International Federation of Clinical Chemistry
Recommendations and Related Documents, Volume 1

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Clinical Chemistry

Recommendations and Related Documents
Volume I, 1978–1983

Quantities and Units
Quality Control
Enzymes
Proteins
Instrumentation
Diagnostic Kits and Reagents
pH and Blood Gases
Education

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Preface

The first document from the International Federation of Clinical Chemistry (IFCC) was a monograph – R. Dybkær and K. Jørgensen: Quantities and Units in Clinical Chemistry, Including Recommendation 1966 of the Commission on *Clinical Chemistry of the International Union of Pure and Applied Chemistry and of the International Federation for Clinical Chemistry* (Munksgaard, Copenhagen, and Williams & Wilkins, Baltimore, MD, 1967). In 1975 *Clinica Chimica Acta* agreed to publish IFCC Sections, and *Journal of Clinical Chemistry and Clinical Biochemistry* also published these from the beginning. Since then a great number of IFCC documents and recommendations have been published, all of them in these two journals, and in some other leading journals of the field as well, e.g. *Clinical Chemistry, Clinical Biochemistry, Journal of Clinical Laboratory Automation* and *Clinical Chemistry Newsletter.* Translations into Italian, Spanish and Russian have also appeared in national or regional journals.

In 1983 a milestone was passed when the Expert Panel on Nomenclature and Principles of Quality Control in Clinical Chemistry completed its task and the Council approved the six recommendations it had produced. The great interest in its work is evidenced by the fact that National Groups in Italy, Spain and Latin America have produced booklets containing translations of these documents even before some of them had been finalized.

The present book contains the set of approved recommendations on quality control in clinical chemistry. It also contains the approved recommendations on quantities and units in clinical chemistry which have had a substantial impact on the field. The Executive Board of the IFCC decided that other completed projects also should be included. It should be emphasized, however, that an approved recommendation or a completed project may not be the final word on the matter. As progress continues, some texts may become at least partially obsolete, and additional aspects may require attention. Nevertheless, it is hoped that the publication of this volume will aid clinical chemists and related professionals by bringing together the relevant documents scattered throughout the literature as they were published in the cooperating journals over the years.

The book contains references to all documents and recommendations published in English. In addition it contains information on the activities and terms of reference of the various Expert Panels. It is hoped that this will enhance the usefulness of the collection. Future volumes will appear at suitable intervals as projects are completed.

Nils-Erik Saris

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Introduction

The International Federation of Clinical Chemistry

René Dybkær, President 1979–1984

We have to live today by what truth
we can get today and be ready
tomorrow to call it falsehood.
William James

With this first collection of published papers from the International Federation of Clinical Chemistry (IFCC), it may be useful to present the structure and functions of the Federation because they influence the product.

There is no official *definition* of "Clinical Chemistry", but the following may serve the purpose: The paraclinical discipline called clinical chemistry is a special branch of medicine dealing with measurement and interpretation of the physico-chemical condition and dynamics in healthy and diseased humans, thus contributing to a pathophysiological understanding and thereby to the prophylaxis, diagnosis, therapy, prognostication and research of disease. Such designations as "clinical biochemistry" and "chemical pathology" cover the same field and, in practice, there are substantial overlaps between clinical chemistry and other clinical laboratory sciences, especially haematology, immunology, physiology and pharmacology.

It is characteristic that clinical chemists are asked to measure many different types of quantities of widely different nature, in large numbers, within a short time, and on small specimens presenting great matrix problems. Therefore, the clinical chemical laboratory, perhaps more than other analytical laboratories, has had to utilize a wide selection of quite different techniques evolved from physics, chemistry, radiochemistry, biochemistry, immunology and microbiology. Due to the potential seriousness of "false" results, great stress has been put on quality control, and to cope with the increasing workload sophisticated mechanization and electronic data processing have been applied.

The analytical part of clinical chemistry, in spite of its many exciting challenges, must not obscure our main goal: to participate in the elucidation of the physiological and disease process of each patient. In fact, the development of clinical chemistry should be guided by the effort to solve pathobiochemical problems.

With the increasing complexity of our discipline, the need to exchange and pool knowledge and experience resulted in the *formation* of National Societies, starting with the Societé Française de Biologie Clinique in 1942. Soon, a formalized relation between the national groups became natural, and an international embryo was formed in 1952 as another aspect of the clinical chemical activites within the International Union of Pure and Applied Chemistry (IUPAC). In 1967 the IFCC achieved its independence, yet maintaining strong and useful links with the IUPAC.

The *goals of IFCC* are "to advance the science and practice of clinical chemistry and to enhance its service to health and medicine" in the interest of all peoples of the world. The *objectives* are to encourage high professional standards and the formation of National Societies as well as to promote international cooperation and free exchange of professional information among clinical chemists and with neighbouring disciplines.

The Federation comprises a governing *Council* composed of one National Representative for each member society, of which there are at present 43. The Council elects the officers of the *Executive Board*, which conducts business in the interims between the triennial Council meetings at the International Congresses of Clinical Chemistry.

The IFCC is convinced that many industrial or professional corporate groups share its objectives, and since 1978 such organizations can become Corporate Affiliates of the Federation. The more than 30 groups in this category form an important part of the IFCC expertise and potential.

In view of the many tasks of the Federation and the common interests with other professional organizations, our international relations have been continuously expanded to minimize duplication and to utilize resources optimally. Our closest contact is with the IUPAC and its Clinical Chemistry Division, with which we enjoy a pleasant and fruitful collaboration as evidenced by the joint papers in this volume. An increasingly important and demanding collaboration has evolved due to our official relation to WHO, whose worldwide channels of communication and stature increase the impact of clinical chemical joint projects on the national health services, including those in countries that do not yet have IFCC Members.

The Federation also values its excellent working relations with the International Committee for Standardization in Haematology, the International Organization for Standardization, the International Union of Bio-

chemistry, the International Union of Immunological Societies, and the World Association of Societies of Pathology, as well as its participation in a general information exchange between many standards-setting bodies such as the European Committee for Clinical Laboratory Standards, the International Organization of Legal Metrology, the National Bureau of Standards (US), and the National Committee for Clinical Laboratory Standards (US).

In addition to participating in the international work of the Federation, some clinical chemical societies have formed regional groups, and we are happy to acknowledge collaboration with our colleagues in the Latin American Confederation of Clinical Biochemistry and the Asian and Pacific Federation of Clinical Biochemistry.

In the structure of IFCC, four bodies are concerned with organizational matters: the *Awards Committee,* the *Congress Committee* with its Regional Committees for Europe and for African, Mediterranean and Near Eastern countries, the *Nominations Committee,* and the *Publications Committee.* Three groups supervize and conduct studies that may lead to IFCC Recommendations or Documents: the *Education Committee,* the *Office of Reference Materials and Methods* (ORMM) and the *Scientific Committee* (SC). These bodies may form Expert Panels (EPs) or Working Groups (WGs) on specific subjects. At present, the ORMM has a WG on Reference Methodology using Mass Spectrometry and the SC has an Analytical Section comprising EPs on Apolipoproteins, Core Clinical Laboratory, Enzymes, Evaluation of Diagnostic Reagent Sets, Instrumentation, pH and Blood Gases, Quality Control, Quantities and Units as well as a WG on Plasma Protein Standardization; the Clinical Section includes EPs on Drug Effects, Nutrition, Theory of Reference Values, and a WG on Effectiveness of Quantities. In addition, there are two groups to address specific problems put to IFCC by WHO: a Task Force on Essential Tests for WHO Intermediate Laboratories and another on Simple Tests.

The many colleagues working within this structure and its numerous national and international relations produce the means to achieve our objectives in the form of congresses and other international and regional meetings, national or regional courses in theoretical and practical aspects of our field, and study reports of various kinds. It is the last mode of operation that is our concern here.

The present volume is the direct outcome of the interaction between the draft-producing Committees, Expert Panels, Working Groups and Task Forces, and an extensive net of commentators from all over the world. The Federation stresses the usefulness of *consensus* documents and, therefore, follows a rigorous process of draft circulation to Associate Members of Expert Panels, both from National Societies and Corporate Affiliates, as well as to the National Representatives and Corporate Affiliate Representatives, to pertinent international bodies and individual experts. After revision, the paper may be published as an IFCC Document or as a provisional recommendation for further comment, revision, and Council ballot to be republished as an IFCC-Recommendation. All such papers appear in *Clinica Chimica Acta* and *Journal of Clinical Chemistry and Clinical Biochemistry;* selected papers are also published in other journals.

If the reader finds the present documents widely differing in character, this is to be expected when an international organization tries to produce a wide spectrum of offerings so as to provide useful material for nearly everyone.

The Nature of IFCC Documents and Recommendations

Robert Zender, Chairman of the Scientific Committee 1979–1982

IFCC documents are intended either to become recommendations approved by the Council, or to summarize present-day international expertise in a given field. In the latter case approval of the Council is not always solicited when the document is non-controversial (a list of references for instance) or when a reasonable consensus was reached by draft circulation of proposals that will very likely be modfied later (an analytical method for instance).

Recommendations and documents are prepared with two aims in view: to promote quality in clinical chemistry practice, and to introduce norms (written standards) attuning methods, securing control materials and harmonizing modes of expression. IFCC documents can be categorized into those pertaining to clinical practice and the interpretation of laboratory data, those more closely related to biochemistry and physiology, and those touching on methodological aspects, i.e. analytical chemistry.

IFCC documents can also be classified according to their intended use, education for instance, and they likewise fall into categories according to their intended readership. The latter classification is not obvious, and some documents were misunderstood by readers who found them esoteric, obvious or simply irrelevant to their particular field. We would like to lay stress on this aspect of the problem.

Some recommendations are intended more for standardization groups or scientific committees of national societes than for each and every member. For instance reference methods proposed by the Expert Panel on Enzymes are designed to serve as international "yardsticks" rather than as routine bench methods. According to prevailing conditions and usages it is the responsibility of the local, national or regional organizations to implement such reference methodology or to harmonize existing technology with the yardstick. Fortunately, our world is varied and diverse; thus yardsticks are necessary, and only an international body such as the IFCC can provide them with some chance of succeeding.

Other documents and recommendations are written with a view to filling in the existing gap between our discipline and the more basic sciences. Papers, for instance on spectroscopy, or on physicochemical quantities, prepared by the Expert Panel on Quantities and Units or the Expert Panel on pH and Blood Gases, are of this kind. These documents may seem esoteric to most of us, but is it not our personal responsibility to expand and further our knowledge? Furthermore such documents prepared by clinical chemists, both MDs and PhDs, are also addressed to our colleagues in the basic disciplines, who have found some of them quite useful because, as Tom Whitehead wrote some years ago, clinical chemistry is a view from a bridge in which both banks, medicine and chemistry, seem closer and more familiar. Such documents serve also to improve the image of clinical chemistry.

The Expert Panels of IFCC

Most of the work in the preparation of documents and recommendations is carried out in the Expert Panels of the Scientific Committee, the Education Committee, and the Office of Reference Materials and Methods. While the expertise in the Panels is truly international, specific tasks may be carried out by local Working Groups. The Expert Panels which have successfully produced published documents or are in the process of doing so, are presented briefly below. The general field of activity is indicated by the name of each Expert Panel. The terms of reference define the tasks in greater detail. The Panels are presented in the order in which they were established.

Expert Panel on Quantities and Units

The Panel was created in 1968 under the chairmanship of R. Dybkær (Copenhagen, DNK). The present Chairman is H. P. Lehman (New Orleans, USA). Its terms of reference are:

1. Examination of recommendations on nomenclature and rules of quantities, kinds of quantities and units from pertinent international bodies.
2. Active cooperation with relevant international bodies concerned with making recommendations in the same field, especially the International Union of Pure and Applied Chemistry, Section of Clinical Chemistry, Commission of Quantities and Units in Clinical Chemistry.
3. Drafting recommendations or advocating use of the recommendations of other bodies relevant to the panel's general field of activity. The final approval of a recommendation will rest with the Scientific Committee and ultimately with the IFCC Council.
4. As far as possible the proposals of the Panel should be in accordance with the decisions of international bodies allied to clinical chemistry.
5. Suggesting ways and means of implementing the international use of the approved recommendations.

Expert Panel on Proteins

The Panel was created in 1969 under the chairmanship of T. Freeman (London, GBR). In 1980 the Panel was dissolved and its tasks transferred to a Working Group on Protein Standardization under the chairmanship of B. G. Johansson (Malmö, SWE). According to the terms of reference, the following point should be examined for each protein:

1. Definition of protein, nomenclature and units.
2. Definition of a reference preparation: physical and chemical properties (including reactive properties), purity, storage conditions, stability, production and control.
3. Description of one (possibly two) reference method(s) for the determination of the protein in pertinent biological materials.
4. Availability and distribution of reference preparation.
5. As far as possible, the proposals of the Panel should be in accordance with the decisions of international bodies allied to clinical chemistry.
6. Implementation of the international use of recommendations (when finally approved).

Expert Panel on Nomenclature and Principles of Quality Control

The Panel was created in 1969 under the chairmanship of J. Büttner (Hannover, DEU). It was dissolved in 1983 after having completed its tasks. Its terms of reference were:

1. Preparation of a list of English terms and definitions in the field of quality control in clinical chemistry (QC). Translation into German and French.
2. Intralaboratory QC techniques. Description and use. Collection of data and statistical treatment. Self-prepared and commercial reference materials.
3. Interlaboratory QC techniques. Descriptions and use. Collection of data and statistical treatment.
4. Preparation of a general plan for standardization of clinical chemical methods utilizing results from items 2 and 3.
5. Preparation of a list of recommended reference materials and corresponding methods.
6. Recommendations on intra- and interlaboratory QC and on minimal requirements of routine accuracy and precision.

7. Recommendation to manufacturers for preparation of commercial reference materials.
8. As far as possible the proposals of the Panel should accord with decisions of international bodies allied to clinical chemistry.
9. Implementation of the international use of recommendations (when finally approved).

Expert Panel on the Theory of Reference values

The Panel was created in 1970 under the chairmanship of R. Gräsbeck (Helsinki, FIN). The present Chairman is H. E. Solberg (Oslo, NOR). Its terms of reference are:

1. Nomenclature. Kinds of reference values ("normal values").
2. Ways of selecting the individuals constituting a group yielding data for study.
3. Factors influencing reference values.
4. Transformation of data. Calculation of parameters characterizing the distribution of data.
5. Combination of data-yielding groups.
6. Ways of presenting reference values for research workers and for clinicians.
7. Ways of presenting single measurements as related to appropriate reference values.
8. As far as possible the proposals should be in accordance with the decisions of relevant international bodies.
9. Advice on the implementation of the international use of recommendations (when finally approved).

Expert Panel on Enzymes

The Panel was created in 1971 under the chairmanship of G. N. Bowers (Hartford, Conn., USA). Its present Chairman is R. Rej (New York, N.Y., USA). Its terms of reference are:

1. Definition of selected enzyme(s) nomenclature and units.
2. Definition of properties of a reference preparation for the enzyme(s), production and control included.
3. Description of one (possibly two) reference method(s) for the determination of the enzyme(s) in pertinent biological materials.
4. As far as possible, the proposals of the Panel should be in accordance with the decision of international bodies allied to clinical chemistry.
5. Suggestions for implementation of the international use of recommendations (when finally approved).

Expert Panel on Instrumentation

The Panel was created in 1974 under the chairmanship of F. L. Mitchell (Harrow, GBR). Its present Chairman is T. D. Geary (Adelaide, AUS). Its terms of reference are:

1. The following points should be examined for the major classes of instruments (such as centrifuges, pipettes, chromatographs, mass spectrometers, multichannel automatic analyzers) and recommendations made.
2. Definition of terms, with special reference to performance characteristics, for:
   a) instruments in general
   b) the main classes of instruments.
   These definitions should be in accord with the definitions and decisions of other Expert Panels and should take note of the decisions of other bodies allied to clinical chemistry.
3. Prepare one or more protocols for the testing and evaluation of instruments, with particular reference to the ease of use, performance, safety and susceptibility to interference from external sources such as temperature, humidity, dust, vibration, electricity supply, etc.
4. Recommend standards of safety for instruments used in clinical chemistry laboratories, with due emphasis upon chemical, electrical, mechanical, microbiological and radioactive hazards.
5. Recommend standards for the presentation and content of instruction manuals, with special emphasis on:
   a) preventive maintenance
   b) repair facilities, particularly for laboratories remote from manufacturers workshops in developing countries.
6. Make general recommendations upon the requirements for instruments used in developing countries.
7. Advice upon the implementation of these recommendations.

Expert Panel on pH and Blood Gases

The Panel was created in 1977 under the chairmanship of H. Maas (Utrecht, NLD). Its terms of reference are:

1. Review of definitions of quantities used for description of the components related to hydrogen ions, carbon dioxide and oxygen in systems of clinical chemical importance.
2. Recommendations concerning preferred quantities and their definitions.
3. Recommendations of preferred units.
4. Recommendations of symbols for quantities and units.