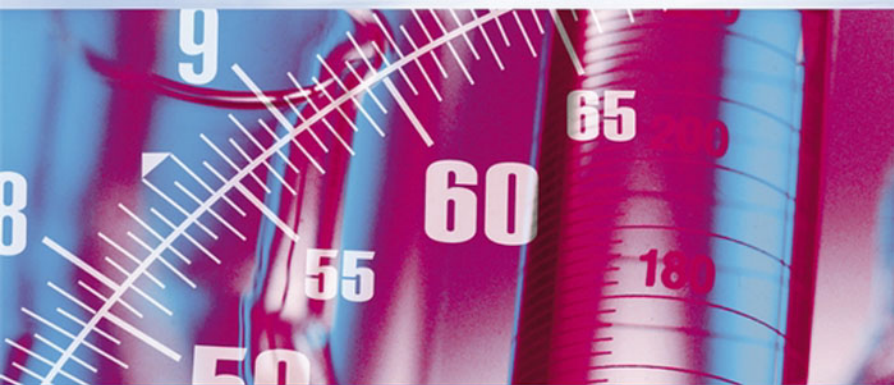


**Elizabeth Prichard**  
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# Series Preface

There has been a rapid expansion in the provision of further education in recent years, which has brought with it the need to provide more flexible methods of teaching in order to satisfy the requirements of an increasingly more diverse type of student. In this respect, the *open learning* approach has proved to be a valuable and effective teaching method, in particular for those students who for a variety of reasons cannot pursue full-time traditional courses. As a result, John Wiley & Sons, Ltd first published the Analytical Chemistry by Open Learning (ACOL) series of textbooks in the late 1980s. This series, which covers all of the major analytical techniques, rapidly established itself as a valuable teaching resource, providing a convenient and flexible means of studying for those people who, on account of their individual circumstances, were not able to take advantage of more conventional methods of education in this particular subject area.

Following upon the success of the ACOL series, which by its very name is predominately concerned with Analytical Chemistry, the *Analytical Techniques in the Sciences* (AnTS) series of open learning texts has been introduced with the aim of providing a broader coverage of the many areas of science in which analytical techniques and methods are increasingly applied. With this in mind, the AnTS series of texts seeks to provide a range of books which covers not only the actual techniques themselves, but *also* those scientific disciplines which have a necessary requirement for analytical characterization methods.

Analytical instrumentation continues to increase in sophistication, and as a consequence, the range of materials that can now be almost routinely analysed has increased accordingly. Books in this series which are concerned with the *techniques* themselves reflect such advances in analytical instrumentation, while at the same time providing full and detailed discussions of the fundamental concepts and theories of the particular analytical method being considered. Such books cover a variety of techniques, including general instrumental analysis, spectroscopy, chromatography, electrophoresis, tandem techniques, electroanalytical methods, X-ray analysis and other significant topics. In addition, books in

this series also consider the *application* of analytical techniques in areas such as environmental science, the life sciences, clinical analysis, food science, forensic analysis, pharmaceutical science, conservation and archaeology, polymer science and general solid-state materials science.

Written by experts in their own particular fields, the books are presented in an easy-to-read, user-friendly style, with each chapter including both learning objectives and summaries of the subject matter being covered. The progress of the reader can be assessed by the use of frequent self-assessment questions (SAQs) and discussion questions (DQs), along with their corresponding reinforcing or remedial responses, which appear regularly throughout the texts. The books are thus eminently suitable both for self-study applications and for forming the basis of industrial company in-house training schemes. Each text also contains a large amount of supplementary material, including bibliographies, lists of acronyms and abbreviations, and tables of SI Units and important physical constants, plus where appropriate, glossaries and references to literature and other sources.

It is therefore hoped that this present series of textbooks will prove to be a useful and valuable source of teaching material, both for individual students and for teachers of science courses.

*Dave Ando  
Dartford, UK*

# Preface

This book is a very much revised edition of the book, *Quality in the Analytical Chemistry Laboratory*, published as part of the ACOL Series about twelve years ago. This version covers in more detail the technical requirements of the International Standards adopted by many laboratories, i.e. method validation, traceability and measurement uncertainty. At the time of writing the ACOL book, analytical measurements were beginning to play an increasing role in many of the world economies. During the last ten years the number of countries wishing to trade internationally has increased. In addition, the need for reliable measurements, carried out in a cost-effective way, brings new demands on analytical scientists. Analysts are required to measure more quickly samples in many different matrices, often with the analyte present at a very low concentration. In addition, the customers of analytical laboratories are also requiring some third-party evidence that they can trust the work of the laboratory. This is why the sections dealing with International Standards and Proficiency Testing schemes have been extended. Increasingly, a knowledge of quality assurance and quality control is important. The principles of reliable measurements need to be integrated into a scientist's work early on in his/her career.

LGC has a strong interest in the quality of analytical measurements and played a lead role in the development of the UK's initiative on Valid Analytical Measurement (VAM). This is a programme supported by the UK government as part of the DTI programmes supporting the national measurement system.

The aims of the VAM programme are as follows:

- to improve the quality of analytical measurements made in the UK;
- to facilitate mutual recognition of analytical data across international boundaries;

- to develop a robust and transparent infrastructure aimed at achieving international comparability and traceability of chemical and biochemical measurements.

These aims reach much further than the UK as evidenced by other international organizations which have developed, partly as a result of the work in VAM. They include Eurachem (a network of organizations in Europe having the objective of establishing a system for the international traceability of chemical measurements and the promotion of good quality practices) and CITAC (Co-operation on International Traceability in Analytical Chemistry). A wide variety of issues have been identified, all of which need to be addressed to ensure that analytical measurements made in different countries or at different times are comparable.

This book sets out to describe how ‘best practice’ can be achieved through adopting the VAM principles (see Chapter 2). It describes the international standards that can provide laboratories with a structure to work to, as well as third-party assurance of their competence. It takes the analyst through the complete analytical process. The text starts with defining the problem fully, thus enabling analysts to identify a method that is likely to provide results that are ‘fit for purpose’. This is ensured through appropriate method validation and suitable calibration leading to results that are traceable to international standards. This is followed by sampling and sample pre-treatment. Layout of the laboratory and inappropriate choice of chemicals can result in poor data. The internal quality control and external quality assessment are both described, as well as sections covering evaluation of the uncertainty of the measurement results. The analytical results end with the report being written and this is described with all of the other documents which ensure the smooth operation of a laboratory.

Issues of quality extend far beyond organizational arrangements. The analyst and the employer must both accept the equally important aspect of quality in professional skills and competences. Analysts need more help in order to learn about good laboratory practice and to work competently and professionally on a day-to-day basis within the framework of the VAM principles. This book offers analysts a new learning route to achieving these aims, and employers a convenient way to introduce quality assurance procedures.

The production of this book has been made possible through support from the VAM programme. The technical content of the book has also benefited through the results of work which has been carried out by LGC, often in collaboration with others, on specific technically based VAM, Eurachem and CITAC projects.

*Elizabeth Prichard and Vicki Barwick*

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The authors take full responsibility for any errors or omissions.

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# Acronyms, Abbreviations and Symbols

|         |                                                                            |
|---------|----------------------------------------------------------------------------|
| °C      | temperature on Celsius scale                                               |
| abv     | alcohol by volume                                                          |
| Ac      | acceptance number in a sampling plan                                       |
| ANOVA   | analysis of variance                                                       |
| AOAC    | Association of Official Analytical Chemists                                |
| AQL     | acceptance quality limit                                                   |
| ASTM    | American Society for Testing and Materials                                 |
| B       | measurement bias                                                           |
| BAM     | Federal Institute for Materials Research and Testing (Germany)             |
| BCR     | Bureau Communautaire de Référence                                          |
| BIPM    | Bureau International des Poids et Mesures (Bureau of Weights and Measures) |
| BP      | British Pharmacopeia                                                       |
| BS      | British Standard                                                           |
| BSI     | British Standards Institute                                                |
| CEN     | European Committee for Standardization                                     |
| CFR     | Code of Federal Regulations                                                |
| CI      | confidence interval                                                        |
| CITAC   | Co-operation on International Traceability in Analytical Chemistry         |
| CONTEST | Contaminated Land Proficiency Testing Scheme                               |
| COSHH   | Control of Substances Hazardous to Health                                  |
| CRM     | Certified Reference Material                                               |
| CUSUM   | cumulative sum                                                             |
| DTI     | Department of Trade and Industry                                           |

|                  |                                                                                                          |
|------------------|----------------------------------------------------------------------------------------------------------|
| EC               | European Commission                                                                                      |
| EFQM EEA         | European Foundation for Quality Management Excellence Award                                              |
| EP               | European Pharmacopeia                                                                                    |
| EPTIS            | A Proficiency Testing information system                                                                 |
| EQA              | external quality assessment                                                                              |
| ERM              | European Reference Material                                                                              |
| Eurachem         | European network of analytical chemistry laboratories                                                    |
| FAPAS            | Food Analysis Performance Assessment Scheme                                                              |
| FDA              | Food and Drug Administration (USA)                                                                       |
| GC               | gas chromatography                                                                                       |
| GC–ECD           | gas chromatography with electron-capture detection                                                       |
| GC–FID           | gas chromatography with flame-ionization detection                                                       |
| GLP              | Good Laboratory Practice                                                                                 |
| GNP              | gross National product                                                                                   |
| HMSO             | Her Majesty's Stationery Office                                                                          |
| HPLC             | high performance liquid chromatography                                                                   |
| HPTLC            | high performance thin layer chromatography                                                               |
| ICP–MS           | inductively coupled plasma–mass spectrometry                                                             |
| ICP–OES          | inductively coupled plasma–optical emission spectroscopy                                                 |
| IDL              | instrument detection limit                                                                               |
| IEC              | International Electrotechnical Commission                                                                |
| ILAC             | International Laboratory Accreditation Cooperation                                                       |
| IMEP             | International Measurement Evaluation Programme                                                           |
| IP               | Institute of Petroleum (now called the Institute of Energy)                                              |
| IQC              | internal quality control                                                                                 |
| IRMM             | European Commission, Joint Research Centre, Institute for Reference Materials and Measurements (Belgium) |
| ISO              | International Organization for Standardization                                                           |
| IUPAC            | International Union of Pure and Applied Chemistry                                                        |
| LC               | liquid chromatography                                                                                    |
| LEAP             | Laboratory Environmental Analysis Proficiency                                                            |
| LIMS             | Laboratory Information Management System                                                                 |
| LoD              | limit of detection                                                                                       |
| LoQ              | limit of quantitation                                                                                    |
| MAD              | median absolute deviation                                                                                |
| MAD <sub>E</sub> | estimate of robust standard deviation                                                                    |
| MAPS             | Malt Analytes Proficiency Testing Scheme                                                                 |
| MDL              | method detection limit                                                                                   |
| MS               | mass spectrometry                                                                                        |
| MS <sup>n</sup>  | multiple stages of mass spectrometry                                                                     |
| MU               | measurement uncertainty                                                                                  |
| NIST             | National Institute of Standards and Technology                                                           |

|        |                                                                    |
|--------|--------------------------------------------------------------------|
| NPD    | nitrogen–phosphorus detector (also known as a thermionic detector) |
| OECD   | Organization for Economic Co-operation and Development             |
| PAH(s) | polyaromatic hydrocarbon(s)                                        |
| PT     | Proficiency Testing                                                |
| QA     | Quality Assurance                                                  |
| QC     | Quality Control                                                    |
| QP     | Quality Procedure                                                  |
| QMS    | Quality Management's Quality in Microbiology Scheme                |
| QWAS   | Quality Management's Quality in Water Analysis Scheme              |
| R      | recovery ratio                                                     |
| Re     | rejection number in a sampling plan                                |
| RICE   | Regular Interlaboratory Counting Scheme                            |
| RM     | reference material                                                 |
| SI     | Système International (d'Unités) (International System of Units)   |
| SIM    | selected-ion monitoring                                            |
| SOP    | Standard Operating Procedure                                       |
| SRM    | Standard Reference Material                                        |
| TLC    | thin layer chromatography                                          |
| UKAS   | United Kingdom Accreditation Service                               |
| USP    | United States Pharmacopeia                                         |
| UV     | ultraviolet                                                        |
| VAM    | Valid Analytical Measurement (Programme)                           |
| VIM    | International Vocabulary of Basic and General Terms in Metrology   |
| VIS    | visible                                                            |
| WASP   | Workplace Analysis Scheme for Proficiency                          |
| WI     | Work Instruction                                                   |
| CV     | coefficient of variation                                           |
| $E_n$  | score in PT scheme                                                 |
| $k$    | coverage factor used to calculate the expanded uncertainty         |
| $K_s$  | sampling constant                                                  |
| $n$    | number in a sample data set                                        |
| $N$    | number in a population of results                                  |
| $r$    | repeatability and correlation (regression) coefficient             |
| $R$    | reproducibility                                                    |
| $RSD$  | relative standard deviation                                        |
| $RSZ$  | rescaled sum of z-scores                                           |
| $s$    | sample standard deviation                                          |
| $s^2$  | sample variance                                                    |
| $s_r$  | repeatability standard deviation                                   |
| $s_R$  | reproducibility standard deviation                                 |

|                |                                                           |
|----------------|-----------------------------------------------------------|
| $s(\bar{x})$   | standard deviation of the mean                            |
| $SDM$          | standard deviation of the mean                            |
| $SSZ$          | sum of squared $z$ -scores                                |
| $t$            | Student $t$ -value                                        |
| $T$            | target value                                              |
| $u$            | standard uncertainty                                      |
| $u(a)$         | standard uncertainty of $a$                               |
| $u_x$          | standard uncertainty of $x$                               |
| $U$            | expanded uncertainty                                      |
| $\bar{x}$      | sample mean                                               |
| $x_i$          | datum point $i$                                           |
| $x_0$          | accepted reference value                                  |
| $X$            | assigned value in PT scheme                               |
| $\bar{y}$      | mean response (of a calibration set)                      |
| $z$            | score in PT scheme                                        |
| $z'$           | score in PT scheme                                        |
| $\alpha$       | probability of a value being outside of a specified range |
| $\theta$       | angle used in construction of CUSUM V-mask                |
| $\mu$          | population mean                                           |
| $\nu$          | number of degrees of freedom                              |
| $\sigma$       | population standard deviation                             |
| $\sigma^2$     | population variance                                       |
| $\sigma'$      | between-laboratory standard deviation                     |
| $\sigma_r$     | repeatability standard deviation                          |
| $\sigma_R$     | reproducibility standard deviation                        |
| $\hat{\sigma}$ | target range in PT scheme                                 |

# About the Authors

**Elizabeth Prichard, B.Sc., Ph.D., FRSC, CChem.**

Elizabeth Prichard obtained a first degree in Chemistry from the University College of Wales, Aberystwyth, where she went on to obtain her doctorate studying infrared spectroscopy. After a Civil Service Research Fellowship, she moved into academia, initially at Bedford College and then Royal Holloway and Bedford New College, University of London before moving to the University of Warwick as a Senior Research Fellow. While at London University, she continued her research in spectroscopy, as well as some work in biophysical chemistry. At the University of Warwick, she researched the release profiles of steroids from implanted contraceptive devices. During her time at London University, Elizabeth spent sabbatical periods at the Division of Materials Application, NPL, the Biophysics and Biochemistry Department, Wellcome Research Foundation, Beckenham and then as Associate Professor sponsored by the British Council at the University of Gezira and at the University of Khartoum, Sudan.

In 1992, Elizabeth was seconded from the University of Warwick to the Laboratory of the Government Chemist (which became LGC in 1996) to manage the production of the first edition of this book which was part of the ACOL Series. Elizabeth had been an editor for this series since its inception in the late 1980s. In 1997, Elizabeth joined the staff of LGC as Head of Education and Training. She developed there a Quality Assurance Training Programme and continues to deliver these courses. As part of the Valid Analytical Measurement (VAM) programme, she also developed courses in analytical science appropriate for A-level chemistry teachers and a Proficiency Testing (PT) competition for the students. She has been involved in the production of a number of quality assurance products for all levels of learning from school to the professional analyst, including books, videos, CDs and web-based e-learning material. In addition, Elizabeth has been a partner in EU projects in the area of quality assurance – these include the QUACHA and SWIFT-WFD projects.

During the last fifteen years, Elizabeth has lectured and delivered training courses on quality assurance topics in the UK, Europe and USA.

### **Vicki Barwick, B.Sc**

Vicki Barwick obtained a first degree in Chemistry from the University of Nottingham. She then joined the Laboratory of the Government Chemist (which became LGC in 1996) as an analyst in the Consumer Safety Group. Vicki was involved with a number of projects to assess the safety of consumer products, including developing test methods for the identification of colourants in cosmetics and the quantitation of phthalate plasticizers in child-care items.

After five years as an analyst, Vicki moved within LGC to work on the DTI-funded Valid Analytical Measurement (VAM) programme. In this role, she was responsible for providing advice and developing guidance on method validation, measurement uncertainty and statistics. One of her key projects involved the development of approaches for evaluating the uncertainty in results obtained from chemical test methods. During this time, Vicki also became involved with the development and delivery of training courses on topics such as method validation, measurement uncertainty, quality systems and statistics for analytical chemists.

In 2002, Vicki moved into a full-time education and training role at LGC. She is currently the Project Manager for VAM knowledge transfer projects aimed at promoting the adoption of the principles of valid analytical measurement. This involves the production of training resources and the organization of workshops for A-level students and their teachers, undergraduate and postgraduate students, and professional analysts. Vicki is also responsible for the development and delivery of LGC's Quality Assurance Training Courses.

Over the last ten years, Vicki has lectured extensively on quality assurance topics and has co-authored a number of papers, books and guides.

## Chapter 1

# The Need for Reliable Results

### Learning Objectives

- To understand why analytical measurements need to be made.
- To understand the importance of producing reliable results.
- To be able to define what is meant by 'quality'.

## 1.1 Why Analytical Work is Required

Measurements affect the daily lives of every citizen. Sound, accurate and reliable measurements, be they physical, chemical or biological, are essential to the functioning of modern society. For these reasons, advanced nations spend up to 6% of their Gross National Product (GNP) on measurements and measurement-related operations.

Informed debate and decisions on such important matters as the depletion of the ozone layer, acid rain and the quality of waterways all depend on the data provided by analytical chemists. Forensic evidence also often depends on chemical measurements. National and international trade are critically dependent on analytical results. Chemical composition is often the basis for the definition of the nature of goods and tariff classification. In all of these areas not only is it important to get the right answer but it is essential that the user of the results is confident and assured that the data are truly representative of the sample and that the results are defensible, traceable and mutually acceptable by all laboratories.

The role of the analytical chemist has not changed since the time analysts discovered that naturally occurring products were composite materials. For example,

when it was discovered that carrots helped prevent ‘night blindness’ it was an analytical chemist who separated out the various components of carrot, characterized the compounds and identified the active component as  $\beta$ -carotene. What have changed are the questions that are asked by society; they have become more demanding. Much of the interest today is centred on levels of unwanted materials that are present at a very low concentration, such as  $\text{ng g}^{-1}$ . In addition, the range of materials being analysed has increased enormously, with the results being required very quickly, as cheaply as possible and to the best quality.

## 1.2 Social and Economic Impact of a ‘Wrong Analysis’

The social and economic impact of the analyst getting a wrong result and the customer consequently reaching a false conclusion can be enormous, for example:

- In forensic analysis, it could lead to a wrongful conviction or the guilty going unpunished.
- In trade, it could lead to the supply of sub-standard goods and the high cost of replacement with subsequent loss of customers.
- In environmental monitoring, mistakes could lead to hazards being undetected or to the identification of unreal hazards.
- In the supply of drinking water, it could lead to harmful contaminants being undetected.
- In healthcare, the incorrect medication or the incorrect content of active ingredient in a tablet can be catastrophic for the patient.

Just think of the huge costs, both in terms of financial and other resources, and in terms of the distress to individuals and their families, that could be caused by such mistakes. In all areas of application ‘getting it wrong’ leads to loss of confidence in the validity of future analytical results. Confidence is an important commodity. At one extreme, loss of confidence puts the future existence of the particular analytical laboratory at risk, but more generally it leads to costly repetition of analyses and, in the area of trade, inhibits the expansion of the world economy.

Many of you will be able to call to mind reports in the papers, or on TV, where the analytical chemist has apparently made a mistake. Some of these may be notorious but remember the many million times that the analytical chemist gets it right without any publicity. We are all aware of the debate over global warming; just think of how important it is that action taken in the future is based on information that gives a true picture of the composition of the global

atmosphere. This book, by covering the majority of relevant basic issues, is designed to put you on the right path to quality in the analytical laboratory.

You might think that results obtained these days are more reliable than they were in the past. This may be true. The technologies have improved, tools for quality control, e.g. Certified Reference Materials, are available and new, more specific quantitative methods have been developed. However, there is ample proof that there are data being produced that are not fit for their intended purpose. Much of the evidence for unreliable results has come from studies involving a number of experienced laboratories all measuring samples of the same material. These may be from studies called collaborative studies or from the results produced during rounds of a Proficiency Testing Scheme (see Chapter 7) or from results published by the International Measurement Evaluation Programme (IMEP) [1]. This programme was set up to demonstrate the degree of equivalence of results of chemical measurements on a global scale. Figure 1.1 shows results for cadmium analysis from IMEP 9 where the participating laboratories have analysed samples of water containing trace metals. It is clear from this figure that many laboratories are not producing results which are 'fit for purpose'. This can be because of human error or because the results are not linked to a traceable reference value.

The issue is that the level of quality control that analysts have applied to their measurements in the past has been insufficient to meet the new challenges of today's analytical problems. There are many reasons why a laboratory might

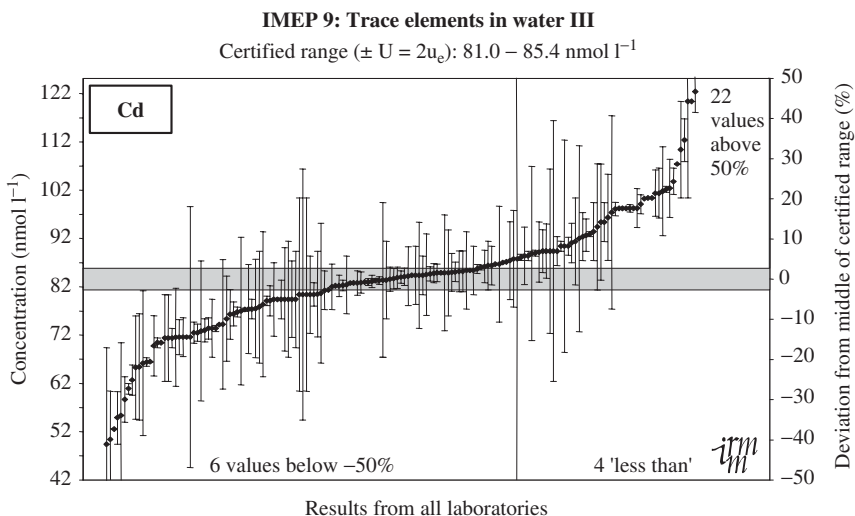


**Figure 1.1** Results from an international intercomparison, IMEP 9, where  $U$  is the expanded uncertainty and  $u_c$  the combined standard uncertainty [1] (see Chapter 6, Section 6.3). Reproduced by permission of EC-JRC-IRMM (Philip Taylor) from IMEP 9, 'Trace elements in water III, Cd, certified range  $81.0 - 85.4 \text{ nmol l}^{-1}$ '.

quote incorrect results. A result may be incorrect because of an error in a calculation or an instrument that is out of calibration so that the scale reading no longer shows the correct value. However, more often the error is in the method used for the analysis. If the method used is not suitable for the analysis then the result will be incorrect. This could be because the analyte concentration is outside the range for which the method has been validated (see Chapter 4, Section 4.6). The method may be unable to detect the low levels required. Another reason could be that there is an interfering substance present, which is being detected along with the analyte. This is termed, ‘lack of selectivity’. A more subtle reason may be that the method does not measure exactly what the customer requires. The method may measure ‘total iron’ in a tablet although the customer wished to know the amount of iron that is extracted by stomach acid. In addition, the method used may be very sensitive to some small changes that have been made to a validated method, e.g. in the concentration or the amount of material added, scaling up/down of components, temperature or pressure, etc. The extent to which a method can be modified without significant loss of accuracy is a measure of the ‘ruggedness’ of the method (see Chapter 4, Section 4.6.5).

Whatever the reason for obtaining it, a chemical measurement has a certain importance since decisions based upon it will very often need to be made. These decisions may well have implications for the health or livelihood of millions of people. In addition, with the increasing liberalization of world trade, there is pressure to eliminate the replication of effort in testing products moving across national frontiers. This means that quantitative analytical results should be acceptable to all potential users, whether they be inside or outside the organization or country generating them.

## 1.3 What do we Mean by ‘Quality’

This book is about quality in the analytical chemistry laboratory, but what do we mean by ‘quality’? It is easier to understand when dealing with various products, e.g. cars or clothes. All successful manufacturers have to produce goods that they can sell. Car manufacturers will have a range of products to suit their customers’ needs. They will all be made to a high standard so that they comply with legislation; however, they will be aimed at people with different needs. You can compare this with an analytical laboratory. Analytical chemists produce results that are passed on to someone else (the customer) who will use them to solve a problem. The laboratory is providing a service.

### DQ 1.1

What do you think quality means in terms of the results obtained in the analytical laboratory?

*Answer*

Quality in this context is not necessarily getting the most accurate results – it is matching the service with the requirements of the customer. This is achieved by providing results that:

- meet the specific needs of the customer;
- attract the confidence of the customer and all others who make use of the results;
- represent value for money.

This is often referred to as *fitness for purpose*.

**DQ 1.2**

List the factors you think need to be considered to ensure that you provide a customer with results of acceptable quality.

*Answer*

There are a number of things to consider, but the most important is understanding the needs of the customer. Is the total sugar content of the product required or the lactose content? The level of uncertainty in the result that is acceptable also helps focus on the choice of method. Once the method is chosen and validated, it is then important to ensure that all of the equipment is available and in a proper state of calibration. Then, all that remains is to have sufficient trained staff to carry out the analysis. Once the experimental results have been obtained and the data treatment is complete, the report can be written. The report also has to meet the customer requirements and should be written in an unambiguous way which is clear to the non-specialist.

## 1.4 Customer Requirements

To ensure that analytical results are fit for purpose, there has to be a discussion with the customer before the analysis is started. You must remember that a customer who is a member of your laboratory is just as important as the customer from outside your organization.

It goes without saying that you should make all measurements to the best of your ability. However, a value to the highest level of precision and trueness is not always required. The aim is that the result produced should be accurate enough to be of use to the customer, for the intended purpose (see Chapter 4). Customers may want the technical details of the method used but more often this will not be

required. It is therefore vital that the exact requirements are discussed with the customer prior to the analysis and mutually agreed. The customer will require enough evidence to give confidence that the data are accurate and are suitable for their intended purpose. The data need to be backed-up by documentary evidence, such as computer printouts and record books that have been signed and dated, and checked. These documents may be required as evidence in cases of disputes or complaints. Every result you produce should have included with it an estimate of the uncertainty associated with the value (see Chapter 6).

There are several different categories of analysis, which might be required by a customer. Each requires a different approach. Analysing to a 'specification' where there is a maximum or minimum limit, for which a product or component concentration passes or fails, requires a different analytical approach from that required for a screening method requiring a 'yes/no' analysis. However, the customer requirement of fitness for purpose stays the same. A screening or 'yes/no' method is used when you have a large number of samples so you need a quick method to select which ones should be subjected to additional testing. The guidance on the maximum level of arsenic in contaminated land is  $40 \text{ mg kg}^{-1}$ . The analysis needs to be quantitative, accurate and reproducible at the  $40 \text{ mg kg}^{-1}$  level. However, the method does not need to be accurate over a wide range of concentrations of the analyte to be determined, e.g.  $1 \text{ mg kg}^{-1}$  to  $100 \text{ mg kg}^{-1}$ . If the land is contaminated above the guidance limit, it does not matter whether it is  $45 \text{ mg kg}^{-1}$  or  $145 \text{ mg kg}^{-1}$ ; the land is 'condemned'. Similarly, if the concentration is less than, say  $10 \text{ mg kg}^{-1}$  it does not matter if the error is 100%. Where the customer does need assurance is how reliable the information is and what confidence can be placed on the data at or around the  $40 \text{ mg kg}^{-1}$  level. Is  $41 \text{ mg kg}^{-1}$  or  $39 \text{ mg kg}^{-1}$  unacceptable or acceptable? All of the procedures have to be fully documented (see Chapter 8), so that answers can be found to the following questions:

- What is the precision and accuracy of the method?
- Was the method tested with known samples to show that it was suitable in terms of the analyte and the concentration range, i.e. validated?
- What data are available concerning sampling, extraction procedures and the end measurement?

Forensic analysis is usually required for the collection of data in the course of determining whether legislation has been infringed. The customer requires that, above all, there is an unbroken chain of evidence from the time the samples were taken to the presentation of evidence in courts of law. In the laboratory this will include documentation and authorization for sample receipt, sample transfer, sub-sampling, laboratory notebooks, analytical procedures, calculations and observations, witness statements and sample disposal. All of these aspects can be called as evidence in court.

Every analytical chemist should be asking the same questions, i.e. ‘Am I using a method which is appropriate and fit for purpose, has it been validated and what are the sources of uncertainty in the method and in my technique? What confidence do I have in the final answer?’ Scientists are increasingly replacing the notion of *error* by that of *uncertainty*. Just because an instrument shows a scale reading of 3.4276 does not mean that the figures are all true and are known to the same level of certainty. It will depend on the state of calibration and on the machine having been used in a proper manner. Even the simplest titration will have a degree of uncertainty at several stages. For example, if a 25 ml burette is used in an acid–base titration, the reading on the burette may be 10.50 ml at the end-point. However, there is an associated uncertainty from two sources in this reading. First, there is an uncertainty in the visual measurement due to parallax and the interpretation of the meniscus and secondly the uncertainty of the calibration of the burette itself. This will depend on the grade of burette used. The reason for this and the way to go about making an assessment of uncertainty in a chemical measurement is explained in Chapter 6.

As an analyst you understand the meaning of the scientific data you produce. However, it must be remembered that laymen often do not and so the data need to be documented in a form that is easily understood. For example, the chromatographic analysis of hydrocarbon oil from an oil spill can produce a chromatogram with over 300 components. Explaining the significance of such data to a jury will be of little benefit. However, overlaying it with a standard trace can demonstrate pictorially whether there is a similarity or not. The customer requires information from the analyst to prove a point. If the data are not fully documented, then the point cannot be proven. A customer who has confidence in a laboratory will always return.

## 1.5 Purpose of Analysis

Analysis involves the determination of the composition of a material, i.e. the identification of its constituent parts and how much of each component is present and, sometimes, in what form. Before starting work on a sample, it is vital to enquire why the work is required, what will happen to the result(s) and to find out what decisions will be taken based on the numerical values obtained.

The purpose of an analysis and the use to which the analytical report or certificate of analysis might be put are numerous. A few examples are listed below:

- Preparation of a data bank of figures to establish trends, e.g. changes in pesticide residue concentration in foods with season, or from year to year.
- Acceptance/rejection of a chemical/product used in a manufacturing operation.
- Assessment of the value of a consignment of goods before payment.

- Prosecution of a company for selling a product not up to the stated specification, e.g. a sausage containing insufficient meat or containing pork instead of beef.
- Providing evidence in a case for or against an individual charged with being in possession of illegal drugs.

In all cases, there could be serious consequences depending on the particular investigation.

An error in the data bank figures may become apparent as further work is completed. If the error is a simple calculation error it can be corrected. However, if a mistake was made because of selection of an unsuitable method or in the calibration of instruments or in the choice of reagents used, it may not be possible to correct the error. This is particularly true if the original samples have been used up or if they have deteriorated in storage. Nevertheless, the error may not be serious where trends are under investigation, e.g. trends over a period of time or trends produced as a result of different treatments. This is because the absolute value of the measurement is of far less importance than the change from day to day, treatment to treatment, etc. Hence, so long as errors remain constant, differences between results will be real. This may not be true if different methods and/or different equipment are used or when trends are being monitored by a number of different laboratories.

Acceptance/rejection or valuation cases may cost (or save) a company a great deal of money depending on the error in the analysis and size of production runs. The prosecution of a company may give rise to a fine, or in the most severe cases, imprisonment of individuals. The arrest of an individual for possession of drugs (or explosives) could have very serious consequences; the individual concerned may be convicted. If the identification of the substance was made in error, the convicted person will have suffered unnecessarily and there could subsequently be huge compensation claims.

Hence, the choice of method and the validation of the method selected become increasingly more critical for those analyses resulting in actions towards the bottom of the list than for those at the top. You now need to pause to consider what the consequences of poor analytical work could be in your own particular job. Do not forget to include longer-term implications as well as the immediate problems. Poor or wrong data also result in the loss of reputation – customers who never come back.

## Summary

This chapter sets the scene for the rest of the book. It gives examples of why analytical measurements are made. This then leads on to why the reliability of these results is so important. Quality is often a misunderstood word in the

context of services and products. This chapter explains what it means in terms of analytical results.

## Reference

1. IMEP 9, 'Trace Elements in Water III, Cd, Certified Range 81.0–85.4 nmol l<sup>-1</sup>', European Commission, Joint Research Centre, Institute for Reference Materials and Measurements (EC-JRC-IRMM), Geel, Belgium (1998). [[www.irmm.jrc.be/html/interlaboratory\\_comparisons/imep/index.htm](http://www.irmm.jrc.be/html/interlaboratory_comparisons/imep/index.htm)] (accessed 30 November, 2006).



## Chapter 2

# General Principles of Quality Assurance and Quality Control

### Learning Objectives

- To appreciate the need for quality assurance.
- To understand the importance of setting up a quality management system.
- To be able to define what is meant by quality assurance and quality control.
- To be aware of some of the international quality standards.

## 2.1 Introduction to Quality Assurance

The analyst provides scientific evidence on which important decisions are made. The work of an analyst is devalued if it is merely considered to be making measurements and reporting results. There has to be some added value. This is provided when it can be demonstrated that the results produced have been obtained in an organization that operates a quality management system. It is because of the importance of the work that the quality has to be assured. This means that all of the necessary actions have been taken to make sure that any factor which has an influence on the final result has been considered, understood and reported in a permanent record – that the appropriate measurements have been made and these have been carried out correctly using a validated method.

No one deliberately produces incorrect results. You may have noticed how often people remind you of the mistakes you have made but rarely of the good work. If your results prove to be wrong, it is not just your reputation that will

**Table 2.1** Trace metals in sea water ( $\mu\text{g l}^{-1}$ )

| Metal   | 1965 | 1975 | 1983  |
|---------|------|------|-------|
| Lead    | 0.03 | 0.03 | 0.002 |
| Mercury | 0.03 | 0.03 | 0.001 |
| Nickel  | 2.0  | 1.7  | 0.46  |
| Copper  | 3.0  | 0.5  | 0.25  |
| Zinc    | 10.0 | 4.9  | 0.39  |

suffer, your customers and subsequently your organization will also suffer. Everyone makes mistakes but when you do, you must always try to find out why it happened, thereby reducing the chances of it happening again.

There is ample proof in the literature that there are data being produced that are not fit for their intended purpose. Table 2.1 shows the accepted representative values of the concentration of trace metals in the open ocean over a 20-year span. The values given might suggest that there has been a dramatic decrease in the level of these metals, e.g. the lead levels appear to have dropped 15-fold. The reasons for the apparent reduction in metal content in the sea water over the period studied could be a reduction in polluting materials, change in sea flow or improvement in the selectivity of the analytical technique. However, the concentration of metals in open ocean water is expected to remain fairly constant over time. There are a number of problems with this type of study. These include difficulty of sampling and storing of samples and the delays in carrying out the analysis, as well as the analysis itself. Unfortunately, there is no way of giving a definitive answer as to why laboratories have reported values which may differ by a factor of  $10^4$ . There is insufficient documentary evidence of how the earlier measurements were made and one cannot get a 1965 sample to repeat the measurement! Therefore, there is no basis from which to draw conclusions.

It is important that a measurement made in one laboratory by a particular analyst can be repeated by other analysts in the same laboratory or in another laboratory, even where the other laboratory may be in a different country. We aim to ensure that measurements made in different laboratories are comparable. We are all confident that if we measure the length of a piece of wire, mass of a chemical or the time in any laboratory, we will get, very nearly, the same answer, no matter where we are. The reason for this is that there are international standards of length, mass and time. In order to obtain comparable results, the measuring devices need to be calibrated. For instance, balances are calibrated by using a standard mass, which can be traced to the primary mass standard (see also Chapter 5). The primary standard in chemistry is the amount of substance, i.e. the mole. It is not usually possible to trace all of our measurements back to the mole. We generally trace measurements to other SI units, e.g. mass as in  $40\text{ mg kg}^{-1}$  or trace back to reference materials which are themselves traceable to SI units.

In analytical chemistry, we do not have a standard mole. Therefore, solutions made up to a well-defined concentration using very pure chemicals are used as a basis from which we can compare other solutions or an instrument scale. This process is 'calibration'. For some analyses, the chemical used may be a Certified Reference Material which has a well documented specification, e.g. in terms of the concentration of a particular species and the uncertainty of the specified value. However, it is not sufficient just to calibrate the apparatus/equipment used, it is important that the complete method of analysis is validated from extraction of the analyte from the sample to the final measurement.

The biggest benefit of producing reliable and traceable data is the mutual acceptance of those test data both nationally and internationally, by manufacturers, regulators, traders and governments. In this context, metrological traceability is as defined in the *International Vocabulary of Basic and General Terms in Metrology* (VIM) [1]. Metrological traceability is 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. (A new version of VIM is being produced and so the definition may change slightly in the near future.) In terms of international trade, it is important that countries within a trading community accept each other's results. This can only happen if all of the countries agree the standard of quality testing and calibration. To achieve this, everyone must use the same reference points and be third-party assessed.

The increasing concerns of the public and the need for monitoring very low concentrations of toxic compounds means that detection at levels below  $\mu\text{g kg}^{-1}$  are required in many areas of analysis. Pesticides in the food chain, toxic materials in incineration and waste products and traces of nitro-compounds in 'finger washings' of a person suspected of handling explosives, all involve analysis for low concentrations.

If data are produced which are not fit for their intended purpose, there is both the financial penalty and the possible legal penalty to be considered. For instance, if a manufacturer of pharmaceuticals produces a pharmaceutical tablet containing the incorrect amount of active ingredient, the consequences could be disastrous, causing, in the worst circumstances, loss of life.

Contaminated land is a 'never to be forgotten' high profile area of environmental pollution. However, to do anything with the land, so that it can be made fit for future uses, assessment has to be made on the basis of reliable analytical data. If the sampling and analysis are performed appropriately, then a set of results can be produced which can be used with confidence to make decisions about how the land can be made suitable for use. Random or unintelligent sampling can miss patches or 'hot spots' of pollution, which can have disastrous effects (see Chapter 3 for a discussion of sampling). If bad sampling has resulted in a high concentration of phenols or sulfate from an old gas works being undetected, the concrete in the piles for a new multi-story building could be attacked with the

eventual weakening of the structure. It is also possible that if assessment of land is not performed reliably, then if the land is used for gardens, the vegetables grown on that land may provide a source of toxic metals which can end up in the food chain.

The benefits of producing good data are therefore broad and impinge on all of our daily lives, whether it is food, environment, health or trade. Laboratories that produce valid measurements have a higher status in the analytical world, since they produce data that are demonstrably traceable to a reference standard and reliable, with the cost of correcting bad data being lower. This means that such laboratories have a better chance of competing in the open market.

## **2.2 Quality Management System, Quality Assurance (QA) and Quality Control (QC)**

Quality appears to have a language of its own and some definitions or explanations are required. This is what is covered in this section. A quality management system is a set of procedures and responsibilities that an organization puts in place to make sure that the staff have the facilities, equipment and resources to carry out their work effectively and efficiently. For the quality management system to be formally recognized and audited, it must be based on an internationally recognized standard that means something to its customers and other organizations across the world. There are a number of aspects of a good management system that should be put in place. These include the quality policy statement, general organization of the laboratory, roles and responsibilities, quality procedures, document control and reporting of results, auditing, review and subcontracting. It should be remembered that a quality management system should only be as comprehensive as that which is required to meet the needs of the customers. This means it may exceed the expectation of any individual customer.

Briefly, the quality management system is a combination of quality management, quality control and quality assurance. Quality assurance and quality control are components of the laboratory's quality management system. There is often confusion over the meaning of quality control and quality assurance and regrettably they are often used interchangeably. This is possibly because some quality control and quality assurance actions are interrelated. The definition of the terms can be found in the International Organization for Standardization (ISO) Standard, ISO 9000:2005 [2].

Quality assurance is the part of quality management focused on providing confidence that quality requirements will be fulfilled. It is all the planned and systematic activities implemented within the quality system, and demonstrated as needed, to provide adequate confidence that the analytical service will fulfil the requirements for quality. Quality assurance is the essential organizational infrastructure that supports all reliable analytical measurements. It encompasses

a number of different activities. Included are staff training, record keeping, appropriate laboratory environment for the particular activities, adequate storage facilities to ensure the integrity of samples, reagents and solvents, maintenance and calibration schedules for instruments and the use of technically validated and documented methods.

Quality control is the part of the quality management system focused on fulfilling quality requirements. It is the planned activities designed to verify the quality of the measurement, e.g. analysing blanks or samples of known concentration. There are two types of quality control – internal quality control and external quality assessment (also known as external quality control). Internal quality control provides confidence to the laboratory management while external quality assessment provides confidence to the customer. Internal quality control is the operations carried out by the staff as part of the measurement process which provide evidence that the system is still operating satisfactorily and the results can be accepted (see also Chapter 5). Evidence is required that the performance of the laboratory is not only consistent but also comparable with other laboratories making similar measurements; this is provided by external quality assessment. Laboratories taking part in formal or informal intercomparisons achieve this. Formal intercomparisons are termed Proficiency Testing (PT) (see Chapter 7).

## 2.3 Different Standards and their Main Features

Standards dealing with the quality of a service have been developed by a number of national and international organizations. The requirements of an analytical laboratory depend on its size, the range of its activities and the type of analysis carried out. There are therefore a number of Standards that should be considered by an analytical laboratory. These Standards will be covered in more detail in Chapter 9.

### DQ 2.1

Is there a difference between the processes of certification and accreditation?

*Answer*

There is a subtle difference in the meaning of these two terms and it is important to be clear about this difference. This is explained in the following paragraphs in terms of two Standards which you may encounter in your work.

The International Standard, ISO 9001:2000, Quality Management Systems – Requirements, is a general standard that applies to all types of organizations,

regardless of size [3]. This Standard specifies the requirements for a quality management system where an organization, (a) needs to demonstrate its ability consistently to provide a service that meets customer and applicable regulatory requirements, and (b) aims to enhance customer satisfaction through the effective application of the system, including processes for continual improvement of the system and the assurance of conformity to customer and applicable regulatory requirements. If this meets the needs of the organization, it will seek certification by a third-party against this Standard. Certification is the procedure by which an external, independent auditing body (third-party) gives written assurance that a product, process or service conforms to specified requirements [2]. Independent third-party certification is offered by, e.g. BSI British Standards, the UK National Standards Body and, on an international scale, BSI Management Systems or Lloyds Register of Quality Assurance. This Standard does not check the competence of the organization but the control of the processes.

Another International Standard, ISO/IEC 17025:2005, General Requirements for the Competence of Testing and Calibration Laboratories, is far more specific [4]. This Standard applies to all laboratories performing tests and/or calibrations. It covers the competence of the laboratory and its staff. Laboratories seeking accreditation to this Standard will develop their management system for quality, administrative and technical operations in line with the clauses in this Standard. Accreditation is the formal procedure carried out by the relevant authority, which confers formal recognition that a laboratory is competent to carry out certain tasks [5]. This includes the management issues dealing with administration and those quality issues that are within certification. Accreditation is usually for a specific combination of analyte, matrix and method, although there are opportunities for flexible scope. Guidance on the implementation and management of flexible scopes of accreditation is produced by the International Laboratory Accreditation Cooperation (ILAC G18) [6] and many national accreditation bodies, e.g. UKAS LAB 39 [7]. The national accreditation body usually carries out the accreditation in that country. The United Kingdom Accreditation Service (UKAS) is the competent body in the UK.

Medical laboratories have some specific needs and these are incorporated in ISO 15189:2003, Medical Laboratories – Particular Requirements for Quality and Competence [8]. The requirements of both ISO 9001 and ISO/IEC 17025 are incorporated within this Standard. It is a customized version of ISO/IEC 17025 for medical laboratories. In the UK, UKAS have designated Clinical Pathology Accreditation (UK) Ltd as the authoritative body to accredit against this Standard.

Test facilities in the OECD (Organization for Economic Co-operation and Development) member countries that conduct regulatory studies must comply with the OECD Principles of Good Laboratory Practice (GLP), as set out in Council Decision C(97)186/Final. These are referred to as GLP Principles. GLP came into prominence in the late 1970s in response to some malpractice in research and development activities of pharmaceutical companies and contract

laboratories used by them. The malpractice included some cases of fraud, but the majority was a result of poor management and organization of the studies carried out as part of the registration process for prospective pharmaceutical products. Problems were first highlighted in the United States and as a consequence the Food and Drug Administration (FDA) developed, in 1976, a set of principles for such studies which had to be adhered to before a regulatory authority could accept data from the studies. A harmonized set of regulations was required to ensure that international trade was not impeded. These were produced by the OECD and the initial set of principles was adopted in 1981. These were subsequently revised and published in 1998. The purpose of the GLP principles is to promote the development of quality test data. The principles set out a quality system dealing with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported. There needs to be sufficient information available for the study to be reconstructed at a future date. In the European Union and many other parts of the world, e.g. the USA and Japan, it is a regulatory requirement that studies undertaken to demonstrate the health or environmental safety of new chemical or biological substances shall be conducted in compliance with the principles of GLP. Each country has to have a monitoring authority that assesses the study to ensure it meets the requirements of the GLP principles. In some countries there may be more than one authority. In the United Kingdom, the GLP requirements are contained within The Good Laboratory Practice Regulations, Statutory Instrument 1999 No. 3106 with the amendments set out in Statutory Instrument 2004 No. 994 [9, 10]. These regulations require that any test facility which conducts, or intends to conduct, regulatory studies must be a member of the UK GLP Compliance Monitoring Programme. In these regulations, a 'regulatory study' is defined as a non-clinical experiment or set of experiments:

- (a) in which an item is examined under laboratory conditions or in the environment in order to obtain data on its properties or its safety (or both) with respect to human health, animal health or the environment;
- (b) the results of which are, or are intended, for submission to the appropriate regulatory authorities;
- (c) for which compliance with the principles of Good Laboratory Practice is required in respect of that experiment or set of experiments by the appropriate regulatory authorities.

The Department of Health has responsibility for the monitoring in the UK through the GLP Monitoring Authority.

### 2.3.1 Common Features of ISO 9001, ISO/IEC 17025 and ISO 15189

The three Standards, ISO 9001, ISO/IEC 17025 and ISO 15189, have much in common but there are subtle differences. Figure 2.1 shows the common features. These will be covered briefly here and in more detail in Chapter 9. In matters relating to the management structure and responsibility for quality matters, the Quality Manager (however named) usually acts on behalf of the Chief Executive. The management structure is laid out in the Quality Manual which is the top-level document. It shows clearly how the organization is structured and the roles and responsibilities of the managers and their teams. The Quality Manual also contains all of the top-level documents relating to central functions and possibly some business areas. This will be supported by local documentation, e.g. Work Instructions and Standard Operating Procedures. It is important that all matters relating to a particular sample can be tracked from contract review, through the receipt of the sample to the delivery of the results to the customer. This means that all of the instrument results, validation and calibration data and quality control results must be uniquely identified as relating to the sample. Such records will have to be kept for the period of time set down in the Quality Manual or as agreed with the customer. Increasingly, organizations are expected to be able to demonstrate the competence of their staff. How this is achieved may also be laid down in the Quality Manual. In order to demonstrate to the senior management that the appropriate procedures are in place and being implemented, internal checks are carried out on a regular basis – these are called internal audits. These provide a means of ensuring correct implementation of the quality system. In addition, to gain either certification or accreditation, to a particular standard, there has to be third-party assessments by appropriate authorities. To ensure that all the requirements of the particular Standard and the needs of the business are satisfied, the quality management system is reviewed by top management once a year.

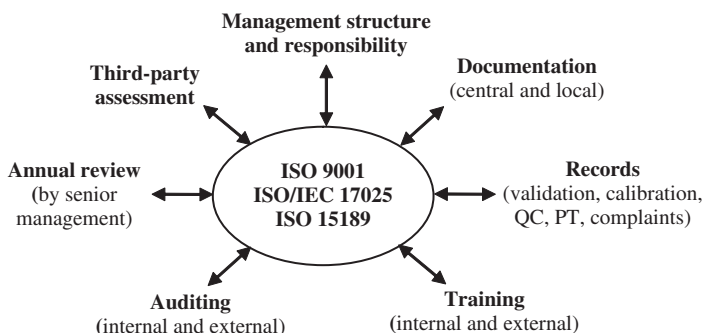


**Figure 2.1** Main components of a quality management system.

### 2.3.2 Features of ISO 9001:2000

The quality management systems Standard, ISO 9001:2000, promotes the adoption of a process approach when developing, implementing and improving the effectiveness of a quality management system, to enhance customer satisfaction by meeting customer requirements. This is on the basis that any activity that uses resources to convert 'inputs' into 'outputs' can be considered to be a process. Figure 2.2 is based on Figure 1 from ISO 9001:2000, indicating how the Standard may be interpreted for a laboratory carrying out chemical analysis.

This Standard is a very general document and does not cover technical aspects. However, analytical laboratories increasingly have selected certification to ISO 9001 to cover the broader aspects of their activities. The earlier versions of this Standard had the term 'quality assurance' in the title but this has now been removed. The reason is that the current standard requires more than quality assurance of the service. Enhancement of customer satisfaction is also expected, along with evidence of continuous improvement. In Figure 2.2, this is covered in the box dealing with evaluating the results.

Changes take place in the laboratory system to take into account customer feedback and/or laboratory and office feedback. This could be after the completion of the work or as a result of the internal audit. Management review will evaluate the whole system and provide resource to enable changes to take place, e.g.

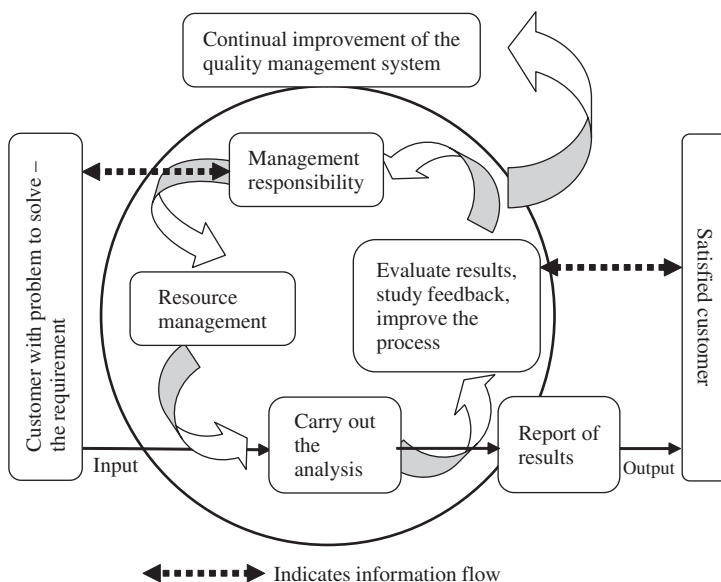


**Figure 2.2** Model of an analytical problem in terms of a process-based management system.

extra/different equipment or staff. There is a great deal of emphasis on assessing the performance and having measures in place that demonstrate customer satisfaction.

### **2.3.3 Features of ISO/IEC 17025:2005**

The ISO/IEC 17025 Standard, General Requirements for the Competence of Testing and Calibration Laboratories, is about competence and ways of demonstrating it. Whereas the ISO 9001 Standard is very general, ISO/IEC 17025 is very specific. Accreditation is given for specific tests in terms of the scope, i.e. the analyte, the matrix, method and concentration range. This Standard has two main sections – one dealing with the management requirements and the other with the technical requirements. To comply with the requirements of this Standard, the laboratory must operate a quality management system that meets the principles of ISO 9001. The technical section deals with the extra requirements of a laboratory wishing to demonstrate its competence in carrying out testing and/or calibration. Topics covered include method validation, measurement uncertainty and the use of reference materials and reference standards to achieve traceability of the reported results. Sampling that takes place in the laboratory is also covered along with the maintenance of sample integrity. As a means of assuring the quality of results, a laboratory is expected to participate in interlaboratory comparisons such as Proficiency Testing programmes (see Chapter 7).

### **2.3.4 Features of ISO 15189:2003**

This Standard was prepared specifically to cover medical laboratories. These laboratories carry out testing or examination of materials derived from the human body. Such studies are carried out for the purpose of providing information for the diagnosis, prevention and treatment of disease or assessment of the health of an individual. ISO 15189 covers a whole range of tests relating to clinical measurements, e.g. chemical and microbiological. This Standard is based on ISO 9001 and ISO/IEC 17025 and contains a correlation between the clauses and those in ISO 9001 and ISO/IEC 17025.

The terminology used in this Standard is slightly different from the others in that it is appropriate for the particular discipline. For example, the term, ‘referral laboratories’ in paragraph 4.5 of ISO 15189 is used in a slightly different sense to the comparable clause in ISO/IEC 17025. Included in this section are consultants who may provide a second opinion. If the referral laboratory is an external laboratory, to which samples are submitted for a supplementary or confirmatory examination procedure and report, it is much the same as a ‘contract laboratory’ in ISO/IEC 17025. There is an extra Annex in this Standard which covers the ethics applicable to laboratory medicine.

### 2.3.5 Good Laboratory Practice (GLP)

The layout of the GLP principles is different from the Standards covered in the earlier sections but has much in common with the management sections within those Standards. It is narrow in its application but is a legal requirement for all laboratories carrying out regulatory work. Laboratories may wish to apply the principles if they are working in a different area but they are not eligible to register with the GLP Compliance Programme.

The aim of GLP is to encourage scientists to organize the performance of the study in such a way that ensures the production of reliable results. However, the GLP principles do not deal with the technical or scientific content of the research programme. They do not aim to evaluate the scientific value of the studies. However, it is expected that the methods used will be 'fit for purpose'. Use of standard methods of analysis is encouraged but the validation studies are not generally inspected during a quality assurance audit. It is important that the procedures used are fully documented, along with any changes made during the course of a study. Carrying out method validation under GLP compliance is not required by all monitoring authorities.

Emphasis is placed on the following organizational elements:

- resource, in terms of organization, personnel, facilities and equipment;
- written procedures and protocols;
- characterization of test items and test systems;
- documentation of raw data, final report and archiving;
- independent quality assurance unit;
- archiving.

It can be seen that the GLP principles do cover similar requirements to both ISO 9001 and ISO/IEC 17025 but data generated solely under these standards would not generally satisfy the principles of GLP. This is mainly in the area of documentation.

## 2.4 Best Practice

Implementing a quality management system for a laboratory is a formal way of implementing and demonstrating good laboratory practice or 'best practice' so as not to confuse it with GLP. It is possible for laboratories to achieve the implementation side, of the management standards already mentioned, by adopting some basic principles, without going for formal accreditation. In the UK, the Department of Trade and Industry (DTI) has funded research into achieving valid analytical measurements in the area of chemical measurement (and other areas

of measurement) through the VAM programme [11]. Some years ago, an interdisciplinary group of measurement scientists suggested what are known as ‘The six principles of valid analytical measurement’. These have subsequently been widely adopted and are given below. If you study the Principles and ISO/IEC 17025, you will see there is a great deal of common ground.

## VAM Principles

1. Analytical measurements should be made to satisfy an agreed requirement.

*What does the customer want to know?*

2. Analytical measurements should be made using methods and equipment which have been tested to ensure they are fit for purpose.

*Make sure everything works as it should and that the method used is capable of providing a useable result.*

3. Staff making analytical measurements should be both qualified and competent to undertake the task.

*Use trained staff and do not use equipment unless you have been trained to use it competently.*

4. There should be a regular and independent assessment of the technical performance of a laboratory.

*Take part in External Quality Assessment, formally through Proficiency Testing schemes and informally by taking part in intercomparison studies.*

5. Analytical measurements made in one location should be consistent with those made elsewhere.

*Use Reference Materials so that your scale of measurement is acceptable at a national and international level.*

6. Organizations making analytical measurements should have well defined Quality Control and Quality Assurance procedures.

*Implement a quality management system or at least the elements of such a system.*

There are other ways of demonstrating that an organization implements best practice. One of these is obtained through the European Foundation for Quality Management (EFQM). The EFQM excellence model was introduced in 1992 as a framework for assessing applications for the European Quality Award which has since been replaced by the EFQM Excellence Award (EEA). The EFQM

model provides a non-prescriptive framework currently based on eight fundamental concepts of excellence. These are as follows:

- **Results Orientation**

*Excellence is achieving results that delight all the organization's stakeholders.*

- **Customer Focus**

*Excellence is creating sustainable customer value.*

- **Leadership and Constancy of Purpose**

*Excellence is visionary and inspirational leadership, coupled with constancy of purpose.*

- **Management by Processes and Facts**

*Excellence is managing the organization through a set of interdependent and interrelated systems, processes and facts.*

- **People Development and Involvement**

*Excellence is maximizing the contribution of employees through their development and involvement.*

- **Continuous Learning, Innovation and Improvement**

*Excellence is challenging the status quo and effecting change by utilizing learning to create innovation and improvement opportunities.*

- **Partnership Development**

*Excellence is developing and maintaining value-adding partnerships.*

- **Corporate Social Responsibility**

*Excellence is exceeding the minimum regulatory framework in which the organization operates and to strive to understand and respond to the expectations of their stakeholders in society.*

More information can be obtained from the EFQM website [12].

## Summary

This chapter outlines the means by which results which are fit for purpose are achieved. There are examples of how unreliable results can affect all of our lives. It explains some of the nomenclature encountered in quality management and why a quality management system is important. There is a brief description of the international standards that are applicable to a chemical analysis laboratory.

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## Chapter 3

# Sampling

### Learning Objectives

- To understand the importance of sampling.
- To be able to identify different types of samples.
- To understand the importance of sampling plans and appreciate the legal and statutory requirements.
- To appreciate the importance of correct sample handling and storage.
- To be aware of the various problems associated with subsampling and the different techniques used.

This chapter gives an introduction to sampling. Devising a sampling plan or procedure may apply to your current position but it is more likely that the only sampling you are involved with is taking a test sample from the laboratory sample which has been submitted for analysis. However, you should be aware of the complete sampling process because this allows you to discuss sensibly the previous history of the material which comes into the laboratory. This will help to ensure that you measure the correct parameter.

The area of sampling is confused by the use of the same words in several different contexts. An IUPAC paper (1990) goes some way towards clarifying the definitions [1]. There is available also specific guidance on terminology in soil sampling [2]. In the foods sector, the Codex Alimentarius Commission has prepared draft general guidelines on sampling which were accepted by the Commission in July 2004 [3].