

## EXPERT COMMITTEE ON THE UNIFICATION OF PHARMACOPOEIAS

### REPORT ON THIRD SESSION<sup>1</sup>

*Held at the Palais des Nations, Geneva, 15-23 October 1948*

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The Expert Committee on the Unification of Pharmacopoeias held its third session in Geneva from 15 to 23 October 1948. The following members were present :

Professor H. Baggesgaard-Rasmussen, Chairman, Chemical Division, Danish Pharmacopoeia Commission, Copenhagen, Denmark

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

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

H. Flück, Dr.Sc.Nat., Professor of Pharmacognosy, Eidgenössische Technische Hochschule, Zürich, Switzerland ; Membre de la Commission fédérale de la Pharmacopée

Dr. C. H. Hampshire, Secretary, British Pharmacopoeia 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

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

The committee noted that :

(a) the first World Health Assembly had approved the establishment of a section on the unification of pharmacopoeias in the Secretariat of WHO and of an expert committee, and had made budgetary provision for the publication in 1949 of an international pharmacopoeia in English, French and Spanish ;

(b) the Executive Board at its first session had decided to set up an expert committee with an initial membership of seven.

#### 1. Matters arising from Report on Second Session<sup>2</sup>

##### 1.1 *Negotiations for the Establishment of a single International Secretariat for Pharmacopoeias*

The committee noted a telegram received from the Belgian Government intimating that the Belgian Government would prefer the international secretariat for pharmacopoeias to remain in Brussels. A confirmatory letter was stated to be on the way.

##### 1.2 *Pan American Pharmacopoeia*

The committee noted a letter which had been received from the Deputy-Director of the Pan American Sanitary Bureau with reference to the proposed Pan American Pharmacopoeia. After hearing a statement from the Secretariat on the present state of the negotiations for the integration of the Pan American Sanitary Bureau with WHO, the committee agreed that the Secretariat should pursue the question of the proposed Pan American Pharmacopoeia.

##### 1.3 *Table of Usual and Maximal Doses<sup>3</sup>*

After discussing the table submitted by Professor Hazard, the committee decided that a note should be inserted to the effect that a physician may exceed the dose, but that if he does he must indicate that there is no mistake.

The committee agreed that the corrected list prepared by Professor Hazard should be circulated to the members of the committee for the opinion of physicians of their respective countries.

#### 2. Preparation of an International Pharmacopoeia

The greater part of the session was devoted to the consideration of monographs and reports.

<sup>2</sup> *Off. Rec. World Hlth Org.* 11, 62

<sup>3</sup> WHO. IC/Pharm/31, unpublished working document

<sup>1</sup> The Executive Board, at its second session, "noted the report of the ad hoc Expert Committee on the Unification of Pharmacopoeias on its third session and decided to publish this report without comments". *Off. Rec. World Hlth Org.* 14, 24

## 2.1 Consideration of Draft Monographs

The 105 draft monographs, which had been prepared by the members since the first and second sessions of the committee, were placed before the committee. Of 91 draft monographs considered, 59 were approved with amendments, additions, or subject to reports by members of the committee, 15 were deferred, 3 were transferred to class B, and 14 were withdrawn from the programme of the committee. The list of the draft monographs considered, with the action taken, is given in Annex 1 (p. 41).

2.1.1 *Hormones*. In a general discussion on the melting range of hormones and hormone compounds, it was pointed out that the new French Codex will contain narrower ranges, since purer preparations were now available. The committee agreed that these more precise figures would be discussed again, after consultation with manufacturers.

2.1.2 *Antitoxins (sera antitoxica)*. After discussion on the nomenclature, the committee agreed that antitoxins should be designated as "sera antitoxica". The committee recommended that this international designation should be inserted as a synonym in the national pharmacopoeias.

The committee agreed that in the section on labelling two additional paragraphs should be added, stating:

1. that the name of the manufacturer and the manufacturer's reference number should be given on the labels and wrappers;
2. that the name and proportion of bacteriostatics added should also be given.

The committee decided that, for each of the monographs on sera antitoxica, tests for potency and toxicity should be proposed and accepted on the understanding that they would not be obligatory.

The committee further decided to include a fourth gas-gangrene antitoxin, namely Serum Antihistolyticum, and the chairman agreed to prepare a draft monograph.

2.1.3 *Toxoids*. The committee decided that toxoids should be removed from the programme of the committee until such time as international standards for them had been established by the Expert Committee on Biological Standardization.

2.1.4 *Vaccinia*. The secretary of the Expert Committee on Biological Standardization questioned whether vaccines should be included as no international standard had yet been established. He thought that probably all that could be done for the present was to adopt minimum requirements. The only exception was Tuberculinum Pristinum, for which an international standard existed.

The committee decided that, with the exception of Tuberculinum Pristinum, the inclusion of other vaccines should wait until international standards were available.

## 2.2 Consideration of Draft Reports

The committee considered a number of reports which had been prepared by members of the committee. These were adopted with amendments where necessary.

## 2.3 Synonyms

After consideration of a report<sup>4</sup> by Professor Fullerton Cook, the committee agreed that synonyms should be confined to exceptional cases and inserted when finally reviewing monographs.

Professor Fullerton Cook submitted a proposal for the preparation of a list giving the name of the same drug in the principal languages of the world. After discussion, the committee decided to defer the proposal for the time being.

## 2.4 The Title "International Pharmacopoeia"

A letter had been received from Professor Fullerton Cook expressing the views of the Board of Trustees of the United States Pharmacopoeia, which was opposed to the use of the title "International Pharmacopoeia".

Professor Fullerton Cook explained to the committee that his Board was in complete sympathy with the work of the expert committee. It was objecting only to the word "Pharmacopoeia" in the title.

The committee pointed out that there was no intention that the suggested international pharmacopoeia should take the place of any national pharmacopoeia.

The committee considered that any objection to the title "International Pharmacopoeia" could be applied equally to the title "Pan American Pharmacopoeia", the compilation of which was on the agenda of the first Pan American Congress of Pharmacy, to be held at Havana, 1 December 1948. Although the committee was reluctant to drop the word "Pharmacopoeia", the members felt, at the same time, that it was desirable to endeavour to reach general agreement. Alternative names were considered by the committee, and the following was thought to be most suitable for further consideration: Codex Medicamentarius Internationalis.

The committee agreed that the chairman should write a letter to Professor Cook for submission to his Board, giving a résumé of the discussions of the committee on the question of the title. As the members of the committee expressed the wish to think over the question, and to have further consultations in their own countries on this subject, a final decision was deferred until the next session.

## 2.5 List of Common Designations of Medicaments

A report<sup>5</sup> by Professor Hazard was deferred for consideration to a later session.

## 2.6 General Principles discussed and approved

2.6.1 *Chromatographic analysis*. The committee considered a report submitted by Professor van Os on aluminium oxide for quantitative chromatographic analysis.

The chromatographic method in general and the quality of aluminium oxide to be used were discussed. It was agreed that the matter should be rediscussed at the next session and that members should produce reports.

<sup>4</sup> WHO/Pharm/39, unpublished working document

<sup>5</sup> WHO. IC/Pharm/35 and Annex, unpublished working document

2.6.2 *Botanical nomenclature.* The committee agreed that the botanical nomenclature should follow the international rules of nomenclature approved by the International Botanical Congress, Amsterdam, 1935.

2.6.3 *Melting range and boiling range.* The committee considered a report on melting range and temperature submitted by a working group consisting of Professors Baggesgaard-Rasmussen, Fahmy, Flück and van Os, and accepted it with amendments.

The committee agreed that the figures for the melting range and boiling range which had already been approved in the monographs accepted should be reviewed. Professors Baggesgaard-Rasmussen, Fahmy, Flück and van Os agreed to collaborate in this work.

2.6.4 *Chemical nomenclature.* The committee decided that the chemical nomenclature should be inserted with the formula in every monograph.

2.6.5 *Ultraviolet absorption.* The committee decided that ultraviolet absorption should be mentioned in all cases where it is considered useful, and that a method should be included in a general appendix.

2.6.6 *Potent tinctures.* The committee decided that, in the international monographs on all potent tinctures, two concentrations of the active principle should be recognized, one expressing the quantity of active principle per unit-volume of the tincture, the other expressing the same quantity per unit-weight of the tincture, and a note added, stating that "the country concerned will decide which of these concentrations will be adopted for that country".

### 3. Relations with other Expert Committees

#### 3.1 *Expert Committee on Biological Standardization*

The committee agreed that the appendices on the determination of the therapeutic potency of Sulfarsphenamina and of Neoarsphenamina should be decided after consultation with the Expert Committee on Biological Standardization.

The committee noted that the Expert Committee on Biological Standardization at its forth-

coming meeting would probably be dealing with liposoluble vitamins.

The committee agreed that the collaboration of the Expert Committee on Biological Standardization should be invited in regard to the tests for potency of sera antitoxica and of Tuberculinum Pristinum.

#### 3.2 *Expert Committee on Habit-forming Drugs*

The committee agreed that monographs on narcotic drugs should first be completed and the comments of the Expert Committee on Habit-forming Drugs obtained.

#### 3.3 *Expert Committee on Malaria*

The committee agreed that the monograph on Quinini Sulfas<sup>6</sup> should be submitted to the Expert Committee on Malaria with the following comment: "The Expert Committee on the Unification of Pharmacopoeias discussed fully the quality of Quinini Sulfas to be prescribed in an international pharmacopoeia. The degree of purity, as expressed by the Kerner-Weller ammonia test, was selected as 6.5 ml. of ammonia solution, this representing a lower quality than that of the Dutch and some other pharmacopoeias. The committee believed that any higher standard, that is to say any lower proportion of other cinchona alkaloids, would inevitably raise the price, and be to the disadvantage of the world control of malaria."

The committee agreed that suggestions for the inclusion of antimalarial drugs should be invited from the Expert Committee on Malaria, and that the chairman should prepare draft monographs on any drugs so recommended.

The attention of the committee was drawn to the report on the second session of the Expert Committee on Malaria,<sup>7</sup> which contained a critical review of modern antimalarial drugs.

### 4. Date of Next Meeting

The committee recommended that its next meeting should be held towards the end of April 1949, the dates 20-30 April being suggested.

<sup>6</sup> WHO. IC/Pharm/Mon/6. Rev. 1, unpublished working document

<sup>7</sup> *Off. Rec. World Hlth Org.* 11, 43

## Annex I

### LIST OF MONOGRAPHS CONSIDERED<sup>8</sup>

Monographs have been listed under the nomenclature adopted at this session. Names in parentheses represent the previous nomenclature.

#### 1. Monographs accepted with amendments or subject to reports

WHO.IC/Pharm/Mon/		WHO.IC/Pharm/Mon/	
44	Acidum Benzoicum	58	Neoarsphenamina
52	Thiopentalum Natricum cum Natrii Carbonas (Thiopentalum Sodium)	59	Sulfarsphenamina
56	Tinctura Digitalis	App. 60-64	Sera Antitoxica (Antitoxina)
		60	Serum Anti-Vibrio Septicum (Anti- toxinum Septicum)
		61	Serum Antiperfringens (Antitoxi- num Welchicum)

<sup>8</sup> Unpublished working documents

WHO.IC/Pharm/Mon/		WHO.IC/Pharm/Mon/	
62	Serum Antioedematiens (Antitoxicum Oedematicum)	124	Oleoresina Aspidii
63	Serum Antitetanicum (Antitoxicum Tetanicum)	125	Oleum Ricini
64	Serum Antidiphthericum (Antitoxicum Diphthericum)	126	Oleum Chenopodii
73	Acidum Nicotinicum	127	Opium
74	Nicotinamidum	128	Pulvis Opii
75	Oleum Jecoris Aselli (Oleum Morrhuae)	148	Picrotoxinum
76	Oleum Jecoris Hippoglossi (Oleum Hippoglossi)	151	Phenolum Liquefactum
77	Calciferol	152	Solutio Kalii Arsenitis
78	Menadionum	154	Amphetamina
80	Riboflavinum	155	Chloramina
81	Thiaminae Hydrochloridum	160	Amyleni Hydras
82	Aether Vinylicus	161	Cresol
87	Carbonei Dioxidum	164	Amphetaminae Sulfas
96	Digoxinum	166	Tuberculinum Pristinum
97	Lanatosidum C	168	Biological Assay of Tuberculinum Pristinum
102	Mepacrinae Hydrochloridum	169	Pentetrazol (Metrasolum)
103	Methyltestosteronum	170	Chiniofonum
104	Oxidum Nitrosum	174	Tetrachloraethylenum
105	Oestradiol	176	Carbacholum
106	Oestradiolis Benzoas	177	Solutio Formaldehydi (Liquor Formaldehydi)
107	Oestronum	178	Mersalyum
108	Oxygenium	182	Neostigminae Bromidum
112	Progesteronum	184	Tribromethanolum
113	Testosteroni Propionas	185	Pethidinae Hydrochloridum
		188	Phenantoinum
		191	Neostigminas Methylsulfas
		197	Ouabainum

### 2. Monographs consideration of which was deferred

WHO.IC/Pharm/Mon/		WHO.IC/Pharm/Mon/	
70	Heparinum	162	Benzylls Benzoas
79	Menadioni Sodii Bisulfis	167	Tuberculini Derivatium
95	Digitoxinum		Proteinicum Purificatum
98	Injectio Insulini	180	Tabellae Glycerylls Trinitratis
99	Injectio Zinco-Insulini Protaminati	187	Injectio Mersalyli et Theophyllini
111	Injectio Pituitarii Posterioris	195	Dicoumarol
129	Tinctura Opii	196	Injectio Diodoni
130	Tinctura Opii Benzoica	198	Stibophenum

### 3. Monographs transferred to Class B

WHO.IC/Pharm/Mon/		WHO.IC/Pharm/Mon/	
121	Acetum Scillae Mellitus	123	Aloinum
122	Aloe		

### 4. Monographs removed from the programme of the committee

WHO.IC/Pharm/Mon/		WHO.IC/Pharm/Mon/	
133	Codeini Sulfas	202	Toxinum Diphthericum Detoxicatum
149	Strophanthinum-K	203	Vaccinum Choleraicum
179	Vaccinum Antirabicum	203	Vaccinum Pestis
183	Acriflavina	203	Vaccinum Typhosum
189	Proflavinae Sulfas	203	Vaccinum Typho-paratyphosum
200	Toxinum Tetanicum Detoxicatum	204	Vaccinum Febris Flavae
201	Toxinum Diphthericum Diagnosticum	205	Vaccinum Vaccinae

## Annex 2

### PREPARATION OF DRAFT MONOGRAPHS, REPORTS AND EXPERIMENTAL INVESTIGATIONS

Professor Baggesgaard-Rasmussen agreed :

To prepare a draft monograph on Phenantoinum Natricum

To check an assay of Menadionum to be supplied by Professor Cook with that in the British Pharmacopoeia (with Professor Fahmy)

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

To review the figures for the melting range and boiling range in monographs accepted (with Professors Fahmy, Flück and van Os)

To report on the following :

The chromatographic analysis of Butacaine  
The chromatographic test for the assay of Tetracainae Hydrochloridum and chromatographic tests in general (with Professor van Os)

Specific gravity and refractive indices for the General Notices

The general principles of ultraviolet absorption  
The limits of ash, acid-insoluble ash and sulphated ash

A bulkiness test for Bismuthi Subcarbonas (with Professor Flück)

Professor Fullerton Cook agreed :

To prepare draft monographs on :

Amino Acid Preparations  
Gonadotrophinum Chorionicum  
Streptomycin

To supply an assay of Menadionum

To report on Heparinum

To report on the tests for Arseniuretted Hydrogen, Phosphoretted Hydrogen and Carbon Monoxide in the British Pharmacopoeia monograph on Oxidum Nitrosum

To submit chemical and physical tests for the draft monograph on Digitoxinum

Professor Fahmy agreed :

To check an assay of Menadionum to be supplied by Professor Cook with that in the British Pharmacopoeia (with Professor Baggesgaard-Rasmussen)

To report on the chromatographic assay of Pilocarpinae Hydrochloridum (with Dr. Hampshire, Professors van Os and Flück)

To review the figures for the melting range and boiling range in monographs accepted (with Professors Baggesgaard-Rasmussen, Flück and van Os)

To report on tests to control the qualities of glass to be used as containers (with Professor Hazard)

Professor Flück agreed :

To prepare an assay of Metacresol (with Professor van Os)

To review the figures for the melting range and boiling range in monographs accepted (with Professors Baggesgaard-Rasmussen, Fahmy and van Os)

To report on the following :

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

Chromatographic assay of Pilocarpinae Hydrochloridum (with Dr. Hampshire, Professors van Os and Fahmy)

Vegetable drugs in general

Ash and insoluble ash

Monographs concerning Herba Belladonnae and Herba Hyosciami

Dr. Hampshire agreed :

To prepare draft monographs on :

Serum Antihistolyticum  
Any antimalarial drugs suggested by the Expert Committee on Malaria  
Dichlorophenarsinae Hydrochloridum  
Oxophenarsinae Hydrochloridum  
Penicillinum

To report on :

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

Chromatographic assay of Pilocarpinae Hydrochloridum (with Professors van Os, Fahmy and Flück)

The methods of preparing sterile solutions for injections

To prepare

A list of reagents  
A list of qualitative and limit tests  
The standardization of Ergot

Professor Hazard agreed :

To report on :

Tests to control the qualities of glass to be used as containers (with Professor Fahmy)

Professor van Os agreed :

To prepare an assay of Metacresol (with Professor Flück)

To review the figures for the melting range and boiling range in monographs accepted (with Professors Baggesgaard-Rasmussen, Fahmy and Flück)

To report on :

Chromatographic assay of Pilocarpinae Hydrochloridum (with Dr. Hampshire, Professors Flück and Fahmy)

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