See also
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Assuring Quality of Analytical Measurement Results: The IUPAC Role

by Ales Fajgelj

Over the past 30 years the value of world trade has risen dramatically. In 2005 it amounted to almost USD 17 trillion (trillion = 10^{12}; see figure 1). A large proportion of this trade is dependent upon chemical analyses, since food, pharmaceutical products, medicines, ores, and chemical products in general represent the largest groups of trading items. To gain acceptance in the trading process, the quality of analytical measurement results needs to be assured and demonstrated. The term *quality of analytical measurement results* encompasses, among others, comparability of analytical results, their accuracy, reproducibility, metrological traceability, measurement uncertainty, and more.

IUPAC has a long tradition of activities related to quality assurance of analytical measurement results. The formation of the IUPAC/ISO/AOAC Working Party for Harmonization of Quality Assurance Schemes in 1978 was an important milestone. At that time, efforts were focused on harmonizing requirements related to method validation studies (or laboratory collaborative studies), which had been conducted by a number of organizations around the world. IUPAC, offering a completely neutral scientific forum for harmonization activities, was identified as the most appropriate body to host the working party. Today, after almost 30 years, that working party is the IUPAC Interdivisional Working Party for Harmonization of Quality Assurance (WPHQA), which is part of the Analytical Chemistry Division (ACD). The short description of activities that follows and the documents cited here are aimed at highlighting the important role that IUPAC, and specifically the WPHQA, plays in ensuring the quality of analytical measurement results.

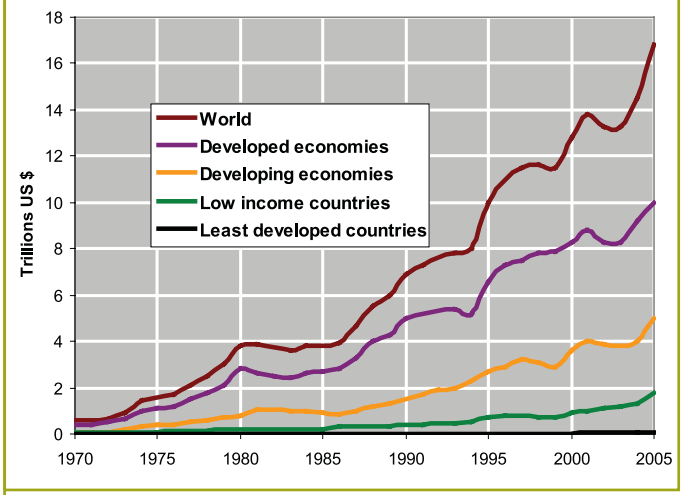


Figure 1: World Trade Development 1970–2005 in Trillions of USD (Source: United Nations Conference on Trade and Development).

Method Validation

The use of standardized methods of analysis in analytical chemistry is one of the most traditional ways of achieving comparability of measurement results. Especially in food analysis, agrochemicals, organic analysis, and other analytical areas where unstable samples and/or measurands are analyzed, the use of standardized methods is often prescribed by legislation.

Two IUPAC internationally harmonized protocols have for many years served as a basis for validation and adoption of standardized analytical methods (procedures). The first is the IUPAC "Protocol for the Design, Conduct, and Interpretation of Collaborative Studies,"[1] and the second the "Harmonized Protocols for the Adoption of Standardized Analytical Methods and for the Presentation of their Performance Characteristics."[2] These principles of collaborative studies for method validation are still widely applied by the AOAC International, as well as by the International Standards Organization (ISO). However, the world is changing rapidly and with the fast development of analytical instrumentation and the availability of new analytical techniques and procedures the prescription of methods to be used is sometimes a limiting factor. Responding to the situation, the WPHQA has opened the door for single-laboratory method validation, also known as in-house method validation. The principles presented in the IUPAC "Harmonized Guidelines for Single Laboratory Validation of Methods of Analysis"[3] and in the proceedings of the Joint AOAC Int./FAO/IAEA/IUPAC International Workshop on the *Principles and Practices of Method Validation*, held in 1999 in Budapest, Hungary,[4] have been accepted as official guidelines by the CODEX Alimentarius Commission.

Quality Control and Proficiency Testing

Established internal quality-control practices and regular laboratory participation in proficiency testing constitute another very important pillar of quality assurance in analytical chemistry. Again, the contributions of the WPHQA have been indispensable. Two IUPAC internationally harmonized documents, namely the "International Harmonized Protocol for the Proficiency Testing of (Chemical) Analytical Laboratories"[5] and the "Harmonized Guidelines for Internal Quality Control in Analytical Chemistry Laboratories"[6] still provide the basic rules, which have received wide international acceptance and utilization.

Assessment of laboratory performance based on a z-score evaluation introduced in the IUPAC proficiency testing protocol became the most frequently used approach in evaluation of laboratory performance. Considering the experience gained over 13 years, the protocol has been updated and a revised version titled "The International Harmonized Protocol for the Proficiency Testing (PT) of Analytical Chemistry Laboratories" was published in 2006.[7] To supplement this so-called classical PT approach, the WPHQA recently initiated a separate project on the Selection and Use of Proficiency Testing Schemes for Limited Number of Participants (Chemical Analytical Laboratories).[8] In case of a small number of participants, some limitations on statistical applications may appear and this project is aimed at elaborating some additional approaches for evaluation of participants' results and their reporting.

However, neither of the above described external quality assurance schemes replaces the internal laboratory quality control. They actually should go hand in hand. The ISO/IEC 17025 standard, which serves as a basis for laboratory accreditation, is very general and brief in its Clause 5.9 titled "Assuring the Quality of Test and Calibration Results."[9] It urges laboratories and accreditation bodies to use separate guidance, specifically prepared for their field of application. The large number of citations in scientific literature and translations of both IUPAC documents into numerous languages, including the translation by the Japan Chemical Laboratory Accreditation into Japanese in 2001, reflect the importance of this IUPAC activity for quality in chemical analytical laboratories.

Metrological Traceability and Recovery

One of the most important parameters defining the quality of analytical measurement results is comparability. Comparability of measurement results is based on metrological traceability, which allows results to be compared independently of the time, place, analyst, and procedure used. Two aspects of this description are very much IUPAC's concern. The first is the metrological traceability of chemical measurement results. It is a term often used and cited, but without a firm agreement within the measurement/scientific community regarding associated concepts, their understanding, and requirements. In recent years, IUPAC representatives have been deeply involved in the ongoing revision of the *International Vocabulary of Basic and General Terms in Metrology*, trying their best to assure that specifics of chemical measurements are considered in this guide.

comparability: property of measurement results enabling them to be compared because they are metrologically traceable to the same stated metrological reference; independent of:

Time | Place | Laboratory/operator/procedure

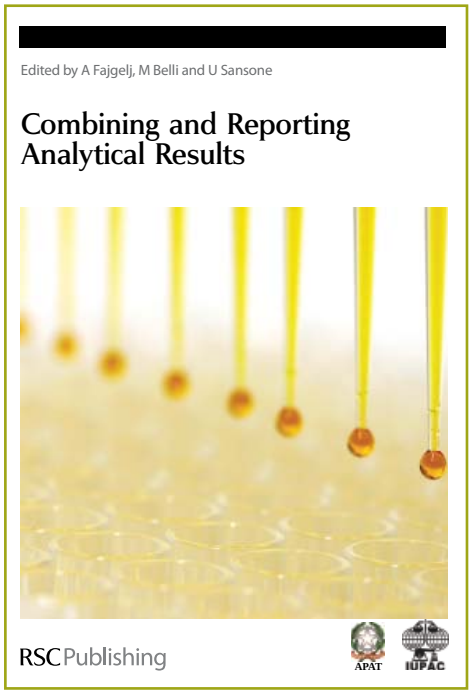
Comparability of measurement is the ultimate goal of quality assurance and is a prerequisite for smooth trade at the national, regional, and global level.

In addition, the WPHQA-coordinated project Metrological Traceability of Measurement Results in Chemistry[11] is also dealing with this issue. Concepts developed in the framework of this project will be underpinned with examples (various scenarios) for establishing traceability in chemical measurement, to provide clear and practical explanations for all levels of laboratories—from field laboratories to metrology institutes. The guide will clarify terms like metrological reference, traceability chain, and metrological hierarchy, and describe the different roles that organizations

in the global metrological infrastructure (metrology institutes, reference material producers, laboratories, etc.) have in establishing metrological traceability. The guide is to be presented during the IUPAC General Assembly in Torino, Italy, in August 2007.

In discussions about metrological traceability of measurement results one frequently hears the claim that the traceability chain in chemistry has been broken. This claim is often related to the chemical process, destructive analysis, where the sample and measurand are converted into the physical and chemical form suitable for the selected measurement technique/instrument. Such conversions (digestions, extractions, etc.) may result in the loss of measurand, incomplete conversion into the required chemical/physical form, or even contamination, and are very much dependent on the procedure used.

In the context of this article, recovery is defined as the proportion of the amount of analyte, present or added to the analytical portion of the test material, which is extracted and presented for measurement. It can be illustrated with the practical example of the determination of pesticide residues in food. The amount of the extracted, and consequently measured, pesticide residue will depend on the procedure used. In the discussion above, the use of standardized methods has been identified as a possible solution to the problem. However, this is only part of the overall process assuring the comparability of measurement results. There is also different legislation in different regions of the world. The European legislation in this specific case requires reporting of results corrected for recovery; this is not the case in the USA. It was a major IUPAC success when IUPAC, ISO, and AOAC Int. agreed on the technical principles for recovery determination provided in the "Harmonized Guidelines for the Use of Recovery Information in Analytical Measurement,"[12] including the fact that recovery values need to be established as a part of the method validation process and be available if necessary, whether or not recoveries are reported or results are corrected. On this basis measured values can always be converted to corrected values and vice versa, thus enabling comparability of results on a global scale.



Combining and Reporting Analytical Results

The correction of results for recovery, or not, is only one illustrative problem related to reporting of analytical results. There are many more. Combining measurement results obtained by one analyst in one laboratory employing one measurement procedure, and using one measurement technique is the starting point for the two questions: How to report the associated measurement uncertainty? and How to establish and demonstrate the metrological traceability of combined results? The complexity of these questions expands with the increasing number of measurement procedures/techniques, and with the number of laboratories and measurement results that need to be considered.

Continuing the tradition of organizing workshops and symposia, the WPHQA, together with the Italian Agency for Environmental Protection and Technical Services, organized the international workshop Combining and Reporting Analytical Results—The Role of (metrological) Traceability and (measurement) Uncertainty for Comparing Analytical Results, in March 2006 in Rome, Italy. The wide international interest in the topics covered by the workshop program was reflected in the number of cosponsoring organizations, namely: Centro Svillupo Materiali. S.p.A, the International Atomic Energy Agency, the Consultative Committee for Amount of Substance—Metrology in Chemistry (CCQM), International Bureau of Weights and Measures, the Co-operation on International Traceability in Analytical Chemistry, the

ISO Committee on Reference Materials and the United Nations Industrial Development Organization.

Most lectures were prepared as full text for the proceedings book published by the Royal Society of Chemistry.[13] Contributions provide an overview of current practices used in different laboratories from different scientific fields to combine and report measurement results, at the same time they describe some basic scientific considerations as well as discussions related to legislative aspects. Practical examples from environmental monitoring laboratories, reference material producers, clinical chemistry, and the top metrological level are included.

Although the workshop was a successful event, it represented only one small step forward in providing answers for dilemmas analytical chemists face in combining and reporting analytical results. Much still needs to be done. In April 2007 a workshop was organized by CCQM focusing on calculating the CCQM Key Comparison Reference Values.

Harmonization Today

From this article, the reader should recognize that in its harmonization efforts IUPAC has never been working alone. There has always been cooperation with relevant bodies and other organizations. Cooperation is considered the only possible approach to achieving agreement at a global level. However, in the 1970s and early 1980s, the international standardization and harmonization scene was smaller than today. Cooperation between AOAC Int., ISO, and IUPAC was sufficient for assuring appropriate arrangements and the flow of information. The situation has changed drastically in the last 20 years. Metrology, accreditation, and standardization infrastructures have developed at all levels.

A careful look into the distribution of the most influential organizations and bodies related to standardization and harmonization in the area of analytical chemistry reveals that there is a strong concentration in the northern hemisphere. The fact is that barriers of trade exist and are still growing between developed and developing economies. One reason for this is the standardization and application of very strong quality requirements in the accreditation process, without provision of the required assistance and support to developing countries. In this respect, the role of independent, non-commercial, non-profit scientific organizations like IUPAC is of utmost importance. The second important way of overcoming such differences is by open access to scientific literature (e.g., via the Internet). The IUPAC journal *Pure and Applied Chemistry* is a valuable example.

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