

[WHO.IC/204]

5 June 1948

**12. EXPERT COMMITTEE ON THE UNIFICATION OF PHARMACOPŒIAS****REPORT ON THE SECOND SESSION <sup>1</sup>***Held 31 May - 5 June 1948, Palais des Nations, Geneva**Contents*

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**1. Introduction**

The Expert Committee on the Unification of Pharmacopœias held its second session in Geneva from 31 May to 5 June 1948. The committee noted that the report on the first session had been accepted at the fifth session of the Interim Commission for submission to the first Health Assembly,<sup>2</sup> and that in accordance with the recommendations contained in it the membership of the committee had been enlarged by the appointment, with the approval of the governments concerned, of the following experts:

H. Flück, Dr.Sc.Nat., Professor of Pharmacognosy, Eidgenössische Technische Hochschule, Zurich, Switzerland

Professor D. van Os, Professor of Pharmaceutical Chemistry and Toxicology, University of Groningen; Chairman of the Netherlands Pharmacopœia Commission, Groningen, Netherlands

The following members were present:

Professor H. Baggesgaard-Rasmussen, Chairman, Chemical Division of the Danish Pharmacopœia Commission, Copenhagen, Denmark

E. Fullerton Cook, M.Sc., Chairman, Committee of Revision of the Pharmacopœia of the United States of America, Philadelphia, United States of America

I. R. Fahmy, Ph.D., Professor of Pharmacognosy, Fouad I University, Cairo, Egypt; Secretary of the Egyptian Pharmacopœia Commission

H. Flück, Dr.Sc.Nat., Professor of Pharmacognosy, Eidgenössische Technische Hochschule, Zurich, Switzerland

Dr. C. H. Hampshire, Secretary of the British Pharmacopœia Commission, General Medical Council Office, London, United Kingdom (Chairman)

Dr. R. Hazard, Professeur de Pharmacologie et de Matière médicale à la Faculté de Médecine de l'Université de Paris, France, was absent because of illness. The expert from South America has still not been appointed.

M. J. Volckringer, Pharmacien Inspecteur principal de la Santé, Secrétaire technique adjoint à la Commission permanente du Codex français, attended in advisory capacity.

**2. Matters arising from report on first session***2.1 Proprietary Drugs and Trademark Names*

The Secretary summarized the legal advice which had been obtained on the inclusion of proprietary drugs, and submitted two documents: a letter from the International Bureau for the Protection of Industrial Property, Berne, and a note by Professor Hazard.<sup>3</sup>

After a general discussion, the committee agreed that proprietary drugs could, and should be included in the international pharmacopœia. As to the question of whether the firms owning the patent drugs should be consulted, it was decided that the committee would prepare monographs and then invite comments from the firms concerned.

On the question of trademarks, the committee agreed that these should not be used save in exceptional cases, for which special explanatory notes would be provided.

*2.2 Standards for fineness of powders*

The Secretary submitted two papers<sup>4</sup> on this question. The committee decided to defer discussion.

<sup>1</sup> This report was referred by the Interim Commission to the Health Assembly for consideration.

<sup>2</sup> *Off. Rec. WHO*, 7, 253

<sup>3</sup> Document WHO.IC/Pharm/18, unpublished working document

<sup>4</sup> Documents WHO.IC/Pharm/14 and WHO.IC/Pharm/17, unpublished working documents

### 2.3 *Negotiations for the establishment of a single International Secretariat for Pharmacopœias*

The Secretary outlined the background to this question for the benefit of new members of the committee and said that unofficial approaches had been made. Further negotiations would have to be undertaken by the World Health Organization.

### 2.4 *Pan American Pharmacopœia*

The relationship of the future international pharmacopœia to a proposed Pan American Pharmacopœia was discussed, and it was decided to ask the Pan American Sanitary Bureau how far such proposals had progressed.

### 2.5 *Doses*

After an exchange of views as to the responsibility for the compilation of a list of usual and maximal doses, the committee decided to ask Professor Hazard to compile such a list in association with Dr. Hampshire. The list, when completed, would be circulated to members of the committee for comment by the medical profession in their respective countries.

The question of doses for children was raised but the committee felt that for the moment no action should be taken.

It was agreed in the case of injections to specify the route of administration.

## 3. **Preparation of International Pharmacopœia**

The greater part of the session was devoted to the active preparation of the international pharmacopœia.

### 3.1 *General Notices*

The committee discussed the General Notices in detail, and made adjustments in form and amendment where considered necessary. The section on biological assays was deferred until the draft monographs on antitoxins were considered.

### 3.2 *Consideration of Draft Monographs*

159 draft monographs, which had been prepared by the members since the first session, were placed before the committee. The time allowed permitted the consideration of only 71 draft monographs, 58 of which were approved with amendments or subject to reports by members of the committee, 11 of which were postponed, and 2 withdrawn. The list of the draft monographs considered will be found in appendix 1.

### 3.3 *Additions to the List of Drugs and Preparations for inclusion in the International Pharmacopœia*

Several new drugs and preparations were proposed for inclusion in the international pharmacopœia. Decision on their inclusion was deferred.

The question of the inclusion of tablets and injections was discussed, but the majority of the committee felt that, in view of the necessity for producing the international pharmacopœia as soon as possible, these should be omitted from the first edition.

## 4. **Standardization of nomenclature of new drugs**

After comprehensive general discussion, the committee considered a letter sent to the Secretariat by Dr. G. M. Findlay, Editor of *Abstracts of World Medicine*, concerning this subject.

It was pointed out that an international agreement on trademarks and patent rights already existed, and it was suggested that the Secretariat should communicate with the International Bureau for the Protection of Industrial Property for information.

## 5. **Consultation with other Expert Committees**

### 5.1 *Antimalarial Drugs*

The committee decided to consult with the Expert Committee on Malaria on all monographs relating to antimalarial drugs.

### 5.2 *Narcotic Drugs*

The committee decided to consult with the Expert Committee on Habit-forming Drugs on all monographs relating to narcotic drugs.

### 5.3 *Liver Preparations*

The Expert Committee on Biological Standardization brought to the notice of the committee the fact that a unit of activity for liver-extract preparations had been accepted by the US Pharmacopœia, based upon admittedly variable interpretation of their clinical effect on patients with pernicious anæmia and not in terms of a standard preparation. The committee was asked to consider this matter in connexion with monographs on liver preparations. Its attention was drawn to the need in all countries for assuring the clinical efficacy of liver-extract preparations by tests on pernicious anæmia patients, and to the possible dangers of adulteration of the extracts, by the addition of folic acid in quantities sufficient to stimulate a reticulocyte response comparable with that induced by the anti-anæmic principle of liver extract itself.

The committee felt that a unit not based on a given weight of an international standard was undesirable and further that there might be objections in certain countries to the assay of a preparation in terms of experiments based on a clinical response in man. They also recognized the danger of the addition of folic acid in a

quantity which might simulate the therapeutic effect of an active liver preparation.

In view of recent work on the isolation of certain active liver factors, it was decided to defer the monographs on liver preparations to a later date.

### 6. Date of next meeting

The committee recommended that its next meeting should be held during the latter part of October or the first part of November 1948.

It was considered desirable that the duration of the next session should be extended.

## Appendix 1

### LIST OF MONOGRAPHS CONSIDERED DURING THE SECOND SESSION<sup>5</sup>

WHO.IC/Pharm/Mon/		WHO.IC/Pharm/Mon/	
33	Sulfanilamidum	108	Oxygenium ( <i>Postponed</i> )
34	Sulfadiazinum	109	Pilocarpini Nitras ( <i>Withdrawn</i> )
35	Sulfathiazolum	109 Rev. I.	Pilocarpini Hydrochloridum
36	Sulfaguanidinum		( <i>Postponed</i> )
37	Sulfadiazinum Sodium	110	Pituitarium Posterius
38	Sulfamerazinum	111	Injectio Pituitarii Posterioris
39	Sulfamerazinum Sodium		( <i>Postponed</i> )
40	Sulfathiazolum Sodium	114	Tetracainæ Hydrochloridum
41	Succinylsulfathiazolum	115	Theophyllina cum Æthylenediamina
42	Antimonii et Sodii Tartras	116	Totaquina ( <i>Postponed</i> )
43	Antimonii et Sodii Thioglycollas	131	Colchicinum
45	Ergometrinæ Maleas	132	Codeinum Phosphoricum
46	Acetarsole	133	Codeinum Sulfuricum ( <i>Postponed</i> )
47	Carbarsonum	134	Ephedrinum
48	Tryparsamidum	135	Morphinum Hydrochloricum
50	Solutio Iodi Aquosa	136	Morphinum Sulphuricum
51	Solutio Iodi Spirituosa	137	Æthylum Chloratum
52	Thiopentalum Sodium ( <i>Postponed</i> )	138	Amylium Nitrosum
71	Emetinæ Hydrochloridum	139	Carbonei Tetrachloridum
83	Æthisteronum	140	Barii Sulfas
84	Æthylis Aminobenzoas	141	Ferrosi Sulfas
85	Butacainæ Sulfas	142	Ferrosi Sulfas Siccatus
86	Butylis Aminobenzoas	143	Ferri et Ammonii Citras
88	Desoxycorticosteroni Acetas	144	Bismuthi Subcarbonas
89	Diethylstilbestrol	145	Bismuthi Subsali-cylas
90	Epinephrina ( <i>Withdrawn</i> )	146	Theobromini et Natrii Acetas
91	Liquor Epinephrina ( <i>Postponed</i> )	147	Theobromini et Natrii Salicylas
92	Histaminæ Phosphas	150	Apomorphini hydrochloridum
93	Injectio Oxytocini	156	Argenti Nitras
94	Injectio Vasopressini	157	Calcii Lactas
98 & Add.	Injectio Insulini ( <i>Postponed</i> )	158	Calcii Gluconas
99	Injectio Zinco-Insulini Protaminati ( <i>Postponed</i> )	159	Natrii Bromidum
100	Liquor Hepatis ( <i>Postponed</i> )	163	Kalii Bromidum
101	Injectio Hepatis ( <i>Postponed</i> )	165	Natrii Salicylas
104	Nitrogen Monoxidum ( <i>Postponed</i> )	171	Natrii Citras
		172	Kalii Iodidum
		173	Natrii Iodidum
		175	Argentoproteinum

<sup>5</sup> Unpublished working documents

## Appendix 2

### PREPARATION OF REPORTS AND EXPERIMENTAL INVESTIGATIONS

Professor van Os agreed to report on :

The different methods of assay of Theophyllina cum Æthylenediamina

The different methods of assay of Theobromini et Natrii Salicylas

Chromatographic assay of Pilocarpine Hydrochloridum (with Dr. Hampshire, Professor Flück and Professor Fahmy)

The testing of oxidizable impurities in Carbonei Tetrachloridum

The chromatographic test for the assay of Tetracainæ Hydrochloridum and chromatographic tests in general (with Professor Baggesgaard-Rasmussen)

Professor Baggesgaard-Rasmussen agreed to report on :

The assay of Ferri et Ammonii Citras (with Professor Fahmy and Professor Flück)

A bulkiness test for Bismuthi Subcarbonas (with Professor Flück)

A limit test for nitrates

The chromatographic analysis of Butacaine

The chromatographic test for the assay on Tetracainæ Hydrochloridum and chromatographic tests in general (with Professor van Os)

Specific gravity and refractive indices for the General Notices

The general principles of ultra-violet absorptions

The limits of ash, acid-insoluble ash and sulphated ash

and to prepare a table giving details of weights and measures, and abbreviations

Professor Hazard was asked to prepare :

A table of usual and maximal doses (in association with Dr. Hampshire)

And to report on :

Tests to control the qualities of glass to be used as containers

Dr. Hampshire agreed to prepare :

A table of usual and maximal doses (in association with Professor Hazard)

And to report on :

Sulfadiazinum. The test in lines 56-58 and the method suggested by Professor Baggesgaard-Rasmussen

Chromatographic assay of Pilocarpinæ Hydrochloridum (with Professor van Os, Professor Fahmy and Professor Flück)

The methods of preparing sterile solutions for injections

Thiopentalum Natricum. Is Thiopentalum itself ever used? (with Professor Fullerton Cook)

A list of reagents

A list of qualitative and limit tests

The standardization of Ergot

Professor Flück agreed to report on :

A bulkiness test for Bismuthi Subcarbonas (with Professor Baggesgaard-Rasmussen)

Chromatographic assay of Pilocarpinæ Hydrochloridum (with Dr. Hampshire, Professor van Os and Professor Fahmy)

Assay of Ferri et Ammonii Citras (with Professor Baggesgaard-Rasmussen and Professor Fahmy)

Will also report on :

Vegetable drugs in general

Ash and insoluble ash

Monographs concerning :

Herba Belladonna

Herba Hyoscyami

Assay of Aspidium

Professor Fahmy agreed to report on :

The assay of Ferri et Ammonii Citras (with Professor Baggesgaard-Rasmussen and Professor Flück)

Chromatographic assay of Pilocarpinæ Hydrochloridum (with Dr. Hampshire, Professor van Os and Professor Flück)

Conditions of storage

Definitions of acidity and alkalinity

and to prepare monograph on Ephedrinum Hydratum

Professor Fullerton Cook agreed to report on :

The use of the iodine method of assay on Antimonii et Natrii Thioglycollas

Thiopentalum Natricum. Is Thiopentalum itself ever used? (with Dr. Hampshire)

Tetracainæ Hydrochloridum—check the figures in lines 3-6

The use and inclusion of synonyms

The application of spectrophotometric methods to pharmacopœial work

### Appendix 3

#### PREPARATION OF DRAFT MONOGRAPHS STILL OUTSTANDING

Professor Baggesgaard-Rasmussen agreed to prepare draft monographs on :

Suraminum Sodium

Unguentum Hydrargyri

Professor Fullerton Cook agreed to prepare draft monographs on :

Amino-acid Preparations

Aneurinæ Hydrochloridum

Gonadotrophinum Chorionicum

Streptomycin

Professor Fahmy agreed to prepare draft monographs on :

Ephedrinum Hydratum

Liquor Potassii Arsenitis

Dr. Hampshire agreed to prepare draft monographs on :

Dichlorophenarsinæ Hydrochloridum

Oxophenarsinæ Hydrochloridum

Penicillinum

Toxinum Diphthericum Diagnosticum

Toxinum Scarlatinum

Toxinum Tetanicum Detoxicatum

Toxoida Diphtherica Alumen-Præcipitata

Toxoida Diphtherica et Tetanica

Toxoidum Diphthericum

Vaccinum Choleraicum

Vaccinum Febris Flavæ

Vaccinum Pestis

Vaccinum Typhi Exanthematici

Vaccinum Typho-Paratyphosum

Vaccinum Typhosum

Vaccinum Vaccinæ

## Appendix 4

LIST OF GENERAL PRINCIPLES WHICH WERE DISCUSSED AND APPROVED  
DURING THE CONSIDERATION OF DRAFT MONOGRAPHS

*Spelling of Sulpha derivatives.* The committee decided to spell all sulpha derivatives with an "f" instead of "ph".

*Methods of Preparation.* The committee thought that it would not be desirable in the International Pharmacopœia to define methods of preparation.

*Purity Tests.* After a general discussion on the question of including a large variety of purity tests, the committee agreed that, although in the case of products from reputable manufacturers a large variety of such tests was not essential, in other cases the inclusion of such tests was necessary. It was therefore decided that whatever tests were necessary for the detection of any possible impurity should be included.

*Colour Nomenclature.* The committee decided that reference to standard colours rather than to vague terms should be made.

*Ash.* The committee decided to use the term "residue on ignition" instead of "ash" in non-vegetable drugs.

*Molecular Weights.* After a discussion on the number of significant figures to be given in molecular weights,<sup>6</sup> the committee decided that at a later stage all molecular weights should be calculated on the latest international atomic weights then available. The molecular weights of compounds are given at the beginning of monographs, where applicable. The number of significant figures in these molecular weights is determined as follows: the addition of the atomic weights, or multiples thereof, is made with all the figures of the International Atomic Weights and the total is rounded off to four significant figures if the initial digit is 1, 2, 3, 4 or 5, or to three significant figures if the initial digit is 6, 7, 8 or 9; the last digit being

<sup>6</sup> Document WHO.IC/Pharm/3, unpublished working document

increased by 1 when the part rejected exceeds one half unit of the last digit taken, and being taken unchanged where this does not exceed it.

*Pure Products.* The committee decided that whenever in the International Pharmacopœia the pure product was referred to, it should be referred to by its chemical formula and not by its name.

*Use of term "ion".* The committee decided that the modern practice of using the term "ion" should not be followed throughout.

*Specific Rotation.* The committee decided that in relation to specific rotation the temperature used must be given in each monograph.

*Epinephrina.* The committee decided to consider at a later date whether new names should be given to solutions of epinephrina.

*Arsenic Tests.* The committee decided that the same arsenic tests should always be used throughout the monographs.

*Monograph on Poisonous Substances.* The committee agreed that in monographs on very poisonous substances a cautionary notice should be inserted.

*Organic Compounds.* The committee decided that the chemical name of organic compounds should be mentioned in all monographs dealing with organic compounds.

*Latin Abbreviations.* The committee decided that official Latin abbreviations should be included immediately under the name of each monograph.

*Translation.* The committee noted that it might be useful if the names of drugs used in the International Pharmacopœia could be translated into various languages.

*"PH. I".* The committee considered it desirable that in references to the International Pharmacopœia the term "PH. I" should be used.