

World Health Organization
Technical Report Series
No. 12

EXPERT COMMITTEE
ON THE UNIFICATION
OF PHARMACOPOEIAS

Report on the Fifth Session

Geneva, 26 September – 5 October 1949

	Page
1. Matters arising from report on fourth session	3
2. Preparation of the <i>Pharmacopoea Internationalis</i> (Ph.I) . .	4
3. Consultation with other expert committees	8
4. Other matters	10
Annex 1. Monographs to be inserted in the supplement . .	11

WORLD HEALTH ORGANIZATION
PALAIS DES NATIONS
GENEVA
MAY 1950

EXPERT COMMITTEE ON THE UNIFICATION OF PHARMACOPOEIAS

Fifth Session

Members :

H. Baggesgaard-Rasmussen, Ph.D., Professor of Pharmaceutical Chemistry, Danish School of Pharmacy, Copenhagen, Denmark ; Member of the Danish Pharmacopoeia Commission

Professor E. Fullerton Cook, Pharm.D., 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., Professeur de Pharmacognosie à l'Ecole Polytechnique Fédérale, 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 ; Membre de la Commission permanente du Codex

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

Secretary :

P. Blanc, Chief, Pharmaceutical Section, WHO

The report on the fifth session of this committee was originally issued in mimeographed form as document WHO/Pharm/88, 7 November 1949.

EXPERT COMMITTEE ON THE UNIFICATION OF PHARMACOPOEIAS

Report on the Fifth Session ¹

The Expert Committee on the Unification of Pharmacopoeias held its fifth session in Geneva from 26 September to 5 October 1949.

1. Matters Arising from Report on Fourth Session ²

1.1 *Decisions of the Second World Health Assembly and of the Executive Board*

The committee noted that the reports on the third and fourth sessions of the committee had been approved by the Executive Board ³ and the Second World Health Assembly, ⁴ that an allocation had been included in the regular budget allowing for two sessions of the committee during 1950, that budgetary allocation had been approved for the publication of an English edition of the *Pharmacopoea Internationalis* (Ph.I.) during 1949 and French and Spanish editions in 1950, and that the volume could be distributed as soon as published without further administrative procedure.

Regarding the distribution of the *Pharmacopoea Internationalis*, the committee agreed that it would be inadvisable to send advance copies to manufacturers.

¹ The Executive Board, at its fifth session, adopted the following resolution :
The Executive Board

(1) NOTES the report of the Expert Committee on the Unification of Pharmacopoeias on its fifth session ; and

(2) AUTHORIZES its publication ; . . .

² *World Hlth Org. techn. Rep. Ser.* 1950, 1

³ *Off. Rec. World Hlth Org.* 14, 24 ; 22, 3

⁴ *Off. Rec. World Hlth Org.* 21, 21

2. Preparation of the Pharmacopoea Internationalis (Ph.I.)⁵

The greater part of the session was devoted to the revision of the monographs and appendices which will appear in the first edition of the *Pharmacopoea Internationalis*. Suggested changes and reports submitted by members were considered, particularly those referring to chemical assays, congealing, melting- and boiling-temperatures, usual and maximal doses, densities, solubilities, storage, chemical formulae and names, test solutions, and reagents.

Ninety-four monographs, the general notices, and the appendices were accepted ; it was decided that all monographs and appendices not considered in detail should be revised by the Chairman and the Secretary, taking into consideration the general principles agreed upon and the amendments submitted by members.

It was agreed that Professor Baggesgaard-Rasmussen should be responsible for any laboratory work concerning the verification of the densities of substances.

A number of draft monographs for the French edition were examined, and a French terminology, corresponding to the English technical expressions for assays, reagents, etc., was established.

The proposed arrangements for the printing and publication of the *Pharmacopoea Internationalis* were approved by the committee.

2.1 Consideration of draft monographs

Fourteen draft monographs which had been prepared since the fourth session of the committee, or on which decision had been deferred, were considered.

The following seven monographs were accepted with amendments where necessary : Quinidini Sulfas, Kalii Hydroxydum, Solutio Kalii Hydroxydi, Quinini Hydrochloridum, Mepacrini Methanosulfonas, Pamaquinum, and Pentaquini Phosphas.

Consideration of the following four monographs was deferred : Streptomycinum, Penicillinum G Potassicum, Penicillinum G Natricum, and Digitoxosidum (synonym : Digitoxinum). It was decided that they should be included in a supplement, after further verifications had been made.

⁵ The Executive Board, at its fifth session, adopted the following resolution :

The Executive Board...

(3) RECOMMENDS the adoption of the following resolution by the Third World Health Assembly :

The Third World Health Assembly

(1) APPROVES of the *Pharmacopoea Internationalis* ; and

(2) RECOMMENDS the eventual inclusion of its provisions in the national pharmacopoeias after the adoption of the said provisions by the authorities responsible for the pharmacopoeias.

Three monographs—Toxinum Diphthericum Calefactum, Toxinum Diphthericum Diagnosticum, and Toxinum Diphthericum Detoxicatum—were referred to the Expert Committee on Biological Standardization for re-examination before inclusion in the Ph.I.

2.2 *Graphic formulae and chemical names*

The committee considered graphic formulae and chemical names which had been proposed by Professor Baggesgaard-Rasmussen, and drawn up in accordance with the Patterson Ring Index System,⁶ and with the nomenclature for radicals recommended by the International Union of Chemistry.

All the graphic formulae as revised were adopted, with the exception of Lanatosidum C, which it was agreed should be investigated in consultation with the manufacturer.

The chemical names were also revised and adopted.

2.3 *Atomic weights ; molecular weights ; melting-range, melting-temperature, congealing-temperature, boiling-range, and boiling-temperature ; densities ; solubilities*

The committee agreed that the table of atomic weights, taken from the International Table of Atomic Weights, 1947, should be limited to those elements mentioned in the monographs or appendices, and that the molecular weights of drugs should be stated in each monograph and not given in tabular form.

Reports and revised figures for melting-range, melting-temperature, congealing-temperature, boiling-range, densities, and solubilities, submitted by members of the committee, were adopted.

2.4 *Table of usual and maximal doses*

The committee considered the revised table of usual and maximal doses.⁷ After discussion it was agreed that doses should not be given for drugs not described in the monographs, and that an extended list could be included in a supplement.

It was agreed that maximal doses need not always be stated, and that the following paragraph should be inserted in the introduction to the table.

Maximal doses are not stated in some instances, either because the drug is not very toxic or because its maximal posology cannot be precisely determined at the present stage of medical knowledge.

⁶ Patterson, A. M. & Capell, L. T. (1940) *The ring index : a list of ring systems used in organic chemistry*, New York

⁷ Unpublished working documents WHO/Pharm/43 Rev. 2, and Add. 1

It was noted that the table of usual and maximal doses had been sent to the World Medical Association, which would discuss it at its meeting in London on 10 October 1949 and would communicate its comments to WHO.

The committee considered the question of the inclusion of doses for infants and children, and decided to insert a statement in the introduction to the table indicating that the doses as given are for adults only and must necessarily be modified for children. Professor Hazard agreed to prepare a table of doses for infants and children for a supplement to the Ph.I.

2.5 *Appendix on sieves and fineness of powders*

After consideration of information supplied by the International Organization for Standardization (ISO), the committee agreed to insert a table of sieves in the Ph.I. The series of preferred numbers prepared by ISO, and already adopted in the French Codex (1937 edition), would be used for the classification of sieves.

The table should also include a classification of powders according to their fineness, the actual dimensions of the opening of sieves, their sequence numbers, and the permissible variation of the opening.

2.6 *Dilution materials for preparation of standardized powders*

Following a discussion on the question of whether starch and lactose should be generally used as dilution materials for the preparation of standardized powders, and after special consideration had been given to the alteration of the degree of potency which might be due to the use of lactose with glycosides, the committee agreed to add lactose and starch as alternative diluents, with the exception that lactose should not be allowed as a diluent for glycosides, particularly in the preparation of the standardized powder of digitalis leaf.

2.7 *List of reagents*⁸

The committee decided :

- (1) to give the concentration of the test solutions as percentages ;
- (2) that the approximate normality should be indicated in brackets, and that an explanatory note should be inserted in the appendix on reagents.

2.8 *Latin names*

The committee considered reports submitted by members, and revised the Latin names adopted for drugs in the *Pharmacopoea Internationalis*.

⁸ Unpublished working document WHO/Pharm/85

2.9 Trademarks and patents

The committee decided to include a general notice in the Ph.I. concerning the names covered by trademarks, on the following lines :

Where any name for a drug appearing in the *Pharmacopoea Internationalis* is a trademark in any part of the world, it may be used only when applied to the product made by the owners of that trademark.

It was also decided that a general notice concerning patents should be included, on the following lines :

In this pharmacopoeia, certain drugs have been included notwithstanding the existence of actual or potential patent rights. In so far as such substances are protected by patent, their inclusion in this pharmacopoeia neither conveys nor implies licence to manufacture.

2.10 Non-proprietary names for drugs⁹

The committee considered the resolution adopted by the Executive Board at its fourth session requesting the Director-General " to study the questions involved in establishing a system of common nomenclature for new pharmaceutical products moving in international commerce, and to

⁹ The Executive Board, at its fifth session, adopted the following resolution :

The Executive Board

- (1) REQUESTS the Director-General to circulate to governments for their information the principles enumerated by the Expert Committee on the Unification of Pharmacopoeias ; and
- (2) RECOMMENDS to the Third World Health Assembly the adoption of the following resolution :

The Third World Health Assembly

Recognizing the desirability that a system of non-proprietary names be established internationally for such new pharmaceutical products as might be contemplated for later insertion in the *Pharmacopoea Internationalis*,

- (1) APPROVES the general principles enumerated by the Expert Committee on the Unification of Pharmacopoeias at its fifth session ; and
- (2) RESOLVES as follows :
 - (a) the Expert Committee on the Unification of Pharmacopoeias should undertake the selection and approval of non-proprietary names for drugs which might be described in later editions of the *Pharmacopoea Internationalis* ;
 - (b) such names as are from time to time selected and approved by the expert committee should be communicated by the Director-General to national pharmacopoeial authorities, together with a recommendation that these names be officially recognized and approved, and, if the substances are eventually included in the national pharmacopoeia, adopted as pharmacopoeial names ;
 - (c) such recommendations shall further include a request that such measures as may be deemed appropriate by States Members be taken with a view to preventing the use of the names selected for unauthorized purposes, and in particular to prevent the granting of exclusive proprietary rights in these names to the manufacturer.

report thereon to the sixth session of the Board",¹⁰ and heard statements by members on the situation and systems existing in their own countries.

Difficulties are to be expected, particularly from a legal point of view, before a system can be consistently introduced, and it was considered advisable to consult with governments, national pharmacopoeial commissions, manufacturers' associations, and the International Union for the Protection of Industrial Property. Meanwhile, lists of important products for which a non-proprietary name should be introduced will be prepared, and information collected on trademarks and regulations in force in the different countries. The establishment of a subcommittee of the Expert Committee on the Unification of Pharmacopoeias to deal with these matters might be found advisable in the future.

The committee considered the principles followed by the British Pharmacopoeia Commission in devising names, and adopted them with the following amendment :

Names already used in the national pharmacopoeias, or officially adopted in any country, or which are included in *New and Non-official Remedies* should receive preferential consideration.

It was agreed that the committee should submit a system of common nomenclature to the Director-General for presentation at the sixth session of the Executive Board.

3. Consultation with Other Expert Committees

3.1 *Expert Committee on Biological Standardization*

3.1.1 *Biological assays.* The committee agreed that a statement should be included in the general notices applicable to all international standards to the effect that national standard preparations corresponding to the international standard preparations may replace the latter.

3.1.2 *Sera antitoxica.* Consideration was given to whether the inclusion in the Ph.I. of appendices on the biological assay of sera was necessary. It was considered that such appendices would serve a useful purpose in many countries, since there is no other international manual of methods of assay for antitoxic sera. The committee therefore decided that the assays should be included in the Ph.I.

It was agreed that the monographs and appendices should be revised taking into account the amendments submitted by members of the Expert

¹⁰ *Off. Rec. World Hlth Org.* 22, 3

Committee on Biological Standardization, and should then be published without further submission to members of the present committee.

The committee agreed that an additional monograph, on Serum Anti-histolyticum, should be prepared and inserted in the first edition.

3.1.3 *Folium Digitalis and Tinctura Digitalis*. It was agreed that the pigeon test should be added to the appendix on biological assay of *Folium Digitalis* and *Tinctura Digitalis*.

3.2 *Expert Committee on Drugs Liable to Produce Addiction*

After consideration of comments by members of the Expert Committee on Drugs Liable to Produce Addiction on the monographs on addiction-producing drugs, the committee decided :

(1) that the text of the monograph on opium should be retained without amendment ;

(2) that dihydrocodeinone bitartrate, metopon, amidone, and such other addiction-producing drugs as may be recommended by the Expert Committee on Drugs Liable to Produce Addiction, should be included in a supplement.

3.3 *Expert Committee on Malaria*

The committee noted that monographs had been prepared on all the drugs recommended for inclusion in the Ph.I. by the Expert Committee on Malaria, with the exception of isopentaquine mono-oxalate. Information on this drug would be supplied by the Secretary of the Expert Committee on Malaria, and a monograph would be prepared for inclusion in a supplement.

3.4 *Expert Committee on Mental Health*

The committee noted a recommendation received from the Expert Committee on Mental Health¹¹ that a list of the drugs most frequently used in psychiatric practice should be prepared showing for each the different proprietary names under which it is sold. Similar recommendations had been received from other WHO sections concerning drugs used in their specialities.

The committee agreed that a list of synonyms, including non-proprietary names and trademarks, should be submitted for the drugs appearing in the *Pharmacopoea Internationalis*, and for important drugs moving in international commerce. It was felt that this list could be published in 1950 as a supplement to the *Bulletin of the World Health Organization*.

¹¹ *World Hlth Org. techn. Rep. Ser.* 1950, 9

4. Other Matters

4.1 *Thirteenth General Assembly of the International Pharmaceutical Federation*

After a report on the Thirteenth General Assembly of the International Pharmaceutical Federation, held in Amsterdam, 28 August to 3 September 1949, by the Secretary of the Expert Committee on the Unification of Pharmacopoeias, who attended as WHO observer, the committee noted the following resolutions which had been adopted at the Assembly :

- “(1) that the control of proprietary medicines be organized everywhere with a large participation by the pharmaceutical organizations of the nation concerned ;
- (2) that the basis of all control shall be registration and compulsory approval of each medicine before it is put on the market ;
- (3) that every product put on the market should bear clearly and without ambiguity the fullest possible statement of its composition ;
- (4) that the prevention of frauds requires a regular examination of the products currently on the market. ”

The committee expressed the view that work concerning the control of biological, pharmaceutical and similar products moving in international commerce, as well as the advertising and labelling of these products, had been delegated by virtue of its Constitution to WHO.

The committee agreed to study the matter further, particularly with regard to the labelling of these products.

4.2 *Pharmacopoea Internationalis — supplements*

In consequence of the rapid advances in the knowledge of certain drugs and their chemical or biological assay, it was not found possible to complete the monographs on those drugs in time for publication in the first edition of the Ph.I.

The committee therefore recommended that a first supplement to the *Pharmacopoea Internationalis* be prepared by the committee, and issued in English and in French in 1950, and in Spanish in 1951.

The committee compiled a list of monographs and appendices to be included in this supplement, and allocated the preparation of the necessary monographs among the members, as shown in Annex 1.

Annex 1**MONOGRAPHS TO BE INSERTED IN THE SUPPLEMENT****New Draft Monographs to be Prepared by Members
of the Committee**

Professor Baggesgaard-Rasmussen agreed to prepare draft monographs on :

Amidonum
Dichlorophenarsini Hydrochloridum
Metoponum
Oxophenarsini Hydrochloridum
Thyroideum (assay)

Professor Fullerton Cook agreed to prepare draft monographs on :

Acidum Folicum
Aureomycinum
Chloromycetinum
Tyrothricinum
Vitaminum B₁₂
Injections
Blood-transfusion solutions
Tablets

Professor Fahmy agreed to prepare draft monographs on :

Dihydrocodeinonum Bitartaricum
Dihydromorphinonum Hydrochloridum
Oxydihydrocodeinonum Hydrochloridum

Professor Flück agreed to prepare a draft monograph on :

Thyroideum (description)

Dr Hampshire agreed to prepare draft monographs on :

Dimercaprolum
Dihydrostreptomycinum
Gonadotrophinum Chorionicum
Gonadotrophinum Chorionicum Serum
Isopropylthiouracilum
Suraminum Natricum

Professor Hazard agreed to prepare draft monographs on :

Aspergillinum
Digitoxosidum (revision)

and to continue his work on the French text of the monographs and chemical names.

Professor van Os agreed to prepare draft monographs on :

DDT
Isopentaquini Mono-oxalas

Monographs Already Drafted for the Supplement

Penicillinum G Potassicum
Penicillinum G Natricum
Streptomycinum
Tinctura Aconiti
Tinctura Belladonnae
Tinctura Colchici
Tinctura Hyoscyami Mutici
Tinctura Hyoscyami Nigri
Tinctura Ipecacuanhae
Tinctura Strychni
Tinctura Scillae
