information about their materials in the form of reports, certificates and statements, but also to demonstrate their competence in producing RMs of appropriate quality.

The first edition of ISO Guide 34 set out specific guidelines on the interpretation of ISO/IEC Guide 25 and the ISO 9000 series standards in the context of RM production. The more general requirements of these standards were omitted. Since ISO Guide 34 was first published in 1996, the assessment of the competence of RM producers has gained considerable impetus and the present Guide now sets out all the general requirements in accordance with which a RM producer has to demonstrate that it operates.

Pharmacopoeial standards and substances are established and distributed by pharmacopoeial authorities following the general principles of this Guide. It should be noted, however, that the pharmacopoeial authorities to give the user the information provided by certificates of analysis and expiration dates use a different approach. Also, the uncertainty of their assigned values is not stated since it is negligible in relation to the defined limits of the method-specific assays of the pharmacopoeias for which they are used.

ISO Guide 35:1989 *Certification of reference materials – General and statistical principles* (**Under revision**)

The purpose of this Guide is to give a basic introduction to concepts and practical aspects related to the CRMs. The quality of a measurement based on the use of a CRM will depend in part on the effort and care expended by the certification body on determining the property value(s) of the candidate CRM. Hence the process of certification should be carried out using well-characterized measurement methods that have high accuracy as well as precision and provide property values traceable to fundamental units of measurement. Furthermore, the methods should yield values with uncertainties that are appropriate to the expected end-use of the CRM. Two clauses are devoted to the two most important technical considerations in the certification of CRMs – measurement uncertainties and material homogeneity. It assists in understanding valid methods for the certification of RMs and also to help potential users to better define their technical requirements. The Guide should be useful in establishing the full potential of CRMs as aids to assuring the accuracy and interlaboratory compatibility of measurements on a national or international scale.

This Guide is being revised taking into account the development both in the statistical approach and the requirements of quality systems.

ANNEX 2

ACTIVITIES OF ISO/DEVCO–ISO/REMCO

The success of the ISO 9000 series of International Standards has had an impact on the requirement in quality in laboratories. Laboratories are expected to present correct measurement data that were obtained using validated measurement – methods by well-trained analysts that have adequate instrumentation and take part in proficiency testing. Laboratories should have their quality assurance procedures and they have to use CRMs in order to ensure traceability to SI units.

In many developing countries laboratories do have well-trained analysts and quite often adequate instrumentation as well. In most cases they follow validated measurement – methods: ISO Standards, AOAC methods, etc.

However, it is not easy for laboratories in developing countries to participate in proficiency testing and quite often they do not have appropriate CRMs.

This is why ISO/DEVCO and ISO/REMCO have launched a joint programme to be at the assistance of laboratories in more than 40 developing countries. After having established and tabulated their needs for CRMs generous donations have been received from Members of REMCO, producers of CRMs. These have been dis-

tributed together with relevant ISO/REMCO and IUPAC documentation.

As a second phase "training materials" have been received as donations[2] and distributed to the above laboratories as "unknown" for analysis. This was intended to be performed as a replacement of the real proficiency testing. The results have been evaluated at the Central Secretariat (using the analytical data received together with the training materials). The laboratories were then informed in confidentiality on their performance and also on the real analytical values of the training material. Therefore these can be used now as RMs. In case of problems alternative analytical methods have been proposed and other suggestions were given to improve their performance.

The success of this help became widely known and now there are more and more laboratories that would like to join to this exercise. Further donations of Standard Reference Materials have been received.[3] The above exercise, which took place in 1994 and 1995, was extremely well received by the participating laboratories. One of them, the Trinidad and Tobago Bureau of Standards (TTBS) took the initiative to propose to other laboratories in the Caribbean to carry out a project for upgrading analytical laboratories in that region with support from ISO.

Between 1997 and 2000 three missions were organized: two experts, one in food analysis and testing and one in general chemical analysis and quality assurance in laboratories visited 3–3 Developing Countries:

1997: Jamaica, Trinidad and Tobago, and Barbados
1998: Ecuador, Peru, Bolivia,
2000: Botswana, Mauritius, and Mozambique.

[2] Donation by Mr. P.D. Ridsdale, Bureau of Analysed Samples Limited, Middlesbrough, UK.
[3] Donation by NIST National Institute of Standards and Technology Gaithersburg, USA

The missions had been preceded by the following preparatory activities:

- Dispatch of relevant literature
- Dispatch of unknown samples
- Instructions for carrying out calibration of instruments (by calibration authority or in-house)
- Instructions for carrying out analyses of the samples (in accordance with relevant ISO or AOAC or ASTM or BS documents.).

During the mission experts undertook the following activities:

- Organized a two-day training seminar for personnel from all participating laboratories on Quality Assurance for Laboratories, (ISO/IEC Guide 25) ISO/IEC 17025 on laboratory accreditation.
- Visited the participating laboratories and provided advice on good laboratory practice in the areas of interest.
- Discussed the organization of interlaboratory comparisons
- Discussed the possibility preparing in-house RMs

Follow-up activities to the missions have been proposed and implemented according to the needs as they became apparent during the mission. The missions were well received by the Member Bodies of the countries visited as well as by the interested laboratories as well. There is a need for CRMs and "training materials" mainly in the food, agriculture, biological and environmental fields. Further donations are being requested. If and when received these will be sent to laboratories in Developing Countries in Africa, Asia and in Central and South America.

There is a demand for more such missions and also for donations both training materials and RMs.

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2. [a] ISO Guide 30:1992 (1992) Terms and definitions used in connection with reference materials. ISO, Geneva
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9. [b] ISO/REMCO List of producers of certified reference materials (Information document of Task Group 3 "Promotion")
10. CITAC Guide 1 (1996) International guide to quality in analytical chemistry.

[a] Six ISO Guides prepared by REMCO, published by ISO
[b] This reference is updated once a year. A dynamic listing is obtainable by searching the COMAR database for CRMs (www.comar.bam.de)