EXPERT COMMITTEE ON THE UNIFICATION OF PHARMACOPOEIAS

Report by the Director-General

The Expert Committee on the Unification of Pharmacopoeias, which the Executive Board has decided to maintain as an ad hoc Committee, will meet in October 1948.

A progress report of the work of the Committee will be submitted to the Executive Board at its second session.

To give effect to a recommendation made by the Expert Committee (WHO.10/127) and approved by the Interim Commission at its fifth session (Off. Rec. WHO, 7, p. 253) the Belgian Government has been approached regarding the establishment of a single international secretariat of pharmacopoeias under the aegis of the World Health Organization. It is hoped that the views of this Government will have been received before the Executive Board meets.
EXPERT COMMITTEE ON THE UNIFICATION OF PHARMACOPEIAS

Report by the Director-General

Addendum

The Director-General has the honour to transmit herewith to members of the Executive Board document WHO/Pharm/40 Rev.1, "Expert Committee on the Unification of Pharmacopoeias - Report on the Third Session". This report is noted on the provisional agenda of the second session of the Executive Board (Document EB2/42 Rev.1) under item 17.2.2.

CONSEIL EXECUTIF

Deuxième Session

COMITE D'EXPERTS POUR L'UNIFICATION DES PHARMACOPEES

Rapport du Directeur général

Addendum

Le Directeur général a l'honneur de communiquer ci-après aux membres du Conseil Exécutif le document WHO/Pharm/40 Rev.1, "Comité d'experts pour l'Unification des Pharmacopées - Rapport sur les travaux de la troisième session". Ce rapport est mentionné dans l'ordre du jour provisoire de la deuxième session du Conseil Exécutif (Document EB2/42 Rev.1) sous le numéro 17.2.2.
The Expert Committee on the Unification of Pharmacopoeias
held its third session in Geneva from 15 - 23 October 1948.
The following members were present:

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

E. Fullerton Cook, M.Sc., Chairman, Committee of Revision
of the Pharmacopoeia 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
Pharmacopoeia Commission

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

Dr. C.H. Hampshire, Secretary of the 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 of
the 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 WHO Secretariat 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.

3.1 MATTERS ARISING FROM REPORT ON SECOND SESSION

3.1.1 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.

3.1.2 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.

3.1.3 Table of Usual and Maximal Doses (WHO/IC/Pharm/31)

After a discussion on the table submitted by Prof. 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 Prof. Hazard should be circulated to members of the committee for the opinion of physicians of their respective countries.

3.2 PREPARATION OF AN INTERNATIONAL PHARMACOPOEIA

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

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

3.2.2.1 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, after consultation with manufacturers, these more precise figures would be again discussed.

3.2.1.2 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 manufacture 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.

3.2.1.3 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.

3.2.1.4 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 the adoption of 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.

3.2.2 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.

3.2.3 Synonyms

After consideration of a report by Prof. Fullerton Cook (WHO/Pharm./39), the committee agreed that synonyms should be confined to exceptional cases and inserted when finally reviewing monographs.

Prof. 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.

3.2.4 The Title "International Pharmacopoeia"

A letter had been received from Prof. 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".

Prof. 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 La 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 Prof. 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 of the title, and to have further consultations in their own countries on this subject, a final decision was deferred until the next session.

3.2.5 List of common designations of medicaments

A report by Prof. Hazard (WHO/IC/Pharm/35 and annex) was deferred for consideration to a later session.

3.2.6 General principles discussed and approved

3.2.6.1 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.

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

3.2.6.3 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.

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

3.2.6.5 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.

3.2.6.6 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".

3.3 RELATIONS WITH OTHER EXPERT COMMITTEES

3.3.1 Expert Committee on Biological Standardization

The committee agreed that the appendices on the determination of the therapeutic potency of Sylfarsphenamina 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 forthcoming 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 Antitoxinum and of Tuberculinum Pristinum.

3.3.2 Expert Committee on Habit-forming Drugs

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

3.3.3 Expert Committee on Malaria

The committee agreed that the monograph on Quinini Sulphas (WHO/IC/Pharm/Mon/6.Rev.1) 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 Sulphas to be prescribed in an international pharmacopoeia. The degree of purity as expressed by the Kerner-Weller ammonia test was selected at 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, which contained a critical review of modern antimalarial drugs.

3.4 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.
APPENDIX 1 - LIST OF MONOGRAPHS CONSIDERED

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

<table>
<thead>
<tr>
<th>WHO/Pharm./40 Rev.1</th>
<th>Monograph</th>
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<tbody>
<tr>
<td>52</td>
<td>Acidum Benzoicum</td>
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<tr>
<td>54</td>
<td>Thiopeptalum Natricum cum Natrii Carbonas (Thiopeptalum Sodium)</td>
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<tr>
<td>56</td>
<td>Tinctura Digitalis</td>
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<tr>
<td>58</td>
<td>Neoarsphenaminina</td>
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<tr>
<td>59</td>
<td>Sulfarsphenaminina</td>
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<tr>
<td>Appendices 60-64</td>
<td>Sera Antitoxica Antitoxina</td>
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<tr>
<td>60</td>
<td>Serum Anti-Vibrio Septicum (Antitoxinum Septicum)</td>
</tr>
<tr>
<td>61</td>
<td>Serum Antiperfringens (Antitoxinum Welchicum)</td>
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<tr>
<td>62</td>
<td>Serum Antioedematiens (Antitoxinum Oedematicum)</td>
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<tr>
<td>63</td>
<td>Serum Antitetanicum (Antitoxinum Tetanicum)</td>
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<td>64</td>
<td>Serum Antidiphthericum (Antitoxinum Diphthericum)</td>
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<td>73</td>
<td>Acidum Nicotinicum</td>
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<tr>
<td>74</td>
<td>Nicotinamidum</td>
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<tr>
<td>75</td>
<td>Oleum Jecoris Aselli (Oleum Morrhuae)</td>
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<tr>
<td>76</td>
<td>Oleum Jecoris Hippoglossi (Oleum Hippoglossi)</td>
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<tr>
<td>77</td>
<td>Calciferol</td>
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<tr>
<td>78</td>
<td>Menadionum</td>
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<tr>
<td>80</td>
<td>Riboflavinum</td>
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<tr>
<td>81</td>
<td>Thiaminae Hydrochloridum</td>
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<tr>
<td>82</td>
<td>Aether Vinylicus</td>
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<tr>
<td>87</td>
<td>Carbonii Dioxidum</td>
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<tr>
<td>96</td>
<td>Digoxinum</td>
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<tr>
<td>97</td>
<td>Lanatosidum C</td>
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<tr>
<td>102</td>
<td>Mepacrinae Hydrochloridum</td>
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<td>103</td>
<td>Methyltestosteronum</td>
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<td>104</td>
<td>Oxidum Nitrosum</td>
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<td>Oestradiol</td>
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<td>Oestradiolis Benzoas</td>
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<td>107</td>
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<td>108</td>
<td>Oxygenium</td>
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<td>Progesteronum</td>
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2. **Monographs consideration of which was deferred**

<table>
<thead>
<tr>
<th>WHO.IC/Pharm./Mon/</th>
<th>Description</th>
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<tr>
<td>70</td>
<td>Heparinum</td>
</tr>
<tr>
<td>79</td>
<td>Menadioni Sodii Bisulfis</td>
</tr>
<tr>
<td>95</td>
<td>Digitoxinum</td>
</tr>
<tr>
<td>98</td>
<td>Injectio Insulini</td>
</tr>
<tr>
<td>99</td>
<td>Injectio Zinco-Insulini Protaminati</td>
</tr>
<tr>
<td>111</td>
<td>Injectio Pituitarii Posterioris</td>
</tr>
<tr>
<td>129</td>
<td>Tinctura Opii</td>
</tr>
</tbody>
</table>
3. Monographs transferred to Class B.

WHO.IC/Pharm/Mon/130  Tinctura Opii Benzoica
162  Benzylis Benzoas
167  Tuberculin Derivatumin Proteinicum Purificatum
180  Tabellae Glycerylis Trinitratis
187  Injectio Mersalyli et Theophyllini
195  Dicoumarol
196  Injectio Diodoni
198  Stibophenum

4. Monographs removed from the programme of the Committee.

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

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APPENDIX 2

List of Reports, etc. to be prepared

Prof. H. Baggesgaard-Rasmussen agreed:

To prepare a draft monograph on Phenantoinum Natricum

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

To review the figures for the melting range and boiling range in monographs accepted (with Prof. Fahmy, Flick and van Os), and to report on the following:

The chromatographic analysis of Butacaine

The chromatographic test for the assay on Tetracaine Hydrochloridum and chromatographic tests in general (with Prof. van Os)

Specific gravity and refractive indices for the General Notices

Prepare a table giving details of weights and measures, and abbreviations

The general principles of ultraviolet absorption

The limits of ash, acid-insoluble ash and sulfated ash.

Prof. E. Pullerton Cook agreed:

To supply an assay of Menadionum

To report on Heparinum


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

To prepare draft monographs on:

Amino Acid Preparations

Gonadotrophi num Chorionicum

Streptomycin
Prof. I.R. Fahmy agreed:

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

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

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

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

Prof. H. Fltck agreed:

To prepare an assay of metacoesol (with Prof. van Os)

To review the figures for the melting range and boiling range in monographs accepted (with Prof. Baggesgaard-Rasmussen, Fahmy and van Os); and to report on the following:

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

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

Vegetable drugs in general

Ash and insoluble ash

Monographs concerning Herba Belladonna and Herba Hyoscin.

Dr. C.H. 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 Prof. Baggesgaard-Rasmussen.

Chromatographic assay of Pilocarpinae Hydrochloridum (with Prof. van Os, Fahmy and Flüeck)

The methods of preparing sterile solutions for injections; and to prepare:

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

Prof. R. Hazard agreed:

To report on:

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

Prof. D. van Os agreed:

To prepare an assay of metacresol (with Prof. Flüeck)

To review the figures for the melting range and boiling range in monographs accepted (with Prof. Baggesgaard-Rasmussen, Fahmy and Flüeck); and to report on:

Chromatographic assay of Pilocarpine Hydrochloridum (with Dr. Hampshire, Prof. Flüeck and Fahmy)

The chromatographic test for the assay of Tetracainae Hydrochloridum and chromatographic tests in general (with Prof. Baggesgaard-Rasmussen).