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 defendable, 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,

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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 ß-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 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

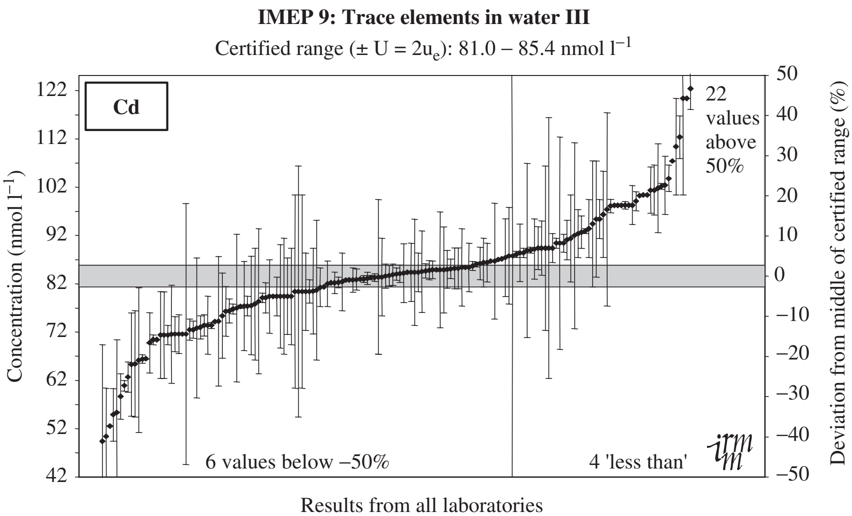

Figure 1.1 Results from an international intercomparison, IMEP 9, where U is the expanded uncertainty and u_e the combined standard uncertainty [1] (see Chapter 6, Section 6.3). Reproduced by permission of EC-JRC-IRMM (Philip Taylor) from IMEP 9, 'Trace elements in water III, Cd, certified range 81.0–85.4 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 mg kg^{-1}. The analysis needs to be quantitative, accurate and reproducible at the 40 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 mg kg^{-1} to 100 mg kg^{-1}. If the land is contaminated above the guidance limit, it does not matter whether it is 45 mg kg^{-1} or 145 mg kg^{-1}; the land is 'condemned'. Similarly, if the concentration is less than, say 10 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 mg kg^{-1} level. Is 41 mg kg^{-1} or 39 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^{-1}', 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] (accessed 30 November, 2006).