METROLOGY IN CHEMISTRY

Metrology is defined[1] as "*the science of measurement".* Over the past ten years or so much work has been undertaken in the generic and sectorial areas of chemical measurement and testing in order to develop quality systems and to put in place a measurement and testing infrastructure. The development of an overall system for metrology in chemistry will necessitate building on past achievements, developing synergy and exchanging expertise between the various categories of laboratories in the sectorial areas.

"The ability to make accurate measurements is one of the essential foundations of an advanced industrial society"[2]. This ability is the pivot around which trade, commerce and society revolve. Every year many millions of chemical measurements are made for a wide variety of purposes within the EU and important decisions are based on those measurements. Examples of these purposes include:

- safeguarding the quality of food and the purity of air,
- developing new products and materials, such as pharmaceuticals or ceramics,
- monitoring conformity assessment and product specification,
- protecting the consumer against fraud and counterfeit products,
- assisting a hospital physician with a medical diagnosis,
- supporting the justice system in the fight against drugs and organised crime,
- providing forensic evidence for litigation including EU policies,
- gathering revenue for Governments (Customs and Excise),
- underpinning the free movement of goods within the Single Market and trade agreements with third countries such as the USA

Thus chemical analysis spans a wide variety of activities and has important social and economic consequences. Undertaking reliable chemical analysis is, however, complicated by the dependence of the chemical measurement process on the sample matrix and in many instances the necessity to separate the analyte from the sample matrix. The instrumental measurements used for virtually all applications do not usually take place directly on the original sample; they are often the final step of a complex analytical method involving chemical pretreatment (destruction of the sample matrix) or separation of the analyte from the sample matrix. Hence, in most applications calibration of the instrument is insufficient in-order to achieve reliable and comparable analytical results.

The sample matrix problem has given rise to the development of two approaches to achieving reliable and comparable chemical measurements:
(a) matrix reference materials and
(b) inter-laboratory comparisons.
The matrix-matched, certified reference material (CRM) is a unique type of chemical standard commonly used to validate complete measurement methods and is sometimes used for instrumental calibration (eg in XRF, NIR). Such standards are prepared to

correspond to each required analyte/matrix combination and while there are thousands of CRMs in use, there are still many strategic areas where reference materials are required particularly in relation to manufacturing industry, trade, health and the environment. The production of CRMs is both costly and time consuming and many organisations are involved in their certification. It is necessary to ensure that their role in the traceability chain is fully recognised and utilised and that a synergy is developed between the various certification bodies.

Similarly, inter-laboratory comparisons are undertaken for each relevant analyte/matrix combination in order to establish comparability of their measurement data. These comparisons range from 'round robin' studies, which collaboratively test a new method, to formal proficiency testing (PT) schemes which assess agreement between laboratories on an on-going basis.
It is impracticable to organise comparisons for every routine application or to organise a world-wide comparison involving all the laboratories requiring comparability for each measurement application.
Mechanisms are required which will permit interlinking (overlapping) of regional and national PT schemes.

These problems have long been recognised as a significant technical and economic limitation in delivering sound chemical analytical data. The situation is continually being exacerbated with increasing demand from purchasers of data and by regulators for proven comparability of measurements. Global expansion of trade, means more countries and more laboratories need to be brought into each inter-laboratory comparison. In addition, increasing numbers of measurements are used in support of regulations, for which there is an expanding requirement for rigorously proven reliability and comparability. Finally, increasing use of sub-contracted measurements, due to commercial pressures on laboratories, requires not only conformity of contractors to quality systems but also demonstration of the comparability of data from different contractors.

To ensure reliable and comparable chemical measurements in the 21st Century, it is necessary to have unified national/regional/international systems in place which will enable analysts to attain and demonstrate the comparability and traceability of their measurements. In order to achieve this requires a measurement and testing infrastructure, the building blocks of which are:

- Validated methods
- Procedures for determining measurement uncertainty
- Procedures and tools for establishing traceability
- Pure substance reference materials and calibration standards
- Matrix reference materials
- Proficiency testing
- Third party accreditation to an international standard

"Metrology in Chemistry is concerned with the development of a structured support system based on traceable standards and analogous to the systems that have been used to underpin physical measurements for over 100 years."[3] Chemical measurements have developed more or less on a sectorial basis and in a different culture, so that in very many cases the laboratory support systems developed for physical measurements by National Measurement Institutes (NMIs) cannot easily be applied to the field of chemical or indeed biological measurement.

However, common areas do exist and there are measurement problems in chemistry which are similar to those experienced with physical measurements. These include the difficulty of obtaining reliable estimations of measurement uncertainty and the frequent disparity between calibration standards and the "real" samples or artifacts on which measurements are made.
Some of the problems are being addressed at the highest level through the CCQM (Consultative Committee on Amount of Substance), EUROMET and EURACHEM. Others are being addressed in sectorial areas where a "bottom up" up approach is being adopted.
This approach is based on quality systems, CRMs, PT and laboratory accreditation (EN45001) coupled to a laboratory networking system. This approach is widely adopted in the food and agricultural fields and in certain instances is underpinned by legislation.

A recent survey conducted under the SMT programme[3] showed that for generic metrology three countries had systems in place and were in a position to claim traceability to SI (Système International) for a small number of measurements. A lesser number claimed traceability to other standards. In some of the sectors surveyed the activities at a metrological level were almost nil whereas the activities at the comparability level (working level) were quite high. The environmental and industrial sectors were the most advanced in claiming traceability to SI (numbers being about 6).

It was clear from both this survey and from a series of workshops[4] held between 1997 – 1999 that the development of system(s) for metrology in chemistry are at varying stages of evolution. The developments that are underway in the Member States are also taking place practically in isolation from one another although the above interactive workshops have led to positive outcomes.

There is a need for a coordinating role by the Commission supported by the Framework programme, to facilitate and harmonise those developments.

A two pronged approach is required

1. The development of a harmonised European chemical measurement infrastructure for all sectors of chemical measurement, which will contribute to and be compatible with systems being developed around the world. This work should be carried out in close co-operation with CCQM, EUROMET and EURACHEM.

2. Disseminating traceability and the principle of metrology in chemistry from the top level to the working level by developing, demonstrating and evaluating concepts, systems, strategies and tools.

Some work areas requiring attention in both 1 and 2 above are:

- Evaluation and development of measurement uncertainty strategies and procedures.
- Development of traceability strategies and initiation of demonstrator projects showing how traceability could be achieved from high level international standards to working level measurements.
- Development of high level (primary) reference materials.
- Development of reference values for proficiency testing schemes
- Evaluation of EU legislation with regard to limits based on chemical measurements. and development of relevant European and international "key comparisons" to assist trade and other cross border issues.
- Education and training for metrology in chemistry.
- Development and validation *of methods including* primary methods.
- Development and validation of pre-treatment techniques as a means of managing matrix effects in analytical methods.
- Technology transfer and networking between primary and reference measurement laboratories.
- Development of metrological standards and tools for biotechnology applications (analytical molecular biology and microbiological measurements).

These work areas are discussed in Annex I.

In order to make progress it is recommended that priority be given to the following project areas:

- The development of a blue-print for metrology in chemistry in Europe.
- Dissemination of traceability from metrology institutions to laboratories.
- Development of the metrological tools necessary to attain the above.

An outline of the rational, the work programme and the expected outputs for each of these project areas is given in Annex II.

References

1. International Vocabulary of Basic and General Terms in Metrology, ISO, Geneva, 2nd edition 1993
2. Quinn Report on BCR Programme (1988-1992)
3. Metrology in Chemistry EUR 19074 en
4. TRAC, Special Issue, Metrology in Chemistry, Sept/Oct 1999, **18**, 569-655

ANNEX I

Work Areas

1. **Measurement Uncertainty.**
   The key requirement of traceability is a full understanding of the uncertainty of the entire chemical measurement procedure. Measurement uncertainty and traceability are closely interlinked. Traceability chains can only be built up if methods are available to evaluate the uncertainties of the links in the chain. The ISO guide to the expression of uncertainty provides a unified way to evaluate these uncertainties. EURACHEM is already active in this field and has developed a guidance document, which interprets the ISO Guide to Uncertainty Measurements (GUM) for chemical measurement. However there is an urgent need to develop strategies for primary and reference measurements. In addition user-friendly examples relevant for routine analysis and training for "field laboratories" are required. For most chemical measurement methodology the process of uncertainty estimation, for sample preparation and pre-treatment, is largely on an empirical basis which relies heavily on professional judgement. Hence studies are needed to gain a better understanding of the major sources of uncertainty. Consideration must also be given to the development of systems for biological measurements. There is also a necessity to develop measurement uncertainty strategies and tools for qualitative (identification) analysis and for sampling.

2. **Traceability Issues.**
   A guidance document for field laboratories which would elaborate mechanisms for the attainment of traceability in all areas of chemical measurement is required. In addition practical examples are needed of how traceability could be achieved from reference laboratories to working level measurements. In addition it will be necessary to evaluate and extend the range of applicability of the limited number of high level standards available. Consideration should be given to measurements where it is neither possible nor practicable to achieve traceability to the highest metrological levels.

3. **Development of high level (primary) reference materials.**
   The need for large numbers of application-specific CRMs has lead to fragmented production without a logical hierarchy to interlink CRMs produced for different applications. There are also relatively few traceable chemical measurement standards in the sense used for physical measurement standards. Hence there is a need for high level (primary) reference materials of both pure substances and matrix materials which would be linked to working level reference materials.

4. **Reference values for proficiency testing schemes**.
   Consideration should also be given to the role of PT in traceability and the interlinking of schemes between countries and regions. At present such schemes aim to evaluate competence but adoption of reference instead of consensus values could facilitate the attainment of traceable measurements.

5. **European legislative issues**
   The legal aspects of interpretation of EU Regulations and Directives are currently fraught with difficulties and sectors within the DGs are currently addressing this on an individual basis, without any harmony between the approaches. There is an urgent requirement for a common approach and development of a guidance document for the interpretation of regulatory and specification limits.
   Inter comparisons between national laboratories are essential for regulatory purposes and as a means of establishing comparability.

6. **Education and training.**
   The development of guidance documents, workshops and training sessions is an essential ingredient in the establishment of system for traceability and hence metrology in chemistry. Examples related to measurement uncertainty are described above but similar needs exist with regard to validation of methods, production and use of reference materials or calibration standards, and good metrological practice.

7. **Development and Validation of Primary Methods**.
   Primary methods provide the links to SI and work is required on the analytes and matrices using both classical and modern instrumental methods. In addition to the development and validation of existing techniques such as, IDMS, NMR, etc. there is a need to investigate emerging technologies.

8. **Method Validation and Matrix Effects**.
   The main complicating difference between chemical and physical measurement is the vast array of different types of measurement made in chemistry. The influence of the matrix is the biggest source of inaccuracy and techniques for digestion, extraction, separation and recovery are often inadequately validated due to the difficulty of evaluating measurement bias

9. **Technology Transfer and Networking.**
   There is a requirement to cross-fertilise, harmonise and share the cost of world comparisons and to establish a standard European chemical measurement system. In addition to networking connected with specific projects there is a need for collaboration and discussion between the representatives for both NMIs and national reference laboratories across the EU.

10. **Biotechnology**.
    This area of measurement is of growing strategic importance but as of yet there has been very little consideration of measurement quality issues. There is a need to

develop and validate strategies for assessing quality including the use of reference and primary methods.

ANNEX II

Priority projects

1. Development of a Blue-Print for Metrology in Chemistry in Europe.

Previous studies have clearly shown that significant work is in progress, in certain sectors and in some of the Member States. However, there are major sectorial deficits and in a number of Member States little or no activity currently exists. Also although there is some emerging clarity about how all the parts of the jig-saw could fit together there is no blue-print for an overall structure.

Research into the following areas is needed.

- Studies of the existing work and existing responsibilities for metrology in chemistry in the Member States and the candidate countries at both the generic and sectorial levels.
- Consultation and joint studies with officials from the Member States and candidate countries on both policy issues and technical requirements.
- Investigation of trade barriers, with particular emphasis on those areas which relate to EU Directives & EU-USA trade, which have been occasioned by problems with analytical data arising from poor measurement traceability.
- Investigation of the existing linkages and the requirements for further interaction between work on generic issues in DG XII and work in specific sectors under the remit of the other DGs.

Outputs from the above would include:

1.1 A detailed blue-print for the establishment of a European infrastructure for metrology in chemistry, with particular emphasis on;

- interfaces between high level international metrology (CCQM), European level activities and Member State activities,
- linkages between high level metrology laboratories, reference laboratories and field laboratories,
- linkages between generic metrology work and sectorial activities.
- division of responsibilities between the Member States and the EU,
- plans for establishing virtual laboratories,
- key requirements related to concepts, systems, strategies and tools.

1.2 Recommendations on priorities and strategies for addressing;

- technical barriers to trade,
- a harmonised approach to the formulation, implementation and interpretation of EU regulations and Directives which rely on chemical/biological measurement,

- technology transfer to assist Member States and candidate countries not yet active in the area of metrology in chemistry to acquire the requisite expertise and to establish the appropriate infrastructures,
- technology transfer to promote metrology concepts and tools to field laboratories across Europe,
- specific measurement problems.

2. Dissemination of Traceability from Metrology Institutes to Laboratories

The benefits of developing a chemical metrology infrastructure in Europe can only be realised if it is possible to trace everyday measurements of field laboratories to reference measurements derived from international chemical metrology. This requires development of a network of European centers of excellence linked into international chemical metrology.

At the top of the metrology chain the CCQM and designated regional metrology organisations are organising a series of *key comparisons* which reflect applications relevant to industry, trade, health, environment, etc. It is essential that participating laboratories are experts and that they have measures in place for disseminating traceability to field laboratories.

In most European countries governmental expertise in chemical measurement is more widely dispersed than is the case for physical measurements which are mainly focused on a single National Measurement Institute (NMI). As a result there is presently no co-ordinated group of European centers of excellence in analytical measurement which are able to fill the requisite role.
It is therefore necessary to stimulate participation by the relevant expert chemical laboratories and to support their development of both metrological expertise and methodology for disseminating traceability to field laboratories.
This requires research to address issues such as:

- Method development, which enables expert analytical laboratories to participate in European comparisons at the metrological level
- The delivery of European key comparisons in areas where analytical measurements are supporting EU priorities in industry, regulation or trade
- The development of services which will establish traceability of a wide range of materials, methods and laboratories to the relatively small number of key comparisons which are planned
- Vertical demonstration of the concept of traceable chemical measurements extending from a key comparison to measurements made by reference and field laboratories

Outputs from the above would include:

- Published reports addressing key measurement problems.

- High level European certified reference materials (CRMs) providing traceability for commercially produced CRMs in key application areas.
- Calibration services for CRM producers, suppliers of calibration standards, PT organisers, field laboratories, etc, requiring means to establish direct traceability of their products or services.
- European interlaboratory studies with traceable independent reference values.

3. Development of Metrological Tools to attain sections 1 and 2 above

The mechanisms for establishing traceability to a common reference will vary with the nature and type of analysis being performed. It may for example be to SI units, a CRM or a reference method. To achieve this objective the analyst requires a set of tools and procedures and research necessary to deliver on these objectives is outlined below.

- Procedures and guidance to elaborate the mechanisms for establishing traceability for the complete spectrum of chemical analyses (including hybrid areas, such as immunochemistry, chemometrics,). Technology transfer measures to disseminate the above.
- Procedures and guidance, for the estimation of measurement uncertainty in quantitative and qualitative analyses, including the utilisation of data from PT schemes, method validation studies, internal quality control data and CRMs for the estimation of uncertainty.
- Technology transfer measures to disseminate the above.
- The development of pure substance and matrix reference materials and calibration standards.
- The interlinking of national and regional PT schemes.
- Networking between, national monitoring laboratories, national reference laboratories and EU centers of excellence in the various measurement sectors.
- Interlinking of national sectorial centers of excellence (national reference laboratories)

Outputs will include:

- Procedures and guidance documents on the attainment of traceability and the estimation of measurement uncertainty.
- Strategies and mechanisms for the dissemination of metrological principles and the establishment of the traceability chain for all types of analyses performed by analytical chemists.
- A demonstration of traceability from European field laboratories to two or more European reference laboratories which have ascertained their international measurement equivalence through CCQM key comparisons.
- Workshops and other systems of technology transfer.
- Pure substances certified reference materials, calibration standards and artefacts.
- Assigned values for PT schemes

- An evaluation of the relative merits of the conventional and metrological approaches to achieving comparable analytical data.

The development of a synergistic culture and a collegial approach to metrology in chemistry throughout all sectors and categories of laboratories who utilise the discipline of chemistry to generate analytical data which is “fit for purpose”