

V Quality control : guidelines for achieving quality in trace analysis

V.1 Introduction

This chapter explains those matters in trace chemical analysis to which special attention should be paid in order to obtain reliable results (such as the analysis of inorganic and organic compounds at concentrations less than 100 ppm). This chapter describes general methods for both quality control and techniques for trace analysis. For example, requirements for the ‘ideal laboratory’, and concerns about apparatus, analytical methods, and routine analysis. Specific analytical methods are not discussed, and the nature and size of errors and the technology required to decrease such errors are not mentioned. One way to use this chapter is as a concise outline or as technical notes which should be followed in the laboratory.

As analytical technology improves, so instrument sensitivities are improved and the amount which can be detected becomes smaller. One consequence of this instrumental improvement is that, unless analysts pay attention to such matters as contamination or leakage at the time of trace measurement, the accuracy of data becomes unreliable and errors in the data can be large. It is absolutely necessary to make strenuous efforts to maintain low and constant blank values, and important to prevent contamination. Advanced analytical instruments and contamination management can make the evaluation of lower concentration samples possible. Needless to say, evaluation of the results of such trace analysis must also be paid sufficient attention.

V.2 Apparatus and instruments

Ideally, all apparatus and instruments used for trace analysis should be located and maintained separately from equipment used for general analysis. If that is not possible, some management strategies to prevent the risk of contamination when apparatus and instruments are shared, have to be adopted.

Trace analysis is very different from macroanalysis. Essentially, this is because small amounts of contamination in the final sample solution (the solution used for determination) causes the bulk

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of the error. Such contamination can be derived not only from the apparatus or reagents but also from such things as building materials, the environment, or analytical operations and procedures, etc. To prevent contamination the area or areas used for trace analysis should preferably be completely separated from those used for macroanalysis. If such areas are not available, one must use contamination free cabinets or a part of the laboratory for trace analysis.

Apparatus used for trace analysis should be exclusive to such trace analysis studies. One must take special care not to share laboratory, solvent, glassware, or other apparatus to avoid contamination problems. If it is possible, use disposable glassware or plastic apparatus. Also, one must consider what other operations are being conducted in the same area. Wash apparatus or equipment severely, and contamination must be minimal for blank samples. Do not bring samples which contain high concentrations of target compounds into the trace analysis area.

V.2.1 Laboratory

The laboratory and associated equipment should be designed to allow analysts to work easily. The materials from which the laboratory is built may affect the analytical results. Building materials should be resistant to corrosion caused by the chemicals being used.

a) The working environment should be appropriate for trace analysis. There should be minimal possibility of contamination of samples. Activities such as eating, drinking, smoking, and applying make-up should all be banned in the laboratory.

Sometimes special laboratories built as clean rooms are necessary. When clean rooms are not available because of lack of budget or other restrictions, a minimally contaminated area or clean cabinet should be used. Consider what the other work is being undertaken in the same room or next door laboratory. If there are gases or particles in the atmosphere, it is possible to decrease their potential contamination effect by exchanging air. If the working area is small, it is good idea to cover apparatus and instruments to prevent particle adhesion. One must also consider the different requirements of trace inorganic and organic compounds determination. Cosmetics or jewels should be avoided because they are possible sources of contamination. Hair should be covered. Gloves reduce contamination compared to using bare hands. However, one must be careful which gloves one chooses, because the gloves themselves might pollute samples (rubber gloves contain dithiocarbamate as a vulcanisation agent, and plastic gloves may contain metals).

b) In order to gain reliable analytical results, the temperature in the laboratory should be well controlled, and a record should be maintained.

Indoor temperature may have an effect on the physical measurement conducted in the laboratory. For example, the volume of volumetric glassware is determined at a certain temperature. There are some operations effected by temperature such as extraction with ether, or degradation of target compounds during sample separation. Change of ambient temperature affects the character of HPLC columns and other instruments. When experiments are conducted at specific, non-ambient temperatures, the temperature should be measured and a record maintained.

V.2.2 Analysts

To obtain good results for trace analysis, staff must always consider the details of their work, which aspects should be paid particular attention, what aspects specifically affect results. Good results rely on the experience and cautiousness of the analysts. To obtain consistent results, staff must take pride in their work.

a) The analyst must be carefully chosen from those who are experienced and have both a deep understanding and knowledge of the requirements of trace analysis.

The analyst must thoroughly understand the analysis and related matters, and be able to scientifically answer questions about their analytical results. The analyst must understand well specific analyses, and be able to evaluate the “suitability for purpose” of the adopted method.

b) Other technical staff working under the analyst must also be well trained, analytically skilled, and have experience of dealing with the apparatus, instrument operation, data analysis. Such staff should know the purpose of the experiments, the problems inherent in each level of operational procedure, the necessity of considering special problems specifically related to the samples, the importance of accurate operation, and the size and relevance of the inevitable errors.

Staff must, ideally, understand the basic principles of the analytical operations and the necessity of quality control systems. If any member of staff has little experience in these matters then the whole process should be closely supervised by an experienced person. An inexperienced staff member should not be allowed to report on his own responsibility until he obtains sufficient

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analytical skill under the supervision of the experienced person. All staff have to be familiar with the operation of general experimental apparatus such as balances, volumetric apparatus, and know both how to use such equipment and the error generated in their use. Staff must undertake training seminars and programs related to analytical methods and their work.

c) Records concerning the training history (external in-house seminars and training programs) experience and personal character of all analytical staff should be kept.

Laboratories and institutes should plan regular seminars, the subjects of which are based the operational requirements and general experience of staff.

V.2.3 Laboratory infrastructure

a) Laboratories should be provided with stable and guaranteed quality supplies of electricity, gases, and water.

It may seem self-evident, but a stable supply of electricity, water and gas is important to conduct reliable trace analysis. A stable electric supply is necessary to allow many instruments work in a reliable and stable manner. Many laboratory operations require deionised water. Many institutes provide a centralised deionised water supply system, but it is often necessary to re-purify such deionised water depending on the nature of the analysis. Purity of gases have to be checked regularly. Gases can be purified by using such filters such as molecular sieves, anhydrous salts, activated charcoal, or deoxygenating traps.

b) It must be stressed that for trace analysis to be conducted in a laboratory, the condition of reagents, solvents, and experimental apparatus should be appropriate for such investigations.

Reagent and solvent blanks must be measured (checked) regularly to confirm that there is no contamination. If blank value show high concentrations of target analytes, check all reagents to find the source of contamination. It is relatively easy to measure reagent contamination using the same analytical method as ones used to measure samples. In addition, purified water must be analysed regularly to determine if the water contains target compounds or other interference. If detergents are used for washing glassware, one must rinse the glassware thoroughly so there is no detergent residue. Depending on the purpose of apparatus, organic solvents, acid, or alkaline may have to be used for the last rinse.

c) Keep records confirming the good condition and maintenance of all apparatus.

These rules apply equally to specific analytical instruments as well as general apparatus in the laboratory. The temperature of refrigerator and freezer s in which samples and standards are stored should be monitored and recorded.

It may be necessary to adjust or reconfigure instruments, including making calibration curves as mentioned in V.4.5. This type of adjustment corrects problems to do with the character of the instruments. For example, there are chemical scale adjustments, wavelength scale adjustments of ultraviolet spectrophotometer, or mass adjustments of mass spectrometer.

An instrumental “Ability Test “ may have to be performed under the supervision of the chief analyst in order to check if capability of the instruments is at an appropriate level. Such tests include measurement of single or multiple standard solutions to check sensitivity, resolution, noise, and baseline drifting. The frequency of such tests depends on change in instrument capability. When instruments don’t work as they are supposed to, indicate by means of a warning note that the instrument may not be in an appropriate condition for use. And before the instrument is used again, the proper repairs, re-calibration, re-tuning, etc. have to be done. Also even if there are no problems, regular maintenance is necessary. Records of routine maintenance and re-calibration must be kept along with the analytical results.

V.2.4 Analytical standards and reference materials

The term “analytical standards” is widely used by and between analysts. However, the term “analytical standard” used in this chapter means compounds and solutions which are used for making calibration curves or used for instrument checks. The ISO distinguishes this definition from that of “reference materials” as a piece of basic and general terminology required by analysts.

a) In the laboratory, analytical standards whose purity or composition is known have to be used.

Use commercial standards which come with appropriate purity notes and quality control warranties. Purchase the best standards possible. Certified reference materials designated for use in the preparation of calibration curves are recommended if they are available. If it is not

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possible to purchase standards whose concentration or compositions are known, prepare your own analytical standards, then determine the concentrations according to designated methods.

b) Standards have to checked for reliability and certainty before use in trace analysis.

Check to see if the material is of the designated grade reagent. An easy way to confirm this is to compare newly obtained standards to old ones. If there is difference, it will be necessary to investigate the discrepancy further.

c) When standards are used, the concentration of the standards, and how accurately the concentration has been determined, should be known. It is necessary to examine thoroughly whether the concentrations and the accuracy of their determination are sufficient for the purpose of the analysis.

The concentration of analytical standard solutions has to be known with sufficient accuracy to make sure it wouldn't cause analytical errors. In order to evaluate the inaccuracy of the whole analytical procedure, the accuracy of the standards has to be known. Control of standard stock solutions can be achieved by limiting use, keeping an appropriate reserve, and recording use. Make a standards log book to keep records. Standard stock solutions and the diluted standard solutions should be prepared by a designated person. Records of measured weights of standards, volumes of flasks and pipettes used for the preparation should be kept with signature of the person who prepared the standards.

d) Analytical standards and standard stock solutions have to stored under such conditions that will not cause their concentration to change. The preparation dates and expiry dates should be clarified on the labels on the bottles.

Analytical standards should not be stored with samples, or in places which may causes contamination.

Analytical standards and standard stocks deteriorate as time goes by. The expiry date of such solutions depends on the target compounds, their stability in the solvent, the stability of the solvent, and storage conditions. Expiry dates can be obtained from literature data, information from other analysts in the same field, and experiments. Keep detailed records of how the length of storage was determined. It is necessary to describe in the analytical methods about how long and how analytical standards and stock solutions should be stored.

Reagents for making standard solutions and analytical standards also have to stored. In this

case, in sealed containers in the dark at 1 - 5°C. Working standards (low concentration standard solutions in frequent use) should not generally be used for more than 2 - 3 months. Compounds which easily evaporate and are decomposed should of necessity be prepared every time.

e) Traceability of measurement results must be secured using standards with guaranteed values.

Traceability is important to allow comparison of data from different institutes and countries. If analytical methods don't cause systematic errors and standards for calibration curves are assured in nationally or internationally, traceability can be secured. Traceability of physical measurement is easy, but traceability of chemical analysis can be secured by analysing certified reference materials (CRM) which have a similar composition to one's samples and whose composition has been determined nationally or in international institutes. If ideal reference materials cannot be obtained, use the best available substitutes. For example CRM which have similar composition may cause the same problems from the point of analysis as actual samples. It is inevitable that one may have to purchase reference materials which don't contain clear information about traceability. In such cases obtain additional information from the maker. NIST (USA), NRC (Canada), BCR, IAEA (EC), and NIES (Japan) all provide environmental reference materials.

V.3 Methods

V.3.1 Plan

A good plan is indispensable for successful trace analysis. When formulating the plan, consider the purpose of the analysis, analytical quality control, the sampling regime, the choice of analytical methods, the accuracy and precision of the methods, and report contents etc.

Consider comparative analyses to evaluate contamination levels. The analytical uncertainty has to be evaluated and reported as a part of routine work of laboratories.

V.3.2 Selection / development of analytical methods

a) Cautious selection and development of analytical methods is crucial to obtain reliable results.

There are several analytical methods that may be applied to most studies. The following list shows, in order of importance, which methods might be applied for most purposes:

- (1) Official analytical methods being simultaneously compared and unified at multiple institutions at a very high technical level.
- (2) Analytical methods whose adequacy has been confirmed at more than two institutes, or which are recommended by specialist committees.
- (3) Analytical methods have been developed by institute itself and whose adequacy has been confirmed. Original methods from the literature, books or various manuals.

b) Important factors that influence the choice of analytical method are whether sufficiently reliable results can be obtained under such limitations as available experimental apparatus, instruments, required time and time limits, budget and other restrictions.

Analysts can generally obtain accurate results by using common, familiar analytical methods instead of using completely new methods. In order for analysts to be able to apply an adopted an unfamiliar, analytical method to samples with special problems having never personally applied the method, it will be necessary for the analysts to check for themselves both if the method is appropriate, and if the method is as reported. (Ref. V.3.3)

Ideally, one should use the largest quantity of sample possible given the limits of sample size and analytical constraints. This is especially important when target compounds are not evenly distributed in the sample matrix. Large amount of samples contain more target compounds, there are less contamination effects, and decreased operational losses. The most important technical points for choosing analytical methods are:

- (1) How much analytical accuracy is necessary? Does the chosen method satisfy this requirement?
- (2) Are measurement results within the range of the calibration curve used?
- (3) Is the detection limit of the chosen analytical method lower than the expected concentration of the constituent in the sample ?
- (4) Are there any interferences in the samples? Was a spike recovery test done using actual samples (spiked amount is equivalent to the amount in the sample)?

- (5) Are instruments, reagents, apparatus ready for analysis? Were staff appropriately trained to operate the analytical methods?
- (6) According to historical data for the selected analytical method, did results of inter-laboratory analysis or the repeatability reported by each institute agree well? How much difference is there between standard deviations of repeatability test within the same samples and that of one test operated on the whole process?

c) The two most important factors which decrease opportunities for contamination and loss of target compounds are a decrease in the number and complexity of analytical operations. However, interferences which have effects on the measurement results of the target compounds should be removed until the effects the interferences cause can be neglected.

Any reduction in the number of procedures is always related to removal of interference. Increasing the number of procedures increases the possibility of contamination, and decreases accuracy. For example, when target compounds are extracted from samples with solvents, direct measurement of the extracts is highly accurate, compared to extraction of target compounds through additional operations such as reverse extraction and solvent removal.

V.3.3 Adequacy

a) Accuracy and precision have to be checked through the whole analytical process. Precision can be checked by analysing standards. If standards are not available, precision can be confirmed by comparing the data being collected with that from another analytical method whose principles are different and whose reliability has been confirmed.

Accuracy has to be checked not only at the last determination step, but throughout the whole process. Accuracy can be checked by analysing multiple, homogeneous samples which contain multiple target compounds. Precision may also be checked by analysing spiked samples. Inclusion (systematic error) can be checked by analysing samples of known composition such as standards or determining recovery of spiked samples.

b) Confirmation and evaluation of the causes of inaccuracy should be undertaken.

It is important to know the difference between inaccuracy and error. Inaccuracy of analysis gives data incompleteness. Analytical error is a value that causes the analytical value to deviate from the true value. Therefore, if the analytical error is known, data can be adjusted to the true

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values.

V.3.4 **Quality control system**

It is necessary to establish internal quality control systems which are clearly regulated, in order to monitor performance of instruments, reliability of calibration curves and dispersion or inclination through the whole analytical procedure. This can be checked by regularly analysing compounds which are close to the composition of the samples.

Systematic internal quality control has to be conducted as a part of normal quality control in order to investigate everyday or batch analytical conditions. Prepare a manual which clearly explains the procedures. The nature of quality control system depend on the importance and character of analysis, the frequency of analysis, batch size, automation capacity, difficulty of the analytical method and reliability. Confirmation of analytical results by quality control should be done for each batch. If the check samples are outside prescribed limits, abandon the results of all samples after the last check samples which give a normal result. Then conduct appropriate improvement before re-analysis of samples. Samples for quality control (QC) have to be typical samples, stable, and in a sufficient amount to be used for long periods. During the study period, whether the analytical methods fits in a prescribed range can be checked by plotting analytical values of QC samples on a normal chart. The amount of QC that has to be conducted depends on the nature of the study, but must be sufficient to prove the reliability of the analytical data. For example, it is normal to analyse one QC sample after every 20 samples. For complicated analyses, analysis of 30 % of samples as QC samples is not uncommon, sometimes more than 50 % is necessary. If the analysis is rarely conducted, analysis character tests have to be undertaken each time the method is used. This includes analysis of standards (reference materials) whose concentration are known, double analysis, and recovery tests. If the analysis is conducted more often, systematic QC using control charts and check samples has to be undertaken.

Essentially, quality control plans have to include the following :

- **Regular checks for contamination.**
- **Regular recovery tests using analyte concentrations similar to that in the samples to evaluate analytical method operation. Use the same matrix as sample for recovery test.**
- **Analysis of check samples for each group of sample.**

V.3.5 Documenting analytical methods

The analytical methods and all routine operating procedures have to be documented. The document should contain information detailing the collection and nature of samples, details of the analytical procedure, detection limits, methods for calculating analyte concentrations. Also it has to be clear who is responsible for the analytical methods and who has authority to change the method.

The document should be stored for a pre-determined period of time, and if some changes and improvements happen, the changes have to be made obvious in the documentation. Written methods are described and sorted as “analytical methods”, “standard analytical methods”, “standard operation procedure”, “business order?”, “protocol” etc.

V.4 Analysis

No part of analytical procedure must change the composition of the samples, or affect the concentration or determination of the target compounds.

V.4.1 Receiving and storage of samples

A reliable system for the registration and record of samples in the laboratory must be established. Samples which are brought in and the requested form of analysis should be compared and checked. Make records of any damage, or abnormality of the sample containers and the samples at the time they are received. Record the dates and the time the samples are received. Open any packages carefully, in a safe place and with the appropriate level of safety precautions, and in a place which has no, or minimal, risk of contamination. Mark the sample with unique numbers (codes) which can be used from the moment of sample receipt, through the analysis to the reporting of the results.

Analyse unstable samples immediately. If this is not possible, or treat and store the sample in a manner which prevents sample decomposition or change. There are several things to remember when storing and preserving samples. Although light affects only certain kind of compounds,

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shielding is generally necessary. To prevent evaporation of volatile compounds, it is necessary to pay special attention to temperature, exposure to sunlight, and the integrity of container seals. The stability of samples, standards, and standard solutions is a function of standing time at each step of the analytical procedure. Samples must be stored in appropriate containers under appropriate conditions which prevent cross contamination with other samples, do not allow decomposition by external factors such as light and heat, and preserve the sample. High concentration standards and samples should be stored separately from calibration curve standards because of the possibility of contamination.

V.4.2 Taking sub-samples

Check visually if the samples contain objects which have to be removed. If there is any doubt about homogeneity of samples, mix the sample thoroughly. When not all of the sample is used for analysis, take representative sub-samples. Be careful of contamination and chemical changes of target compounds or sample matrices when separating samples.

When sub-samples are taken from inhomogeneous samples, special care is necessary. It may be possible to determine from exceptional data which component of the samples has to be chosen. However, most of the time samples have to be homogenised evenly.

V.4.3 Sample preparation

Make sure that extraction or dissolution conditions (temperature etc.) do not cause decomposition or decrease of concentration of target compounds in the sample. Reduce interferences and contamination. Pay attention not to spill sample solutions or cause any loss by adsorption and desorption.

V.4.4 Measurement

Describe the operation of analytical instruments clearly, so there is no chance of any misunderstanding. Conduct regular maintenance of instruments at appropriate intervals. Mention anything which may affect instrument sensitivity. One MUST operate the instruments

within the limits of the range of the calibration curve or optimum operating range. Check reproducibility for sample measurement beforehand.

Describe in detail in written analytical methods the making of calibration curves, the frequency of measurement of blanks, standards and check samples. Write down details of the operating range of instruments. Conduct work according to such outlines of operations e.g. for steps such as set up of instruments, judgement of ability, operating conditions and operations.

Describe in detail the possibility of interference and appropriate adjustment methods. Adjustments are done by using solutions which contain known concentrations of both target compounds and other compounds whose concentrations are the same as samples.

V.4.5 Making calibration curves

Measure standards repeatedly at designated intervals to make instrument calibration curves and to adjust results for changes in instrument sensitivity during measurement. Measure reagent blank as necessary in order to check if there is any residual contamination after standard measurement. Measurement of standards is also used to check if the reproducibility of results is within an acceptable range.

It is hard to stress how important it is to make calibration curves properly in order to gain accurate results. There are several kinds of calibration curves, and which one to choose depends on the character of the samples to be analysed and the analytical instruments to be used.

- The absolute calibration curve method (external calibration curve) measures concentrations of standard solutions in an operation distinct from that of sample analysis. A standard solution containing a single concentration of the target analyte is analysed and a concentration-response factor (RF) determined. By using standard solutions of multiple concentrations a calibration curves can be plotted. Once the calibration curve is produced, the response of the target analyte in the samples is used to determine the concentrations of the target compounds in the sample.
- The internal standard method is used to decrease errors for chromatography or atomic absorption spectrometry. There are two types of internal standard method as the following:
 - (1) General internal standard method. Calibration curves are produced in a similar manner to the external standard method for compounds of similar chromatographic behaviour to

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the target analytes. Thereafter, known amounts of these compounds are added to the sample mixture either prior to any sample preparation or just prior to chromatography. The ratio of the response of the internal standard and the response of the target analyte in the samples is used to determine the concentrations of the target compounds in the sample. A variation of this method is the isotope dissolution method for mass spectrometry.

- (2) Standard addition method. Used to determine the change in response caused by the solution being introduced into analytical instruments. Internal standards are added to both standard solutions and samples, the standard and samples are measured together, and the response of the additional target analyte in the sample is used to determine the concentrations of the target compounds in the sample.

Calibration curves should be made regularly in order to confirm the sensitivity and / or drift in sensitivity of analytical instruments. Record all apparatus parameters at the time of taking data for calibration curves because change in apparatus parameters can affect the slope of calibration curves. Calibration conditions can change abruptly depending on continuous parameter change or conditions of analytical operation. In order to cope with this, most laboratories conduct regular re-calibration. Regular calibration is indispensable for formal quality assurance schemes.

V.4.6 Signal management

a) Signal management in analytical methods is very important. The technology involved should not readily be changed without special reasons. If the technology has to be changed, write down the reasons for the change as well as details of the alterations.

Signal management technology is used to change the electrical signals originating from the detectors to forms more meaningful for analysis. Signal management includes signal amplification, alternating current signal rectification, reduction of background signal, exchange from analogue to digital, and integration etc.

b) Data can be used only when the S/N ratio is more than the value specified in the analytical methods.

Accuracy of measurement relies on the S/N ratio at the time of measurement. The permitted S/N ratio is given in the analytical methods, the S/N ratio during the analysis of a series of samples should be above that. Otherwise the data obtained will not be in the range determined by the

methods.

c) It is necessary to pay attention to signals produced by blanks. If such signals are not within tolerance limits, all measurement data at that time are invalid.

If blank values have an adverse affects on analytical results, the blank cannot be accepted. If the response of blank is extremely large, contamination from reagent or solvent may be the reason. The reason of contamination has to be searched because contamination gives analytical results uncertainty.

V.4.7 Confirmation analysis

If more reliability and accuracy than normally obtained by the method of analysis is required, conduct additional confirmatory analysis. This can be done by using different analytical methods or different standards. Confirmation of detected and not-detected concentrations is also important. Both determination and confirmation of concentration of target compounds are necessary. It is sometimes indispensable for trace analysis to confirm both compound identity and concentration by another analytical method.

To confirm is to analyse by more than two analytical methods. Reproducibility can be evaluated by analysing several times by one analytical method. Only reproducibility information can be gained by repeating analysis using the same analytical instruments. Elemental analysis can be confirmed by analysing by two analytical methods based on different physical principles.

When the results are unexpected, extremely big or small , a second and third sub-sample should be analysed by another analytical method to confirm the results.

V.4.8 Dealing with raw data and reports

a) Analysts must follow recognised protocols if data adjustment have been made on the basis of recovery data. A report generally has to accompany the results explaining such matters as how data was calculated and data handling procedures etc. When more than two analytical systems are used to produce results, describe how the two sets results are linked together. When new or complex statistics or mathematical methods are used to calculate the results, it is necessary to explain how and why the methods are appropriate. Data values which are less than detection limits should not be reported.

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If data adjustment is made on the basis of recovery data, write down the details of the calculation and make the values before adjustment available.

b) It is necessary to determine detection limits, determination limits and report limits. Laboratory institutes have to evaluate their own detection limits and determination limits using samples.

Institutes have to confirm determination limits by using spiked samples or samples with known concentrations of target compounds. Spiked samples are made by adding target compounds whose concentrations are around expected determination limits into samples which don't contain target compounds.

c) All results have to be reported in a clear format (generally written documents). Reported results have to relate clearly to analysed samples' names. Also report limit values and determination limit values, and an estimation of the uncertainty of results must be described. An outline of the analytical methods used can be inserted in order to aid understanding of the results and the limits of their application. Data which must be reported are blank values, recovery results, and results of repeated examination. All reports have to be checked for mistakes by the person or persons in charge.

The results of calculations using electric calculators and computers are often un-necessarily detailed (too many significant figures) so they have to be rounded up to more appropriate numbers.

When analysis has been repeated, show results with an average \pm standard deviation if the number of repeats is large enough. If the number of repeats is small, show results as range. Standard deviation numbers are rounded up to one significant figure, and averages are rounded up to the appropriate number of significant figures balancing accuracy and the standard deviation.

V.4.9 **Maintenance of records and storage of data**

All data related to the analytical results must be stored for a specified period of time to allow investigations of each step of analysis if required afterwards. Data that must be stored are analysis request forms, estimates, sample record book, analytical results (data sheets from analytical instruments), calculation processes, record sheet of results, experiment note book, calibration curves, operation procedure, conditions of analytical instruments, etc.

Each record has to be correlated to samples, and reserved with sign of the analyst with dates in order to be able to specify all records about analysis when necessary.

V.5 Monitoring and inspection

a) Using confirmed analytical methods, professional analytical institutes, and veteran analysts does not always guaranteed reliable analytical results. In order to decrease the chance of causing errors, all analytical procedures have to be conducted using a system which guarantees the quality of the analytical results.

Quality assurance in trace analysis requires analysts to maintain a control chart. A control chart is useful for error detection. However it only can correct errors, it cannot prevent errors which arise at the beginning. Quality assurance systems prevent errors. Therefore quality goes up and efficiency increases because of error elimination.

b) At regular intervals, internal and external inspections have to be conducted to guarantee that the quality assurance program is working appropriately.

c) Institutes should participate in technology confirmation tests or inter-laboratory research as a quality control on their analytical results. Such tests make direct comparisons of in-house results with results for the same samples obtained by other institutes, and it is useful for checking technology. If possible, when conducting such tests, add check samples into routine analysis so the analysts can conduct the analysis under the normal, working conditions. Quality control systems should be established.

V.6 Appendix

Some especially important subjects that influence quality control in a chemistry laboratory are :-

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V.6.1 Staff

- (1) Train staff appropriately and keep accurate and up-to-date training records.
- (2) Check the analytical ability of staff.
- (3) Tests of analytical ability of staff have to be done by analysts who have both authority and the ability themselves.

V.6.2 Apparatus

- (1) Gain certification of apparatus correction.
- (2) Stick the label about correction of apparatus or clarify it.
- (3) Write down instruments correction operation and store the correction records.
- (4) Use apparatus which is appropriate for the purpose.
- (5) Maintain instruments properly and store maintenance records.
- (6) Microapparatus such as analytical balance, thermometer, glassware, watch, pipettes are corrected and make appropriate manual of standard level.
- (7) Conduct performance test if the apparatus can give full ability.

V.6.3 Analytical methods

- (1) Write down home-made analytical methods completely and discuss their propriety.
- (2) Approval has to be gained when analytical methods are changed.
- (3) Use the latest analytical methods.
- (4) Conduct analyses following defined analytical methods.

V.6.4 Standard reagents and reference materials

- (1) Keep standards which are needed for experiments.
- (2) Use standards of guaranteed purity, or the best ones available.
- (3) Write down the methods of preparation of standards for calibration curves.
- (4) Store standards and reference materials in containers with their names or codes written clearly in an appropriate manner.

- (5) Compare new batches of standards with the old ones before use. Use prescribed grade of reagents during such an examination.
- (6) Keep a copy of the purity certificate when standard reagents are purchased.

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- (1) Make calibration curves for each experiment.
- (2) Ensure performance is within the prescribed range in the case of using control charts.
- (3) Analyse QC samples regularly by pre-determined methods. Record the values obtained and, if the values exceed the limits, correspond with appropriate treatment.
- (4) Analyse samples at random to check that results compare with the originally determined values.
- (5) Get good results by using well considered experimental plans. Satisfy comparison results of interlaboratory examination. Don't have marked problems. Do some treatment if function is not enough.

V.6.6 Control of samples

- (1) Make a document control system which clearly shows the receipt of samples, confirmation of samples against request form items, procedure of analytical development, fate of samples etc.
- (2) Stick labels on samples and store properly.

V.6.7 Records

- (1) Make records in notebooks or worksheets covering examination dates, analysts, items of analysis, detail of samples, examination records, all calculation, data of analytical instruments (output data), calibration curves data etc.
- (2) Write down in notebooks or worksheets with ink and correct mistakes by crossing out. Also leave analysts' signatures.
- (3) Sign corrections if mistakes are corrected.
- (4) Copy data or check calculations following procedures which have been determined by institutes.
- (5) Problems shouldn't happen about a series of inspection of random samples. (For example, check about samples, inspection of all procedure about from sample receiving to producing reports)

V.6.8 Definition of terminology

(1) *Accreditation (Laboratory)*

An accredited laboratory is an institute which is formally acknowledged by a designated public organization as a laboratory which has met specific analytical performance criteria. Being an accredited laboratory means the laboratory has both technical ability and fairness as an institute (sometimes it just means having the technical ability). Accreditation is generally given when the laboratory passes an ability evaluation (a test) as a institute. Accreditation is regularly re-evaluated.

(2) *Accuracy (ref. Error and Uncertainty)*

Accuracy refers to the difference between the average of several analytical values (of concentration), or each analytical values, and the true value (guaranteed value). When the term of accuracy is applied to a set of multiple observations of value, accuracy is the sum of accidental and systematic errors or bias. It is desirable to show the range of results within confidence limits in order to show accuracy of results from a standpoint that results have a certain doubtfulness. The true value is included within the range of confidence limits.

(3) *Analytes*

The compounds or elements in samples or standards which are directly or indirectly determined.

(4) *Batch*

A group of samples which is treated at the same time in order to determine the same analytes.

(5) *Bias*

Systematic errors which are caused by analytical operations. Average bias of analytical values from true values.

(6) *Blank Analysis (Blank Determination) (ref. Reagent Blank)*

This term is used for the analysis of a blank or non-contaminated matrix. This term is also used widely to describe experimental operations which are conducted without samples. For example, blank analysis is undertaken by following the adopted method using all reagents, solvents and procedures that would be followed for the analysis of the sample, but either no sample or a

non-contaminated sample is used. The purpose is to check contamination levels during the analytical procedures..

(7) *Blank Matrix (Blank Sample, Blank Solution)*

A blank matrix has the same composition as samples but it does not contain the target compounds. at levels above their detection limits. Blank matrices can be prepared as solutions. In this case matrix solutions have the same composition as sample solutions but do not contain target compounds.

(8) *Calibration*

A concentration series or value set which is established under special conditions. The relationship between the true concentrations of standards and the values gained from the analytical instruments.

(9) *Certified Reference (Matrix) Material, CRM (ref. Reference Material)*

Reference materials which are certified as containing specified concentrations of target compounds. They are produced by having independent laboratories using either the same, similar or different methods obtain specified analyte values. Certified values have always confidence limits.

(10) *Check Sample (ref. Reference Material, Quality Control Sample)*

Samples which contain target compounds of known concentration and whose compositions are similar to target samples. Check samples are analysed along with samples for quality control. In general check samples are made in-house and not appropriate for long term storage.

(11) *Collaborative Study*

Research in which multiple analytical institutes prepare, analyse and evaluate the same samples by the same analytical methods in order to confirm adequacy of the analytical methods. Also this term can be used as substitute for Interlaboratory Study.

(12) *Contamination*

In trace analysis, contamination is the unintentional mixing of the sample with target compounds or other compounds which then cause analytical interference and errors. Contamination tends to happen during analytical operations. To check whether there is contamination or not, blank analysis or analysis of reference materials are conducted as quality control.

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(13) *Control Charts (ref. Quality Control Charts)*

(14) *Error (ref. Uncertainty, Accuracy)*

Analytical results, even the best analytical results, contain errors. These errors are the difference between true values and the analytical values. Errors include systematic errors and random errors.

- systematic errors: definite difference from true values when multiple analysis are conducted under the same conditions; errors which change the determined value from the true values according to a certain ratio when conditions are changed.
- random errors: irregular scatter which cannot be estimated when multiple analyse of the same amount are conducted under the same conditions.

For trace analysis, it is desirable to estimate the uncertainty of the results because true values are rarely known.

(15) *Interferent*

A constituent in samples which affects analysis measurements and results.

(16) *Interlaboratory Study*

A series of measurement in which a given set of samples is analysed independently at multiple analytical institutes. This term is sometimes used as substitute for Collaborative Study, and the study is conducted as a 'round robin' or 'ring test'.

(17) *Limit of Detection*

The detection limit, or limit of detection, of an analytical method is the least amount of target analyte in a samples which can be detected. The limit of detection is not the smallest amount of analyte for which the true value can be determined (see below). Detection limits of the concentration C_L , or amount q_L , are calculated from the value of the least amount of analyte which can be detected, X_L , accompanied by an certain uncertainty. X_L is calculated by the following formula.

$$X_L = X_{bL} + kS_{bL}$$

X_{bL} is average value of the blank, and S_{bL} is standard deviation of the blank, k is a coefficient which is determined by necessary confidence limits. Detection limits which are generally used are $3S_{bL}$ or three times the S/N ratio.

(18) *Limit of Determination*

The limit of determination of an analytical method is the smallest amount of target compounds

in a samples which can be determinate (measured) for a given uncertainty. It is also Limit of Quantitation, and it is effectively 10 times the S/N ratio.

(19) *Linearity*

Linearity of analytical methods means that relationship of concentrations and the signals obtained from the instruments follow a linear regression of the form $y=mx+c$ in a certain range. m , c are coefficients.

(20) *Method (ref. Standard)*

All systematic operations which are used to undertake an analysis. This includes not only last measurement but all of the procedures related to analysis.

(21) *Precision (ref. Reproducibility, Repeatability)*

The degree of agreement of the results of measurements obtained from multiple examinations under the designated conditions.

(22) *Qualitative (ref. Quantitative)*

The term qualitative analysis means chemical analysis which is devised so as to confirm the components of a material or mixture, but which does not determine the exact quantity of components in the material or mixture.

(23) *Quality Assurance*

Systematic and intentional work which is undertaken to give definite reliability to analytical results.

(24) *Quality Control*

Specified work which institute staff undertake during analytical operations or measurements in order to judge if the analytical values are sufficiently reliable.

(25) *Quality Control Chart*

Graphs which are made from the results of measurements of Quality Control Samples which are prepared to check the reliability of the analytical results.

(26) *Quality Control Sample (ref. Check Sample)*

Samples of known concentration and similar composition to sample matrix. It is analysed with samples as an internal quality control.

(27) *Quantitative*

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The term quantitative analysis means chemical analysis which is devised to determine numerical data values for one or more components of a material or mixture to specified certain confidence limits.

(28) *Range*

This term has two meanings.

1. the range of concentrations, from the smallest to the largest, of target compounds in samples to which the analytical methods can be applied.
2. the difference between the smallest and the largest values of data.

(29) *Reagent Blank (Solvent Blank) (ref. Blank Analysis)*

A Reagent Blank is a solution obtained after conducting all of the analytical process without using samples.

(30) *Recovery*

Recovery of a compound when more than one analytical procedure is conducted.

(31) *Reference Material (ref. Check Sample)*

This is a stable material in which the concentrations of one or more component is well established, and which is used for the confirmation of the calibration curves of analytical instruments, evaluation of analytical methods, or designation of the value of a material.

In the field of trace analysis, reference materials are briefly categorised into two types of reference materials.

1. Chemical substances of known purity that are used for the preparation of analytical standard solutions and calibration curves.
2. matrix standards : materials with the same or similar compositions to the analytical samples and in which the concentrations of target compounds are known. Matrix standards are used for the development of analytical methods, confirmation of the adequacy of the analytical methods, and comparison of results between laboratories or methods.

(32) *Repeatability (ref. Precision)*

The term Repeatability (r) refers to the range of values resulting from the difference in results when two samples are analysed by the same analytical method under the same conditions (by the same analysts, apparatus, laboratory and using the same experimental duration). Use 95 % as probability when there is no specific instruction.

(33) Reporting Limit (ref. Limit of Detection, Limit of Determination)

The Limit of the values of the analytical results which can be reported. Usually this is determined by agreement between analysts and their clients?.

(34) Reproducibility (ref. Repeatability)

The term Reproducibility (R) refers to the range of values resulting from the difference in results when two same samples are analysed by different analytical methods under different conditions (by different analysts, apparatus, and laboratory). Use 95 % as probability when there is no specific instruction.

(35) Robustness

The term Robustness refers to the sensitivity, or lack of sensitivity, of the analytical operations i.e. the ability of the parameters of the analytical methods to not be affected by trivial things. This becomes index of reliability when general samples are analysed.

(36) Selectivity

The degree to which non-target compounds affect the measurement of the analytical target compounds for a given analytical method.

(37) Signal-to-Noise Ratio (S/N ratio)

The ratio of the intensity of a controlled signal to the background instrument noise. Usually this value is the signal divided by the standard deviation of the background signal. (ref. Limit of Detection, Limit of Determination)

(38) Spiked Samples

“Spiking samples” is a common term used to imply the addition of solutions of target compounds of known concentrations to sample itself or to a matrix which is similar to the samples. (This is also called fortification of samples.)

(39) Standard (all types)

Standards are materials which are established by the acknowledged agreement of designated organizations. As for use of this regulation, standards are applied to materials, solutions (for example, organic compounds and metal solutions whose purity is known), and documents (for example, analytical methods and quality control system).

In this manual the following terms are used as standards.

- analytical standards (standard solutions) : solutions and matrices which contain target compounds which are used to confirm analytical methods or the ability of instruments.

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- standard solutions for calibration curves : solutions and matrices whose concentrations are known, and which are used for making calibration curves from the response of instruments.
- internal standards : compounds which are spiked into samples, and have similar characteristics to target compounds and which are analysed together.
- external standards : generally target compounds are used, and analysed separately from samples.
- standard analytical methods : a series of written operational procedures for conducting chemical analysis, and which are acknowledged by a formal organisation.

(40) *Stock Solution*

Stock standards are solutions of standards or the sample prepared in relatively high concentrations and whose stability is well known. Standard solutions are prepared by diluting small amounts of stock solutions.

(41) *Sub-sample*

A part of the sample which represents the whole.

(42) *Traceability*

The term traceability refers to the ability to relate analytical data to appropriate standards such as international or domestic reference materials.

(43) *Ultra Trace Analysis*

This term, Ultra Trace Analysis, generally means analysis of concentrations less than 1 mg/kg, or 1 mg/L.

(44) *Uncertainty (ref. Accuracy, Error)*

Data has a certain range. True values exist at the confidence limit level within the range.

(45) *Validation*

This is the process which measures the ability of the chosen measurement operation to perform the desired task, and confirms if the method is capable of reaching a pre-determined level.

V.6.9 Check List

V.6.9.1 Check List Example of recording documents

a) Record (logbook) of entry to and exit from the analytical centre (room)

Date	Name	Time In	Time Out	Work Undertaken	Signature

*Logbooks should be located at the entrance of key rooms, such as sample storage room, clean room, etc.

b) Instrument logbook

Date	Name	Start Time	Finish Time	Sample Contents	Sample Numbers	Qualitative/ Quantitative	Comments (instrument condition etc.)	Signature

c) Sample storage logbook

Date	Name of person who brought sample	Sample Name	Numbers Weights	Sample state Liquid/solid /etc.	Container No.	Storage section	Comments	Signature

*Logbooks (use, preparation, and storage record) should be made for reagents, standard solution, and standard substances.

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V.6.9.2 **Instrument check list**

a) Before use

Contents		Tick mark
1)	Did you record all details in the logbook?	()
2)	Are the instruments and room tidy?	()
3)	How is room air status?	(room temp. °C, humidity %)
4)	Ventilation duct	()
	Power supply line	()
	Gas supply line	()
	Cooling system line	()
	Other connected lines	()

b) While running

Contents		Tick mark
1)	Any problem at start up?	()
2)	Is OS working normally?	()
3)	Is base line signal (blank intensity) normal?	()
4)	Standard solution for calibration curves	
	Name of operative who prepared the solution	()
	Date on which solutions were prepared	()
	Type and numbers of standard solutions	()
	Concentration range	(~ ppm)
5)	Analytical samples	
	Name of client	()
	Sample name	()
	Sample numbers	()
	Sample condition : comments about existence of suspended particles etc.	
	Required analytical level	Qualification, semi-quantitative, quantitative analysis, close analysis
6)	Cross check samples?	No / Yes (kinds :)
7)	Blank samples?	No / Yes (How many?)
8)	Effects of interferences?	No / Yes (Was level of interference checked? ())
9)	Stability of instruments?	()

c) After analysis

Contents		Tick mark
1)	Was all analysis completed? (analytical samples, blank, standard solution for check, etc.)	()
2)	Confirmation of data output, and saving of data	()
3)	Are instruments and room tidy?	()
4)	Check power supply and other lines.	()
5)	Entry in logbooks	()

V.6.9.3 Check list for data analysis

Contents		Tick mark
1)	Cross check between entry items of analytical samples etc. and data file names of analytical samples	()
2)	Entry of analytical procedures	()
3)	Calculation of detection limits and quantitative limits Calculation of upper limit allowance range?	() ()
4)	Are data of standard solutions and check substances within allowance limits from start to end of analysis?	()
5)	Examination of dispersion because of repetitive analysis of each data.	()
6)	Decision on significant figures	()
7)	Is it necessary to adjust data? (If yes, method of adjustment)	() (contents:)
8)	Confirmation of cross check between list of analytical requirements and results report.	()
9)	Explanation, agreement and signature of manager of analyst	()
10)	Storage of raw data, calculation data, note of calculation procedure, and report of last results.	()
11)	If requested analysis, are explanations in the client's report appropriate?	()