TECHNIQUES IN MARINE ENVIRONMENTAL SCIENCES

No. 6

Control procedures: Good laboratory practice and quality assurance

F.A.J.M. Vijverberg and W.P. Cofino

Ministry of Transport and Public Works
Public Works Department
Tidal Waters Division
Hooftskade 1, P.O. Box 20907
2500 EX The Hague
The Netherlands

INTERNATIONAL COUNCIL FOR THE EXPLORATION OF THE SEA
CONSEIL INTERNATIONAL POUR L'EXPLORATION DE LA MER

Palægade 2-4, DK-1261 Copenhagen K, Denmark

December 1987

ISSN 0903-2606

INDEX

1. General Introduction

Good Laboratory Practice (GLP) is one of the manifestations of the increased attention being paid to quality control measures in general. It provides a framework designed to bring the quality of laboratory results into accord with predefined standards and to maintain the quality at this level. The need for such a framework arises from the economic, political, and scientific implications that laboratory studies may have, which place demands on the reliability and comparability of the results.

The value of Quality Control became clear in the 1950s during the reconstruction of Japanese industry, which had acquired a reputation for manufacturing cheap products of poor quality. During the reconstruction process, the work of Deming, an American pioneer in quality control, was used to advantage (20, 37).

In the 1970s the U.S. Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) collaborated closely in the development of Good Laboratory Practice regulations (8, 13). The motive for developing such guidelines was the lack of reliable and comparable methods of obtaining results. In 1979 the principles of Good Laboratory Practice were made mandatory for U.S. Government contractors.

During 1979/1980 in Europe a group of experts under the auspices of the Organisation for Economic Co-operation and Development (OECD) produced the document "OECD Principles of Good Laboratory Practice" (1). The purpose of this document was to promote the development of data of high quality, because good comparability of test data is a prerequisite to mutual acceptance of the data among countries. Legislation on this document was enacted in 1981 by members of the OECD.

At first, the principles of Good Laboratory Practice were only prescribed for laboratories engaged in toxicological research for the pharmaceutical industry. Both the FDA and OECD guidelines mentioned above have this aim. Today the principles of Good Laboratory Practice have a wider scope.

This overview provides a brief introduction to GLP and Quality Assurance. The aim of this paper is to give insight into the available literature on these topics. The several components of GLP and Quality Assurance are reviewed but not discussed in detail. Detailed information is provided in the reference list.

2. Definitions

Good Laboratory Practice

The OECD states: Good laboratory practice is concerned with the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported. (1)

F.M. Garfield describes GLP as "a set of rules, operating procedures, and practices as established by a regulatory agency that are adequate to ensure the quality and integrity of data generated by a laboratory."(3)

Quality

The International Organization for Standardization (ISO) definition is: The totality of features and characteristics of a product, process or service that bear on its ability to satisfy stated or implied needs.

Quality is an estimation of acceptability for a given purpose of an object, item, tangible, or intangible thing.(2)

Quality Assurance

The ISO definition is: All those planned and systematic actions necessary to provide adequate confidence that a product, process or service will satisfy given quality requirements.

F.M. Garfield states: "Quality assurance is a planned system of activities whose purpose is to provide assurance that the quality control program is actually effective".(3)

According to J.K. Taylor, a quality assurance is a system of activities whose purpose is to provide to the producer or user of a product or a service the assurance that it meets defined standards of quality. It consists of two separate but related activities, quality control and quality assessment.(2)

Quality Control

The ISO definition is: The operational techniques and activities that are used to satisfy quality requirements.

According to J.K. Taylor: The overall system of activities whose purpose is to control the quality of a product or service so that it meets the needs of users. The aim is to provide quality that is satisfactory, adequate, dependable, and economic.(2)

F.M. Garfield states: Quality control is a planned system of activities whose purpose is to provide a quality product.(3)

Quality Assessment

The overall system of activities whose purpose is to provide assurance that the quality control activities are being done effectively. It involves a continuing evaluation of performance of

the production system and the quality of the products produced.(2)

Quality Assurance Program

Quality Assurance Program means an internal control system designed to ascertain that the study is in compliance with the principles of Good Laboratory Practice.(1)

3. Introduction to GLP and Quality Assurance

3.1. Description of Good Laboratory Practice and Quality Assurance

Good Laboratory Practice guidelines are rules for laboratory research on chemical materials. GLP describes how a laboratory should work, how it should be organized and how it can produce valid data. It does not prescribe the analytical methods that have to be used. GLP is a policy for all the aspects in the laboratory which influence the quality of the analytical work, for laboratory spaces in which the work is done, for staff, analysts and technicians, for safety of equipment, handling of chemicals, for reporting and filing the results etc.

GLP applies to all the tests carried out by a laboratory. Guidelines are implemented through a quality assurance program, which is in compliance with GLP.

3.2. The Quality Assurance Manual

The quality assurance program of a laboratory is delineated in a quality assurance manual. In a quality assurance manual the objects mentioned in section 3.1 are described explicitly and the methodology is given to assess and to monitor the quality of the data, and to maintain it on an accepted level.

The items in a quality assurance manual will be taken as the basis for the following sections. For all items relevant topics are discussed.

4. Items of importance in a Quality Assurance Manual (1-19)

In a quality assurance manual the quality assurance program is embodied. The major items are:

- **Test Facilities, Organization, and Personnel**
  - location of the laboratories and safety aspects
  - structure of the organization and the allocation of responsibilities
  - education
  - management
- **Quality assessment**
  - interlaboratory and intralaboratory testing programs
  - reference material
- **Statistical quality control**
  - control charts

- **Apparatus, chemicals, reagents, and blank**
  - apparatus
    - preventive maintenance and maintenance
    - calibration
    - cleaning glassware and non-glassware
  - chemicals
    - registration
    - quality control checks
    - rules for storage of waste
    - handling and storage
  - reagents
    - standard solutions
  - blank
- **Sampling and storage**
  - sampling strategy
  - way of sampling
  - storage and preservation
  - sample identification
- **Laboratory analysis**
  - test-sample
  - vendor laboratories
- **Documentation**
  - study
  - methods
  - work-sheets
  - notebook
- **Reporting of results**
  - not computerized
  - computerized
- **Archiving of results**

4.1. Test facilities, organization, and personnel (1-21)

4.1.1. Location of the laboratories and safety aspects

The location of, the construction of, and the spatial planning in the laboratories should meet the needs to perform research correctly, free of contamination and without danger for the health of the personnel.

All the safety rules should be compiled in a safety handbook and be accessible to everybody in the laboratory. (Each person should have a copy of his own).

The properties of all chemicals used in the laboratory must be known and a manual on properties of these chemicals should be present and in reach of all personnel.

4.1.2. Structure organization and the allocation of responsibilities

An organization chart and a document in which responsibilities of staff members, analysts, and technicians are laid down must be present. (11)

4.1.3. Education

The tests should be performed by well-trained and educated persons. Further training must be stimulated. Participation in analytical workshops is to be encouraged and where appropriate visits to expert laboratories should be arranged to gain additional experience and expertise (4).

Technicians should follow courses for handling the equipment they use or be trained by the manufacturer.

4.1.4. Management

Staff members, analysts, and technicians must see the importance of a Quality Assurance Program and must be motivated to do their job accordingly. In a laboratory there are three levels on which quality assurance can take place. (03,21)

First level : Technicians and analysts performing sampling, analyses etc.
The activities are well planned. Protocols are taken into account. Attention is given to critical aspects (e.g. contamination). Relevant observations and details are written down.
Instruments are calibrated and control-data are checked. The data gathered from the analysis are compared with references and standards checked (control charts). The progress control system is up to date and accessible to all laboratory personnel.

Second level : Chief of a laboratory sector. Controls and validates the data. Evaluates the control charts and is responsible for the performance of the quality assurance program.

Third level : Management level. Must stimulate to work according the quality assurance program which is in compliance with GLP. Has to appoint personnel for keeping the program up to date and evaluating the system (a quality assurance unit; (3)). Is responsible for having audits.

The importance of a motivating and stimulating management was recognized by Deming, as is clear from the following nine guidelines for quality control formulated by him (cited by E.J.M. Kobus (20)):

- do not control the quality afterwards but have a preventive control program;
- plan statistical quality control;
- motivate personnel;
- plan a good education program;
- have a good sphere of action where everybody can express himself;
- avoid and/or stop parochialism;
- use modern techniques for the education;
- the structure of the organization must be adapted to fulfil the above guidelines;
- management/staff have to approve above ideas and stimulate the implementation.

4.2. Quality Assessment (22-34,63)

The credibility of a laboratory lies in its quality assessment. Quality assessment is a form of control in which intralaboratory and interlaboratory testing programs play a major role.

4.2.1. Intra- and interlaboratory Testing Programs

To get an overall view of the quality of the data produced by a laboratory it is necessary to have an intralaboratory testing program for periodic checks of performance to determine precision and accuracy. Examples include analysis of duplicate and check samples, peer check of chart readings and calculations, and validation of methodology.

Interlaboratory testing programs determine the ability of the participating laboratories to achieve comparable results when the same samples are analysed. On evaluation of interlaboratory tests participating laboratories can obtain insight to the performance of their methods, and needs for refinements of the applied procedures. These interlaboratory evaluations should be conducted periodically.

4.2.2. Reference Materials

According to J.K. Taylor (22) the most general terminology of a reference material is the following:

> A reference material is a substance for which one or more properties are established sufficiently well for use to calibrate a chemical analyser or to validate a measurement process.

J.K. Taylor distinguishes several kinds of reference materials (22):

- Internal Reference Material (IRM)
  Is a material developed by the laboratory itself and for its own internal use.
- External Reference Material (ERM)
  Is a reference material developed by someone else than the end-user.
- Certified Reference Material (CRM)
  Certified reference material is a reference issued and certified by an organization generally accepted to be technically competent to do so. The US National Bureau of Standards designates their CRM as Standard Reference Material (SRM).

S.S. Berman uses an another subdivision (24).

- Certified Reference Material (CRM)
  Reference material containing concentrations certified by an expert laboratory.
- Uncompromised Reference Material (URM)
  Reference material for which concentrations of the material are unknown to all participants but the coordinator of an international exercise.
- Compromised Uncertified Reference Material (CURM)
  Surplus materials after an international exercise has been

carried out.

The analysis of appropriate reference materials represents the most direct way to investigate bias during analysis or to test the reliability of the results of an analytical method. (Appropriate refers in this context to materials that closely simulate the analytical samples which are analysed e.g. same matrix). Every test or sequence should include the analysis of reference material (IRM or ERM) and certified reference material should be analysed on a regular basis. The frequency of testing a reference material must be established for each analytical method used in the laboratory.

In general the following information regarding purchased reference material must be recorded:
- the date;
- the amount purchased;
- the stability;
- the distribution;
- the amount used for a test and the kind of test;
- the amount left after using;
- the goal;
- the preparation (if necessary);
- the results of the tests (see control charts).

4.3. Statistical Quality Control (22,35-48)

Statistical control may be defined as the attainment of a state of predictability (22). Statistics play an important role in the manipulation and interpretation of laboratory data. Some relevant aspects are:
- applications of descriptive statistics e.g. definition of detection limits, limits of confidence, rounding intervals etc.
- application of inferential statistics;
  - setting up sampling schemes;
  - methods to evaluate quality control results such as intracalibration and intercalibration tests, control charts, etc;
  - interpretation of results when the significance of difference between methods, laboratories, etc. is being judged.

A variety of statistical tests can be used: parametric or non-parametric procedures, standard or orthogonal regression techniques, the Student or t-test, the F-test, analysis of variance (ANOVA) etc. An extensive discussion of statistical methods is beyond the scope of this paper. Reference is made to standard texts on statistics.

Training of analysts in this field is recommended.

4.3.1. Control Charts (see also annex 1)

A control chart is a graphical way to interpret test data and to monitor the measurement process or the status of an instrument. It provides the feedback for process control. Results of several

quality parameters like reference materials, blanks, recordings of signals of instruments (e.g. sensitivity), standard solutions etc. should be recorded on a control chart. The control chart in a real-time mode provides an important means to monitor precision and changes in accuracy.

It is recommended (25) that laboratories maintain charts for the mean (X) and the difference (R) of duplicate determinations (02). For the mean (X) chart (02,61) both the 2s and the 3s limits should be utilized.

Another type of charting is the "cusum system" (03, 05, 21). In the cusum chart the sum of the differences between the analytical value and the true or average value of the control sample are plotted against every analysis of that sample. In this way one has a good overview about the stability of the process. If the plot is horizontal the process is in control.

4.4. Apparatus and Reagents (1-18,49-50)

4.4.1. Apparatus

A manual should be present nearby every instrument. In addition a short version of the manual in the local language is recommended. The latter manual consists of a description of the instrument and its operation and a part about trouble shooting.

4.4.1.1. Calibration

The optimizing of the instrument is as important as the calibration. Before calibration takes place the optimizing of the instrument should be carried out. The calibration of an instrument should be described in a procedure. In such a document the way the calibration is performed (e.g. which standards, intervals, concentrations) and the frequency of calibration is noted (the latter only if it is not necessary to calibrate the instrument every time it is used).

A point for attention is control of graduated glassware, syringes, micro-pipettes, balances etc. When applicable, procedures have to be developed and documented.

4.4.1.2. Preventive Maintenance

To enhance performance of the instruments a maintenance contract with the supplier of the instruments is recommended. The maintenance should be done with a check list and this list should be filed. A record of all the problems which occur should be kept and the way the problem is solved should be noted in an instrument journal.

Someone should be appointed who is responsible for the instruments and contacts the supplier in case difficulties arise that cannot be solved by the operator himself.

4.4.1.3. Cleaning Glassware and Non-Glassware

Each laboratory must establish sound cleaning procedures for glassware and non-glassware used in various types of determinations. Every determination can have its own procedure of cleaning the glassware and non-glassware.

4.4.2. Chemicals

4.4.2.1. Registration

For the storage of chemicals special accommodation should be created. All chemicals and reagents should be recognizable and the following items recorded:
- supplier;
- purity;
- date received and the date of tenability;
- the conditions of storage (cooled, dark, etc);
- toxicity etc.

4.4.2.2. Quality Control Checks

Keep a record of all the chemicals used in the laboratories on which control checks are important. Every time a new batch is purchased a control check must take place.

4.4.2.3. Rules for Storage of Waste

Rules for handling, storage, and the removal of waste should be embodied in the safety manual.

4.4.2.4. Handling and Storage

All inorganic and especially organic chemicals should be stored in rooms with a good air ventilation. Cross contamination should be avoided. The toxic chemicals should be stored behind lock and a file of distribution should be kept. In the laboratory should be a manual in which the properties of chemicals are mentioned.

4.4.3. Reagents

4.4.3.1. Standard Solutions

Standard procedures must be established to prepare standard solutions and there should be a system to control the new standard solutions on their actual concentration. Guidelines for the acceptance of a new standard should be present. The stability of a standard solution must be known and the day of preparation must be noted on the standard, likewise the day the standard is not valid any more.

4.4.4. Blanks

Blank determinations should be made by exactly the same procedure as that used for the preparation of the sample and should be carried through the entire analytical procedure. Problems seen in the analysis of the analytical blank can be reduced to four principal sources, namely (49):

- the environment in which the analysis is performed;
- the reagents used in the analysis;
- the apparatus used for the analysis;
- the performance of the analyst/technician;

J.K. Taylor discusses the statistical considerations in applying the blank correction in trace analysis. (50)

4.5. Sampling and Storage (51-60)

4.5.1. Sample Strategy

Sampling is as important as the analytical methods used to analyse the sample. Unrepresentative samples will lead to poor data and are a waste of work, time, and money.

Before sampling starts it is necessary to have a sampling model and a sampling plan. In a sampling plan all steps of sampling and all protocols used during the sampling are specified and documented.

Several questions should be addressed, for example:
- what is the goal of the study?
- what should samples be analysed for?
- in which environmental compartment should samples be collected?
- where should samples be collected?
- when should samples be taken?
- what type of samples should be collected? (the single discrete or the composite)
- what is the size of the sample?
- what is the number of samples that should be taken?
- what is the frequency of sampling?
- what is the storage and holding time?

Important aspects are:

4.5.2. Way of Sampling

The way of sampling depends upon the parameter to be analysed, the environmental compartment and the goal of the study. Great care must be taken for selecting the right method of sampling for each parameter. The sampling must be carried out by qualified personnel well trained in the procedures and in use of the sampling equipment so that bias and contamination are minimized. A written protocol for the sampling itself and procedures before and after sampling must be specified and should be provided. (e.g. conditions during transport).

4.5.3. Storage and Preservation

The type of containers in which the samples are stored depends also on the parameter to be analysed and the compartment. For each combination the cleaning procedure of the containers per parameter must be written down in a protocol. Also a protocol of the storage procedure and preservation must be present and known by the technicians.

4.5.4. Sample Identification

For each sample or group of samples a document should be present on which several data are recorded. These are items such as
- conditions during sampling;
- time;
- sampling point description;
- lot number etc.

4.6. Laboratory Analysis (8,61-67)

It has been stated that there are six possible sources of bias or systematic error in water analyses (61):
- unrepresentative sampling;
- instability of samples between sampling and analysis;
- interference effects;
- biased calibration;
- a biased blank correction;
- inability to determine all forms of determinand.

The above six sources are also valid for analyses in sediments and biological material. An addition is contamination and losses of analyte during the working-up of the sample before the instrumental analysis.

Apart from knowing where specific errors or bias may occur, the expertise of the analysts is also a major factor in detecting possible errors or bias during the analysis of the sample. The analysts and technicians must be alert to recognize problems such as:

- Contamination
  Great care should be taken in the handling of samples. Contamination of the samples should be avoided and losses of analyte should be kept to a minimum. To check on contamination procedural blanks should be processed in the same way as samples.
- Matrix effects
  To overcome matrix effects for certain analyses it is necessary to analyse the sample and spiked samples. In some analyses a solution is provided by adding reagents which suppress matrix interferences.
- Poor recovery
  For certain analyses it is necessary to check the recovery by analysing a sample with a known concentration of the analyte.
- Bad instrument settings
  For each instrumental analysis, the basic settings per parameter per instrument should be written down in a manual.

4.6.1. Test-sample

Every test-sample should be uniquely identified so no confusions can arise to the identity of the test-sample. The sample should be stored in an adequate way before and after the tests. If a test-sample is to be divided into sub-test-samples, care must be taken to ensure no contamination of the sample has occurred and that the homogeneity of the sample is maintained.

4.6.2. Vendor Laboratories

If analyses are contracted out to vendor laboratories it is necessary to have a program in which the qualifications and the control of their quality assurance program is specified. Audits of the quality assurance programs of vendor laboratories should be made during the study. (An example in a related situation: ref. 27)

4.7. Documentation (1-19)

4.7.1. Study

At the start of a study, a study plan (1,8,11) is made. A study should have a descriptive name and the study plan should at least contain the following information:

- name and address of the laboratory including the names of the responsible management members and name of the principal;
- the name of the study director;
- the nature and the goal of the study;
- the nature and the identification of the study object;
- the date the study starts and the estimated date the study will stop;
- a description and a justification of the way the experimental work is carried out e.g.:
  - the sampling methods and frequency (see section 4.5);
  - the analytical methods;
  - instruments;
  - parameters to be analysed.
- the statistical methods to be used to compute the data;
- the names and addresses of vendor laboratories if analytical work is contracted out.

4.7.2. Methods

A definition by A.L. Wilson is as follows (quoted in an article by C.J. Kirchmir (61)).

> An analytical method is to be regarded as the set of written instructions completely defining the procedure to be adopted by an analyst in order to obtain the required analytical result. It is clear that a method should meet the analytical requirements of the goal of the test.

Methods which are not used for routine laboratory tests should be well documented and archived.

Methods which are used for routine laboratory tests are written down as Standard Operating Procedures (SOP). According to the Guidelines for GLP of the OECD (01) the definition of a SOP is the following:

> Standard Operating Procedures (SOPs) means written procedures which describe how to perform certain routine laboratory tests or activities normally not specified in detail in study plans or test guidelines.

In the descriptions of methods a standard glossary should be employed (18). If possible the use of National or International Standard Methods is preferred (e.g. British Standards BS, Dutch Standards NEN, Deutsche DIN, ISO, American ASTM etc.). When modifications in an analytical method do occur then the reason of the modification, the date of validation, and the date on which the new version of the method is used should be recorded. A description of all the methods which have been used should be archived.

4.7.3. Work Sheets

It is essential to have a well-designed work sheet (3,8) to avoid unnecessary problems when computing results or when questions are asked at the end of the study. On the work sheet all the raw data and the results of the analyses should be noted. Print-outs from instruments are added to the work-sheet file.

4.7.4. Notebook

If during a test the analyst deviates from a standard method the reason why the deviation took place and the way the test was conducted must be documented so questions about results and about the test itself can be answered afterwards. Likewise all observations during the tests must be recorded in a notebook. The pages in such a notebook should be numbered. At the end of the test this notebook should be archived.

4.8. Reporting of results (1-18)

4.8.1. Not computerized

The report should be made in a standard format and should be include at least the following information.

- All pages should be numbered or identified in another way and the total number of pages should be mentioned;
- The name and address of the laboratory;
- The name and address of the principal;
- The name of the study director and of other responsible personnel involved in the study;
- The disposition and the aim of the study. The information should be laid down in the study plan. Changes made should be noted in the study plan or a revision should be made;
- The date or the period of time in which the study took place and the date of the report;
- All relevant information about the samples as it is stated in section 4.5;
- All relevant information about the analysis performed for the study. Any deviation from the proposed method in the study should be noted;
- If appropriate the way the quality of the test is assured. Results of reference samples should be reported. A statement of the person who is responsible for the quality assurance program should be added to the final report;
- A presentation of all the results, including transformation and calculation of the data. Statistical methods used for the handling of the data;

- The location where all samples, specimens, raw data and the final report is stored.

The report should be signed by the responsible manager of the laboratory and if appropriate also by the technician or analyst responsible for a certain part of the analysis. Any changes or additions should be done in the form of an addendum.

4.8.2. Computerized

In case the results are reported to the principal by means of an automatic data transmission system the transmission should have an identification of the study and a code of the person who is responsible for the transmission (5). If possible also security codes must transmitted to check the transmission after it is performed.

Regular back-ups of computerized files should be made.

4.9. Archiving of Results (1-18)

All the relevant documents that might be needed for the reconstruction of the study should be archived for a predetermined time period.

Rules for retention of records should be made and followed.

5. Audits (5)

The quality assurance program must be evaluated on a regular basis. The evaluation can be performed by the quality assurance unit of the laboratory itself or by an external organization.

6. Concluding Remarks

In this paper an overview is given on Good Laboratory Practice and Quality Assurance. The coverage of the literature is not complete, but aspects which need or deserve attention have been dealt with. Additional references may be found in the consulted literature. The material may serve as a starting point for reconsideration of an existing program or for establishing a new program.

Acknowledgement

The authors thank Dr (Ms.) M.A.T. Kerkhoff of Tidal Waters Division for critically reading the manuscript.

References

01. OECD "Principles of Good Laboratory Practice"
1981.

02. Taylor J.K. "Principles of quality Assurance of Chemical measurements."
NBSIR 85-3105 U.S. Department of Commerce, National Bureau of Standards
February 1985

03. Garfield F.M. "Quality Assurance Principles for Analytical Laboratories."
Publisher : Association of Official Analytical Chemists, Inc.
1984 ISBN : 0-935584-26-9

04. "General guidance for good laboratory practice in relation to collection and analysis of marine samples."
Document MCWG 1986/7.4 of ICES meeting in Helsinki, Finland on 18-21 february 1986.

05. Aitio A. "Quality Control in the Occupational Toxicology Laboratory."
Interim document 4 - European Cooperation on Environmental Health Aspects of the Control of Chemicals, World Health Organization, Regional Office for Europe Copenhagen 1981.

06. Stanley T.W. & Verner S.S "The U.S. Environmental Protection Agency's Quality Assurance Program."
Quality Assurance for Environmental Measurement ASTM STP867, J.K Taylor and T.W. Stanley, Eds., American Society for Testing and Materials, pp 12-19.
ASTM Publication Code Number 04-86700-16.
1985 ISBN : 0-8031-0224-0

07. Taylor J.K. "What is Quality Assurance?"
Quality Assurance for Environmental Measurement ASTM STP867, J.K Taylor and T.W. Stanley, Eds., American Society for Testing and Materials, pp 5-11.
ASTM Publication Code Number 04-86700-16.
1985 ISBN : 0-8031-0224-0

08. Beyermann K. "Organic trace analyses" Chapter 2.7 p 62.
Publisher : Ellis Horwood Limited, Chichester.
1984 ISBN : 0-85312-638-0

09. ISO Guide 25 "General requirements for the technical competence of testing Laboratories."
Ref No.: ISO/IEC Guide 25-1982(E).

10. ISO Guide 38 "General requirements for the acceptance of testing Laboratories."
Ref No.: ISO/IEC Guide 38-1983(E).

11. Dutch Standard: Ontwerp NEN 2653, October 1985; "Quality Assurance - General conditions for quality systems of Laboratories."

12. British Standard 6460, part 1, 1983: "Accreditation of testing Laboratories."

13. Smeenk J.G.M.H. & Olrichs S.H.H. "De Kwaliteits-beheersing van het laboratorium proces." (Dutch)
Chemisch Magazine 1986, november, pp 827-835.

14. Taylor J.K. "Quality Assurance of Chemical Measurement."
Thalassia Jugoslavica 1980, 16 (2-4), pp 111-124.

15. Taylor J.K. "Essential Features of a Laboratory Quality Assurance Program."
Statistics in the Environment Sciences, ASTM STP845, S.M. Gertz and M.D. London, Eds., American Society for Testing and Materials, 1984, pp 66-73

16. ISO Guide 2 "General terms and definitions concerning standardization, certification and testing laboratory accreditation."

17. Horwitz W. "Good Laboratory Practices in Analytical Chemistry."
Anal.Chem. 1978, 50(6), pp 521A-524A

18. ISO 6107/1 - 6107/6 "Water Quality Vocabulary"

4.1. Test facilities, Organization and Personnel

19. Eggenberger L.M. "Establishing an Environmental Quality Assurance Program."
Quality Assurance for Environmental Measurement, ASTM STP867, J.K Taylor and T.W. Stanley, Eds., American Society for Testing and Materials, pp 391-405.
ASTM Publication Code Number 04-86700-16.
1985 ISBN : 0-8031-0224-0

20. Kobus E.J.M. "Management van kwaliteit of kwaliteit van management." (Dutch)
H_2O (19) 1986 no 16 pp 364-366.

21. Smeenk J.G.M.M. "Good Laboratory Practice." (Dutch)
Internal Report Gemeente Waterleiding Amsterdam.

4.2. Quality Assessment

22. Taylor J.K. "Standards Reference Material: Handbook for SRM Users."
NBS Special Publication 260-100. U.S. Department of Commerce, National Bureau of Standards (1985).

23. Alvarez R. "The role of NBS standard reference material in Quality Assurance of environmental Measurements."
Quality Assurance for Environmental Measurement ASTM STP867, J.K Taylor and T.W. Stanley, Eds., American Society for Testing and Materials, pp 349-356.
ASTM Publication Code Number 04-86700-16.
1985 ISBN : 0-8031-0224-0

24. Report of the ICES Marine Chemistry Working Group
Copenhagen, 26 february - 1 march 1985.
C.M. 1985/C:2, Ref E.

25. Taylor J.K. "Reference Materials - What They Are and How They Should be Used."
Journal of Testing and Evaluation, 1984, vol 11, no 6, pp 385-387.

26. Taylor. J.K. "The Importance of Intercalibration in Marine Samples."
Thalassia Jugoslavica 1978, 14 (1/2), 221-229

27. Ehler C.N. & Calder J.A. "Monitoring Environmental Quality."
Sea Technology 1986, april, pp 32-37

28. Taylor J.K. "Role of Collaborative and Cooperative Studies in Evaluation of Analytical Methods."
National Bureau of Standards, Gaithersburg, MD 20899.

29. Taylor J.K. "The Quest for Quality Assurance."
American Laboratory, October 1985, pp 67-75.

30. Tetlow J.A. & Hunt D.T.E. " Analytical Quality Control in the United Kingdom Water Industry, with Particular Reference to the Harmonised Monitoring Scheme for River Water Quality."
July 1984
Anglian Water, Huntingdon, Cambs
Water Research Centre, Medmenham, Marlow, Bucks

31. Berman S.S et al "Preparation of the Seawater Reference Material."
Mar. Pollut. Bull., 1983, vol 14, no 2, pp 69-73

32. Thompson J.F. & Mann J.B. "Analytical Quality Control in Pesticide Residue Laboratory."
IUPAC 3rd International Congress on Pesticides Chemistry, Helsinki 1984, pp 32-39

33. Thompson J.F "Storage, Handling and Preparation of Pesticide Analytical Reference Standards."
IUPAC 3rd International Congress on Pesticides Chemistry, Helsinki 1984, pp 47-50

34. Aspila K.I., White R.E. & Clark J.L. "Interlaboratory Quality Assurance aspects of the International Joint Commission's great Lakes Monitoring Programs."
Quality Assurance for Environmental Measurement ASTM STP867, J.K Taylor and T.W. Stanley, Eds., American Society for Testing and Materials, pp 406-424.

ASTM Publication Code Number 04-86700-16.
1985 ISBN : 0-8031-0224-0

4.3. Statistical quality control

35. ASTM Committee E-11. ASTM Manual on Presentation of data and control chart analysis,
STP-15D, ASTM, Philadelphia, PA 19103.

36. Grant E.L. and Leavenworth R.S. "Statistical Quality Control."
Publisher : McGraw-Hill, Inc.
1974 ISBN : 0-07-024114-7

37. Ishikawa K. "Guide to Quality Control."
Publisher : Asian Productivity Organization, Tokyo.
1971 ISBN : 92-833-1035-5

38. Montgomery D.C. "Introduction to Statistical Quality Control."
Publisher : John Wiley and Sons Inc., New York.
1985 ISBN : 0-471-80870-9

39. Currie L.A. "Chemometrics and Analytical Chemistry." "Chemometrics, mathematics and statistics in chemistry." Kowalski B.R., Eds, NATO ASI Series, Serie C vol 138
pp 115-146.
Publisher : D. Reidel Publishing Company, Dordrecht.
1984 ISBN : 90-277-1846-6

40. Glaser J.A., Foerst D.L., McKee G.D., Quave S.A. & Budde W.L. "Trace Analyses for Wastewaters."
Environ. Sci. & Technol. 1981, vol 15, no 12, pp 1426-1435.

41. Juran J.M., Seder L.A. & Gryna F.M. "Quality Control Handbook." (3rd ed, 1974)
Publisher : McGraw-Hill, New York.

42. Kateman G. & Pijpers F.W. "Quality Control in Analytical Chemistry."
Publisher : John Wiley & Sons, New York
1981 ISBN : 0-471-46020-6

43. Long G.L. & Winefordner J.D. "Limit of Detection, closer look at the IUPAC definition."
Anal.Chem. 1983, vol 55 (7), 712A-724A.

44. Wakkers P.J.M, Hellendoorn H.B.A, Op de Weegh G.J. & Heerspink W. "Applications of statistics in clinical chemistry. A critical evaluation of regression lines."
Clin.Chim.Acta 1975, vol 64, 173-184.

45. Helsel D.R. "Advantages of nonparametric procedures for analysis of water-quality data."
Paper presented at the 2nd Scientific Assembly of the International Association of Hydrological Sciences, Budapest, Hungary (1986). Address author: Water Resources Division, U.S. Geological Survey, 410 National Center, Reston, Virginia

22092 USA.

46. Youden W.J. & Steiner E.H. "Statistical Manual of the AOAC." Publisher : AOAC,1111 North Nineteenth Street, Suite 210, Arlington, Virginia 22209,USA
1982, 3rd printing; ISBN 0-935584-15-3

47. Wernimont G.T. & Spendley W. "Use of Statistics to Develop and Evaluate Analytical Methods." Publisher : AOAC,1111 North Nineteenth Street, Suite 210, Arlington, Virginia 22209,USA
1985 ISBN 0-935584-31-5

48. Steven Porter P. "A description of measurement error near limits of detection." Monitoring to Detect Changes in Water Quality Series, Proceedings of the Budapest Symposium,july 1986). IAHS Publication no.157, 1986,305-315. IAHS Press, Institute of Hydrology, Wallingford, Oxfordshire, OX10 8BB, United Kingdom.ISBN 0-947571-70-1

4.4. Apparatus and reagents

49. Murphy T.J. "The Role of the Analytical Blank in Accurate Trace Analysis." Accuracy in Trace Analysis: Sampling, Sample Handling, and Analysis. National Bureau of Standards Special Publication 422, Vol. 1, 1976 pp 509-539

50. Taylor J.K. "Guidelines for Evaluating the Blank Correction" Journal of Testing and Evaluation, vol 12, no 1, jan 1984, pp 54-55.

4.5.4. Sampling and storage

51. Kratochvil B., & Taylor J.K. "Sampling for Chemical Analysis." Anal. Chem. 1981, vol 53, pp 924A-938A.

52. Kratochvil B., Wallace D. & Taylor J.K. "Sampling for Chemical Analysis." Anal. Chem. 1984, vol 56, no 5, pp 113R-129R.

53. Chapman P.M., Romberg G.P. & Vigers G.A. "Design of monitoring studies for priority pollutants." Journal WPCF 1985, vol 53, no 3, pp 292-297.

54. Berman S.S. & Yeats P.A. "Sampling of Seawater for Trace Metals." CRC Crit. Rev. Anal. Chem. 1985, vol 16, no 1, pp 1-14.

55. Segar D.A. & Stamman E. "Fundamentals of Marine Pollution Monitoring Programme Design." Marine Pollution Bulletin 1986, vol 17, no 5, pp 194-200.

56. Kateman G. "Sampling."
"Chemometrics, mathematics and statistics in chemistry."
Kowalski B.R., Eds, NATO ASI Series, Serie C vol 138
pp 177-205.
Publisher : D. Reidel Publishing Company.
1984 ISBN : 90-277-1846-6

57. Robertson D.E. "The adsorption of trace metals is sea water on various container surfaces."
Anal. Chim. Acta 1968, vol 42, pp 533-536.

58. Walker D.G. "A Question of Sampling."
Effluent and Water Treatment Journal, 1982, may, pp 184-191.

59. Kramer C.J.M. "Monitoring of abiotic compartments for trace metals: Difficulties, Strategies and the use of surveys."
Environmental Monitoring and Assessment 1986,7,pp 169-187.

60. Harris W.E. "Sampling, Manipulative, Observational and Evaluative Errors."
Amer. Lab. 1978, 10, pp 31-41

4.6. Laboratory analysis

61. Kirchmir C.J. "Quality Control in Water Analyses."
Environ. Sci. Technol. 1983, vol 17, no 14 pp 174a-180a.

62. Taylor J.K. "On validation of Analytical Data."
Marine Chemistry 1986, vol 18, pp 115-119.

63. Taylor J.K. "Quality Assurance for a Measurement Program."
Environmental Sampling For Hazardous Wastes, Schweitzer G.E. and Santolucito J.A. Eds. pp 105-108.
ACS Symposium Series 267, 1984.

64. Taylor J.K. "Validation of Analytical Methods."
Anal. Chem. 1983, may, pp 600A-608A

65. McCully K.A., & Lee J.G. (1980) "Optimizing Chemical Laboratory Performance Through the Application of Quality Assurance principles."
Garfield F.M. et al (Eds), Association of Official Analytical Chemists. Airlington, VA, "Quality Assurance of Sample Analysis in the Chemical Laboratory," pp 57-86.

66. Keith L.H., Crummet W., Deegan J., Libby R.,Taylor J.K. & G. Wentler "Principles of Environmental Analysis."
Anal. Chem. 1983, vol 55, pp 2210-2218.

67. Griepink B, "Improving the Quality of Environmental Trace Analysis."
Fresenius. Z. Anal. Chem. 1984, 317, pp 210-212.

68. Tuinstra L.C.M.Th., Roos A.H., Griepink B. & Wells D.E. "Interlaboratory Studies of the Determination of selected Chlorobiphenyls with Capillary Gaschromatography using Splitless- and On-Column Injection Techniques"
J High Res Chrom and Chrom Com, 1985, vol. 8, pp 475-480.

Annex 1

Control Charts

1. Introduction

A control chart is a graphical way to interpret test data and to monitor the measurement process or the status of an instrument. It provides feedback for process control and in a real-time mode it is an important means to monitor precision and changes in accuracy.

The professional judgement of competent analysts is required in making decisions as to the number and types of control charts. Results of several quality parameters such as reference materials, blanks, recordings of signals of instruments (e.g. sensitivity), standard solutions, recovery of spikes etc. can be recorded on a control chart. Experience has shown that 5 to 10 per cent of the sample load should consist of control samples in order to monitor the measurement process (02).

Material chosen by a laboratory as a reference material (IRM or ERM) should be analysed every time samples are tested. By plotting the results in a control chart one measures the lack of constancy of the system and one is warned if a result is out of control. A control chart of an IRM or ERM only shows how the analyses vary among themselves. It is a measure for precision. To be sure the method is giving true results a CRM or a SRM should be analysed on a regular basis. Plotting the results of these reference materials gives a view of accuracy and precision of the method used.

The following control charts are adequate for laboratories to maintain.

1. The Shewart chart.
   - 1a. The X and $\bar{X}$ chart.
     Plotting single measurements (X or the mean $\bar{X}$ of a number of measurements) on a control chart may be an indicator of precision and bias.
   - 1b. The difference of duplicate determinations, the R chart.
     Plotting the difference between duplicate measurements gives an indication of the precision only.
2. The Cusum chart.
   Plotting the cumulative sum of the difference between the analytical value and the true or average value of the control sample gives a good view if changes do occur in the average of a serie of values.

In laboratories where Shewart charts are already in effective routine operations, Cusum charts can give additional information about the process providing it is basicly under control. It is not recommended to use Cusum charts on their own. They are to be used in combination with Shewart charts (1a).

2. Setting up a control chart

Before setting up a control chart the method for which a control chart is made must be in control. This means that the analyst must

be familiar with the method and must have explored all the possible sources of error. Once the method has been validated a sample can be analysed several times and the mean value and the standard deviation of all the measurements can be computed. The next time the sample is analysed the analytical value should lie around the calculated mean value. Statistics predicts that 1 in 20 measurements will lie above or under the 2s limits and 1 in 500 will be under or above the 3s limits. So 95.45% or 99.7% of all the measurements are expected to lie within respectively the 2s and 3s limits. (The actual limits are $1.96\sigma/\sqrt{n}$ and $3.06\sigma/\sqrt{n}$. They are rounded to 2 and 3 times $\sigma/\sqrt{n}$.). One obtains the so-called central line by plotting the mean value on a chart against the number of analyses. The 2s limits (mean ± 2s) are called upper or lower warning limits (UWL = mean + 2s and LWL = mean - 2s). The 3s limits (mean ± 3s) are called upper or lower control limits (UCL = mean + 3s and LCL = mean - 3s). In some parts of the world only the 3s limits are used (e.g. USA; ref 42). In the open literature the warning limits are also called inner control limits (ICL = mean ± 2s) and the control limits are designated as outer control limits or action limits: OCL = mean ± 3s).

To compute the central line and the standard deviation of a X or a $\bar{X}$ chart it is necessary to have a set of at least 10 (Dutch NPR 6603) independent measurements. (15 measurements: ref 35; 25 measurements: ref 03). The data of these measurements are not to be obtained the same day but over a certain period of time.

A SRM or a CRM have a known central line, namely the certified value. With these reference materials a method can be validated. An IRM or ERM can be produced out of a sample which is stable over a long period of time. For an IRM or ERM laboratories use the analytical mean value for the central line. Primarily precision can be monitored. However in combination with CRM or SRM accuracy can be monitored as well

In a graph the distance between the mean value and the 3s limit is preferred to be 3 ± 0.5 cm (Dutch Ontwerp NPR 6603).

3. X chart and $\bar{X}$ chart

3.1. X chart (Fig. 1)

For a single measurement at a time the limits are calculated as follows:

$$UCL = \bar{X} + 3s \quad \text{and} \quad UWL = \bar{X} + 2s$$
$$LCL = \bar{X} - 3s \quad \text{and} \quad LWL = \bar{X} - 2s$$

where $\bar{X}$ = mean value of the single measurements
s = standard deviation
calculated with the following formula

$$s = \sqrt{\frac{\sum_{i=1}^{n}(X_i - \bar{X})^2}{n - 1}}$$

where
X_i = the value of the independent measurements
$\bar{X}^i$ = the average of the total number of measurements
n = the number of results used to compute the mean and the standard deviation.

3.2. $\bar{X}$ chart

When $\bar{X}$ of n measurements per analysis is plotted the limits are calculated as follows:

$$UCL = \bar{\bar{X}} + 3s\sqrt{n} \quad \text{and} \quad UWL = \bar{\bar{X}} + 2s\sqrt{n}$$
$$LCL = \bar{\bar{X}} - 3s\sqrt{n} \quad \text{and} \quad LWL = \bar{\bar{X}} - 2s\sqrt{n}$$

where
$\bar{\bar{X}}$ = mean value of the total number of measurements
s = standard deviation (computed by the formula given in section 3.1)
n = the number of measurements per analysis.

3.3. Out of control

The quality is not in control if:
a. the 3s limit is exceeded
b. two times after each other the 2s limit is exceeded on the same side of the mean $\bar{x}$
c. the measured value is for the eleventh time on the same side of the mean $\bar{x}$.

The chance, computed statistically, of having one of the above-mentioned "out of control" appearances is 0.30%, 0.10% and 0.10% respectively (Dutch Ontwerp NPR 6603).

Remark: Exceeding 4 times after each other the 1s limit on the same side of the mean $\bar{x}$ is an indication that the process might be out of control.

4. R chart

By plotting the difference of the duplicate samples on a control chart a one gets a good view of the precision of the measurement
The mean of R is computed from a set of 15 duplicate measurements. Also in this case the data of these 15 measurements are not to be obtained the same day. The limits are computed as follows (ref 22)

$$UCL = 3.267*R$$
$$UWL = 2.512*R$$

where R is the mean of differences of >15 sets of duplicates.

The factor in the formula depends on number of analyses of the sample itself. A table of this factor is given in ref 35.
For the criteria for out of control one is referred to section 3.3. a and b

5. Cusum chart (Fig. 2)

The Cusum technique can be used for:

a. detecting changes in the average of a series of values from some standard values
b. determining when the onset of such changes occurred
c. obtaining a reliable estimate of the new average value following a change

In the Cusum chart the sum of the differences between the analytical value and the reference or average value of the control sample are plotted against every analysis of that sample. In this way one has a good overview about the stability of the process. If the plot is horizontal the process is in control.

Formula:

$$s_i = \sum_{j=1}^{i} (x_j - x_o)$$

where

s_i = cumulative sum
x_i = measured value or mean of the measured values
x_o = reference or average of the control sample.

The performance of a cusum chart depends highly on the correctness of the average value (see Table 1).

If the horizontal distance between the plotted points is regarded as one unit, it is recommended that the same distance on the vertical scale represent approximately $2\sigma/\sqrt{n}$ property units, where σ is the population standard deviation. Also rounded lower values may be chosen (ref 42).

5.1. Out of control

The general way to interpret the Cusum chart is called the V-masked method.
A perspex sheet upon which a 30° half-angle V mask is drawn is needed. The corner of the mask is placed two periods (d=2) ahead of the current or most recently plotted point. Assuming the process is in a state of control all the previous points should lie within the two limbs of the V. If the Cusum cuts one of the limbs of the V there is significant change in the process. Such a change is positive if the lower limb is cut and negative if the upper limb is cut. Performing the V-mask method as described above it is equivalent to the $3\sigma\sqrt{n}$ limits (ref 42).

Additional references

Dutch Ontwerp NPR 6603, october 1986, "Guideline for Internal Quality Assurance by the use of Control Charts with Chemical Analyses"

Lewis C.D. "Statistical Monitoring Techniques"
Med. & Biol. Engng. 1971, Vol 9, pp 315-323.

Dewey D.J. & Hunt D.T.E. "The use of Cumulative Sum Charts (Cusum Charts) in Analytical Quality Control"
January 1972, Technical Report TR 174. Water Research Centre Medmenham. P.O. Box 16, Matlow Vucks, SL72HD.

Table 1.

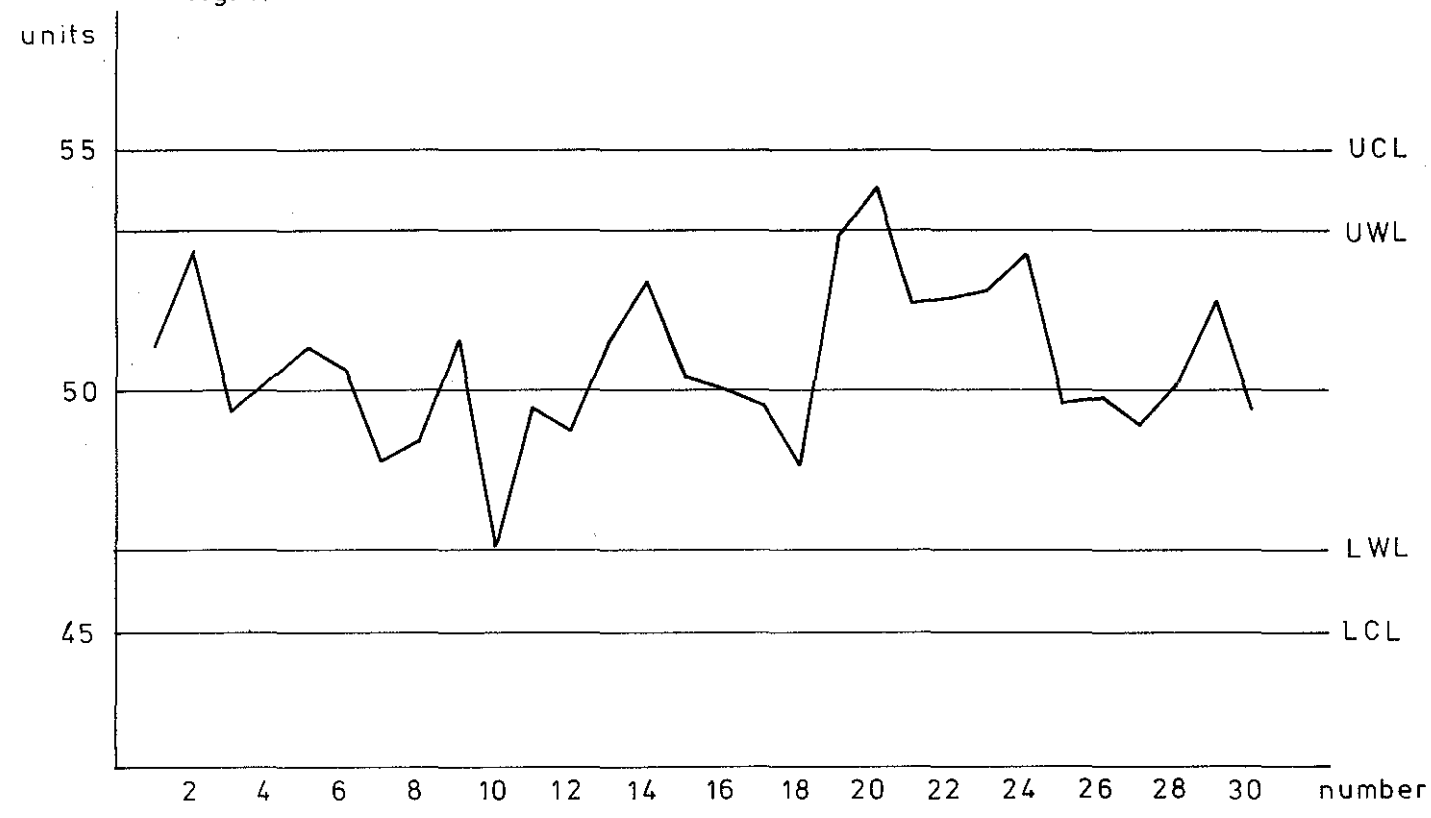
No	Result	Deviation ref value 50	Cusum	Deviation ref value 49	Cusum	Deviation ref value 51	Cusum
1	51.8	1.8	1.8	2.8	2.8	0.8	0.8
2	53.0	3.0	4.8	4.0	6.8	2.0	2.8
3	49.5	-0.5	4.3	0.5	7.3	-1.5	1.3
4	50.2	0.2	4.5	1.2	8.5	-0.8	0.5
5	51.8	1.8	6.3	2.8	11.3	0.8	1.3
6	50.8	0.8	7.1	1.8	13.1	-0.2	1.1
7	48.4	-1.6	5.5	-0.6	12.5	-2.6	-1.5
8	48.9	-1.1	4.4	-0.1	12.4	-2.1	-3.6
9	51.9	1.9	6.3	2.9	15.3	0.9	-2.7
10	46.5	-3.5	2.8	-2.5	12.8	-4.5	-7.2
11	49.6	-0.4	2.4	0.6	13.4	-1.4	-8.6
12	49.1	-0.9	1.5	0.1	13.5	-1.9	-10.5
13	51.1	1.1	2.6	2.1	15.6	0.1	-10.4
14	52.4	2.4	5.0	3.4	19.0	1.4	-9.0
15	50.3	0.3	5.3	1.3	20.3	-0.7	-9.7
16	50.1	0.1	5.4	1.1	21.4	-0.9	-10.6
17	49.7	-0.3	5.1	0.7	22.1	-1.3	-11.9
18	48.3	-1.7	3.4	-0.7	21.4	2.7	-14.6
19	53.4	3.4	6.8	4.4	25.8	2.4	-12.2
20	54.6	4.6	11.4	5.6	31.4	3.6	-8.6
21	51.9	1.9	13.3	2.9	34.3	0.9	-7.7
22	52.0	2.0	15.3	3.0	37.3	1.0	-6.7
23	52.2	2.2	17.5	3.2	40.5	1.2	-5.5
24	53.0	3.0	20.5	4.0	44.5	2.0	-3.5
25	49.7	-0.3	20.2	0.7	45.2	-1.3	-4.8
26	49.8	-0.2	20.0	0.8	46.0	-1.2	-6.0
27	49.2	-0.8	19.2	0.2	46.2	-1.8	-7.8
28	50.1	0.1	19.3	1.1	47.3	-0.9	-8.7
29	51.9	1.9	21.2	2.9	50.2	0.9	-7.8
30	49.5	-0.5	20.7	0.5	50.7	-1.5	-9.3

Limits for ref value : 50

Standard deviation (s) : 1.78
2 * standard deviation (2s) : 3.55
Upper Warning Limit (UWL) : 53.55
Lower Warning Limit (LWL) : 46.45
3 * standard deviation (3s) : 5.33
Upper Control Limit (UCL) : 55.33
Lower Control Limit (LCL) : 44.67

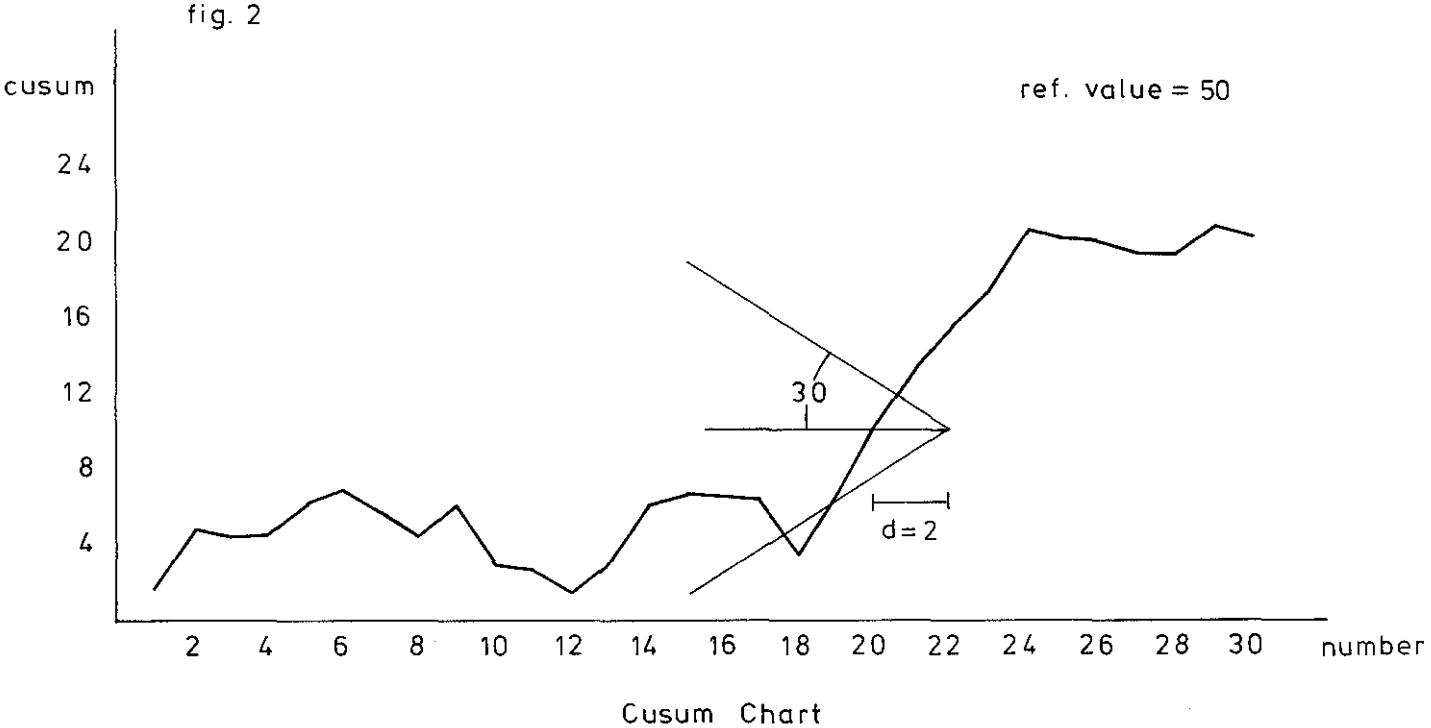
Units vertical axis Cusum : 0.65

fig. 1.



Shewart Chart

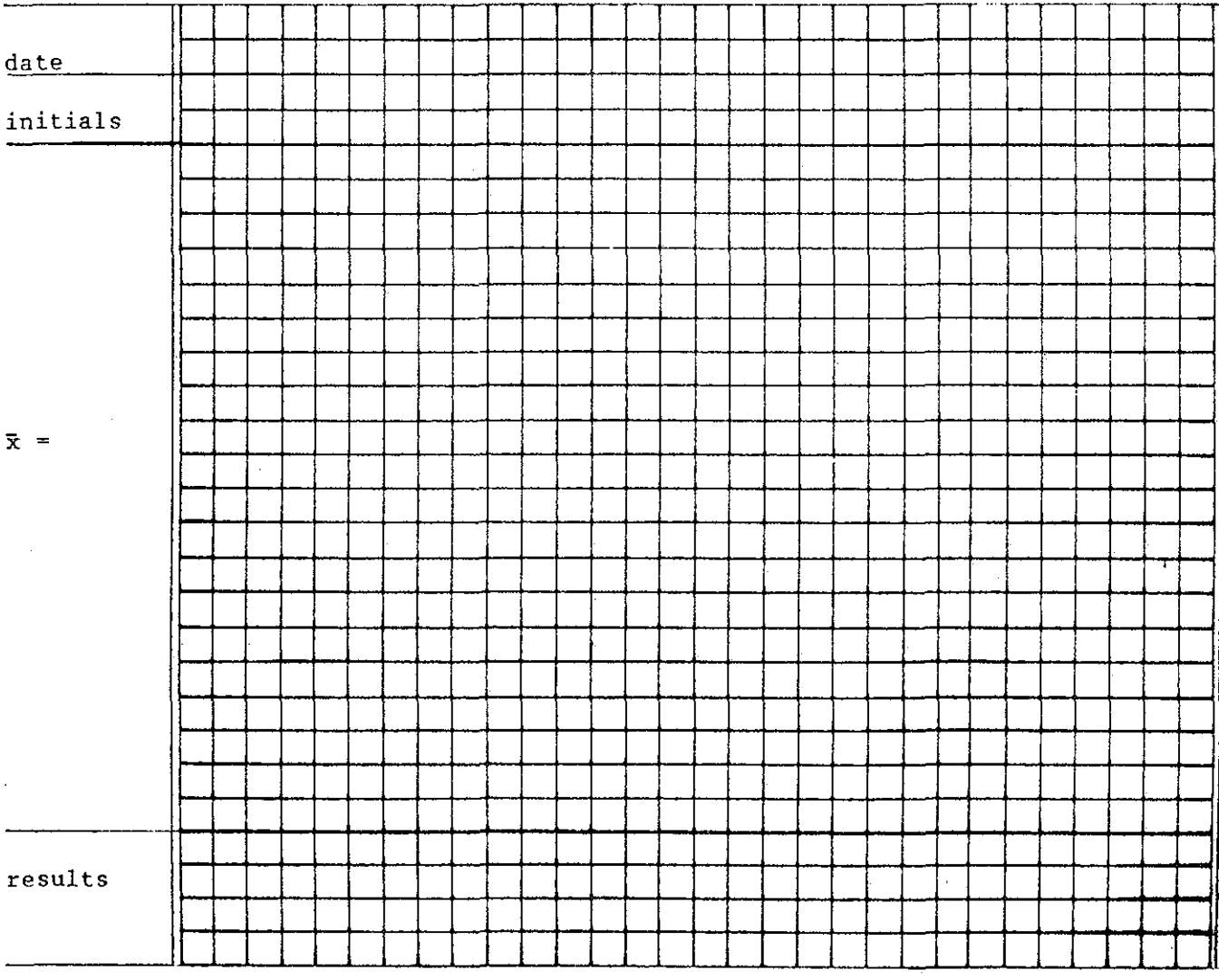
fig. 2



Cusum Chart

parameter :
type of analysis:
units :

laboratory :
chart number:
period :



data of previous periods:
$\bar{x}$ =
s =
N =
Σx_i =
Σx_i^2 =

data of this period:
$\bar{x}$ =
s =
N =

data of all periods:
$\bar{x}$ =
s =
N =
Σx_i =
Σx_i^2 =

remarks

warning limits : $\bar{x} \pm 2s$ (95.45%)
control limits : $\bar{x} \pm 3s$ (99.70%)

Example of a control chart

Annex 2

Overview* of ISO guides and other standards which can be of importance for Quality Systems and Manuals

ISO 5725	Precision of test methods - Determination of repeatability of reproducibility by inter-laboratory test
ISO 8402	Quality Assurance - Vocabulary
ISO 9000	Quality Management and quality assurance standards-guidelines for selection and use.
ISO 9001	Quality Systems - Assurance model for design development, production, installation and servicing capability.
ISO 9002	Quality Systems - Assurance model for production and installation capability
ISO 9003	Quality Systems - Assurance model for initial inspection and test capability.
ISO 9004	Quality Management and quality system elements-guidelines.
ISO/IEC Guide 2	General terms and their definitions concerning standardization and related activities.
ISO Guide 6	Mention of reference materials in international standards.
ISO/IEC Guide 25	General requirements for the technical competence of testing laboratories.
ISO Guide 30	Terms and their definitions used in connection with reference materials.
ISO Guide 31	Contents of certificates of reference materials
ISO Guide 35	Certification of reference materials - General and statistical principles.
ISO/IEC Guide 38	General requirements for the acceptance of testing laboratories.
ISO/IEC Guide 43	Development and operation of laboratory proficiency testing.
ISO/IEC Guide 45	Guidelines for the presentation of test results.
ISO/IEC Guide 49	Guidelines for the development of a Quality Manual for testing laboratories.

ISO — Directory of certified reference materials (CRM)
Geneva, International Organization of Standardization, 1984

OIML — Vocabulary of Legal Metrology.
Paris, International Organization for Legal Metrology, 1978.

BIPM — Le Système international d'Unites (SI)
Paris, Bureau International des Poids et Mesures, Offilib, 4th editions, 1981.

BIPM/IEC ISO/OIML — International Vocabulary of Basic and General Terms and Metrology.
Geneva, International Organization of Standardization, 1984.

BS 5233 — Glossary of terms used in metrology
British Standard

BS 5781 — part 1 - Measurements and calibration systems- Specification of systems requirements;
part 2 - Guide to the use of BS 5781 part 1.
British Standard

BS 6460 — part 1 - Accreditation of testing laboratories- Specification of general requirements for the technical competence of testing laboratories.
British Standard

ILAC doc 1 — General recommendations for the acceptance of accreditation bodies for testing laboratories.
International Laboratory Accreditation Council

ILAC doc 2 — General recommendations for the operations of testing laboratories accreditation systems.
International Laboratory Accreditation Council

*Document of lecture "Laboratorium Erkening" by P.J.H.A.M. van de Leemput
Symposium "Kwaliteit in de Analytische Chemie",
24 april 1987, Amsterdam.

Annex 3

Institutes where reference material can be purchased.

Catalogues

Standard and Reference Materials for Marine Science
National Status & Trends Program
National Oceanic and Atmospheric Administration
Department of Commerce, USA

Catalogue BCR Reference Material
Commission of the European Communities
Directorate-General For Science, Research and Development
Community Bureau of Reference (BCR)

"Survey of Currently Available Reference Materials for Use in Connection with the Determination of Trace Elements in Biological and Environmental Materials"
Muramatsu Y. & Parr R.M.
IAEA/RL/128, december 1985
International Atomic Energy Agency

Europe

International Atomic Energy Agency
Analytical Quality Control Services
Laboratory Seibersdorf
P.O. Box 100
A-1400 Vienna
Austria

For marine reference material contact:

International Atomic Energy Agency
Laboratory of Marine Radioactivity
Oceanographic Museum
Monaco-Ville
Principality of Monaco

Community Bureau of Reference (BCR)
Commission of the European Communities
Directorate General for Science Research and Development
200 Rue de la Roi
B-1049 Brussels
Belgium

Institute of Radioecology and Applied Nuclear Techniques
Komenského 9
P.O. Box A-41
04061 Kosice
Czechoslovakia

PZO Sluzba Vyskumu
Konevo 131
130 86 Praque 3 - Zizkov
Czechoslovakia

Dr. H.J.M. Bowen
Department of Chemistry
The University of Reading
Whiteknights
P.O. Box 224
Reading R66 2 AD
United Kingdom

Institute of Oceanographic Sciences
Brook Road
Wormley, Godalming
Surrey GU8 5UB
United Kingdom

Unites States of America

National Bureau of Standards
Office of Standard Reference Materials
Room B311, Chemistry Building
Gaithersburg, MD 20899
USA

US Environmental Protection Agency
Quality Assurance Branch
EMSL-Cincinnati
Cincinnati, OH 34268
USA

US Geological Survey
Geologic Division Reference Materials
12201 Sunrise Valley Drive
Reston, VA 22092
USA

Japan

National Institute for Environmental Studies
Yatabe-machi
Tsukuba Ibaraki 305
Japan

Sagami Chemical Research Center
Nishi-Ohnuma 4-4-1
Sagamihara-shi 229
Japan

Canada

National Research Council of Canada
Division of Chemistry
Montreal Road
Ottawa, Ontario K1A OR9
Canada

National Research Council of Canada
Marine Analytical Chemistry Standards Program
Atlantic Research Laboratory
1411 Oxford Street
Halifax, Nova Scotia B3H 3Z1
Canada