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AND APPLIED CHEMISTRY

ANALYTICAL, APPLIED AND CLINICAL CHEMISTRY DIVISIONS
INTERDIVISIONAL WORKING PARTY FOR HARMONIZATION OF
QUALITY ASSURANCE SCHEMES FOR ANALYTICAL
LABORATORIES*

**HARMONIZED PROTOCOLS FOR THE
ADOPTION OF STANDARDIZED
ANALYTICAL METHODS AND FOR THE
PRESENTATION OF THEIR
PERFORMANCE CHARACTERISTICS**

Resulting from the Second International Workshop on the Harmonization of the
Adoption and Presentation of Methods Standardized by Collaborative Study,
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Chairman: G. Svehla (Ireland); *Secretary:* M. Parkany (Switzerland); *Members:* S. S. Brown (UK); L. E. Coles (UK); G. den Boef (Netherlands); 1989 B. Griepink (Netherlands); W. Horwitz (USA); S. H. H. Olrichs (Netherlands); W. D. Pocklington (UK).

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Harmonized protocols for the adoption of standardized analytical methods and for the presentation of their performance characteristics

Abstract - The development of two protocols, for the adoption of standardized analytical methods and for the presentation of their performance characteristics, is described. The two protocols were agreed, in principle, by the consensus of 34 participants at the 2nd IUPAC Harmonization Workshop held at Washington, USA in April 1989, and adopted at Lund, Sweden in August 1989 for publication as IUPAC Harmonized Protocols.

The first protocol outlines the criteria to be considered before adopting a method for publication as a standard method. The second protocol is concerned with the aspects of analytical quality control which are to be associated with the texts of all standard methods. Recommended formats for the drafting of essential information on analytical quality control (to be included in compendia of standard methods) are given, together with examples of precision clauses. Annexes list the names of the organisations and individuals who participated in the development of the harmonized protocols.

INTRODUCTION

During the closing discussions at the IUPAC Workshop on the Harmonization of Collaborative Analytical Studies in Geneva, 4-5 May 1987, the view was expressed that there was a need to achieve harmonization in the procedures followed by standards organisations when methods were being considered for adoption as standard methods, and also for harmonization in the presenting of precision and other performance data in the texts of standardized analytical methods.

Subsequent to the Geneva meeting it was proposed at the meeting of the IUPAC (Analytical Chemistry Division) Interdivisional Working Party for the Harmonization of Quality Assurance Schemes for Analytical Laboratories (held on 20-21 August 1987 in Boston, USA) to initiate a project with the following objectives:

To develop protocols, which would be acceptable to industrial, national and international organizations, for: (1) the adoption of methods standardized by collaborative study, and (2) the presentation of performance characteristics in the texts of those methods.

It was agreed that a questionnaire would be drafted and then circulated to the organisations which took part in the international project for the harmonization of collaborative analytical studies. The questionnaire (circulated in February 1988) invited specific comments on:

- a) the criteria to be used for determining if a method, the performance characteristics of which had been determined by collaborative study, warranted publication as a standard, and
- b) the presentation of precision data (and other performance characteristics) in the texts of standardized methods.

A discussion document based on the comments received in response to the questionnaire was prepared and circulated during January 1989. [The names of organizations which responded to the questionnaire are listed in *Annexe I*.] This discussion document outlined recommendations for both the adoption procedure and the presentation of the performance characteristics of standardized analytical methods, and was tabled for discussion at a two day Workshop in Washington, DC, USA, 17-18 April 1989.

Objectives at the 1989 Workshop - The two main objectives set before the Workshop were the drafting of internationally agreed protocols which, if followed by standards organizations, would ensure that:

- 1) all methods published as standard methods met specified minimum requirements as to their performance characteristics, and
- 2) the texts of all methods to be published as standard methods incorporated practical information regarding the precision and other performance characteristics of the methods.

Need for Harmonized Protocols - The need for developing these protocols derives from the fact that:

- 1) methods with unsatisfactory performance characteristics have in certain cases been adopted for publication as standard methods,
- 2) precision clauses in standard methods have often been presented in formats which, although statistically sound, are of little practical value to the user of the standard, and
- 3) other performance characteristics of methods, e.g. accuracy (trueness), limit of detection, etc., have generally not been indicated in the texts of the standardized methods.

* * * * *

The discussions which took place at the Workshop resulted in the drafting of two protocols which were subsequently circulated for comment in May 1989. On the basis of comments received a revised draft of the protocols was prepared for ratification at the 35th IUPAC General Assembly in Lund, August 1989, where the protocols were finalised for publication as IUPAC Harmonized Protocols. The names of individuals and organizations contributing comments on the drafts circulated in May 1989 are given in *Annexe II*, and the names of the IUPAC Interdivisional Working Party are listed in *Annexe III*.

The second protocol, which is concerned with the presentation of performance characteristics in the texts of standard methods, represents what may be viewed as a significant departure from the policy which has generally been followed by standard making bodies, under which precision clauses (and other data of a statistical nature) have been drafted as an integral part of the text of a standard method. The conclusions of the Workshop were that the text of a standard method should not make the obtaining of duplicate tests results mandatory (as may be prescribed in a *number of determinations* clause), nor should it contain detailed statistical data which was of no immediate practical value to the analyst using the standard. It was recognised that standard methods were used for different reasons, e.g. in quality control where the obtaining of a single test result for a laboratory sample might be considered adequate, or for arbitration purposes, when at least two test results for each laboratory sample are required.

It was accordingly recommended that information on *Analytical Quality Control*, which is essential for the satisfactory performance of standardized methods, should be presented in distinct parts and separated from the text of the methods, in the form of both *general principles* and *specific applications*.

* * * * *

The protocols are reproduced on the following page. The protocols are recommended for use by all organisations publishing analytical methods that have been standardized by collaborative studies. An appended document outlines recommended formats for both the *general principles* and *specific applications* of analytical quality control to be associated with standard methods of analysis, and illustrates the application of the principles underlining the second protocol.

* * * * *

[*Note:* The protocols are not directly applicable in the case of qualitative and microbiological methods.]

I. Criteria to be considered when adopting an analytical method for publication as a standard method

Before recommending the adoption and publication of any method as a definitive standard, a standards committee should critically examine the following factors:

1) Were both the organisation of the collaborative studies of the method, and the statistical analysis of the results obtained from those studies, carried out according to the principles outlined in ISO 5725 *Accuracy (Trueness and Precision) of Measurement Methods and Results* and/or the 1987-IUPAC *Harmonized Protocol for the Design, Conduct and Interpretation of Collaborative Studies?* (ref. 1) [*Note:* ISO 5725-1986 is now under substantive revision]

2) Were more than 1 in 5 sets of data (*obtained from the analysis of test samples with different matrices or levels of analyte concentration*) found to contain more than 20% of unexplainable statistically outlying results?

3) Were the calculated values for the reproducibility relative standard deviation [RSD_R]/reproducibility coefficient of variation (in relation to the concentration level), in the case of methods for the determination of constituents/analytes in products such as animal feeds, cosmetics, drugs, fertilisers, foods, minerals, ores, paints, pesticide formulations, standard reference materials, waters, found comparable with those indicated below?

<i>concn. ratio:</i>	10^{-9}	10^{-8}	10^{-7}	10^{-6}	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}	1
RSD_R in %	45	32	23	16	11	8	5.6	4	2.8	2

[*Note:* The RSD_R values cited above have been calculated from $RSD_R = 2^{(1 - 0.5 \log c)}$, where c is the concentration expressed as a decimal fraction. This equation was derived empirically from an examination of more than 3000 collaborative (method performance) studies involving a wide range of analytes, matrices and measurement techniques (refs. 2,3,4). In the absence of overriding information, values within the range 0.5 - 2 times the RSD_R (calculated from the concentration found) may be considered as acceptable precision of method performance *between-laboratories*. *Within-laboratory* method performance (RSD_L), frequently is about one half to two thirds of these values.]

II. Analytical Quality Control for Standard Methods - Minimum Requirements

1) The text of a standard method of analysis must have comprehensive information regarding *Analytical Quality Control* associated with it.

2) This information should include both *general principles*, which are applicable to all methods (e.g. concerning procedures for checking the precision and trueness of test results, etc), and *specific applications* which are directly applicable to an individual method (e.g. repeatability and reproducibility clauses, the method's trueness (bias), sensitivity, limit of detection, limit of determination, and all relevant statistical data that has been derived from the results of interlaboratory tests, etc.).

3) When the standard method forms part of a compendium of methods, the *general principles* for Analytical Quality Control (AQC) should be included as a specific section of the supplementary material in the compendium whereas the *specific applications* of AQC should be annexed to each individual standard method.

References:

1. Horwitz, W., (1988) *Pure and App. Chem.* **60**, 855-867.
2. Horwitz, W., Kamps, L. R., and Boyer K. W. (1980) *J. Assoc. Offic. Anal. Chem.* **63**, 1344-
3. Horwitz, W., (1982) *Anal. Chem.* **54**, 67A-76A. [1354.]
4. Boyer, K. W., Horwitz, W., and Albert, R. (1985) *Anal. Chem.* **57**, 454-459.

I. General Principles

Introduction - The number of test results to be obtained from the analysis of each laboratory sample is related to the purpose for which the analysis is required. Where the analysis is required under the terms of a contractual agreement, or for arbitration purposes, at least two test results for each analyte/parameter will be required. In routine quality control it may be considered sufficient to obtain a single test result for each analyte/parameter. However, for analytical quality control purposes, an analysis in duplicate will be necessary for at least 1 in every 10 determinations of each analyte/parameter.

1) **Precision of Analyses** - when a check on the precision of the analyses is required, two test results for each test sample must be obtained under the conditions of repeatability (i.e. conditions where independent test results are obtained with the same method on identical test material, in the same laboratory by the same operator using the same equipment, within short intervals of time.) [Note: It may also be desirable to obtain two test results under intermediate precision conditions (e.g. when operator and equipment are the same but time is different.)]

2) **Acceptability of Test Results** - when two test results are obtained (under the conditions of repeatability) from two analyses of the same test sample, the *final quoted result* is the mean of the two test results, provided that the requirements of the repeatability clause are met - see the section on *specific applications* of analytical quality control which is appended to the text of the method. If these requirements are not met, reject the results and obtain two further test results (under repeatability conditions). If the requirements of the repeatability clause are again not met, an investigation into the possible sources of error should be carried out. If the source of error cannot be found, the procedure for deriving the *final quoted result*, illustrated in the annexed flow diagram, may be followed. In such a case the final quoted result should be qualified with a statement to the effect that the conditions of repeatability were not met, and the individual test results (with an indication as to how the final quoted result has been calculated) should also be reported.

3) **Utilisation of values for the reproducibility limit (R)** - when test results obtained by two laboratories (from the analysis of identical laboratory samples) are being compared, it should be noted that the values for (R) [determined according to *ISO 5725*] apply in the particular case when each laboratory obtains one test result only. If it is desired to compare *final quoted results* which are the mean results from more than one analysis carried out by each laboratory on identical laboratory samples, the appropriate values for (R) can be calculated as outlined in the *1987-IUPAC Harmonized Protocol* (ref. 1) or *ISO 5725 Part 6 Section 2*. For example, when the *final quoted results* are the mean results from *two* analyses carried out by each laboratory, the formula below applies:

$$R^* = \sqrt{[R^2 - r^2 / 2]}$$

where:

R^* is the adjusted value for the *reproducibility limit*, applicable when the *final quoted results* are the mean results from *two* analyses carried out by each laboratory on identical laboratory samples,

R is the value for the *reproducibility limit** of the method, and

r is the value for the *repeatability limit** for the method

*as determined according to the *1987-IUPAC Harmonized Protocol* or *ISO 5725* from a statistical analysis of the results obtained during the collaborative study of the method.

4) **Trueness of Test Results** - when a check on the trueness of the test results is required, one or more certified (purchased or prepared in-house) reference materials, of similar matrix and analyte concentration to that of the test samples, should be analysed in parallel with the test samples. A decision is then made as to whether the difference, if any, between the expected value(s) for the reference material(s) and that obtained by analysis of the latter, is statistically significant, in the case of:

(contd. overleaf)

a) *certified reference materials* - by reference to the cited confidence limits, or

b) *prepared in-house reference materials* - by use of plotted data such as that on control charts. In this case a test result obtained for the prepared reference material which falls within ± 2 units of the standard deviation (s)* of the accepted mean value* for the analyte of interest may be considered acceptable. If the difference between the test result and the mean value exceeds $\pm 3s$ the test result must be rejected. *[Note: The accepted mean value and standard deviation would be that calculated from the results obtained from not less than 10 analyses of the prepared in-house reference material. Lines drawn on the control chart at $2s$ and $3s$ both above (+) and below (-) the line representing the mean value are regarded as warning and action limits, respectively.]

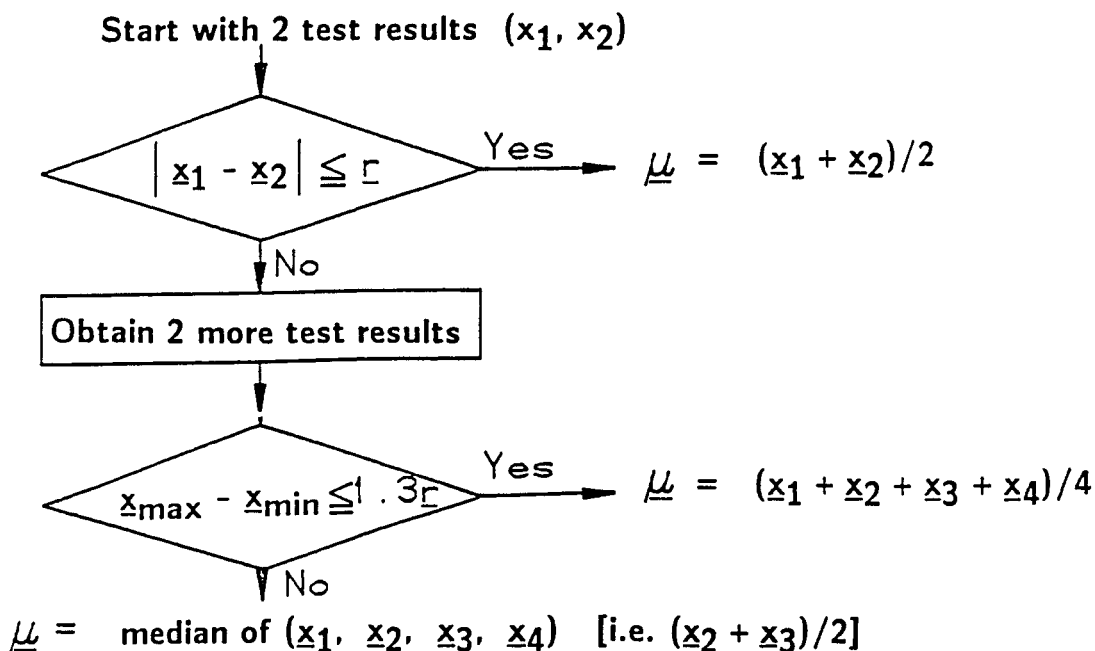
A check on consistent method and individual laboratory *bias* may be made by *spiking* and determining the recovery of added analyte.

Annexe

FLOW DIAGRAM ILLUSTRATING THE DERIVATION OF THE FINAL QUOTED RESULT WHEN TEST RESULTS DO NOT MEET THE CONDITIONS OF REPEATABILITY

r = *repeatability limit* for the method

μ = **final quoted result**



(where x_2, x_3 are, respectively, the second and third smallest test results)

Note: The above flow diagram is based on that appearing in Section 7 of Part 6 of ISO 5725 (long term revision).

Reference:

1. Horwitz, W., (1988) *Pure and App. Chem.*, 60, 855-867.

II. Specific Applications

1) **repeatability and reproducibility clauses** - these should cite values for (*r*) and (*R*)* [as defined in, and derived according to, ISO 5725], wherever suitable and possible, in the following order of preference:

- a) in absolute or relative terms#, or
- b) derived from simple formulae, or
- c) by reference to a table

*[Where available, intermediate repeatability limits applicable to intermediate conditions would also be cited.]

#[In some cases it may be desirable to express values for (*r*) and (*R*) in both absolute and relative terms and applicable to differing levels of analyte concentration.]

Examples of recommended formats for these precision clauses are given in **section IV** below.

2) **performance characteristics of the method** - these should be given in the form of a table of data derived from a statistical analysis of the results obtained from collaborative studies of the method. (An example a table of statistical data is given in **section III** below.) Whilst it may be considered unnecessary to include all the data shown in the table, the following data should at least be included:

- a) the number of laboratories retained (i.e. excluding those submitting outliers [results]),
- b) the mean values of the analytes in the samples studied, and
- c) both the repeatability and reproducibility standard deviations*.

together with the literature reference to the published results of the collaborative studies.

*[*Note:* Although the repeatability/reproducibility limits (*r*, *R*), and relative standard deviations (*RSD*), can be readily derived from the values for the repeatability and reproducibility standard deviations and means, it is of more immediate value to the user of the method if the actual values for (*r*), (*R*), RSD_r , and RSD_R are included in the table.]

3) **bias of the measurement method** - this should be stated, together with a statement regarding the reference against which that bias was determined. Where the bias varies with the level of the test, the data should be given in the form of a table giving the level, the bias as determined, and the reference used in that determination - see *ISO 5725 Part 1: General Principles and Definitions. Section four. Utilization of accuracy data.* The laboratory bias should be defined as the difference of the long-term average value from the true, formulated, or assigned value. The average of all individual laboratory biases is the estimate of the method bias, and the standard deviation of this average (obtained from the values determined by at least eight laboratories) is S_L , i.e. the reproducibility standard deviation without the within-laboratory repeatability standard deviation. (S_R is the reproducibility standard deviation with the repeatability standard deviation.) A note in the text of the method should caution against the direct correcting of analytical test results by the bias.

4)* **the sensitivity, the limit of detection, the limit of determination**, the definitions used, and relevant information regarding possible *interferences* applicable to the method, wherever such data is available, should also be included in the section on specific applications of analytical quality control.

*[*Note:* It may be considered advisable to make reference to this information in the **Scope and Field of Application** section of the method.]

An example of the drafting of the **specific applications** of analytical quality control is given on the following two pages.

III. An Example of Specific Applications

IUPAC Method: 2.310 *Determination of butyric acid by gas-liquid chromatography*

1) *repeatability*

When the mean value [m] of two single test results obtained under repeatability conditions[#], lies within the range of the values cited below, the absolute difference between the two test results obtained should not be greater than the *repeatability limit* (r) deduced by linear interpolation from the data below:

butyric acid content [m] (g/100 g)	0.19	0.35	1.75	3.45
repeatability limit [r] (g/100 g)	0.02	0.04	0.12	0.29

[#]*repeatability conditions*: conditions where independent test results are obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time.

2) *reproducibility*

When the values of two single* test results obtained under reproducibility conditions**, lie within the range of the values cited below, the absolute difference between the two test results obtained should not be greater than the *reproducibility limit* (R) deduced by linear interpolation from the data below:

butyric acid content (g/100 g)	0.19	0.35	1.75	3.45
reproducibility limit [R] (g/100 g)	0.07	0.16	0.43	0.68

*see *utilization of values for the reproducibility limit* in the section on *general principles* of analytical quality control.

***reproducibility conditions*: conditions where test results are obtained with the same method on identical test material in different laboratories with different operators using different equipment.

3) *trueness (bias)* - the bias of the method was demonstrated in the collaborative study of the method (see table of statistical data below) to be negligible when used for the determination of concentration levels of butyric acid at 1.82 and 3.45 g/100g.

4) *the sensitivity, the limit of detection, the limit of determination*, and possible *interferences* have not been established for the method - see also section 1.0 *Scope and Field of Application*.

5) **STATISTICAL AND OTHER DATA DERIVED FROM THE
RESULTS OF INTERLABORATORY TESTS**

Two interlaboratory tests carried out at the international level in 1987 and 1988 (ref. 1) by the IUPAC Commission on Oils, Fats and Derivatives, in which 7 and 13 laboratories participated, each obtaining two test results for each sample, gave the statistical results (evaluated in accordance with the 1987-IUPAC Harmonized Protocol [ref. 2] and ISO 5725) summarised in the following table:

Sample	A	B	C	D
Number of laboratories retained after eliminating outliers	.. 11	7	11	11
Number of outliers (laboratories)	.. 2	-	-	2
Number of accepted results	.. 22	14	22	22
Mean value (g/100 g sample)	.. 0.19	0.35	1.79	3.46
True, or accepted value (g/100 g)	.. -	-	1.82	3.45
Repeatability standard deviation (S_r)*	.. 0.008	0.015	0.044	0.102
Repeatability relative standard deviation	.. 4.2%	4.3%	2.5%	2.9%
Repeatability limit (r)* [2.8 x S_r]	.. 0.02	0.04	0.12	0.29
Reproducibility standard deviation (S_R)*	.. 0.024	0.056	0.155	0.242
Reproducibility relative standard deviation	.. 12.6%	16.0%	8.7%	7.0%
Reproducibility limit (R)* [2.8 x S_R]	.. 0.07	0.16	0.43	0.68

*(expressed as g butyric acid/100 g sample)

* * * * *

References:

1. *Pure and Appl. Chem.*, (1986) 58, 1419-1428.
2. *Pure and Appl. Chem.*, (1988) 60, 855-867.

IV. Examples of formats for precision clauses

(A) Repeatability Clauses

Example 1. [when precision is to be expressed in absolute terms]

"The absolute difference between two single test results obtained under repeatability conditions [Note x]* should not be greater than 0.5 mg/kg."

or, alternatively,

"The absolute difference between two independent single test results, obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time, should not be greater than 0.5 mg/kg."

Example 2. [when precision is to be expressed in relative terms]

"The absolute difference between two single test results obtained under repeatability conditions [Note x]* should not be greater than 2 % relative to the higher of the two test results."

or, alternatively

"The absolute difference between two independent single test results, obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time, should not be greater than 2 % relative to the higher of the two test results."

Example 3a. [when precision is to be related to the analyte concentration]

"The absolute difference between two single test results obtained under repeatability conditions [Note x]* should not be greater than the *repeatability value* (*r*) as calculated from the formula:

$$\text{copper in oil: } r = 0.010 + 0.139 m$$

where *m* is the mean of the two results, expressed in mg/kg."

or, alternatively

"The absolute difference between two independent single test results, obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time, should not be greater than the *repeatability limit* (*r*) as calculated from the formula:

$$\text{copper in oil: } r = 0.010 + 0.139 m$$

where *m* is the mean of the two results, expressed in mg/kg."

Example 3b. [when precision is to be related to the analyte concentration]

"When the values of two single test results obtained under repeatability conditions [Note x]*, lie within the range of the values cited below, the absolute difference between the two test results obtained should not be greater than the *repeatability limit* (*r*) deduced by linear interpolation# from the data below:

copper content (mg/kg)	0.5	5.8	35.8
<i>r</i> (mg/kg)	0.06	0.8	3.6"

#(Note: Linear interpolation may not be valid in the case of non-constant matrices.)

*(ISO definitions of repeatability conditions cited in Note - see foot of next page)

or, alternatively

"When the mean (*m*) value of two independent single test results, obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time, lie within the range of the mean values cited below, the absolute difference between the two test results obtained should not be greater than the **repeatability limit (*r*)** deduced by linear interpolation from the data below:

copper content [<i>m</i>] (mg/kg)	0.5	5.8	35.8
<i>r</i> (mg/kg)	0.06	0.8	3.6]"

(B) Reproducibility Clauses (see Note below)

Example 1. [when precision is to be expressed in absolute terms]

"The absolute difference between two single test results obtained under reproducibility conditions [Note y]" should not be greater than 0.8 mg/kg."

or, alternatively,

"The absolute difference between two single test results, obtained with the same method on identical test material in different laboratories with different operators using different equipment, should not be greater than 0.8 mg/kg."

Example 2. [when precision is to be related to the analyte concentration]

"When the values of two single test results obtained under reproducibility conditions [Note y]*, lie within the range of the values cited below, the absolute difference between the two test results should not be greater than the **reproducibility limit (*R*)** deduced by linear interpolation from the data below:

copper content (mg/kg)	0.5	5.8	35.8
<i>R</i> (mg/kg)	0.2	2.6	11.6"

or, alternatively

"When the values of two single test results, obtained with the same method on identical test material in different laboratories with different operators using different equipment, lies within the range of the values cited below, the absolute difference between the two test results should not be greater than the **reproducibility limit (*R*)** deduced by linear interpolation# from the data below:

copper content (mg/kg)	0.5	5.8	35.8
<i>R</i> (mg/kg)	0.2	2.6	11.6"

#(Note: Linear interpolation may not be valid in the case of non-constant matrices.)

*(ISO definitions of reproducibility conditions cited in Note - see below.)

* * * *

Notes:

Reproducibility clauses, when expressed in relative terms, or by reference to formulae or a range of analyte concentrations, should be drafted along similar lines to the corresponding examples of repeatability clauses given above.

repeatability conditions: Conditions where independent test results are obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time.

reproducibility conditions: Conditions where test results are obtained with the same method on identical test material in different laboratories with different operators using different equipment.

*Annexe I***Names of Organisations Represented in the Development of the Protocols****1) International Organisations****a) International Union of Pure and Applied Chemistry (IUPAC)**

- Analytical Chemistry Division: *Interdivisional Party for Harmonization of Quality Assurance Schemes for Analytical Laboratories*
- Applied Chemistry Division: *Commission on Atmospheric Chemistry
Commission on Oils, Fats and Derivatives*
- Clinical Chemistry Division: *Commission on Toxicology*

b) International Organization for Standardization (ISO) Technical Committees

- TC 6 Paper, board and pulps;
- TC 17 Steel (SC 1);
- TC 34 Agricultural food products (SC 11);
- TC 38 Textiles;
- TC 42 Photography (WG6);
- TC 45 Rubber and rubber products;
- TC 69 Applications of statistical methods (SC 6);
- TC 91 Detergents;
- TC 102 Iron ores;
- TC 183 Copper, lead and zinc ores and concentrates;

c) Other

- Association of Official Analytical Chemists (AOAC)
- International Wool Secretariat
- European Brewery Convention - Analysis Committee
- International Committee for the Unification of Methods for Sugar Analysis (ICUMSA)
- Collaborative International Pesticides Analytical Council (CIPAC)
- Nordic Committee on Food Analysis (NMKL)
- International Committee for Standardization in Haematology (ICSH)
- International Federation of Clinical Chemistry (IFCC)
- International Dairy Federation (IDF/FIL)
- Community Bureau of Reference (BCR)

2) National Organisations

- Food and Drug Administration, Washington, DC, USA
- Istituto Italiano di Idrobiologia (CNR), Pallanza, Italy
- National Institute of Chemistry, Bucharest, Romania
- The Macaulay Land Use Research Institute, Aberdeen, UK
- Public Analyst Laboratory, Dublin, Ireland
- Laboratory of the Government Chemist, Teddington, UK
- Norddeutsche Affinerie, Hamburg, FRG
- State Technical Research Centre, Espoo, Finland
- State Laboratory, Dublin, Ireland
- Inspectorate Griffith, Witham, UK
- Kantonalen Labor, Zurich, Switzerland
- Nederlands Normalisatie-instituut (NNI), Delft, Netherlands
- Shanghai Import & Export Commodity Inspection Bureau, Shanghai, UK
- American National Standards Institute Inc, New York, USA

(contd)

2) **National Organisations (contd)**

- Association française de normalisation (AFNOR), Paris, France
- Max von Pettenkofer-Institute of Federal Health Office, Berlin, FRG
- Water Research Centre, Marlow, UK

- National Institute of Standards and Technology, Gaithersburg, USA
- The United States Pharmacopeia Convention, Inc, Rockville, USA
- Council for Mineral Technology, South Africa

- USDA, Western Human Nutrition Research Centre, San Francisco, USA
- Biologische Bundesanstalt für Land- und Forstwirtschaft, Braunschweig, FRG
- Station Fédérale de Recherches en Chimie Agricole et sur l'Hygiène de l'Environnement, Liebefeld-Berne, Switzerland

- Enterprise for Vegetable Oil, Industry and Detergent Production, Budapest, Hungary
- Cone Mills Corp (AATCC), Greensboro, USA
- CSIRO, Division of Mineral & Process Engineering, Port Melbourne, Australia

- China State Bureau of Standards, Beijing, China
- Instituto Nacional del Carbon, Oviedo, Spain
- Verein Deutscher Eisenhüttenleute, Dusseldorf, FRG
- Standards Association of Australia, Sydney, Australia

- Ministry of Agriculture, Fisheries and Food, London, UK
- Norwegian Institute for Air Research (NILU), Lillestrøm, Norway
- SGS Inspection Services, Mineral Assay Service, London, UK

- United States National Committee on Sugar Analysis, USA
- Standing Committee of Analysts, Department of the Environment, London, UK
- Institut für Standardisierung und Dokumentation im Medizinischen Laboratorium E.V. (INSTAND), Dusseldorf, FRG

Annexe II

Names of organizations and individuals contributing comments on the draft protocols circulated in May 1989

International Union of Pure and Applied Chemistry

Analytical Chemistry Division
 Applied Chemistry Division
 Clinical Chemistry Division [S S Brown]

International Organization for Standardization

ISO/TC 134/SC 4 [P A Hargood]
 ISO/TC 17/SC 1 [H Terashima]
 ISO/TC 69/SC 6 [P T Wilrich]

International Organizations (other than IUPAC or ISO)

International Federation of Clinical Chemistry (IFCC) [R Dybkaer]

(contd)

Names of organizations and individuals contributing comments on the draft protocols circulated in May 1989***National Organisations***

National Institute of Standards and Technology, USA [S D Rasberry]
 Shanghai Import & Export Commodity Inspection Bureau, China
 Central Coal Mining Research Institute, China
 State Laboratory, Ireland [Marie C Walsh]
 Libra Laboratories Inc, USA [T K Blumenthal]
 Nederlands Normalisatie-instituut, Netherlands [R W Zwart]
 Food and Drug Administration, USA [W Horwitz, R Albert]
 Council for Mineral Technology, South Africa [G D Marshall]
 De Danske Sukkerfabrikker, Denmark
 The United States Pharmacopeia Convention, Inc, USA [L T Grady]
 Association française de normalisation (AFNOR) [Roland Hue]
 China State Bureau of Technical Supervision [Jin Guang]
 Labtest Hong Kong Ltd [A S K Tang]

Individuals

Mr C T Ashton (BSI, UK)
 Dr J C Koedam (Netherlands)
 Dr K Pavel (Bayer AG)
 Dr K A Smart (UK)
 Dr R F M Herber (Universiteit van Amsterdam)
 Prof H P Lehmann (Louisiana State University Medical Center)
 Dr R Zender (Hopital de La Chaux-de-Fonds)
 Dr A v Klein-Wisenberg (INSTAND)
 Dr T W Lashof (USA)
 Prof D Thorburn Burns (The Queen's University of Belfast)
 Dr M Thompson (University of London)

Annexe III**Names of the Members of the IUPAC (Analytical Chemistry Division) Interdivisional Working Party for Harmonization of Quality Assurance Schemes for Analytical Laboratories**

Prof G Svehla (Department of Chemistry, University College, Cork, Ireland) - *Chairman*
 Dr M Parkany (ISO Central Secretariat, Geneva, Switzerland) - *Secretary*

Dr S S Brown (Regional Laboratory for Toxicology, Birmingham, UK)
 Prof G den Boef (University of Amsterdam, Netherlands)
 Dr L E Coles (United Kingdom)
 Dr B Griepink (Netherlands)
 Dr W Horwitz (Food and Drug Administration, Washington DC, USA)
 Dr S H H Olrichs (Netherlands Waterworks Testing and Research Institute)
 Mr W D Pocklington (Laboratory of the Government Chemist, Teddington, UK)

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