

WORLD HEALTH
ORGANIZATION

EXPERT COMMITTEE ON THE
INTERNATIONAL PHARMACOPOEIA

ORGANISATION MONDIALE
DE LA SANTÉ

WHO/Pharm/308 Corr.1
11 January 1957

ORIGINAL : ENGLISH

FOURTEENTH REPORT

CORRIGENDUM

Page 8: In the second line of the paragraph headed "Hyaluronidasum"
replace the words "annexed to this report" by "sent out".

COMITE D'EXPERTS DE LA
PHARMACOPEE INTERNATIONALE

WHO/Pharm/308 Corr.1
11 janvier 1957

ORIGINAL : ANGLAIS

QUATORZIEME RAPPORT

CORRIGENDUM

Page 8: A la deuxième ligne du paragraphe "Hyaluronidasum",
effacez les mots "au présent rapport".

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FOURTEENTH REPORT

The Expert Committee on the International Pharmacopoeia held its fourteenth session in Geneva from 26 April to 3 May 1956.

Professor H. Baggesgaard Rasmussen, Professor of Organic Chemistry, Royal Danish School of Pharmacy, Copenhagen, Denmark; Member of the Danish Pharmacopoeia Commission and of the Scandinavian Pharmacopoeia Council.

Dr T. Canbäck, Director of the Pharmaceutical Control Laboratory, Stockholm, Sweden; Vice-Chairman of the Swedish Pharmacopoeia Commission; Member of the Scandinavian Pharmacopoeia Council (Chairman).

Mr T. C. Denston, Secretary, British Pharmacopoeia Commission, London, United Kingdom (Rapporteur).

Professor H. Flück, Professor of Pharmacognosy at the Federal Institute of Technology, Zurich, Switzerland; Member of the Federal Pharmacopoeia Commission.

*Dr F. Hartley, Member of the British Pharmacopoeia Commission, London, United Kingdom.

Professor R. Hazard, Professor of Pharmacology and Materia Medica, Faculty of Medicine of Paris University, France; Member of the Permanent French Pharmacopoeia Commission (Vice-Chairman).

Professor M.-M. Janot, Professor of Galenical Pharmacy, Faculty of Pharmacy of Paris University, France; Technical Secretary of the French Pharmacopoeia Commission.

Dr L. C. Miller, Director of Revision of the Pharmacopoeia of the United States of America, New York, USA (Rapporteur).

Dr B. Mukerji, Director, Central Drug Research Institute, Lucknow, India; Joint-Secretary of the Co-ordination Committee, Indian Pharmacopoeia.

Professor D. van Os, Professor of Pharmacy and Toxicology, University of Groningen, Netherlands; Chairman of the Netherlands Pharmacopoeia Commission.

Dr J. L. Powers, Chairman of the Committee on National Formulary, American Pharmaceutical Association, Washington, D.C., USA.

* Member unable to attend

Professor R. H. Thorp, Professor of Pharmacology, Director of Pharmaceutical Studies, University of Sydney, Australia.

Secretariat

P. Blanc, Chief, Pharmaceutical Section, Division of Therapeutic Substances.
G. R. Brown, Consultant.

Dr Dorolle, Dr Gear, Dr Timmerman, Dr Lourie attended some of the meetings.

The Deputy Director-General opened the meeting by welcoming the members and thanking them for their work, as a result of which Volume II of the first edition of the International Pharmacopoeia had now been published in English and French. He also mentioned the great contribution of the late Dr Hampshire, who as early as 1937 acted as Chairman of the first Technical Commission of Pharmacopoeial Experts of the League of Nations, and whose enthusiasm and devoted collaboration were in large part responsible for the realization of this project in the form of the International Pharmacopoeia.

The main task of the Expert Committee would be to consider draft monographs and comments on them received from members of the Expert Advisory Panel and other specialists, and to prepare the texts for the Supplement to the first edition in order that they can be made available for consultation in the Member States of WHO, and to consider the revision of the first edition.

1. Resolutions of the Executive Board

The Executive Board at its fifteenth session noted the thirteenth report of the Expert Committee on the International Pharmacopoeia and the sixth report of the Sub-Committee on Non-Proprietary Names, and thanked the members for their work.

2. Publication of Volume I and Volume II of the International Pharmacopoeia

Since the last session, Volume II of the first edition of the International Pharmacopoeia was published in the autumn of 1955 after consultation with Member States and integration of the comments received. As for Volume I, and again due to the work of Professor Hazard, it was again possible to issue the French edition at the same time as the English.

Volume I was published by WHO in a Spanish edition in December 1955, thanks to assistance from Professor Sellés of Madrid. A firm published on its own initiative a German edition of Volume I, the translation having been supervised by Professor Flück, and another firm has published a Japanese edition of Volume I, the translation having been supervised by Professor Kariyone. Both firms requested permission, which was granted by WHO, also to translate Volume II for early publication.

Comments and information received on Volumes I and II point to their extensive use as a basis in the compilation of national specifications for pharmaceutical preparations.

3. Supplement to the First Edition of the International Pharmacopoeia

A major part of the session was devoted to an examination of the many documents submitted by members of the Expert Advisory Panel and others for the preparation of a Supplement. Considerable efforts had been made by certain of the experts to check experimentally specific points and to obtain agreement by correspondence so as to have drafts available at the session for comment, criticism and suggestions. The Committee expressed its thanks in particular to the members who had supplied draft monographs and laboratory reports. The earlier correspondence through the Secretariat and the discussions during the session were of importance in achieving a greater unification of symbols, specifications for purity, assays, nomenclature and other aspects of pharmacopoeial work in the different countries.

The Expert Committee reviewed the considerable amount of information supplied by the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations for the preparation of the Supplement and second edition. This information is obtained from laboratories, institutes, universities, national pharmacopoeia commissions, specialists, etc., in many countries and makes possible the drafting of specifications for the more important pharmaceutical preparations, including the tests for identification and purity, assays, and posology. It had been possible to circulate draft specifications to the experts for review. The comments received had been examined and for some preparations it was not possible to agree on the proposed specifications, so that these were held over for examination and possible inclusion in the second edition of the International Pharmacopoeia. The specifications of preparations intended for the Supplement are to be sent to Member States as a separate document.

The Committee expressed the view that, taking into account the number of drafts available, the title "International Pharmacopoeia, First Edition, Volume III" might be more appropriate than "Supplement", the title considered when a smaller publication was envisaged.

The following 123 draft monographs were considered by the Expert Committee:

Acidum Acetrizoicum, Acidum Boricum, Acidum Iopanoicum, Acidum Salicylicum, Aethylis Biscoumacetas, Amobarbitalum, Amobarbitalum Natricum, Amobarbitalum Natricum pro Injectione, Aqua Demineralisata, Atropini Methonitras, Bacitracinum, Benzalkonii Chloridum, Benzethonii Chloridum, Calcii Para-aminosalicylas Hemihydras, Capsulae Oxytetracyclini Hydrochloridi, Carbimazolum, Cetrimonii Bromidum, Chlorcyclizini Hydrochloridum, Chloroquini Sulfas, Chlorpromazini Hydrochloridum, Compressi Acidi Iopanoici, Compressi Amobarbitali, Compressi Apomorphini Hydrochloridi, Compressi Carbimazoli, Compressi Chlorcyclizini Hydrochloridi, Compressi Chloroquini Sulfatis, Compressi Chlorpromazini Hydrochloridi, Compressi Dextro Amphetamini Sulfatis, Compressi Diaethylcarbamazini Citratis, Compressi Dienoestrolis, Compressi Digitoxosidi, Compressi Hexamethonii Tartratis, Compressi Hydrocortisoni, Compressi Hyoscini Hydrobromidi, Compressi Isoprenalini Sulfatis, Compressi Mephenytoini, Compressi Mepyradini Maleatis, Compressi Methamphetamini Hydrochloridi, Compressi Methyltestosteroni, Compressi Morphini Sulfatis, Compressi Natrii Nitriti, Compressi Obducti, Compressi Phenadoxoni Hydrochloridi, Compressi Primidoni, Compressi Promethazini Hydrochloridi, Compressi Pyrimethamini, Compressi Quinini Sulfatis, Compressi Secobarbitali Natrici, Compressi Sulfa-dimidini, Decamethonii Iodidum, Deslanosidum, Dextro Amphetamini Sulfas, Diaethylcarbamazini Citras Dibutylis Phthalas, Dienoestrolum, Diiodohydroxy-quinolinum, Diprophyllinum, Erythromycinum, Fluoresceinum Natricum, Gammabenzeni Hexachloridum, Hexamethonii Tartras, Hyaluronidasum pro Injectione, Hydrocortisoni Acetas, Hydrocortisonum, Injectio Acetrizoici Natrici, Injectio Bismuthi et Kalii Tartratis, Injectio Deslanosidi, Injectio Hexamethonii Tartratis, Injectio Insulini Zinci Globinatis, Injectio Methoxamini Hydrochloridi, Injectio Nalorphini Hydrochloridi, Injectio Natrii Citratis Anticoagulans, Injectio Ouabaini, Injectio Procainamidi Hydrochloridi, Injectio Procaini Benzylpenicillini cum

Benzylpenicillino, Injectio Procaini Benzylpenicillini Oleosa, Injectio Streptomycini et Calcii Chloridi, Injectio Suxamethonii Chloridi, Injectio Testosteroni Propionatis, Isoniazidum, Kalii Nitras, Lidocaini Hydrochloridum, Lidocainum, Mephenesinum, Mephenytoinum, Methamphetamini Hydrochloridum, Methandriolum, Methioninum, Methoxamini Hydrochloridum, Methylthiouracilum, Nalorphini Hydrochloridum, Natrii Tetraboras, Penicillinum Amorphum, Phenadoxoni Hydrochloridum, Phthalylsulfathiazolum, Plasma Humanum Dessiccatum, Polymyxini B Sulfas, Primaquini Diphosphas, Primidonum, Procainamidi Hydrochloridum, Procaini Benzylpenicillinum cum Benzylpenicillino pro Injectione, Pyridoxini Hydrochloridum, Pyrimethaminum, Secobarbitalum Natricum, Solutio Acidi Citratis et Glucosi Anticoagulans, Solutio Benzalkonii Chloridi, Solutio Benzethonii Chloridi, Solutio Natrii Citratis Anticoagulans, Streptomycini et Calcii Chloridum pro Injectione, Streptomycini Hydrochloridum pro Injectione, Streptomycini Sulfas pro Injectione, Sulfadimidinum, Suraminum Natricum, Suspensio Insulini Zinci, Suspensio Insulini Zinci Amorphi, Suspensio Insulini Zinci Crystallisati, Suxamethonii Chloridum, Tetracyclini Hydrochloridum, Tetracyclinum, Trimethadionum, Tyrothricinum, Zinci Oxydum, Zinci Sulfas.

It was agreed that the following monographs, for which drafts had been studied, should not be included in the International Pharmacopoeia:

Compressi Apomorphini Hydrochloridi, Compressi Morphini Sulfatis, Compressi Natrii Nitritis, Compressi Phenadoxoni Hydrochloridi, Decamethonii Iodidum, Injectio Bismuthi et Kalii Tartratis, Injectio Methoxamini Hydrochloridi, Injectio Procaini Benzylpenicillini Oleosa, Injectio Streptomycini et Calcii Chloridi, Methioninum, Penicillinum Amorphum, Phenadoxoni Hydrochloridum, Streptomycini et Calcii Chloridum pro Injectione, Streptomycini Hydrochloridum pro Injectione, Streptomycini Sulfas pro Injectione, Tyrothricinum.

The following drafts were deferred for further investigation and for possible inclusion in the second edition of the International Pharmacopoeia:

Bacitracinum, Compressi Mephenytoini, Compressi Pyrimethamini, Deslanosidum, Diprophyllinum, Injectio Deslanosidi, Injectio Insulini Zinci Globinati, Injectio

Natrii Citratis Anticoagulans, Injectio Ouabaini, Mephenytoinum, Plasma Humanum Dessiccatum, Solutio Acidi Citratis et Glucosi Anticoagulans, Solutio Natrii Citratis Anticoagulans, Tetracyclini Hydrochloridum.

Consultation on the draft specifications

The draft monographs¹ and appendices² for the Supplement on which agreement had been obtained will be sent to the Member States of WHO with the object of obtaining comments. In order to facilitate as wide a study as possible of these draft specifications it was hoped that, as in the case of the specifications included in Volume II of the first edition, the Member States would arrange for a large consultation and that to a limited extent additional copies of these texts might be made available for review upon request. It is expected that all comments and suggestions for amendments would be forwarded by Member States and pharmacopoeia commissions to WHO for discussion with the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations and with other specialists, with a view to incorporating them in the Supplement to the first edition of the International Pharmacopoeia. It is hoped that these comments can be received promptly to facilitate the completion of the text.

In addition to this world-wide consultation throughout the Member States it is expected that the members of the Panel will consult national pharmacopoeia commissions or other authorities dealing with the establishment of specifications for pharmaceutical preparations in their country and submit directly to the Secretary of the Expert Committee any suggestions or other information to be used in the preparation of the text of the Supplement.

¹ Unpublished working documents WHO/Pharm/Mon/Sup/1. to 93

² Unpublished working documents WHO/Pharm/Sup/1 to 6

The Committee wishes to emphasize that the specifications in these monographs are intended only as a basis of study, and may be subject to modification which may be extensive in the light of further information received. They are not intended at this stage of their preparation to be taken as a basis for the establishment of national specifications.

Aqua Demineralisata. A working group of members of the Expert Committee reported on this subject. It was agreed that a separate monograph should be prepared describing water purified by ion exchange techniques in addition to the present monograph on Distilled Water included in Volume II of the first edition. The intention was to provide a specification for the material which is used in large quantities in commerce as the basis of pharmaceutical preparations and analytical solutions. It was agreed to include in the monograph a statement that demineralized water must not be used for preparing injections, although its use in ophthalmic preparations would be permitted providing that it was sterilized immediately before use. The use of demineralized water as an alternative to freshly distilled water would also be permitted for the preparation of Aqua pro Iniectione.

Compressi Digitoxosidi. The Expert Committee examined a new draft monograph, including a chromatographic method of assay, prepared by a working group of members of the Expert Advisory Panel. It was agreed that the text should be considered for inclusion in the Supplement.

Hyaluronidasum. In view of the wide interest in this product it was decided that the draft monograph be annexed to this report for comment, although it was recognized that much work remains to be done. Special attention was drawn to the need to provide adequate directions for the preparation of all the reagents used in the tests.

Preparations of insulin. It was agreed that the monographs prepared on some of the newer preparations of insulin under the titles *Suspensio Insulini Zinci Amorphi*, *Suspensio Insulini Zinci Crystallisati* and *Suspensio Insulini Zinci* should be included in the Supplement. It was agreed that members of the Expert Advisory Panel should be asked to report on the extent to which Injection of Globin Zinc Insulin is still in use.

Injectio Ouabaini. The Expert Committee noted that while this preparation is not employed extensively it is needed in emergencies. It was agreed that the monograph considered by the Expert Committee at its thirteenth session should be revised and considered for inclusion in the Supplement. Members undertook to provide identification tests which, together with a simple chemical method of assay, would provide an adequate control without resort to a biological test for potency.

Suraminum Natrium. The Expert Committee noted that Suramin Sodium is still used in the treatment of trypanosomiasis, although it has to some extent been replaced by pentamidine. Used together the two substances appear to counteract each other as far as toxicity is concerned without impairment of their therapeutic or prophylactic properties. Combined treatment by Suramin Sodium and other trypanocides is therefore of great interest. It was agreed that the draft monograph, as amended, should be considered for inclusion in the International Pharmacopoeia.

Compressi Obducti. The text agreed at the thirteenth session of the Expert Committee describing Coated Tablets intended for oral administration, was further revised and was accepted for inclusion in the Supplement. Among other provisions, it allows for the use of harmless colouring agents in the coating of tablets.

Tablets intended for sublingual administration. Members undertook to report on the maximum and minimum disintegration times desirable for tablets intended for sublingual administration, which could later be included in the monograph.

Synonyms. The Expert Committee discussed the extent to which synonyms should be included in the International Pharmacopoeia, and it was agreed to follow in the Supplement the policy adopted for Volume I and Volume II of the International Pharmacopoeia, first edition, of providing synonyms only in special cases.

Titration in glacial acetic acid solution. The methods previously examined¹ were considered again (in the light of information that in some quarters dioxane or mixtures of solvents including dioxane is used instead of acetic acid as a non-

¹ Unpublished working document WHO/Pharm/232 and Adds. 1, 2, 3, 4 and 5

aqueous medium for perchloric acid titrations). Members reported that glacial acetic acid of suitable quality is readily available and this was agreed upon as a satisfactory medium in all the cases proposed. It was therefore agreed to apply the method as drafted where appropriate in the Supplement. The necessary details of procedure will be given in the individual monographs and the reagents will be described in the appendix on reagents and test solutions.

Tests for glass containers for injections. The text previously prepared by the Expert Committee on the recommendation of a working group¹ was re-examined and amended, taking into account recent work on this subject. It was agreed that the text provides a rapid test which may be carried out by the pharmacist, and that a note should be inserted stating that containers which have passed the test may, after further storage, fail to do so. The test provides separate specifications for containers below and above 100 ml in capacity.

Determination of pH. The Expert Committee examined the appendix on buffer solutions and the determination of pH previously approved, and agreed that this document² as amended should be considered for inclusion in the Supplement.

Posology. A draft of the appendix giving a table of usual and maximal doses of the drugs proposed for inclusion in the Supplement was discussed. It was agreed that an additional column should be added to the table in order to allow for brief comments on some of the doses. It was decided that the table of doses should be circulated to members of the Panel. Comments received from them and from other specialists would be taken into consideration in revising the draft appendix.

Complexone determinations. The Expert Committee examined the draft method of assay which had been investigated by members of the Expert Advisory Panel and others³. It was agreed that the reagents for the method of assay employing disodium ethylenediamine tetraacetate should be given in the Supplement, together with directions for employing them in the determination of calcium, as an alternative to the oxalate method described in Volume I and Volume II.

¹ Unpublished working document WHO/Pharm/134 Rev.5

² Unpublished working document WHO/Pharm/226 Rev.2

³ Unpublished working documents WHO/Pharm/227 and Adds. 1, 2 and 3

Amendments to Volumes I and II. The Expert Committee examined a number of suggestions for amendments to Volume I and Volume II. While the majority of points raised were deferred for consideration in revising the monographs and preparing a second edition, it was considered desirable to revise the published texts in respect to the three items listed below, with an appropriate notice to this effect to be inserted in the Supplement.

(a) Standard dropper. It was agreed to replace the existing specification (Volume I) by the one included in the thirteenth report of the Expert Committee (WHO/Pharm/282 p. 8) which had been investigated by members of the Expert Advisory Panel and reported to be satisfactory.

(b) Digitoxosidum. It was reported that samples of high purity may not comply with the solubility requirements given in Volume II, and it was agreed that the figures should be amended so as to cover material of higher purity.

(c) Serum Antitetanicum. It was noted that through a change in the value of the International Unit of potency of antitetanus serum, the specifications of the monograph in Volume I, page 210, require revision to one-half of the values stated. It was decided to effect the necessary revision.

4. Second Edition of the International Pharmacopoeia

Aims and scope. It was agreed that the International Pharmacopoeia should provide specifications for those pharmaceutical preparations which are selected as being established in medical practice and generally used. The monographs should include a definition, tests for identity and a specification for purity or potency with such experimental details as would be essential to demonstrate compliance with the specifications provided. In accordance with the decisions reached earlier (see Report of Eleventh Session), the standards should reflect a quality of drug readily obtainable from commercial sources and high enough for effective therapeutic use.

In addition to provisions relating to identity, strength, quality and purity, the specifications should include provisions on packaging and on labelling and, where appropriate, on storage, to ensure that the drug continues to meet the purity and potency standards.

In view of the present indications that the proposed specifications of the International Pharmacopoeia are coming into use by pharmacists in certain areas, it appears somewhat desirable to include information on incompatibilities where possible inactivation of the drug concerned is involved.

Information on dosage should continue to be given in such form as agreed upon by the Expert Committee.

It was agreed that the trade-names for the International Pharmacopoeia preparations should not be included, but when a preparation is listed in one or more national pharmacopoeias or other official compendia of specifications under a title differing substantially from that used for it in the International Pharmacopoeia, such titles may be given as supplementary information but not as synonyms. Members of the Expert Advisory Panel would be asked to provide information on the non-proprietary names used in national pharmacopoeias and other official compendia for substances included in Volume I, Volume II or proposed for inclusion in the Supplement.

In respect to the selection of drugs to be described in the International Pharmacopoeia, it was agreed that special study should be given to the subject and that the Secretary should be asked to inquire of several national pharmacopoeial bodies what policy is followed in making the selection for their respective pharmacopoeias.

Appendices should be provided to supply the necessary special and general tests and assays, to describe the solutions needed and to provide suitable specifications for the required reagents.

Appendices should also be included (1) to cover certain broad aspects of analysis and pharmaceutical compounding; (2) definitions of pharmaceutical dosage forms; and (3) to a limited extent, tables of constants.

General notices. The Expert Committee agreed that the General Notices included in Volume I and Volume II of the first edition would form a satisfactory basis for the second edition with relatively few changes. It was suggested that the state-

ment on the status and use of the International Pharmacopoeia should be included in the General Notices rather than the Preface. Suggestions for additions to the General Notices included points about sterilization of injections by methods other than those specified in the general monograph and a statement that solubilities should be regarded as general information except in a few special cases where solubility forms an important test for purity. It was suggested that the information given under "Description" should not be considered part of the standard for the substance provided that other tests ensured adequate control of purity. A limit test for colour of a solution might be introduced. A working group of members of the Expert Committee undertook to prepare a report on the General Notices for the second edition.

Reagents and test solutions. The Expert Committee examined a series of specifications for reagents prepared since the last session by the working group. The working group had also provided an introductory statement including a series of general tests. It was agreed that published specifications should be adapted to fit the needs of the International Pharmacopoeia; they would be considered for publication in the International Pharmacopoeia as soon as the work could be completed. Standard methods of testing would be described and tests would be given for a number of impurities. However, the number of tests to be carried out would be kept to a minimum consistent with defining reagents suitable for ordinary laboratory work having regard to tests for which they are used in the International Pharmacopoeia. Members of the working group undertake to review the draft specifications on introductory material¹ in the light of comments received from members of the Expert Advisory Panel and to continue the work of preparing specifications so as to provide a complete Appendix on reagents and test solutions as soon as possible.

Graphic formulas and chemical names. The Expert Committee noted that by consultation with specialists in correspondence, the Secretariat endeavoured to obtain clear and precise chemical names and graphic formulas for all pure substances

¹ Unpublished working documents WHO/Pharm/Ed.Sec./4, WHO/Pharm/Ed.Sec./4 Add. 14 and 15, and Pharm S. 70

Réactifs et solutions-témoins. Le Comité a examiné une série de spécifications pour les réactifs, qui ont été préparées depuis la dernière session du Comité par le groupe de travail désigné à cet effet. Le groupe de travail a également présenté un exposé introductif décrivant une série d'essais généraux. Il a été décidé que les spécifications devraient être adaptées aux besoins de la Pharmacopée internationale; elles seront examinées en vue de leur publication dans cette Pharmacopée dès que le travail préparatoire aura été achevé. Des méthodes types d'essai seront décrites et l'on indiquera les essais appropriés pour un certain nombre d'impuretés. Toutefois, le nombre des essais à exécuter sera réduit au minimum compte tenu de la nécessité de définir des réactifs qui puissent être utilisés pour les travaux ordinaires de laboratoire, qu'exigent les essais prévus dans la Pharmacopée internationale. Les membres du groupe de travail ont accepté de revoir les projets de spécifications pour réactifs à inclure dans la Pharmacopée¹ à la lumière des observations qu'on fait parvenir diverses personnalités inscrites au Tableau d'experts et ils poursuivront l'établissement de spécifications de manière à pouvoir présenter aussitôt que possible un appendice complet sur les réactifs et les solutions-témoins.

Formules développées et noms chimiques. Le Comité a noté que le Secrétariat a consulté par correspondance un certain nombre de spécialistes afin d'obtenir des noms chimiques clairs et précis, ainsi que des formules développées, pour toutes les substances pures décrites dans les monographies de la Pharmacopée internationale. On peut espérer arriver à l'uniformité en appliquant les principes internationalement admis grâce aux efforts de l'Union internationale de Chimie pure et appliquée et en se conformant aux règles publiées par cette Union. Le Secrétaire de l'Union internationale, divers comités de nomenclatures et d'autres autorités ont été consultés à propos de problèmes particulièrement délicats. Le Comité a reconnu la nécessité d'adopter un mode uniforme de présentation qui soit internationalement acceptable. Il a également reconnu que les dispositions prises par le Secrétariat fournissaient une bonne base de départ.

Détermination de la perte à la dessiccation. Le Comité a décidé que l'on devrait s'efforcer, dans la deuxième édition, de normaliser les températures indiquées

¹ Documents de travail non publiés WHO/Pharm/Ed.Sec./4, WHO/Pharm/Ed.Sec./4 Add.14 et 15 et Pharm S. 70

Peroxide value of fats and oils. The Expert Committee examined a number of methods proposed by members of the Expert Advisory Panel and others¹ and it was agreed to include the method recommended by the International Union of Pure and Applied Chemistry.

Acidity or alkalinity. It was agreed to consider including in the second edition tests to establish definite limits for titrable acidity or alkalinity for the purpose of detecting protolytic impurities such as carbonates, phosphates and silicates in neutral salts and certain alkaloidal salts.

Solutions. It was agreed to add to the General Notices a statement to the effect that unless otherwise specified in the individual monographs, all solutions are to be prepared with distilled water or demineralized water.

Date of manufacture. It was agreed that, in view of the wide variation between definitions accepted in national regulations, this term should not be defined in the International Pharmacopoeia.

Upper limit of purity for assays. It was decided to include a statement to the effect that where no upper limit was given in a monograph for a chemical substance, the figure of 100.5 per cent. should apply.

Definition and determination of "colourless". The Expert Committee considered a report from a working group, and agreed to the text contained in unpublished working document WHO/Pharm/124 Rev.1.

Limit test for turbidity. The Expert Committee agreed that the text proposed should be circulated to members of the Expert Advisory Panel for investigation in connexion with the second edition of the International Pharmacopoeia.

Terms used in spectrophotometry and photometry. It was agreed that the terms defined in the appendix on spectrophotometry and photometry (Volume II, page 237) should be employed where appropriate in the Supplement. The Expert Committee recommended that for the second edition these terms should be reviewed, taking into account the efforts at present being made to achieve uniformity on an international scale. It was agreed to seek information from the International Union of Pure and Applied Chemistry on this matter.

¹ Unpublished working documents WHO/Pharm/Ed.Sec./21 and Adds. 1-4

Optical crystallographic data. It was reported that the importance of this data for the identification of crystalline compounds is increasing and it was agreed that a table should be considered for inclusion in the second edition.

Water-bath and steam-bath. It was agreed that the following wording should be considered for inclusion in the General Notices: "'Water-bath' means a bath of vigorously boiling water. Where heating on a water-bath is prescribed, a bath of free-flowing steam may be used as an alternative. When heating in a water-bath is mentioned, only immersion in a bath of vigorously boiling water may be used."

Units for expression of quantities in the monographs. It was agreed to express quantities less than 0.1 g in milligrams (mg) in the monographs of the second edition. Larger quantities would be expressed in grams (g).

Rubber for pharmaceutical purposes. A progress report was received from a working group, and it was agreed to await a further report before making a recommendation on this subject.

Limit tests for impurities. A working group of members of the Expert Committee agreed to continue work on limit tests for chloride, sulfate, turbidity, arsenic, iron, lead, heavy metals, etc., which have been the subject of previous reports to the Expert Committee.

Preparations of human blood. A number of reports by members of the Expert Advisory Panel were examined and it was agreed to defer consideration of most of the draft monographs until further work had been done on the problems involved. It was agreed to prepare a draft monograph on Dried Human Plasma taking into account the advice of experts on preparations of blood and information received from the International Society for Blood Transfusion.

Solutio Natrii Citratis Anticoagulans. Draft monographs on a series of anti-coagulant solutions were examined by the Expert Committee, but in view of the difficulty in obtaining agreement on the formulas to be used it was agreed not to proceed with these monographs for the present. The members undertook to keep the Secretary informed of developments in their countries in respect of these solutions so that the matter might be reconsidered at a later stage.

Surgical dressings. The Expert Committee received a report on a number of problems which arise in connexion with the use of surgical dressings. Attention was drawn to the difficulties occasioned by the use of optical bleaching agents and artificial fibres. A request had been received to prepare specifications taking these matters into account. It was agreed that at the present time it would be very difficult to prepare specifications for these substances but members of the Expert Committee agreed to collect and assemble information on the standardization of surgical dressings in the various countries for review later. The possibility of including specifications in the International Pharmacopoeia could then be re-considered.

Posology. Members undertook to submit their views on the style to be adopted for the statements on doses in the second edition, including the expression of quantities in terms of milligrams and the statement of maximum and minimum doses. It was agreed that the Secretariat would distribute to the members information on the arrangement of the various pharmacopoeias.

Galenical preparations. A working group of members of the Expert Committee agreed to continue the review of monographs on galenical preparations included in the first edition of the International Pharmacopoeia with the object of revising the monographs and providing some additional ones.

Radioisotopes. The Expert Committee noted that the WHO Study Group on Radiological Units and Radiological Protection had made the following recommendation:¹

"WHO might consider including in the International Pharmacopoeia suitable information on preparations of those radioactive substances which may be utilized in medicine."

It was agreed to ask the Secretary to obtain information which would be considered by members of the Expert Advisory Panel in preparing monographs of pharmaceutical preparations of radioactive isotopes and instructions for storing, handling and dispensing such preparations.

¹ Unpublished working document MH/D8/56

5. Colour spots as a danger signal for pharmaceutical preparations

A proposal to differentiate pharmaceutical preparations according to toxicity by using labels or spots of three different colours was examined by the Expert Committee together with a number of reports and comments on this subject which have been received from members of the Expert Advisory Panel. It was considered advisable to defer further study of this proposal because of the great discrepancies between the various countries in the classification of pharmaceutical preparations with regard to their toxicity in use.

6. International non-proprietary names

The Committee noted that the Executive Board had, at its fifteenth session, adopted the amendments¹ to the procedure for the selection of recommended international non-proprietary names for pharmaceutical preparations and to the general principles for guidance in devising international non-proprietary names. A list of 153 names had been published in the January issue of the Chronicle of the WHO² after having been sent to Member States. It had been possible to obtain withdrawal of a number of the objections received on names selected previously, and in general there was a better understanding and appreciation of the programme and its necessary limitations.

7. Authentic chemical substances

The Committee noted and approved an oral report on the work of the Centre for authentic chemical substances established under the aegis of the WHO at the Apotekens Kontrollaboratorium, Stockholm. Two thousand ampoules of 10 mg of Digitoxoside and 1000 ampoules of 10 mg Ergometrine Maleate have been prepared and are now available at the Centre.

¹ Off. Rec. Wld Hlth Org. 60, 3 (Resolution EBL5.R7)

² Chron. Wld Hlth Org. 1956, 10, 26-35

Concerning Vitamin A, some delays have arisen owing to the difficulty in producing an authentic chemical substance which would be stable for more than two years. The Vitamin Commission of the Food Division of the International Union of Pure and Applied Chemistry and the Committee on Reference Standards of the Pharmacopoeia of the United States had been consulted. The Committee agreed that further investigations would be undertaken.

8. Next meeting

The Expert Committee expressed the view that in order to ensure adequate progress, sessions of the Expert Committee on the International Pharmacopoeia and study groups to deal with special problems on the preparation of the International Pharmacopoeia should be held with sufficient frequency.