Paul De Bièvre · Helmut Günzler (Eds.)

Traceability in Chemical Measurement

Springer

Prof. Dr. Paul De Bièvre
Duineneind 9
2460 Kasterlee
Belgium

Prof. Dr. Helmut Günzler
Bismarckstrasse 11
69469 Weinheim
Germany

Library of Congress Control Number: 2004114857

ISBN 3-540-43989-7 **Springer Berlin Heidelberg New York**

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer. Violations are liable for prosecution under the German Copyright Law.

Springer is a part of Springer Science+Business Media
springeronline.com
© Springer-Verlag Berlin Heidelberg 2005
Printed in Germany

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Cover design: *design & production* GmbH, Heidelberg
Production: LE-TEX Jelonek, Schmidt & Vöckler GbR, Leipzig

Printed on acid-free paper 52/3111/YL - 5 4 3 2 1 0

Preface

Not many terms covering concepts in measurement have circulated over the last ten years in the chemical measurement community around the world so intensely as the term traceability . It appears in the title of CITAC (Cooperation on International Traceability in Analytical Chemistry) since 1993. It is addressed almost yearly in Workshops of EURACHEM (A Focus for Analytical Chemistry in Europe). Documents of ILAC (International Laboratory Accreditation Cooperation) require it to be used in the process of accreditation. Standards and Guides of ISO (the International Organisation for Standardization) mention them frequently and insistingly.

In short, everybody talks and writes about traceability (because everybody talks and writes about traceability ?).

The 2nd edition of the International Vocabulary of General and Basic Terms in Metrology, VIM2, (1993) de nes it as the property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties .

Over the years the problem had arisen that the term traceability became more and more ambiguous because it was used for many different traceability concepts such as traceability of a sample (sample traceability), traceability of a document (document traceability), traceability of an instrument (instrument traceability) or -most important- traceability of a measurement result (measurement traceability). The VIM2 de nition clearly meant it to be related to a measurement result.

The revised edition of the VIM (VIM3), will probably ne-tune the term for traceability of a measurement result to be named metrological traceability . It is also likely that this de nition is improved to read something like property of a measurement result relating the result to a stated metrological reference through an unbroken chain of calibrations or comparisons each contributing to the stated measurement uncertainty .

Metrological traceability of chemical measurement results means the establishment of a relation to a stated metrological reference (a trace). This can be the de nition of a measurement unit which, of necessity, must go through a practical realization or (better: an embodiment) of that de nition. But in case of operationally de ned measurands (no units), metrological traceability can be to the result of an (internationally) agreed measurement procedure, or to the quantity value[1] carried by a measurement standard such as a certi ed reference material. All of these metrological traceabilities must be realized through an unbroken chain of calibrations or comparisons . The chain ensures that the metrological traceability of a measurement result has been established to a metrological reference which must be stated. Only when measurement results are traceable to a *common* metrological reference, is their direct metrological comparability possible, i.e. is their ability assured to be comparable.

This anthology contains 56 outstanding papers on the topic Traceability , published in the Journal Accreditation and Quality Assurance since its inception, but mostly in the period 2000 2003. They re ect the latest understanding of the concept measurement traceability -or lack thereof- and possibly some rationale(s) for the answer to the question why it is important to integrate the concept of measurement traceability into the standard measurement procedures of every analytical laboratory.

For one thing, the wide variety of opinions re ected in the papers demonstrates that we have not yet achieved a common understanding of the concept traceability and therefore not yet international understanding based on a concept which is unambiguously understood in the same way by everybody. Thus the international discussions will (have to) go on for some time because agreement must be reached. Measurement traceability (metrological traceability) is a cornerstone property of any measurement result. Only measurement results which are traceable to a stated common metrological reference (such as a measurement unit), are directly comparable . Comparability of results is essential in any border-crossing context, whether that is the estimate of the monetary value of goods, based on measurement results, or the rejection of goods based on measurement results for toxic substances contained in the goods, or when comparing results of clinical

[1] quantity (German: Messgröße , French: grandeur de mesure , Dutch: meetgrootheid) is not used here in the meaning amount , but as the generic term for the quantities we measure: concentration, volume, mass, temperature, time, etc., as de ned in the VIM.

measurements in case of international business and leisure travel. At least as important is the fact that proper evaluation of measurement uncertainty is only possible after metrological traceability has been established, i.e. after the trace or track has been decided by the analyst along which (s)he will organize the plan of the measurement in order to make sure that metrological traceability to a common metrological reference would be in place. That is needed because the measurement uncertainty in a measurement result can only be evaluated by combining the uncertainty contributions generated by every step along the metrological traceability chain.

This anthology hopefully is of bene t to both the producers and the users of results of chemical measurements: the basic concepts and the basic thinking in measurement are the same for both. Only their measurement uncertainty will differ.

Prof. Dr. P. De BiŁvre
Editor-in-Chief
Accreditation and Quality Assurance
Kasterlee 2004-04-02

Contents

Measurement principles for traceability in chemical analysis 1

Protocols for traceability in chemical analysis. Part I: De nitions and terminology 12

Protocols for traceability in chemical analysis. Part II: Design and use 24

Metrological traceability in laboratory medicine 29

Traceability and analytical chemistry 36

Do interlaboratory comparisons provide traceability? .. 45

From total allowable error via metrological traceability to uncertainty of measurement of the unbiased result ... 50

Practical considerations on the traceability to conventional scales 55

Traceability of (values carried by) reference materials .. 64

What can we learn from traceability in physical measurements? 70

How to achieve international comparability for chemical measurements 74

The key elements of traceability in chemical measurement: agreed or still under debate? 79

The practical realization of the traceability of chemical measurements standards 85

Link to the SI via primary direct methods 93

The role of reference materials 97

The measurement assurance concept in calibration and traceability at NBS/NIST 102

Lifetime of the traceability chain in chemical measurement 105

Pro cienc y evaluation as a traceability link in chemical metrology 109

Achieving traceability in chemical measurement a metrological approach to pro cienc y testing 114

Traceability issues in measurement 121

Comparative study of the presentations at the CCQM workshop on traceability 125

Traceability in laboratory medicine 128

Testing for foods derived from modern biotechnology: opportunities and limitations for metrology 134

A national traceability system for chemical measurements 141

Establishing measurement traceability in clinical chemistry 147

Clinical laboratory reference networks 160

One way of disseminating reference values with demonstrated traceability and demonstrated uncertainty to eld laboratories: IMEP 166

Implementation of traceability needs and perspective of the in-vitro-diagnosticum industry 175

Improvements in ef cienc y of production and traceability for certi cation of reference materials 177

Traceable measurement in clinical laboratories 184

A traceability protocol to the SI by gravimetric analysis 192

Reference samples for analysis of gas impurities in aluminium and titanium alloys: Features of production, certi cation and usage to ensure traceability of results 195

The use of certi ed reference materials in the Romanian traceability scheme 199

Traceable measurements of pH 206

The development of gas standards and calibration techniques for measurements of vehicle, aircaft and industrial emissions, natural gas, occupational exposure and air quality 212

Problems of traceability of total protein and catecholamine determinations in human urine 222

Traceability in routine chemical measurements: an example of application in the determination of CO_2 at atmospheric concentration 226

Traceability of measurement results of the effective acquisition time in gamma-ray spectrometry implemented by the pulser method 230

Practical ways in establishing traceability in chemical and other measurements in Mexico 239

Bene ts of the implementation of a metrological structure for water analyses 245

Validation steps for traceability of linear calibrated chemical measurements 253

Traceability, is it what we really want in our chemical measurements? 259

Traceability in measurement time for an update? 260

On the existence of primary methods of measurement. 262

Traceability and uncertainty A comparison of their application in chemical and physical measurement 264

Traceability and its role in interlaboratory comparisons (pro cienc y testing programmes), modeled on trace element determination in biological materials 267

Traceable property values of in-house reference materials 269

Primary reference materials and traceability chain for gas compositon 272

Traceability to units 275

Traceability without uncertainty: current situation in pharmaceutical industry 277

The role of reference materials in analytical chemistry 279

Meeting ISO/IEC 17025 Traceability Requirements: A New Guide with Worked Examples 284

UK delivery of traceable chemical measurements in the 21st century: building on the foundation of the VAM programme 287

Disseminating traceability in chemical measurement: Principles of a new EURACHEM/CITAC guide 290

CITAC Position Paper: Traceability in chemical measurement 293

Glossary of analytical terms 295

Contributors

Hassan Y. Aboul-Enein
Biological and Medical Research Department, MBC-03, P.O. Box 3354, Riyadh 11211, Saudi Arabia

Freddy C. Adams
Department of Chemistry, University of Antwerpen (UIA), Universiteitsplein 1, B-2610 Wilrijk, Belgium

Des Alphonso
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Elena Amico di Meane
Istituto di Metrologia Gusta vo Colonnetti del C.N.R., Strada delle Cacce 75, I-10137 Torino, Italy

Boris Anisimov
The National Physical Laboratory of Israel (INPL), Givat Ram, Jerusalem, 91904, Israel

V. P. Antipin
All Russia Institute for Light Alloys, Bldg. 2, Gorbunova Street, 121596 Moscow, Russia

Paul Armishaw
National Analytical Reference Laboratory, AGAL, Clive Road 3, Cottesloe, 6011 Western Australia, Australia

Charles M. Beck II
National Institute of Standards and Technology, Gaithersburg, MD 20899, USA

Brian Belanger
Visiting Committee on Advanced Technology (Retired), National Institute of Standards and Technology, Gaithersburg, MD, 20899 1004, USA

William Bell
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Chris Brookes
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Lutz Br g gemann
Department of Analytical Chemistry, UFZ Centre for Environmental Research, Leipzig-Halle, Permoserstrasse 15, 04318 Leipzig, Germany

Mirella Buzoianu
National Institute of Metrology, Sos. Vitan-B rzesti 11, 75669 Bucharest, Romania

Philippe Charlet
Bureau National de MØtrologie Laboratoire National d Essais, 1 rue Gaston Boissier, 75724 Paris Cedex 15, France

Ludmila DabrowskÆ
National Institute of Public Health, robÆrova 48, 100 42 Praha, Czech Republic

Paul De BiŁvre
Institute for Reference Materials and Measurements, European Commission JRC, B-2440 Geel, Belgium

Hansa D Souza
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Steluta Duta
National Institute of Metrology Sos., Vitan-Barzesti 11, 75669 Bucharest, Romania

RenØDybkaer
Department of Standardization in Laboratory Medicine, Frederiksberg Hospital, H:S Copenhagen Hospital Corporation ster Farimagsgade 5, DK-1399 Copenhagen, Denmark

Steve L. R. Ellison
LGC Limited, Teddington, Middlesex, TW11 0LY, UK

John Fleming
LGC Limited, Queens Road, Teddington, Middlesex, TW11 0LY, UK

D. Glavic-Cindro
Jo zef Stefan Institute, Jamova 39, 1000 Ljubljana, Slovenia

Irena Goldfeld
The National Physical Laboratory of Israel (INPL), Givat Ram, Jerusalem, 91904, Israel

Brian Goody
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

A. A. Grigorieva
All Russia Institute for Light Alloys, Bldg. 2, Gorbunova Street, 121596 Moscow, Russia

Bernd G ttler
Physikalisch-Technische Bundesanstalt (PTB), Bundesallee 100, 38116 Braunschweig, Germany

Gill Holcombe
LGC Limited, Queens Road, Teddington, Middlesex, TW11 0LY, UK

Paul E. Holland
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Lars Jorhem
National Food Administration, Box 622, 751 26 Uppsala, Sweden

Robert Kaarls
Netherlands Measurements Institute, AR, 2600 Delft, The Netherlands

Mary M. Kimberly
Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA 30341 3724, USA

Barnard King
Analytical Measurement Consultant, 25 Bolton Gardens, Teddington, Middlesex, TW11 9AX, UK

B. King
National Analytical Reference Laboratory, 1 Suakin Street, Pymble, NSW 2073, Australia

Matjaz Korun
Jo zef Stefan Institute, Jamova 39, 1000 Ljubljana, Slovenia

Jan Kucera
Nuclear Physics Institute, 250 68 Rez u Prahy, Czech Republic

Ilya Kuselman
The National Physical Laboratory of Israel (INPL), Givat Ram, Jerusalem 91904, Israel

Richard Lawn
LGC Limited, Queens Road, Teddington, Middlesex, TW11 0LY, UK

Wang Linzhen
National Research Center for Certi ed Reference Materials, 100013 Beijing, People s republic of China

Markus Lipp
Monsanto Company, 800 North Lindbergh Boulevard, St. Louis, Missouri, 63167, USA

Randie R. Little
Departments of Child Health and Pathology, University of Missouri School of Medicine, Columbia, MO, 65212, USA

M. MÆriÆssy
Slovak Institute of Metrology, KarloveskÆ63, 842 55 Bratislava, Slovakia

A. Marschal
Bureau National de MØtrologie Laboratoire National d Essais, 1 rue Gaston Boissier, 75724 Paris Cedex 15, France

A. MathiasovÆ
Slovak Institute of Metrology, KarloveskÆ63, 844 55 Bratislava, Slovakia

Roderick G. Millar
National Analytical Reference Laboratory, AGAL, Clive Road 3, Cottesloe, 6011, Western Australia, Australia

Martin Milton
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Yoshito Mitani
Centro Nacional de Metrologia, Mexico, Col. Centro, Apdo. Postal 1-100, QRO. 76000 Queretaro, Mexico

Mathias M. M ller
Institute of Laboratory Diagnostics, Kaiser Franz Josef Hospital, Kundratstrasse 3, 1100 Vienna, Austria

Gary L. Myers
Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA 30341 3724, USA

Bernd Neidhart
Philipps-Universit t Marburg, Hans-Meerwein-Strasse, 35032 Marburg, Germany

Ioannis Papadakis
Institute for Reference Materials and Measurements, Joint Research Centre European Commission, Retieseweg, B-2440 Geel, Belgium

H. Steffen Peiser
National Institute of Standards and Technology 638, Blossom Drive, Rockville, MD, 20850, USA

Alejandro Perez-Castorena
Centro Nacional de Metrologia, Mexico, Col. Centro, Apdo. Postal 1-100, QRO. 76000 Queretaro, Mexico

Margherita Plassa
Istituto di Metrologia Gusta vo Colonnetti del C.N.R., Strada delle Cacce 73, I-10136 Torino, Italy

Gary Price
P.O. Box 57, Menai, NSW 2234, Australia

Han Qiao
National Research Center for Certi ed Reference Materials, 100013 Beijing, People s republic of China

Paul Quincey
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Stanley D. Rasberry
National Institute of Standards and Technology, 31 Longmeadow Drive, Gaithersburg, MD, 20899, USA

William P. Reed
National Institute of Standards and Technology, Gaithersburg, MD, 20899, USA

Wolfgang Richter
Physikalisch-Technische Bundesanstalt (PTB), Bundesallee 100, 38116 Braunschweig, Germany

Rod Robinson
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Mike Sargent
LGC Limited, Queens Road, Teddington, Middlesex, TW11 0LY, UK

Michela Sega
Istituto di Metrologia Gusta vo Colonnetti del C.N.R., Strada delle Cacce 73, I-10135 Torino, Italy

Lothar Siekmann
Institut f r Klinische Biochemie, Universit tsklinikum der Universit t Bonn, Sigmund-Freud-Str. 25, 53127 Bonn, Germany

Ilona perlingo vÆ
National Institute of Public Health, robÆrova 48, 100 42 Praha, Czech Republic

Peter Spitzer
Physikalisch-Technische Bundesanstalt, Bundesallee 100, 38116 Braunschweig, Germany

Christoph Tausch
Philipps-Universit t Marburg, Hans-Meerwein-Strasse, 35032 Marburg, Germany

Philip Taylor
Institute for Reference Materials and Measurements, European Commission JRC, B-2440 Geel, Belgium

Milo Tich
National Institute of Public Health, robÆrova 48, 100 42 Praha, Czech Republic

Ian Uprichard
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

B. Vodenik
Jo zef Stefan Institute, Jamova 39, 1000 Ljubljana, Slovenia

Emil V lk ert
Chairman of EDMA WP Standardisation, Roche Diagnostics GmbH, Sandhofer Str. 116, 68305 Mannheim, Germany

L. Vyskocil
Slovak Institute of Metrology, KarlovskÆ63, 842 55 Bratislava, Slovakia

Andrew Wallard
Bureau International des Poids et Mesures, Pavillon de Breteuil, 92312 SŁvres, France

Wolfhard Wegscheider
Institute of General and Analytical Chemistry, University of Leoben, Franz-Josef Strasse 18, 8700 Leoben, Austria

Alexander Weisman
Chemagis Ltd., P.O.Box 9091, Tel-Aviv 61090, Israel

R. Wennrich
Department of Analytical Chemistry, UFZ Centre for Environmental Research, Leipzig-Halle, Permoserstrasse 15, 04318 Leipzig, Germany

Alex Williams
Chairman EURACHEM Working Group on Measurement Uncertainty, 19 Hamesmoor Way, Camberley, Surrey, UK

Peter T. Woods
Centre for Optical and Environmental Metrology, National Physical Laboratory, Teddington, Middlesex, TW11 0LW, UK

Adolf Zschunke
Bundesanstalt f r Materialforschung und -pr fung (BAM), Richard-Willst tter-Strasse 11, 12489 Berlin, Germany

Accred Qual Assur (1996) 1:3–13
© Springer-Verlag 1996

P. De Bièvre
R. Kaarls
H. S. Peiser
S. D. Rasberry
W. P. Reed

Measurement principles for traceability in chemical analysis

Received: 30 June 1995
Accepted: 30 June 1995

This publication is not subject to copyright; it includes contributions from the National Institute of Standards and Technology, an agency of the U.S. Government.

Paul De Bièvre (✉)
Institute for Reference Materials and Measurements, European Commission – JRC, B-2440 Geel, Belgium

Robert Kaarls
Nederlands Meetinstituut,
NL-2600 AR Delft, The Netherlands

H. Steffen Peiser
638, Blossom Drive, Rockville,
MD 20850, USA

Stanley D. Rasberry and William P. Reed
National Institute of Standards
and Technology, Gaithersburg,
MD 20899, USA

Abstract By the definition of the mole as a base unit for amount-of-substance measures within the International System of Units (SI), chemists can make chemical measurements in full compliance with established metrological principles. Since the mole requires exact knowledge of the chemical entity, which is often neither available nor of practical relevance to the purpose of the measurement, the SI units of mass or length (for volume) are unavoidable in the expression of results of many chemical measurements. Science, technology, and trade depend upon a huge and ever increasing number and variety of chemical determinations to quantify material composition and quality. Thus, international harmonization in the assessments of processes, procedures, and results is highly desirable and clearly cost effective. The authors, with relevant experience and responsibilities in Europe and America, have found some consensus in the interpretation of the metrological principles for chemical measurements, but believe open discussion should precede wide implementation by chemical communities. In fostering this dialogue, this paper shows, for instance, that more precise interpretation of the definitions for "traceability," "calibration," and "validation" is needed for present-day chemical measurements. Problems that face scientists in making measurements do not all vanish just by adherence to the SI. However, such compliance can improve communication among chemists and metrologists.

Key words Traceability · Mole · Definition · Measurements · Chemical metrology · Calibration · Validation · Reference materials

Introduction

Science, technology, and commerce require rapidly rising numbers and types of measurements that for good reasons can be trusted [1–4]. Worldwide acceptance of measurement results requires reliable, traceable, and comparable measurements for reduction of costs, efficient production processes, subsequent use of measurement data, realization of fair-trade conditions, and for internationally recognized and accepted laboratory accreditations. Physical measurements made in accordance with the International System of Units (SI), which was introduced under the Convention of the Meter (with status of an International Treaty), have satisfied many of these needs [5, 6]. Such measurements typically rely on a comparison of the measured quantity in the item concerned with the same quantity in a "standard." Chemical measurements are usually not made by comparison with an equivalent chemical "standard." Chemical measurements are not yet widely made in terms of the SI unit of amount of substance, the mole [7]. This paper will explore the possibilities

for bringing a stronger metrological foundation to chemical measurements and will specifically describe a role for reference materials in the traceability of chemical measurements to the SI [8].

Amount-of-substance measurements

Most chemists will agree that the majority of chemical measurements are, or could be, expressed as amount-of-substance measurements. When appropriate, they will in this paper be so described. However, whereas mass or length (volume) measurements at the smallest attainable uncertainty do not generally require a detailed understanding of the material whose property is quantified, amount-of-substance measurements require reference to the exact composition of the measured entity, to interfering impurities, and to the material – by composition, mass, or volume – within which that entity is measured.

In many chemical measurements one neither knows nor, at the time of measurement, wishes to know the exact composition of the matrix. To give an example, a metallurgical firm will receive ore shipments measured by mass in kilograms. Representative samples in the seller's and receiver's laboratories are measured for quality by the amount of substance of a specified metal element or compound per given mass of ore. It is unnecessary and far too complex to attempt amount-of-substance measurements on all components of the bulk. In exactly the same way, a food laboratory might measure the amount of substance (say lead) in orange juice in milligrams per liter (per cubic decimeter). The charm of the SI system lies in a coherence, which makes it possible to express all measured quantities in a combination of base and derived units [9].

Thus, whereas chemists have historically expressed analyses mostly by mass per mass, or as convenient percentages, or by mass per volume, they could express their measurements in amount of a specific substance per mass (mole per kilogram) or per volume. In cases such as pure materials and gases, mole per mole can be used. A percentage statement, or one in parts per thousand, million, or billion, is possible, though not recommended. In the SI system, as originally visualized, such dimensionless numbers as results of measurements are not favored. The quantitative result of any measurement should be expressed by a number "multiplied" by the appropriate unit associated with the measured quantity. As is further discussed below, this original preference proposed for the International System does not fit well with much of current practice in chemical measurements.

Towards harmony in amount measurements

There is no doubt that chemical measurements are and must be widely used in science and research, technology, engineering, and agriculture, as well as in regulatory issues, including boundary crossings, health control, environmental assessment, and commerce. A vast number of chemical measurements is made every year. Ever more will be needed for reasons of increasing complexities in human interactions with the environment [4, 10, 11]. For many measurements worldwide – such as ozone levels in cities and the upper atmosphere – it is necessary to maintain anchor points with long-term stability. More generally, all equivalent measurements should be made in harmony with each other [2], even when the practically needed and achievable reproducibility [9] has to be superior to the best attainable uncertainty in measurement relative to "true value." The relation to true value, however, remains the ultimate test for quality of a measurement [12]. At present it is a rather widely accepted opinion that, even when the relation to the true value is elusive, chemists in different laboratories equipped to make repeatable measurements can still make them comparable to one another by the use of a reference material (RM) [13–15]. The correctness of this concept will be discussed later.

The use of the mole

We seek to understand the reasons why chemists tend not to express their measurements by the mole, the SI unit of amount of substance, which is said to have been introduced at their request and which is appropriate for many chemical measurements. Some of the background has been discussed previously [7, 16, 17]. Here we hope to discuss:

1. Why and to what extent we advocate a coherent implementation of a wider use of "amount of substance" by chemists
2. Why the use of the mole itself does not solve pressing common problems in chemical measurements
3. Why certified reference materials can meet many, but not all, needs of chemists
4. How we hope a consensus either exists or can be achieved regarding the traceability of measurements to SI
5. Why RMs are necessary to promote harmony among chemical measurements worldwide.

The nature of chemical measurements

Measures of a mass, a length, or a time are not dependent on the composition and constitution of the material. By the definition of the mole, need exists for amount-

of-substance measurements to specify the entity among possibly many types of entities in the material under consideration. Amount-of-substance measurements are highly dependent on the composition and constitution of the material. Chemical measurements fall into four groups:

1. Measurements that can be expressed as a mole/mole ratio, the most basic measurements in chemistry, are typified by processes which react, interact, blend, or replace a described amount of substance A with a described amount of substance B. Included are solution concentration measurements when all solutes are known in a known solvent. Note especially that these measurements are independent of the magnitude of the unit mole. Note also that if these measurements are made by mass or volume determinations, the uncertainties in the corresponding atomic or molecular mass values must be taken into account.
2. Measurements that can be expressed as a mole/kilogram or mole/liter ratio are the most commonly made and are typified by a described amount of substance of compound A in an unspecifiable amount of substance B. Note that for these measurements the uncertainty of and relation to the unit mole, just as those applicable to the kilogram or meter, are involved.
3. Measurements that can only be expressed as kilogram/kilogram or kilogram/liter are unusual because they involve amounts of substances of unknown composition. Instances of this type are not really rare. Examples are particulates in air and condensed-ring compounds in tar. Chemists can be reassured that no mention of the mole is made or needed for expressing the results of such measurements.
4. Measurements that are described directly in terms of multiples and submultiples of the kilogram, the liter, or the mole are the measurements that provide the underpinning of chemical measurements in science, technology, and trade. They are typified by calibrations or validations of values of weight sets, reference materials, or instruments, as well as by determinations of the magnitude of the unit mole of a specifie compound (from the quotient of that compound's mass divided by that of a single ^{12}C atom), or of the Avogadro Constant.

Measurements for which reproducibility is more easily obtained than accuracy

Practical chemical measurements are commonly more precise than accurate. By that statement, we mean that the uncertainty of a measurement relative to the true value expressed, in either the mole or the kilogram, is greater than the range for repeated measurements in the same or even different laboratories at different times or by different operators under different environments.

By contrast, satisfactory practical mechanical, electrical, optical, and thermal measurements are often made adequately for the purpose at hand, even if less accurate than corresponds to the optimum achievable uncertainty relative to "true value" expressed under SI. Routine measurements in these fields can thus be expressed conveniently in terms of the relevant SI unit to an uncertainty determined principally by the uncertainty of the practical measurement in the "field." [1] Harmony among most physical and engineering measurements can be achieved to the uncertainty of the measurement in the field by traceability of all measures to the SI unit without invoking an intermediate "standard" [2] or RM.

In physical science there are occasionally instances where measurements need to be more reproducible than the lowest achievable uncertainty relative to the true value in SI units. Chemists, not just occasionally but as a rule, must achieve traceability of measurements by use of some standard, a reference material, a reference instrument, or a reference method [18]. The spread of these measurements made in different laboratories is often required to be smaller than the uncertainty with respect to true value. Nevertheless, one should state any such measurement in moles along with an assessment of the quality of its reproducibility. Such a statement will be different depending on its applicability within a laboratory, between laboratories, for a given method and environment, or in relation to an RM. When an RM is used, one must also include its often larger uncertainty of traceability to the SI unit. This uncertainty of the value of the RM must be included in the total uncertainty of the unknown.

Some important issues in all metrologyy

When discussing traceability of both physical and chemical measurements, one must be clear from the outset on the following conditions applicable to any measurement or measurement capability.

The type of measurement

First, we must specify the type of quantity: a base quantity such as temperature (a property that is coupled to a base unit within the SI), a derived quantity such as pressure (a property coupled to a derived unit, being

[1] The use of "in the field" is intended without detriment to measurements made in laboratories other than those whose main concern is the traceability link to the true value and the SI.
[2] Although for physical measurements one often speaks of various kinds of "standards," there is a functional difference, but no sharp distinction, in current usage between, say, a transfer standard and an RM.

the quotient of two or more base units within the SI), or even a quantity such as a hydrogen-ion concentration (a property that by convention is not commonly coupled to the SI, although perhaps it should be).

The relevant range of measurement

Measurements are needed over a total of many more orders of magnitude of a quantity than any one measurement methodology or instrument can achieve. For electric current, the measurement in a nerve fiber near 1 nA will differ from one applicable to a gigantic TA current in a magnet laboratory. At the two ends of the measurement range there is a non-trivial need to relate any "standard" in the smallest or highest range to the applicable SI unit itself. Needed amount-of-substance measurements, too, may range over more than 12 orders of magnitude.

The uncertainty statement

The uncertainty applicable to a measurement contains components for repeatability and reproducibility [9, 19, 20], caused in part by variability of measurement-relevant parameters. The uncertainty also depends on the individual making the measurement, the laboratory facilities used, and the environment during the measurement. Without some quality control over measurements, statements on relevant traceability can have little meaning. Such controls provide a laboratory with confidence in its operators and credibility to the outside.

Often of general interest is the reproducibility of measurements when operator, equipment or environment is not the same. One must commonly distinguish clearly between uncertainties applicable to measurements at different times (called repeatability [9]) and those made in different places (called reproducibility). A statistical analysis of homogeneity may be needed whenever a measurement is made on a representative sample from the object to be evaluated.

The similarity principle of metrology

In metrology in general, the closer the similarity between two specimens, the smaller the relative uncertainty of the measured difference between them and the easier it is to make a reliable measurement. Thus, by the use of suitable "standards," measurements in the "field" can become highly reliable and far less demanding and costly.

By this similarity principle it is possible to measure precisely and relatively easily small differences from an amount, or ratio of amounts, given by a "standard." RMs thus become very attractive vehicles for measurement traceability and quality. However, there is an associated problem: good reproducibility of comparisons between pairs of similar specimens is liable to mislead and, in practice, often causes underestimations of total uncertainties through failure to consider additional, large error sources.

Fitness for purpose

The achievement of smaller uncertainties than needed is usually uneconomical. In a practical way, realistic uncertainty assessments in relation to true requirements lead to economically sound planning for measurements to be fit for their intended purpose.

The classical measurement pyramid

A simple view of measurement services pictures the International Bureau of Weights and Measures (BIPM) with its international prototype kilogram and the seemingly perfect constants of physics at the peaks of huge pyramidal systems for all types of measurements, each with many levels. The first level below the apex lists the realizations of units at a number of national metrology institutes, passing on slightly more uncertain measurements to a much larger number of laboratories, which in turn service lower-tier measurement laboratories, until at the very bottom of the broad-based pyramids the workbenches receive calibrations that have become a little more uncertain at every intervening level. That system is simple to understand and works well for most industrial and legal services and for the control of small-scale markets, for which the step-by-step losses from impressive accuracies near the appropriate apex level are tolerable. An inverted pyramid may also become useful for illustrating traceability [7].

For chemical measurements, a possibly preferable system is illustrated in Fig. 1. Various possible forms of realization of traceability are given. They range from virtual lack of traceability to a fully "SI-bonded" measurement. The authors tentatively use the term "SI-bonded" to indicate a direct realization of the SI unit, as opposed to being traceably linked by way of measured values. Any user laboratory must seek a reference laboratory that is capable of providing measurement links of the adequate uncertainty and that provides the direct bond to the SI, if that is needed. The reference laboratory can in turn choose the traceability quality that it wishes to maintain, with the responsibility of fulfilling the corresponding competence requirements.

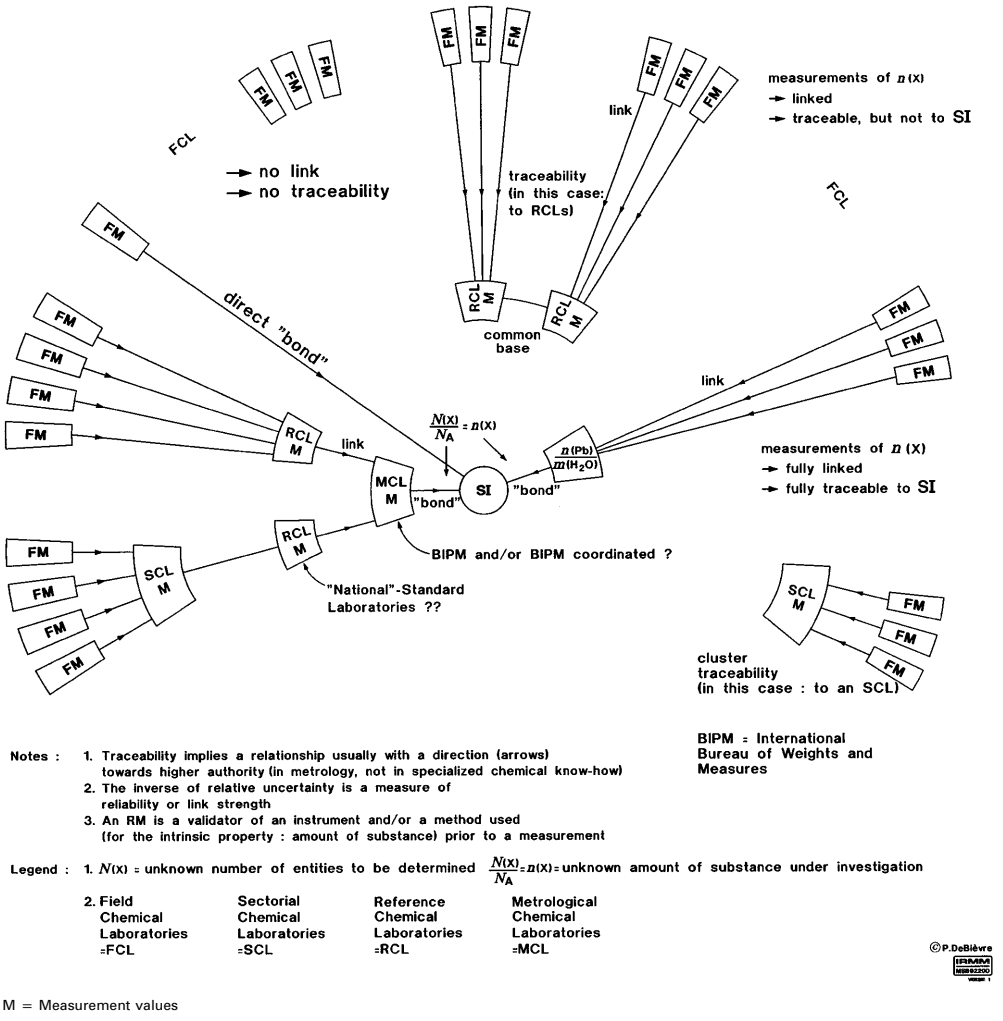

Fig. 1 Traceability Schemes for Field Measurement values (FM)

In modern high-technology situations, however, very high reproducibilities are frequently required. A good metrological system must provide means whereby any measurement station can have access to the highest needed level of the system.

Some important issues for the wider introduction of metrological concepts into chemistry

The above features are common to all measurements. However, some chemical considerations do not have a clear equivalent in physical measurements.

The diversity of chemical measurements

Whereas the types of measurements in physics and engineering do not exceed the numbers of base and derived units of the SI, chemical measurements are virtually infinite, equal to the number of chemical elements and compounds. Whereas the magnitude of, say, mass is defined independently of the entity for which it is measured, the amount-of-substance determination is made specifically relative to one entity. This situation should not lead to confusion, but some chemists fear that it might. For instance the "mole of nitrogen" is not defined until it is said whether reference is made to N_2 or N.

The word "mole"

Other potential difficulties for chemists arise from differences among molecular, molar, and the historic meaning of "mole" in chemistry [16, 17]. Some find the mole unsuited as a base unit in SI because, they argue, it is just a number of entities. Others find the use of "amount of substance" awkward, especially when the entity – for instance an ion – is not generally regarded as a substance. However, true and relevant some of these objections to current nomenclature and defini-

tions are, a consensus is most unlikely to be reached on any related change in the foreseeable future. Discussion on such a change here is therefore not relevant to more immediate opportunities for a useful consensus in amount-of-substance measurements.

The matrix effect

Whereas the measurement of, say, mass depends little on the character (e.g., density) of the object for which it is made, the measurement of amount of substance is strongly dependent on the matrix in which the entity resides. Chemists have always been concerned with interferences, but the general problem has become more important with the introduction of many powerful analytical-chemical instruments, the performance of which depends not only on specific physical properties of the entity to be measured, but also on the matrix within which the entity is contained. Chemists may wish for RMs for all entities to be measured in all kinds of matrices of interest to technology or trade. However, the production of every RM is a time-consuming expensive process. Chemists are thus faced with the unending problem of available resources imposing severe practical limits to the number of RMs that can be produced in conflict with the wide range of matrices of interest. Consequently, a most important contribution that basic chemical science must make is in the development of matrix-independent methods of measurement [21]. The challenge is to separate the one entity to be measured from the influence of all other entities in a mixture. By widespread abilities to do so, metrology in chemistry will reach its most desirable aim to make accurate amount measurements related to the mole unit. In the future, chemical metrology should be directed at the basic science on RMs whose link to SI is strong and at field methods whereby specimens can be compared reliably with the RMs, independent of matrix [7, 22].

SI recognizes derived units (products or quotients of base units)

Whereas the measurement of, say, mass can be stated as a fraction of a total mass (e.g., mass of a sample in a bottle), the amount of substance of a given entity can usually not be stated as a fraction of all amounts of substance in a material. One typically does not even know or care about all the other entities, and one certainly does not generally wish or need to analyze the material in terms of all its constituents. The SI system permits and widely encourages coherently associated units. The substance of interest should, where possible, be expressed in the SI unit, the mole. The other substances, the amounts of which are of no immediate interest to the determination, are quantified in terms of SI units such as the kilogram that do not distinguish entities.

Do physicists use the mole?

Geophysicists generally describe the composition of the universe or of the earth by mass percentages. They could use the mole, the amount of terrestrial substance of, say, aluminum. In the very processes leading to the birth of the elements, amount ratios are of prime interest. The end amount of Al would be expressed in mole per average terrestrial kilogram.

Measurement by ratio

Proponents of the SI for chemistry must consider that proportionality is deeply embedded in chemical thinking.[3] Many of the potentially most reliable analytical techniques – for instance isotope-dilution mass spectrometry – yield ratios in the first place. In complex series of ratio measurements the uncertainty propagation is more straightforward than when sums and differences from standards – such as for mass determinations – are involved. Consistent with the use of SI, the value of a ratio is called a "measurement" when numerator and denominator are multiplied by a unit and the related uncertainties have been evaluated.

Uncertainty about the nature of the entity to be measured

Chemists may not exactly know what is the entity they wish to measure in a material. A common example is moisture, say in grain. There are known to be continuous levels of strengths of chemical bonding of the water molecule in products. Mass loss on heating is routinely used to determine moisture in grain, but may cause error by including in the measured loss volatile compounds other than water and will also depend on the method used, principally on the temperature and time of drying. In giving the result in mole of H_2O per kilogram, one cannot assure that it was free water in the grain, where some of it was present as a different chemical entity. The same may apply to a metal element, say aluminum in an alloy. The user may well be interested in whether a mole of Al per kilogram refers to total aluminum or just the metallically bound – as opposed to oxide – aluminum. The result obtained in a measurement will then depend on the measurement

[3] By contrast, many measurements are initially additive, as is true for mass, time interval, and length.

method that is used. The use of amount-of-substance measurements can neither help nor hinder the chemist's need to carefully distinguish significant entity differences such as those due to chemical bonding and molecular association in a material.

Some vague usages of terms in measurement processes [23]

It is quite common for the chemical community nowadays to use the terms "calibrate" and "calibration" for any process that converts an observed value into a more reliable result, which is then called "corrected," "true," or "calibrated." We must also concede that RMs are sometimes used that do not have a matrix closely similar to that of the sample. To make matters worse, uncertainties associated with that situation are generally ignored. Insofar as the chemical community is aware of these problems, the call goes out for more and more RMs in appropriate matrices beyond available capabilities to produce reliable RMs. In order to arrive at rational conclusions on these issues, it is necessary to examine closely and to understand the proper role of "calibration" and "validation" procedures. In the following paragraphs we describe our views and hope that others will endorse them.

What constitutes a measurement?

A measurement of a specified property in an "unknown" material is a quantitative comparison by ratio or difference made of that property between a reference standard or reference material and the unknown or between relevant settings in an instrument, preferably in the appropriate unit for the quantity under investigation, provided:

a. Measurements of the relevant type and range, at the site where the measurement is made, are subjected to reliable uncertainty assessment.
b. The result (difference or ratio) is proven to be a known function of the true difference or ratio, or appropriately corrected for non-linearity, usually by means of a set of RMs.
c. The comparison applies only to a constituent part of either or both the RM and the "unknown," and the comparison is:
i. proven to be independent of the matrices,
ii. based on knowledge that the matrices are precisely similar, or
iii. quantitatively evaluated for variability with matrix
d. The result is given with its uncertainty including those caused by possible lack of linearity and by the above criteria applied to RMs involved.

Under these conditions, the comparison constitutes a measurement, and the value given of the property in the "unknown" has been determined.

Chemists will have an important reservation concerning this understanding of what constitutes the uncertainty of a measurement. Physicists and engineers may not, but chemists often are subjected to major sampling, stability, blank, and contamination errors. Chemists should include them in their total uncertainty estimates. The distinction between the measurement uncertainty and the degree to which the measured sample fails to represent the relevant larger bulk needs to be debated and discussed for consensus and understanding.

What is a calibration?

Let us begin with the ISO definition [9]: A calibration is a "set of operations that establish, under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure or reference material, and the corresponding values realized by standards." Applied to amount measurements, the "standards" would then be the values assigned to the RMs (of defined composition) at the stated uncertainty relative to the true value of the property, expressed in SI units, or relative to an internationally recognized, certified standard RM for the relevant property, range, and matrix composition.

An instrument or system is said to be calibrated for amount measurements only if, within a specified range, a value versus signal (response) curve has been evaluated against RMs including two near the ends of the range. At the present time, it is unfortunately quite common to use the term "calibration" to describe any process which converts a single observed measurement into a more reliable result.

What is a "validation"?

An RM can validate a measurement procedure (including the measurement instrument) [13] if, prior to its use for an unknown sample, it has been shown to give:

1. A quantitative response for the quantity (in the relevant range) to be measured
2. A response with a defined and acceptable repeatability
3. A response with a defined and acceptable reproducibility over changing times and measurement conditions
4. A defined and acceptable estimate of their overall intrinsic uncertainty

Traceability for chemical measurements

ISO in its vocabulary for metrological terms [9] defines traceability as follows: "property of the result of a measurement or value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties". Thus, the term does not apply directly to laboratories, but should be applied to the results of chemical amount-of-substance measurements. Every link in the traceability chain should consist of comparisons that are measurements in accordance with the above proposed meanings, which include the validation of measurement procedure by RMs. A measurement therefore often has strong links to internationally accepted RMs, but may be only weakly connected to the SI unit. For comparability among measurement laboratories, the strength of the link must be adequate to assure equity in trade. Weakness of the relation to SI may thus be acceptable, but the metrologically minded chemist will be disposed to aim for strongly linked reference measurements, methods, and instruments. They are based on simpler concepts with greater permanence and would be more easily understood by the wider public. Other definitions of traceability have been described [24–26].

Not all chemical measurements are, or should be, traceable to the mole. We have seen instances where the unit of mass was the proper SI unit for a quantitative measurement of a material of unspecified entities. There are chemical measurements that are not, but probably should be, referred, and preferably be traceable, to the SI unit. Color is used either simply as a qualitative attribute not subject to a measurement, or it is measured quantitatively by some spectrometry, where it may inevitably be subject to high uncertainties from both the measurement itself as well as from theory, such as the Lambert-Beer Law, but well understood in relation to SI.

The description of the relation of a measurement to an SI unit encounters a basic difficulty when the desired meaningful measurement result is a ratio, as in many chemical determinations. The magnitude of the unit then becomes irrelevant. Chemists err when they claim that the inaccuracy of their weight set relative to the international prototype is a component in their uncertainty budget. The self-consistency of their weight set is of course of paramount importance. Since that would include tareweights, internal balance weights, and sensitivity weights, the advice to use weights calibrated against the international kilogram is still generally good.

The quality of ratio measurements seems not to be concerned directly with the SI unit. The only essential condition is that the unit for the numerator be the same as that for the denominator. Traceability requirements for many amount-of-substance measurements, therefore, appear to concern not the unit mole, but a standard measured ratio, preferably between pure defined substances in one RM. Nevertheless, the authors propose that by consensus it shall be a rule for all measurements, where a choice could be made, that it shall fall on the SI unit.

Unusual are measurements for which a direct link to the mole is useful. We should probably not talk about traceability in that connection, because that term is defined as a relation between measured values. An acceptable chain of measurements for compound X of established purity, containing element E that has isotope ^{i}E and that would establish a link to the mole, then would take one of the following general routes: the amount of substance $n(X) \rightarrow n(E) \rightarrow n(^{i}E) \rightarrow n(^{12}C)$; or $n(X) \rightarrow n(E) \rightarrow n(C) \rightarrow n(^{12}C)$. The ratio of atomic masses $m(^{i}E)/m(^{12}C)$ is also involved in the definition, but that ratio is known with a negligible uncertainty compared with the other links in the chain. Clearly, only in a few instances will laboratories attempt to execute such a chain of measurements for a link to the SI unit. Is it fear that such a difficult process is involved in every chemical analysis that has kept so many chemists from using the mole as the way to express chemical measurement values? Or is it just habit and the convenience of a balance that subconsciously links amount of substance to amount of mass?

Laboratory accreditation

For laboratory accreditation, based on ISO guide 25 [27] and the EN 45001 standard, as well as for certification, based on the ISO 9000 series of standards [1], it is required that measurement and test results be traceable to international, defined, and accepted physical and physicochemical standards [28]. This requirement includes the use of conventionally expressed quantities and units in conformity with the SI [29]. It also includes the proper use of the concept of measurement uncertainty. All these are necessary conditions for reliance on the measurement results of another laboratory. Accreditation is granted when a laboratory has demonstrated that it is competent and capable of working in the above-mentioned sense. Technical trade barriers then fall away, and the needs and requests from industrialists, traders, and the general public can be met in the interest of open and fair trade, health, safety, and the environment.

For amount-of-substance measurements we include kilogram mass units, which are linked to the amount-of-substance unit in SI by the atomic-weight values. The latter differ greatly in uncertainty for different chemical entities, but are always available, with the best estimates by current knowledge of their uncertainties,

through the International Union of Pure and Applied Chemistry [30, 31].

Reference materials

In the above sections we have already illustrated some of the characteristics and uses of RMs. A more formal definition of RM by ISO is [9]: "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 of assigning values to materials." Extraordinary care in the production of RMs [15] is essential for effective, harmonized chemical measurements. Special features of certified RMs are carefully explained by that ISO document [9, 15] and their designation as measurement standard specifically authorized.

One may be inclined to suppose that for each type of chemical measurement there is a need to build a measurement system based on the pyramid concept [7, 32]. For the practicing chemist, however, this would be seen only as an unhelpful imposition. Previously discussed limitations of such a pyramid system would apply equally to the use of RMs. In addition, there is a major difficulty due to the previously discussed differences between RM matrix and sample matrices. Whereas for extrinsic measurements the composition of an RM or other traveling standard is of little or no concern, intrinsic amount-of-substance measurements are generally affected by the internal composition, structure, and texture of the RM.

The limited number of reliable RMs that can be prepared and made available leads to the use of possibly inappropriate RMs. When the matrix in a sample differs from that of the RM, reliable comparison may be very difficult. A provision for the support of critically important and accurate bench level measurements is needed. In such situations there is a better alternative: from the bench level a specimen with typical matrix properties is sent to a laboratory having competence appropriate for providing a "reference measurement." That value is communicated back to the "bench" where it provides a certified value – a kind of in-house RM – for comparison with routine sample measurements. Thus, the concept of reference measurement emerges as being equally as important as that of the RM. Chemical science has no other choice, since the combined output of RM-producing institutions could not possibly accommodate all the rapidly diversifying demands for all measurands in all matrices of interest.

In order to establish traceabilities of measurements, we advocate the structure shown in Fig. 1 where many types of linkage can be found, including but not limited to those terminating in SI.

A system for describing types of candidate chemical materials for RMs

We would also advocate the optional use of a descriptive materials system for candidate RMs. Firstly, we should have categories depending on the chemical nature of the materials (Table 1). Secondly, we should agree on RM classes dependent upon their degree of traceability (Table 2).

The isotopic composition of an element in a specimen can be established and expressed in abundances – that is amount-of-substance fractions or moles of iso-

Table 1 Categories of reference materials, determined by their chemical nature

Category	Kind of material	Description and criteria in terms of mateiral composition
A	High purity	Pure specified entity (isotope, element, or compound) stoichiometrically and isotopically certified as amount of substance, with total impurities <10 μmol/mol
B	Primary chemicals	As above, but with limits of <100 μmol/mol
C	Pure	One constituent >950 mmol/mol
D	Matrix	Matrix with one or more major constituents >100 mmol/mol
E	With minor constituents	Minor constituents in matrix <100 mmol/kg
F	With trace constituents	Trace constituents <100 μmol/kg
G	With ultra trace constituents	Ultra trace constituents <100 nmol/kg
H	Undefined	Entities unspecified or undefinable

Table 2 Classes of reference materials determined by their traceability

Class	Description and criteria in terms of traceability to SI
0	Pure specified entity certified to SI at the smallest achievable uncertainty
I	Certified by measurement against class 0 RM or SI with defined uncertainty by methods without measurable matrix dependence
II	Verified by measurement against class I or 0 RM with defined uncertainty
III	Described linkage to class II, I, or 0 RM
IV	Described linkage other than to SI
V	No described linkage

tope per mole of element – by comparison to synthetic mixtures of enriched isotope class 0 RMs of that element.

Certification of an elemental class 0 RM can be performed by metrology laboratories having the best scientific procedures for the establishment of traceability routes to the SI system. For every such RM the cost in facilities and experts' time is very high and in practice cannot easily be balanced against sales. Only a long history of the laboratories' reliability and their free and open discussions of problems, coupled with energetic self-criticism, will reassure the scientific and technological communities. Metrological quality, not cost and economy, should be the prime concern of operators within such laboratories.

All other classes of RMs are needed in much greater number and diversity. They are therefore of much greater potential interest commercially. Intercomparison between similar RMs is always helpful. Only one class IV or class V RM should be made available by consensus for a certain purpose, so that all laboratories are encouraged to make their measurements comparable to others through just one RM.

Validation of a measurement procedure including an instrument can be performed with an RM of class 0, I, or II, but only if differences in matrix or impurities are specified, small, and of proven limited influence on the uncertainty. The uncertainty of the RM relative to true value or the mole may be larger than the link between the measurements on the material and the RM. Traceability between measurements can be achieved with the help of all classes of RMs, but requires a clear statement on uncertainty. Traceability to the mole, if not by direct realization of the mole, can be established only by class 0 RMs. Their relation to the unit mole must be established by way of atomic-weight determinations or by direct atomic mass comparisons with carbon 12 atoms.

An example of a class I RM is an RM for which the amount of substance of an element has been measured by isotope dilution against a class 0 RM, provided the measurement has been shown to be in accordance with basic laws [7, 22, 33] of chemistry and physics.

Conclusions

Reliable chemical measurements in future will depend on more RMs with direct links to the SI as well as on RMs of greater diversity than are available now. Chemical science will be assisted by clear consensus definitions of traceability, certification, and validation, as well as by a widely accepted system for describing RMs by material composition, degree of traceability, uncertainty, quality, and purpose. Ultimately, chemists, physicists, and engineers benefit from adherence to the well-grounded and well-established discipline of metrology under a coherent system of units.

Acknowledgement The authors thank two reviewers of the manuscript, Robert Watters and Walter Leight, who provided numerous valuable suggestions.

References

1. International standards for quality management (1992) ISO Series 9000, Geneva
2. King B (1993) Analyst 118:587–591
3. Rasberry SD (1993) Fresenius J Anal Chem 345:87–89
4. De Bièvre P (1993) Int J Environm Anal Chem 52:1–15
5. Quinn T (1995) Metrologia 31:515–527
6. Page CH, Vigoureux P (1975) The International Bureau of Weights and Measures 1875–1975. National Bureau of Standards, GPO Washington
7. De Bièvre P (1994) Fresenius J Anal Chem 350:277–283
8. Terms and definitions used in connection with reference materials (1992) ISO Guide 30, 2nd edn, Geneva
9. International vocabulary of basic and general terms in metrology (1993), 2nd edn. ISO, Geneva
10. De Bièvre P (1993) Quimica Nova 16:491–498
11. Lamberty A, Moody J, De Bièvre P (1996) Accred Qual Assur 1:(submitted)
12. Cali P, Reed WP (1976) National Bureau of Standards, Special Publications, vol 422, pp 41–63
13. Marchandise H (1993) Fresenius J Anal Chem 345:82–86
14. Reed WP (1995) Fresenius J Anal Chem 352:250–254
15. Quality system guidelines for the production of reference materials (1995) ISO Guide 34, Geneva (in press)
16. De Bièvre P, Peiser HS (1992) Pure Appl Chem 64:1535–1543
17. McGlashan ML (1995) Metrologia 31:447–455
18. 5th International Symposium on Harmonization of Internal Quality Assurance Schemes for Analytical Laboratories (1993) Association of Official Analytical Chemists, Washington D.C.
19. Guide to the expression of uncertainty in measurement (1993) BIPM, IEC, IFCC, IUPAC, IUPAP, OIML ISO, Geneva
20. Kaarls R (1981) Metrologia 17:73–74
21. De Bièvre P (1995) Updated from original German, Ch. 7. In: H. Günzler (ed) Akkreditierung und Qualitätssicherung in der Analytischen Chemie, pp 131–156, Springer, Heidelberg (in press)
22. De Bièvre P (1993) Anal Proc 30:328–333
23. Management and quality assurance vocabulary (1986) ISO 8402, Geneva
24. Belanger BC (1980) Standard News 8:22–28
25. Belanger BC (1983) In: 37th Annual ASQC Quality Congress Transactions. American Society for Quality Control, Boston, pp 337–342
26. Rasberry SD (1983) In: 37th Annual ASQC Quality Congress Transactions, American Society for Quality Control, Boston, pp 343–347

27. General requirements for the competence of calibration and testing laboratories (1990) ISO Guide 25, 3rd edn, Geneva
28. Cigler JL, White RV (eds) (1994) National Institute of Standards and Technology Handbook 150
29. Quantities and units (1993) ISO Standards Handbook, Geneva
30. Atomic weight of the elements 1993 (1994) Pure and Appl Chem 66:2433–2444
31. De Laeter JR, De Bièvre P, Peiser HS (1992) Mass Spectrom Rev 11:193–245
32. Taylor JK (1993) National Institute Standards and Technology Special Publication 260–100, pp 1–102
33. De Bièvre P (1990) Fresenius J Anal Chem 337:766–777

Accred Qual Assur (1997) 2:168–179
© Springer-Verlag 1997

Paul de Bièvre
Robert Kaarls
H. Steffen Peiser
Stanley D. Rasberry
William P. Reed

Protocols for traceability in chemical analysis

Part I: Definitions and terminology

Received: 12 January 1997
Accepted: 31 January 1997

P. De Bièvre (✉)
Institute for Reference Materials and Measurements, European Commission – JRC
B-2440 Geel, Belgium
Tel.: 32-14-571-605; Fax: 32-14-591-978

R. Kaarls
Netherlands Measurements Institute, 2600 AR Delft, The Netherlands

H. S. Peiser, retired from National Institute of Standards and Technology, 638, Blossom Drive, Rockville, MD 20850, USA
Tel.: 1-301-762-6860; Fax: 1-301-762-1173

S. D. Rasberry · W. P. Reed, retired from National Institute of Standards and Technology, Gaithersburg, MD 20899, USA

Abstract The authors propose definitions and terminology for protocols on traceability links, generally to the international system of units, for specific chemical-analytical measurements in accordance with recognized principles of science. These definitions and terms could be useful in science, technology, commerce or law. A chain of such links leads from a measurand in a sample up to a unit in the International System of Units or, if unavailable, to a value on an internationally recognized measurement scale. The quality of such a chain is quantified by combining all recognized uncertainties estimated for all its links. These uncertainties of the measured values arise from many potential error sources. The protocols should give details of specific uses of reference materials, measuring instruments and standard measurement methods.

Introduction

This publication is the second of three contributions on traceability in chemical analysis. The first was published in this Journal [1] and deals with the general principles, whereas the third is planned chiefly to present examples, but also to suggest implementation procedures, to assess comments from chemical groups and to introduce possible modifications of concepts and definitions [2, 3].

The second contribution we present in two parts. In this first part we discuss definitions and terminology, mostly from recognized sources [2–9]. Some ideas in this article go beyond established international understandings; they are introduced for debate and possible refinement. The terms used here are responsive to the fundamental concepts under which chemical analysts can formally substantiate and record a traceability link. A chain of such links should lead from the value of a quantity in a sample up to a unit in the International System of Units (SI) [5] or, where that is not possible, up to a unit on an agreed and conventional measurement scale.

We address chiefly individuals or groups of analysts who aim to originate a protocol, that is a document recording the procedures for a specific link. That protocol establishes scientifically reliable measurements for the benefit of equity in trade and industry, as well as for legal interpretations of scientific realities.

A protocol must deal with the quality of the link based upon carefully estimated uncertainties [6, 7] from all foreseen error sources that remain after due precautions have been taken and after significant corrections have been applied where possible. The combined uncertainties of all links in the chain of links will then define the quality of a link to SI[1] or to some other rele-

[1] As has become customary [4], we use "the traceability (or the link) to SI" meaning "the traceability (link) to an appropriate unit or units in the SI"

vant scale unit. This quantitative assessment of quality of traceability to SI from combined uncertainties is not inconsistent with the metrological term of "accuracy" [2, 6]. It differs from popular meanings of "accurate" such as "free from error" and "highly exact". A traceable measurement may be adequate for its intended purpose, yet be inferior compared with the optimum achievable.

Fundamental understandings

By "protocol for *traceability*" [2][2] we here mean a documented *record* of a relationship, consisting of a "*link*", or *chain* of links, emanating from the *value* of a *quantity*[3]. The value is obtained by a *measurement* applicable to the *measurand,* the property of an entity in a *sample* which may consist of a pure material or incorporate the entity in a *matrix.* Each such traceability link is established for a stated chemical purpose and asserted by virtue of that measurement, which relates the forementioned value to another value in a *reference material* (see Fig. 1 for an outline of the use of RMs in typical chemical analyses) or to the response of a calibrated instrument (see Fig. 2). This measurement is carried out in a *responsible laboratory* using planned and described procedures, in a *validity interval* (time period) for a specific type of quantity (such as a concentration or other material property), within a limited *range* of magnitude of the quantity measured. The measurement is characterized, in part, by an observed *repeatability* and invariably by a substantiated estimated *uncertainty* [6] (including especially any arising from matrix effects), which is the sole indication of *quality* of the traceability relationship for each link or, when duly combined, for a chain of links. Thus, the uncertainty becomes the quantified indication of quality for the measured value itself. Wherever possible, the value of that measurement is ultimately made traceable to an SI *unit* (or units) [2, 5, 8], through *realizations* of those units. If not possible, the final link is made to a unit in an internationally recognized scale.

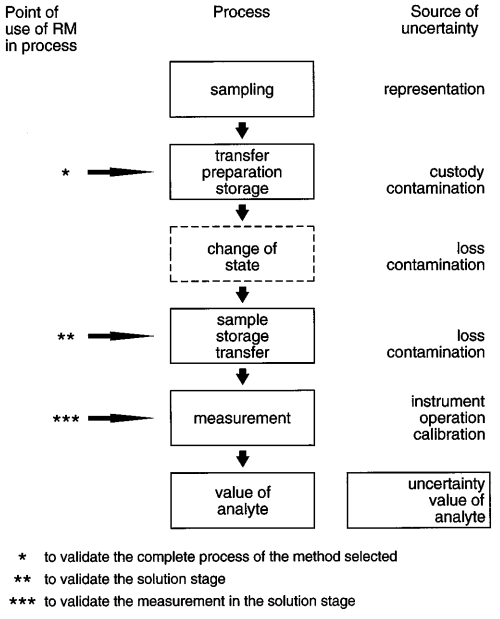

Fig. 1 Schematic of typical chemical analysis

Underlying concepts and definitions

The record

The record of a traceability protocol is a written document that may serve: in science and technology as reference; in product control as procedural "written standard"; in environmental comparisons as precept [10]; in trade and industry as basis for agreement, especially where border crossings are involved; and in courts of law as a means to judge whether specified limits are met[4].

The sample

For a chemical measurement the history and homogeneity of the sample must be established. Subsamples from the original sample are drawn for measurement. Although the selection of a sample in the "field" is important and often of concern to analysts, this paper deals only with the sample as delivered to the laboratory[5]. Two kinds of questions there can profoundly affect the uncertainty associated with the measurement [12]:

[2] Traceability is defined as follows [2]: "property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties"

[3] When using "quantity" [3] we will refer to a property, such as mass, length, amount of substance, or speed of light. We will not use "quantity" for describing a portion or bulk of a material, a chemical, or a sample, but rather consistently use "amount" of a sample or of rubber etc. Furthermore, we will try to distinguish such a general use of "amount" from "amount of substance" which is an SI base quantity requiring specificity of entity in terms of its chemical formula

[4] An elaboration on how a duly recorded traceability protocol might be used outside the professional chemical arena is not the subject of this paper

[5] Questions of chain of custody of samples or "trackability", a term recently proposed [11], and due representation of the population are not addressed in this article

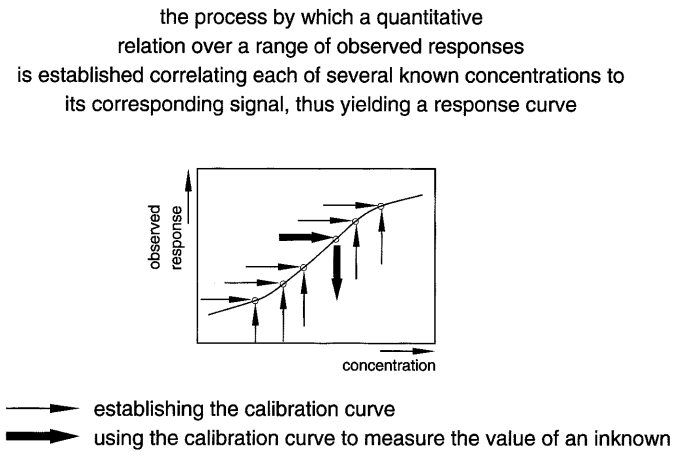

Fig. 2 Instrument calibration for analytical measurements

1. Is the sub-sample on which the measurement is made representative of the undivided sample?
2. Does the measurement of the intended quantity meet the measurement objective?

An important issue, for example, may be whether the measurement value is to apply to a specific sample or to the bulk of its source material. When surface contamination is the purpose of the measurement, total trace-element measurements could be misleading. Thus, surface sampling may have to be part of the protocol. Conversely, measurement methods that give results preferentially for surface layers may not be representative of the bulk of the subsample.

The measurand

The measurand is the selected property to be quantified by measurement of a constituent in a sample. For most analytical measurements, one prefers to select a quantity that is invariant on division of the material. Mass, amount of substance, volume etc. do not remain invariant on division and so are unsuitable for the characterization of a material.

Temperature remains invariant on division, but is unsuitable for characterizing a material because of the dependence of that base SI quantity on the external environment. To a lesser extent, external temperature and pressure conditions affect volume, too. In chemistry, the commonly used ratio of amount of substance (of a stable[6] entity) to mass of the material, in which it is uniformly contained, is not only invariant to contamination-free division, but is also independent of external environmental conditions, as long as they ensure the stability of the entity. In this respect amount-of-substance concentration per mass of material is suitable for characterizing a material, but not unique. Mass per heat capacity has similar invariance on division of the material and independence upon the environment. Concentration by mass per amount of substance has the additional unique property for a pure substance that these two base quantities are related by the molar mass of the entity. Thus, the analyst has the option of measuring either of the base quantities and from it deriving the other base-quantity value and hence the concentration with an appropriate increase in uncertainty.

Issues involved in the choice of measurand may be related to the purpose of measurement, which should be precisely and unequivocally identified and stated in the protocol.

The measurement

The measurement – a quantified comparison by difference or ratio between two values of the same quantity – shall conform to well-accepted principles of the chemical profession and good measurement practice [12–14].

The value

The value is the numerically expressed magnitude of a quantity either in a material or indicated by a calibrated instrument (see Fig. 2). An uncertainty must be associated with every value. Its important estimation is discussed in detail in the section "The uncertainty" below (see also [6, 8]).

Wherever possible, every value and every uncertainty that is cited in a protocol or quoted in the implementation of a protocol shall be expressed in a unit of the SI (with or without prefix) associated with a number commonly called the numerical value [5]. Thus, the value and its uncertainty are multiples or fractions of that SI unit. If an SI unit for the relevant quantity is not in

[6]The meaning of "stable" as here intended does not always indicate constancy of value. For radioactive materials, for example, a quantified change with time is here understood to be "stable"

common use, the value could be associated with an internationally accepted measurement scale or on the scale of a written procedure, perhaps involving an in-laboratory prepared reference material that is properly identified. In some cases, even a commercially available stock solution may serve this purpose. The long-term constancy of such values is an important issue, to be considered in the use of any reference (see section "The validity interval" below). Possible non-negligible instabilities of a reference value used in a protocol must be mentioned and appropriately taken into account.

The unit

In the physical and engineering sciences, the metric International System of Units for measurements [5] has become widely accepted throughout the world. An intended characteristic of all SI units is their unsurpassed stability and their independence of location and time. That characteristic of the SI contributes decisively its unique appeal to measurement science and technology. In technology, the use of SI is gradually gaining acceptance over many customary, especially non-metric, units. Chemists have no problem in using SI for mass comparisons, because of the convenience and sensitivity of analytical balances and the universal acceptance of the kilogram as the unit for mass[7]. Chemists also use SI units for measurements of volume, temperature, and some other quantities, but tend to avoid the use of the mole for amount-of-substance measurements, even when the chemical entity is well defined and although that quantity is the most meaningful for the consideration of chemical formulae, reactions, kinetics, and energy. In such situations the use of the mole in protocols should be expected. Traceability to SI, however, can be claimed relative to any SI unit that is appropriate for the measured quantity. That SI unit can be a base or a derived unit, or even a unit temporarily accepted for use within SI. When traceability is planned to derived units or composed of products or quotients of other SI units, it is often operationally necessary to achieve traceability to these SI units separately. This is the situation for the quantity of greatest interest for characterization of any material by chemical measurement: concentration measured in mole per kilogram or mole per cubic meter. Most laboratories may routinely maintain traceability to the SI units of mass and length at lower uncertainties than is needed for many protocols for chemical analytical measurements.

Whereas mass can be quantified irrespective of the intrinsic nature of a sample, amount-of-substance quantification requires the explicit chemical description of the entity pertaining to the measurand [15]. A description in mole units may be inappropriate for specific purposes when the composition of the chemical entity lacks specificity and would impose an objectionable molar mass or volume uncertainty. This limitation applies frequently in quantifications for purposes of trade, such as when describing amounts of polymers (with large uncertainty of molar mass and additional difficulty in defining its mean), a lithium compound (of variable isotopic composition), sodium carbonate (of undefined hydration), iron oxide (of undefined Fe valency), chlordane (composed of several molecules), nutritional fibers (vague definition), and numerous other substances.

The mole is associated with a specific chemical entity as defined by its chemical formula [15]. Its structural formula, isotopic composition, isomeric form, crystal structure, or chirality may have to be given in order to completely specify the entity of interest. The achievable uncertainty of amount-of-substance measurement is limited by that of its apparent molar mass. This consideration affects not only measurements on entities with variable molar mass, but those on pure substances. It is related to the traditional and important concern about purity.

Ratio measurements in analytical chemistry will often relate values in different units for the numerator and denominator. The most commonly used ratios between SI units are summarized in matrix form in Table 1 (adapted from [5]). Confusion may result when values are stated in different SI quantities. The pharmaceutical industry, for example, is careful to distinguish values in mg/g from values in mmol/g. It is important to retain the two units used in expressing a ratio such as mol/g. Differential measurements are often made, obtaining a ratio of ratios for which the numerator and denominator are generally expressed in multiples of identical pairs of units, e.g. (g/L)/(g/L). For such a ratio of ratios no great harm is done by stating, for instance: "the con-

Table 1 Frequently used ratios of SI units

Quantity	Amount of substance	Volume	Mass
Symbol of quantity	n	V	m
Name of SI unit	mole	(derived) cubic meter	kilogram
Symbol of SI unit	mol	(derived) m^3	kg
	mol/unit of quantity	m^3/unit of quantity	kg/unit of quantity
Unit of quantity/mol	mol/mol	m^3/mol	kg/mol
Unit of quantity/m^3	mol/m^3	m^3/m^3	kg/m^3
Unit of quantity/kg	mol/kg	m^3/kg	kg/kg

[7] In fact, the kilogram is the SI unit most likely to be redefined in the near future. If so, it will be in terms of an atomic-scale mass rather than by an artifact

centration in the numerator equals a (dimensionless) number of times the concentration in the denominator." An unlike pair of units for a ratio of ratios should be avoided, otherwise it becomes imperative to identify explicitly all four units for a meaningful description of the measurement.

On some occasions, protocols may involve SI units of time, electric current, thermodynamic temperature, or luminous intensity. These units are also base units of the SI. Traceability to SI can even refer to realizations of derived SI units, such as those for energy, pressure, and amount of electricity. Solubility per unit pressure may be quoted in $(mol/m^3)/(m \cdot s^2/kg)$ or in $(mol/m^3)/Pa$, but should not be written as $mol \cdot s^2/(m^2 \cdot kg)$ [5, 20], that is: not in reduced form relating to units of quantities not actually measured.

There are chemical measurements for which the decision to use the kilogram or the mole as SI unit depends on the type of deduction that is intended to be made from the measurement. Such examples could arise in polymer studies, in alloying, in isotropic displacements, in assessing electronically active impurities, in effects from variations in isotope abundances, or in those arising from chemical binding states. When documenting a formulation for an industrial reaction process, the use of mass proportions is appropriate even when an entity is known, because weighing devices alone are likely to be available for preparing the needed mixture. In ionic crystals and the alumino-silicates of the earth's crust, especially when dealing with their solid solutions, the concept of a molecular entity has little relevance. Although quantification under those circumstances is best achieved in terms of mass, certain amount-of-substance ratios represent important features of such materials. For instance the ratio of quadrivalent to trivalent ions in feldspars gives meaningful descriptions of attributes of rocks. For abundance of the elements on earth or in space, the common use of kilogram per tonne should with advantage be replaced by the amount of substance per kilogram or by the less common 'Cosmic Abundance Units' (atoms per 10^6 Si atoms).

The dalton is not accepted within SI [9]. It is perceived as a molecular mass of a specific species. In protocols, molar mass, relative molecular mass or unified atomic mass units should be substituted. The last of these, in conjunction with the SI mass unit, is currently acceptable with an added relative standard uncertainty of 10^{-6}.

Realization of an SI unit

A value – whether based on a specific material or on the output of a detector – when traced by a single link to a multiple or submultiple of an SI unit, at a stated low uncertainty, without requiring intermediate standards, reference materials, or significant empirical correction factors, is a realization of that SI unit. The conditions that are involved in a realization of an SI unit include all those involved in the recently proposed definition of a primary method of measurement [4]. Measurements made by a primary method are in principle realizations of an SI unit. For other realizations of an amount of substance, the entity must be defined and the purity of the material containing the entity must be determined. Conceptually, every entity might be deemed to require its specific realization of its mole.

Reference materials (RMs)

In all but a very few chemical measurements, use is made of reference materials (RMs) with appropriate pedigrees [17–19] (Fig. 1). Analytical-chemical RMs are generally certified by properties (such as concentrations) of entities and by values with their uncertainties, and are sometimes provided with limit values [17–19]. These values within their uncertainty ranges remain in-

Table 2 Categories of reference materials, determined by their chemical nature[a]

Category	Kind of material	Description and criteria in terms of constituent(s) certified
		Single major constituent
A	High purity	Pure specified entity (isotope, element, or compound) stoichiometrically and isotopically certified in amount-of-substance ratios with total impurities <10 μmol/mol
B	Primary chemicals	As above, but with limits of <100 μmol/mol
C	Defined purity	As above, but with limits of <50 mmol/mol
		Maxtrix types
D	With major constituents	Major constituents (in matrix) >100 mmol/kg or >100 mol/L
E	With minor constituents	Minor constituents (in matrix) <100 mmol/kg or <100 nmol/L
F	With trace constituents	Trace constituents <100 μmol/kg or <100 μmol/L
G	With ultra trace constituents	Ultra trace constituents <100 nmol/kg or <100 nmol/L
		Undefined
H	Undefined	Entities unspecified or indefinable

[a] A similar table was originally published [1] as basis for discussion. The version here presented incorporates significant changes. Further suggestions for improvements are welcome. – The proposed limits of the concentrations are arbitrary, and, for instance, preclude RM's for most organic entities in category A. Chemists may well use and state their own RM category designations

variant on division into subsamples. RMs are widely regarded and used in chemical analysis, just as are travelling and transfer standards in engineering and physics practice.

Tentative attempts have been made to categorize chemical RMs in terms of their material composition (Table 2) and to classify them by the length and strength of their traceability chain (Table 3). This classification might in future be generalized and expanded in terms of ranges of relative uncertainties.

Whereas an individual value, the result of a measurement, can be said to be "verified" by another measurement, a chemical method or procedure should be "validated", generally by success in application of that method to a certified RM. Validation remains undefined in the ISO vocabulary of terms in metrology [2]. A definition along the following lines is under discussion within EURACHEM/EUROMET: "A validation is a set of operations that establishes, under specified conditions and for a specific range, the suitability of a given measurement instrument, measurement procedure, or measurement method for a measurement of a specified quantity at a stated level of uncertainty." Validation usually is accomplished with the help of RMs and gives an opportunity to forge a link (see next section), but does not verify a given value or its uncertainty.

Table 3 Classes of reference mateirals, determined by the length and strength of their traceability[b]

Class	Description and criteria in terms of traceability to SI
0 Primary	Pure specified entity certified to SI at the smallest achievable uncertainty
I	Certified by measurement against class 0 RM or SI with defined uncertainty (no measurable matrix dependence)
II	Verified by measurement against class I or 0 RM with defined uncertainty
III	Described linkage to class II, I, or 0 RM
IV	Described linkage other than to SI
V	No described linkage

[b] This, like the preceding Table, was originally offered for discussion [1]. Currently it is not widely adopted. The authors welcome proposals for changes

By one convention, illustrated in Fig. 3, the validation of a measurement method, as replicated in the field, succeeds if the certified value of an appropriate RM falls within the estimated measurement uncertainty when the RM is measured using the method. That definition of validation does not require a mutual conformance condition in which the two values (that deter-

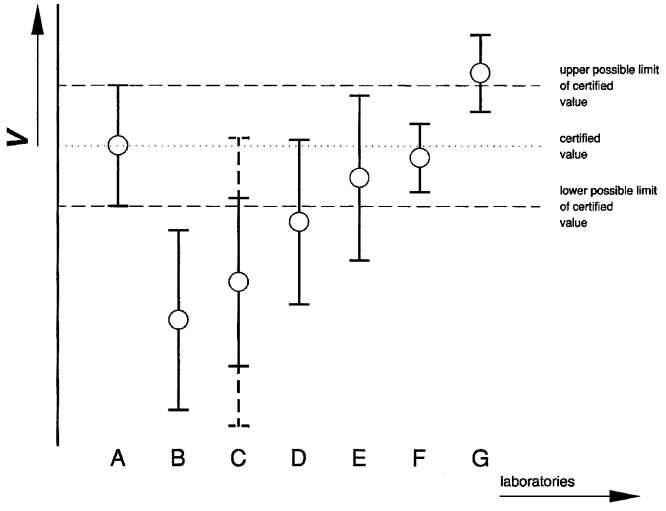

Fig. 3 Issues arising when considering the meaning of a certified value and its uncertainty in a certified reference material

A: is the RM's certified value and its uncertainty. The latter could be used to define the range of permitted values

B: is a measurement of the RM that fails validation as normally understood. An individual protocol, however, may rule that, for a stated purpose, agreement between even wider limits (than indicated by A and B) shall be considered good enough for a purpose at hand

C: is a measurement which - despite overlap of its uncertainty with that of the certified value - would by most definitions fail validation of the method under investigation, unless the uncertainty could be shown to have been underestimated. With this uncertainty corrected (see dotted line) the RM's certified value falls within the measurement's uncertainty range, thus meeting a possible minimum criterion for validation of the method

D: is a measurement by the method to be validated which meets the validation criterion, defined under C

E: is a measurement by the method to be validated that meets the validation criterion under C and the additional possible requirement that its value shall be in the uncertainty range of the RM

F: is a measurement by a new more advanced method also traceable to SI. It does not justify discontinuation of the use of the older RM with its original uncertainty

G: is also a measurement by a new more advanced method traceable to SI. Now the continued use of the older RM might be questioned

mined at the "field" laboratory and that given by the laboratory establishing the protocol) must both lie in each others uncertainties[8].

The values in a sample can be linked to the values in RMs in several ways (see Fig. 1) [14, 16–19]. This relationship can, for example, be established:

1. Directly by a controlled comparison of values from measurements on a sample with certified values for identical entities in closely similar RMs[9], or
2. Indirectly through an instrument calibration established for values for identical entities in closely similar RMs[8]
3. In conjunction with a specified method (or procedure) of measurement [8]
4. To confirm the sensitivity of an instrument or method to detect a trace impurity or contamination.

The link

A trace ("traceability" by definition [2]) is established by a link or an unbroken, single-path (compare footnote 18) chain of links that connects by measurement two or more values of the same indicated quantity in a unidirectional order of authority. One of these values usually refers to a sample that is representative of a material embodying the measurand. The other value may be of that quantity in a reference material, or indicated by an instrument reading, or that of an SI unit (see sections "The value" and "The unit" above (to be continued in the next issue)). Links in a chain, as here discussed, can be thought of as having direction, emanating from a sample and leading progressively through higher levels of authority and perceived expertise to the SI. Each link could then be likened to a vector with the magnitude of its uncertainty. Links without directionality, between laboratories at equal level (see Fig. 1 in [1]), are of great importance to a successful measurement network but are not further discussed in this article. The chain link with the largest uncertainty is the weakest in that chain. It is not exceptional in measurement practice for the link connecting the value in a measurand to the reference chain to be stronger than the rest of the chain is to SI.

The values associated with an established traceability link are given as a difference or ratio and must have an associated uncertainty. This, combined with the uncertainty of the higher link, determines the uncertainty of the value at the lower end of the link.

The responsible laboratory

For every link there is a qualified analyst or team of chemical specialists operating within a laboratory accepting personal and institutional responsibilities for the end result and its uncertainty, in full knowledge of the technical aspects further outlined below [12, 13].

The chemical analyst

In various sections of this paper, the authors appropriately emphasize the needed professional knowledge, experience, integrity and responsibility of the analyst. The handling of samples, the estimation of uncertainties, and the vigilance for unexpected errors also require some familiarity with statistics and possibly the help of a statistician as a consultant. However, the final assignment of uncertainties is the responsibility of the analyst who has actually performed the analyses.

The all-important manipulative skill of the analyst has yet to be underscored. No automated instrumentation or computer software can substitute for the analyst's dexterity and alert observation. Nevertheless, it must be understood that a disparity in this regard exists even between competent analytical analysts. No shame is attached to acknowledging a greater uncertainty in a given analysis than is achieved by the most experienced and the most skilled. During implementation of a protocol, an analyst, estimating a higher uncertainty for his own measurements than indicated in that document, may be demonstrating trustworthiness rather than doubt in his measurements.

Under the enormous ever-growing volume of needed analyses for production controls, environmental needs, and medical test programs, protocols have to be designed to be executed reliably by trained technicians. That protocol development, however, is and must be understood to be exclusively the proper role of the analytical chemist.

The validity interval

The validity interval is the time period during which relevant measurement operations are maintained in control with acceptable repeatabilities by each laboratory involved. This important limitation of validity of a traceability link is provided by design or could be im-

[8] An initially failed validation calls for repeat measurements or a reassessment in order to ascertain whether the uncertainties in the "field" were underestimated. Larger uncertainties may be acceptable for the purpose of the measurement. If so, the original measurement itself may be acceptable

[9] Even minor differences in matrices, however, will require determination of the significance of such differences and their effect on the uncertainties involved

posed from neglect. In order to assign a value to an RM, for example, a laboratory has to work within the validity interval for maintaining all relevant competences and procedures, such as to determine homogeneity and constancy of that RM. Thereafter, however, the measured, preferably certified, value of the RM remains valid, subject only to a validity period based on the RM's stability and requirements for its storage. These should be part of the RM's certificate with the aim of protection against contamination, temperature extremes etc. [18, 19].

The range

The range of values of the measured quantity is defined by the upper and the lower value for which the record is valid. At and between these extremes repeat measurements may not differ by more than an indicated uncertainty (see below). A zero should not be used to specify the lower end of a range. For small values of a measurand, a protocol may indicate the needed repeatability[10] of measurement or specify the smallest required detectable value.

Traceability to the SI

Wherever possible, a traceability chain of measured values terminates in an SI unit. When the base unit for mass is appropriate, this relationship is readily achieved through a mass standard, calibrated in terms of the kilogram prototype. The concept of traceability to SI has to be more carefully considered when conformity to SI depends on the SI concepts in the definition of the SI unit itself.

Basic to chemistry is the numerically simple (stoichiometric) proportion of entities in reaction and in formulae of compounds. The chemical analysts' purposes are therefore well served by comparing numbers of defined entities. The numerical value (see sect. entitled "The measurement" above) for the SI measurement of the amount-of-substance quantity fits those purposes. Historically, however, few were the analytical-chemical methods by which entities could be counted or counts of different entities could even be compared. With the nearly correct assumption that molar masses of the elements from terrestrial sources are constants of nature, chemistry made spectacular progress by measuring mass and converting to amount of substance by the factor of Avogadro's constant. Their measurements were thereby burdened by the uncertainty in that constant – which for many purposes cancels – as well as by the uncertainties in the molar masses – which do not cancel and which become significant as the total uncertainty of a measured value is reduced. For good measurement practice, protocols should therefore prefer traceability to the mole, as is stated in sects. entitled "The value" and "The unit" above.

The SI traceability statement for a chemical composition of a material cannot be completed by the traceability to the mole of one entity. The statement must include reference to another quantity, which could be a mass, a length, some other quantity, or even an amount of substance of another entity. Examples of such traceability statements for chemical composition could refer to a mole and the kilogram for the concentration, say, of a known element in an ore. The source of the element in that ore is then described in terms of the ratio of SI units mol/kg. Similarly by the SI units of mole and meter one could designate the solution of a defined organic compound, that is in mol/L. For some important chemical measurements we need to find traceability to SI for the mole of one entity as well as the mole of another entity. These moles are not identical and need separate traceability chains (see next paragraph). Measurements by mol/mol ratios are appropriate, for instance, for a trace impurity of known composition in a pure compound, or for an amount of isotope-to-element substance ratio (abundance).

The ratio measurement between the numbers of two entities establishes an amount-of-substance ratio that might satisfy the principal purpose of a chemical measurement. In measurement science, however, under the SI system, relative quantities do not fully satisfy the concepts. There remains an underlying requirement for all values to be individually traceable to the appropriate SI unit. For amounts of substance that unit is itself a number, the number of carbon-12 atoms of mass 0.012 kg. The magnitude of a given amount of substance, that is the numerical value of the SI quantity, is the number of defined entities divided by the SI unit number. It follows that equality of amount of substance is equality of the numbers of the two relevant entities.

If, in a ratio of amounts of substance, both of the two numbers of entities are traceable to numbers of carbon-12 atoms, and if the ratio between the entities is obtained by an appropriate measurement, the measurement is perfectly true to the concept of that SI unit. Calling that relationship traceable to SI is thereby reasoned and should be considered correct. Just as for mass measurements, the realization of amounts of sub-

[10] "Repeatability" [2] is defined as the: "closeness of the agreement between the results of successive measurements of the same measurand carried out under the same conditions of measurement." Repeatability should be distinguished from "reproducibility" for which the closeness of the agreement concerns the results of measurements (of the same measurand) that are not necessarily made successively and not under the same conditions, by the same method, or in the same laboratory

stance to SI could be left as a prime responsibility to national measurement laboratories.

That realization will often have larger uncertainty than relative measurements of entities by analysts. This should not surprise; similar conditions commonly apply throughout metrology. One can link the value of a good-quality gram standard to another similar standard with smaller uncertainty than that with which either can be linked to the international prototype kilogram. The designer of the protocol must carefully consider to what extent uncertainties in the realization of the SI unit cancel for the purpose of a given measurement. Not the calibration, but only the self-consistency of a mass-piece set, built-into – or external to – a balance, may enter into the uncertainty of a mass ratio. Similarly, the amount-of-substance ratio may have an uncertainty partially independent of that of the realization of the SI unit.

Summing up conclusions in this section: traceability of chemical measurements to SI involves concepts other than a direct comparison with a physical standard. Uncertainties may relate principally to values produced in the laboratory. The uncertainties of the links of two values of the same quantity to the SI unit may be larger than the uncertainty of the link between these values made in accord with the concepts of the SI.

The repeatability of a measurement

All uncertainty estimates start with that associated with the repeatability of a measured value obtained on the unknown. It is neither required for the sake of quality control, nor could it always be economically justified, to make redundant determinations of each measured value, such as would be needed for complete statistical control. Repeat measurements of a similar kind under the laboratory's typical working conditions may have given satisfactory experience regarding the range of values obtained under normal operational variations of measurement conditions such as: time intervals, stability of measurement equipment, laboratory temperature and humidity, small disparities associated with different operators, etc. Repeatability of routine measurements of the same or similar types is established by the use of RMs on which repeat measurements are made periodically and monitored by use of control charts, in order to establish the laboratory's ability to repeat measurements (see sect. entitled "The responsible" laboratory above). For this purpose, it is particularly important not to reject any outlier, unless cause for its deviation has been unequivocally established as an abnormal blunder. Rejection of other outliers leads a laboratory to assess its capabilities too optimistically. The repeatability in the "field" of a certified RM value represents the low limit of uncertainty for any similar value measured there.

When fewer than about 100 measurements of the same type are needed, the use of control charts becomes impractical. A few repeat measurements made within the routinely encountered range of relevant values is sufficient to estimate the repeatability of a single measurement. Difficulty arises only when a measurement type or procedure is inordinately time-consuming or costly to replicate. Relevant examples are: the measurement of an unusual trace constituent in a sample of minimal size, and a lengthy isotope dilution mass-spectrometric determination. The analyst is then required to depend on general experience of reliability of a method and would be wise to estimate the uncertainty with special care.

Just as the value obtained by measurement of a sample carries an uncertainty, so does the laboratory 'in-field' realization of the certified value of an RM. If the purpose of the measurement is to validate (Fig. 3) a procedure or instrument calibration, the measurement uncertainty estimated by the laboratory should include the certified value of the RM. If the measurement in the laboratory consists of determining the difference of the value in an unknown with that in an RM, the latter is taken as the reference value. Only when evaluating the uncertainty of the unknown to SI, the RM's certified uncertainty must be combined with that of the in-laboratory measurement of the unknown.

The uncertainty

Central to the protocol is the uncertainty[11], symbol u, or, if expanded, U, and u_c or U_c when combined [6]. It is expressed in the same SI units as the value V to which it refers. For propagation of uncertainties by mathematical formulae, relative uncertainties, such as U/V, are often needed.

All uncertainties are estimated and necessarily themselves uncertain. They should not be given to more than two significant figures; that is, to at most 1% of the total uncertainty. Individual smaller uncertainties thus become neglected. Uncertainties are generally given to be symmetric for positive and negative deviations from the evaluated best value[12].

[11] The importance of reliable uncertainties in protocols cannot be overstressed; they distinguish between insignificant differences and dangerous discrepancies

[12] On occasions, chemists designing a protocol recognize good reasons for expecting an asymmetry of likely deviations, such as for analyses of trace constituents that cannot be less than zero, of pure chemicals that cannot be more than 100%, or the molar mass of hydrogen gas (obtained by electrolysis) that cannot have less than zero content of deuterium. Under such circumstances, well-reasoned asymmetries of uncertainties may be introduced into a protocol