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**EXPERT COMMITTEE ON
BIOLOGICAL STANDARDIZATION**

Eighth Report

WORLD HEALTH ORGANIZATION

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Eighth Session

Geneva, 18-23 October 1954

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* Was unable to attend.

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Eighth Report *

The eighth session of the Expert Committee on Biological Standardization was held in Geneva from 18 to 23 October 1954.

The Deputy Director-General of the World Health Organization welcomed the members and thanked them for the preparatory work they had already done, and for being willing to work still further, towards making the session a success. He also expressed appreciation of the continued and valuable co-operation of the Food and Agriculture Organization of the United Nations in those aspects of the Committee's work which are the joint concern of veterinary and medical workers.

IMMUNOLOGICAL

1. Blood-Typing Sera

1.1 Anti-Rh₀ (anti-D) blood-typing serum

The proposed International Standard for Anti-Rh₀ (Anti-D) Blood-Typing Serum was prepared for the characterization of saline-agglutinating anti-Rh₀ (anti-D) sera for routine use. In view of the difficulties experienced by workers in obtaining such agglutinating sera and the relative ease with which albumin-agglutinating anti-Rh₀ (anti-D) sera can be obtained, the Committee authorized the Statens Seruminstitut, Copenhagen, in consultation with the International Blood-Group Reference Laboratory, London, to examine the practicability of preparing a standard anti-Rh₀ (anti-D) serum to be used with albumin or other activating substances.

* The Executive Board, at its fifteenth session, adopted the following resolution:
The Executive Board

1. NOTES the eighth report of the Expert Committee on Biological Standardization;
2. THANKS the members of the Committee for their work; and
3. AUTHORIZES publication of the report.

(Resolution EB15.R4, *Off. Rec. Wld Hlth Org.* 1955, 60, 2)

1.2 *Anti-Rh' (anti-C) and anti-Rh" (anti-E) blood-typing sera*

The Committee noted that the few contributions of anti-Rh' (anti-C) and anti-Rh" (anti-E) blood-typing sera sent to the International Blood Group Reference Laboratory, London, for international standards of these two sera were insufficient for making standard preparations. In view of the expected delay in the establishment of these standards, the Committee wished to draw attention to the alternative method of characterizing anti-Rh' (anti-C) and anti-Rh" (anti-E) sera, whereby the red cells of persons of the correct type who are readily available to the laboratories concerned can be authenticated by the International Blood Group Reference Laboratory, and used as "standard" antigens for the titration of routine anti-Rh' (anti-C) and anti-Rh" (anti-E) typing sera.

2. International Reference Preparations of Cholera Vaccines, Diagnostic Antigens, and Diagnostic Sera

The Committee asked Dr. P. M. Wagle of the Haffkine Institute, Bombay, in association with Dr. M. L. Ahuja of the Central Research Institute, Kasauli, India, and in consultation with the Statens Serum Institut, Copenhagen, to arrange the further collaborative studies of the International Reference Preparations of Cholera Vaccines.¹

The Committee endorsed for publication a memorandum on the preparations, their properties and the ways in which they may be used.²

3. International Reference Preparations of *Clostridium Welchii* (Perfringens) Antitoxins

The Committee noted that the Veterinary Laboratory, Weybridge, Surrey, England, had obtained a batch of serum for each of the proposed new International Standards for *Clostridium welchii* Antitoxins, Types B and D, and had carried out a collaborative examination³ of the suitability of these batches as international standards.⁴ The Committee adopted the

¹ See *Wld Hlth Org. techn. Rep. Ser.* 1954, 86, 7.

² Maaløe, O., unpublished working document WHO/BS/255

³ Participants: Maaløe, O., Statens Serum Institut, Denmark; Mason, J. H., South African Institute for Medical Research, Union of South Africa; Morgan, F. G., Commonwealth Serum Laboratories, Australia; Prigge, R., Paul-Ehrlich Institute, Germany; Stableforth, A. W., Ministry of Agriculture and Fisheries Veterinary Laboratory, England and Wales; Wellcome Research Laboratories, England

⁴ Statens Serum Institut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/281; Stableforth, A. W., unpublished working document WHO/BS/283

materials as International Reference Preparations of *Clostridium welchii* (Type B) Antitoxin and of *Clostridium welchii* (Type D) Antitoxin. The Committee decided that one provisional unit of beta antitoxin is contained in 0.0137 mg of the Type B Preparation and one provisional unit of epsilon antitoxin is contained in 0.0657 mg of the Type D Preparation. It is expected that, until further information is obtained about the properties of these antitoxins, they will be used to assay therapeutic sera and not for the identification of types of *Cl. welchii*.

The Committee recognized that the existing International Standard for Gas Gangrene Antitoxin (*perfringens*) is actually a *Cl. welchii* Type A antitoxin, and recommends that it be studied together with the international reference preparations with a view to assigning unitages to the three antitoxin preparations for the known toxic components of *Cl. welchii*. The Committee authorized the Veterinary Laboratory, Weybridge, and the Statens Seruminstitut, Copenhagen, to organize this collaborative examination.

4. Diphtheria Toxoid and Schick-Test Toxin

4.1 *Diphtheria toxoid, adsorbed*

The Committee noted that the batch of aluminium hydroxide adsorbed diphtheria toxoid prepared by the Paul-Ehrlich Institute, Frankfurt-on-Main, has now been sent to the Statens Seruminstitut, Copenhagen, and authorized that institute to establish it as the International Standard, subject to the approval of participants in a collaborative study of its potency and thermostability.

The Committee noted further evidence of the need for an international standard of this type in a report on assays of a large number of diphtheria toxoid preparations.¹

4.2 *International Standard for Schick-Test Toxin (Diphtheria)*

The Committee considered reports² on collaborative studies³ of a dried preparation of diphtheria toxin and established it as the International

¹ Greenberg, L. (1955) *Bull. Wld Hlth Org.* **12**, 751

² Statens Seruminstitut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/274; Prigge, R., unpublished working document WHO/BS/275 and Add. 1 and 2

³ Participants: Barr, M., Wellcome Research Laboratories, England; Greenberg, L., Biologics Control Laboratories, Canada; Prigge, R., Paul-Ehrlich Institute, Germany; Rostock, O. and Schiebel, I., Statens Seruminstitut, Denmark

Standard for Schick-Test Toxin (Diphtheria). The Committee assigned to the Standard a unitage such that 900 International Units are contained in one ampoule of the Standard Preparation as at present issued.

The Committee agreed that there is no need to provide international standards for Schick-test control reagents.

5. Influenza Vaccines and Diagnostic Reagents

5.1 *Influenza vaccines*

The Committee considered the possibilities of providing a stable reference preparation of influenza vaccine, but emphasized that the technical difficulties appear at present to be insuperable.^{1, 2}

The Committee recommended, however, that in any future field trial of influenza vaccines, concurrent laboratory assays of the vaccines used should be encouraged.

5.2 *Influenza diagnostic reagents*

The Committee considered the question raised by the WHO Expert Committee on Influenza concerning the desirability of providing standard reagents for the differentiation of types of influenza virus.³ The Committee suggested that the Expert Committee on Influenza confirm that typing can be achieved with sufficient precision by means of reference sera alone. If this is so, the Committee will be pleased to give all possible assistance in establishing and distributing diagnostic reference sera for influenza-virus typing.

6. International Reference Preparation for Opacity

The Committee adopted a report⁴ on the International Reference Preparation for Opacity as the memorandum for distribution with issues of this preparation.

¹ National Institute for Medical Research, World Influenza Centre and Department of Biological Standards, London, unpublished working document WHO/BS/258

² Unpublished working document WHO/Influenza/18

³ *Wld Hlth Org. techn. Rep. Ser.* 1953, 64, 10; Payne, A. M.-M., unpublished working document WHO/BS/290

⁴ Maaløe, O. (1955) *Bull. Wld Hlth Org.* 12, 769

7. Pertussis Vaccine and Serum

7.1 *Pertussis vaccine*

The Committee noted that the National Institute for Medical Research, London, had obtained and dried a portion of one of the vaccines which it is hoped will be used in the current field-trials in England. If it is found to have a protective value it might serve as an international reference preparation consisting of material of proven efficacy in man.¹

Collaborative assays of this material, in comparison with the United States and British standards are being arranged by the Statens Serum-institut, Copenhagen.²

7.2 *Pertussis agglutinating serum*

The Committee recognized the desirability of providing a reference preparation for the characterization of agglutinating suspensions of *Haemophilus pertussis*. It requested the Statens Seruminstitut, Copenhagen, to continue the collaborative examination of the serum provided by the Institut Pasteur, Paris, in order to evaluate its suitability as an international reference preparation.²

8. Poliomyelitis Vaccines

On the available information, the Committee decided that the provision of international reference preparations of poliomyelitis vaccines must await further developments in this field.³ The Committee agreed that the provision of international reference preparations of specific neutralizing sera against the three types of poliomyelitis virus is desirable for the characterization both of sera and of vaccines, and agreed to investigate this possibility.

9. International Standard for Anti-Q-Fever Serum

The Committee assigned unitage, on the basis of the result of the collaborative assay,^{4, 5} to the International Standard for Anti-Q-Fever

¹ Perry, W. L. M., unpublished working document WHO/BS/259

² Statens Seruminstitut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/282

³ Dick, G. W. A. & Perry, W. L. M., unpublished working document WHO/BS/260

⁴ Statens Seruminstitut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/276 and Add. 1; Veterinary Laboratory, Weybridge, unpublished working document WHO/BS/296

⁵ Participants: Cox, H. R., Lederle Laboratories, USA; Grasset, E., University of Geneva, Switzerland; Lackman, D., Rocky Mountain Laboratory, USA; Lennette, E. H., California State Viral and Rickettsial Disease Laboratory, USA; Slavin, G., Ministry of Agriculture and Fisheries Veterinary Laboratory, England and Wales; Stoker, M. G. P., University of Cambridge, England

Serum such that one International Unit is contained in 0.1017 mg of the International Standard.

10. Rabies Serum and Vaccine

10.1 *Antirabies serum*

The Committee noted the progress made in the collaborative assay of the proposed International Standard for Antirabies Serum and in testing its specificity and thermostability.¹ The Committee, following its usual practice of equating the International Unit as far as possible with a unit already in common use, recommended that the unit for the International Standard be equated with the unit of the United States Standard Antirabies Serum.

10.2 *Rabies vaccine*

The Committee noted that material had been offered by the National Institutes of Health, Bethesda, Md., USA, and requested WHO to arrange a collaborative investigation of the material as a standard for rabies vaccine.

11. International Standard for Swine Erysipelas Serum, Anti-N

The Committee established the batch of swine erysipelas serum provided by the Paul-Ehrlich Institute, Frankfurt-on-Main, as the International Standard for Swine Erysipelas Serum, Anti-N.^{2, 3}

The Committee considered the progress made in comparing the protective activity of the International Standard with that of the existing German national standard, and agreed that further studies are needed before assigning a unitage such that the International Unit is equal to the German national unit.⁴ The Veterinary Laboratory, Weybridge, Surrey, and the Paul-Ehrlich Institute were authorized to extend the collaborative investigation.

¹ Statens Seruminstitut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/277 and Add. 1; Kaplan, M. M., unpublished working document WHO/BS/294; Veterinary Laboratory, Weybridge, unpublished working document WHO/BS/295

² Veterinary Laboratory, Standards Department, Weybridge, unpublished working document WHO/BS/297

³ Participants: Prigge, R., Paul-Ehrlich Institute, Germany; Schoening, H. W., Animal Disease and Parasite Research Branch, Agricultural Research Service, USA; Stableforth, A. W., Ministry of Agriculture and Fisheries Veterinary Laboratory, England and Wales; van Waveren, G. M., State Serum Institute, Netherlands

⁴ See *Wld Hlth Org. techn. Rep. Ser.* 1954, 86, 11.

12. Syphilis Diagnostic Reagents and Sera

12.1 *Cardiolipin and lecithins*

The Committee noted that the International Reference Preparations of Cardiolipin and Lecithins had been proved to possess a satisfactory degree of thermostability.¹

The Committee noted that the supply of these preparations is running short and authorized the Statens Seruminstitut, Copenhagen, to obtain large batches for replacements.

12.2 *Syphilitic sera*

The Committee noted reports on the progress made by the WHO International Serological Reference Laboratory, Copenhagen, in investigating the possibility of using pooled reactive syphilitic sera as international reference preparations.²

13. International Standard for Purified Protein Derivative of Avian Tuberculin

The Committee noted the results of collaborative assays³ carried out on the batch of purified avian tuberculin prepared by the Veterinary Laboratory, Weybridge, Surrey, and established this material as the International Standard for Purified Protein Derivative of Avian Tuberculin.⁴ The Committee assigned a unitage such that the International Unit is contained in 0.0000726 mg of the International Standard.

14. Typhoid and Paratyphoid Sera and Vaccines

14.1 *Typhoid and paratyphoid agglutinating sera*

The Committee noted that the collaborative assays of the typhoid and paratyphoid agglutinating sera prepared by the Central Public Health Laboratory, London, are in progress.⁵

¹ Statens Seruminstitut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/278 and Add. 1

² Unpublished working document WHO/BS/289; WHO International Serological Reference Laboratory and Statens Seruminstitut, Statistical Department, Copenhagen, unpublished working document WHO/BS/289 Rev. 1

³ Participants: Maaløe, O., Statens Seruminstitut, Denmark; Mitchell, C. A., Animal Diseases Research Institute, Canada; Ottosen, H. E., State Veterinary Serum Laboratory, Denmark; Simms, B. T., Animal Disease and Parasite Research Branch, Agricultural Research Service, USA; Stableforth, A. W., Ministry of Agriculture and Fisheries, Veterinary Laboratory, England and Wales

⁴ Veterinary Research Laboratory, Weybridge, unpublished working document WHO/BS/293 and Add. 1 and 2.

⁵ Statens Seruminstitut, Department of Biological Standards, Copenhagen, unpublished working document WHO/BS/279

14.2 *Typhoid vaccine*

The Committee considered that the field trials of alcoholized and phenolized typhoid vaccines now in progress in Yugoslavia present a unique opportunity for obtaining international reference preparations of proven efficacy in man.¹

The Committee recommended that WHO request that 5 litres of each vaccine be made available to the Statens Seruminstitut, Copenhagen, for detailed collaborative investigations of current laboratory methods of assay. Should the results of the laboratory and field trials be satisfactory, it is hoped to establish a stable international reference preparation of typhoid vaccine.

PHARMACOLOGICAL

ANTIBIOTICS

15. Oxytetracycline

The Committee considered a report² on the material which, subject to the approval of the participants in the collaborative assay,³ will be established by the National Institute for Medical Research, London, as the International Standard for Oxytetracycline, with an international unit. The Committee adopted the report as the memorandum to be sent out with issues of this standard.

16. Newer Antibiotics⁴

16.1 *Tetracycline, erythromycin, and polymyxin B*

The Committee asked the National Institute for Medical Research, London, to obtain suitable batches of tetracycline and erythromycin for

¹ Payne, A. M.-M., unpublished working document WHO/BS/291

² National Institute for Medical Research, Department of Biological Standards, London, unpublished working document WHO/BS/285

³ Participants: Gibbard, J., Department of National Health and Welfare, Canada; Grove, D. C., Food and Drug Administration, USA; Hedger, F. H., Messrs. Chas. Pfizer & Co., Inc., USA; Humphrey, J. H. and Lightbown, J. W., National Institute for Medical Research, Great Britain; Lund, E., Statens Seruminstitut, Denmark

⁴ National Institute for Medical Research, Department of Biological Standards, London, unpublished working document WHO/BS/263

detailed characterization with a view to establishing international standards for these substances.

The Committee noted that there is a British standard for polymyxin B, a portion of which is offered for use as an international standard, and agreed that the National Institute for Medical Research should arrange for this material to be examined collaboratively with a view to its possible establishment as an international standard.

16.2 *Other antibiotics*

The Committee also decided that there was no need to establish international standards for carbomycin, neomycin, and viomycin.

17. Procaine Benzylpenicillin in Oil with Aluminium Monostearate (PAM)

The Committee considered the specifications for procaine benzylpenicillin in oil with aluminium monostearate (PAM) which appear in the fourth report of the Expert Committee on Venereal Infections and Treponematoses,¹ and asked the National Institute for Medical Research, London, to investigate the possibility of establishing an international reference preparation of PAM and of devising suitable laboratory assay methods, including animal tests for persistence of penicillin in the circulation, as a preferable substitute for similar tests in man.

HORMONES (AND PROTAMINE)

18. Anterior Pituitary Hormones

18.1 *Adrenocorticotrophic hormone*

The Committee noted the preliminary results² of the collaborative assays of the proposed Second International Standard for Adrenocorticotrophic Hormone and confirmed the authorization already given to the National Institute for Medical Research, London, to establish this material as the Second International Standard and to assign unitage to it on the basis of all the results obtained in the collaborative study and with the approval of the participants.

¹ *Wld Hlth Org. techn. Rep. Ser.* 1953, **63**, 55

² National Institute for Medical Research, Department of Biological Standards, London, unpublished working document WHO/BS/262 and Add. 1

18.2 *Prolactin*

The Committee noted that the National Institute for Medical Research, London, had been offered a small amount of material expected to be suitable for replacement of the existing International Standard for Prolactin. In spite of the small amount available, the Committee requested the National Institute for Medical Research to arrange a collaborative assay of this material.

18.3 *International Standard for Thyrotrophin*

The Committee noted the report¹ on the collaborative assays of the proposed standard,² and established it as the International Standard for Thyrotrophin. The Committee authorized the National Institute for Medical Research, London, to assign unitage to the Standard on the basis of the results obtained in the collaborative study³ and with the approval of the participants.

19. **Insulin**

The Committee noted that the National Institute for Medical Research, London, had collected material for the Fourth International Standard for Insulin.⁴ The Committee authorized the National Institute for Medical Research to establish this material as the Fourth International Standard for Insulin and to assign a unitage to the Standard on the basis of the results obtained in the collaborative study and with the approval of the participants.

20. **International Reference Preparation of Protamine**

The Committee established as the International Reference Preparation

¹ Mussett, M. V. & Perry, W. L. M., working document WHO/BS/284; to be published in *Bull. Wld Hlth Org.*

² See *Wld Hlth Org. techn. Rep. Ser.* 1954, **86**, 18.

³ Participants: Courrier, R., Académie des Sciences, France; Crooke, A. C., Birmingham United Hospitals, England; Gilliland, I. C., London Postgraduate Medical School, England; Hamburger, C. and Wichmann, R., Statens Serum Institut, Denmark; Morris, C. J. O. R., London Hospital, England; Pugsley, L. I., Department of National Health and Welfare, Canada; Purves, H. D. and Adams, D. D., Dunedin Medical School, New Zealand; Rademaker, R., N. V. Organon, Netherlands; Trikojus, V. M., University of Melbourne, Australia

⁴ National Institute for Medical Research, Department of Biological Standards, London, unpublished working document WHO/BS/267

of Protamine the batch which had been subjected to a collaborative examination.¹

MISCELLANEOUS

21. Dextran Sulfate

The Committee considered a report on the collaborative assays carried out on the existing Author's Preparation of Dextran Sulfate which indicated that it is not valid to express the potency of dextran sulfate in International Units of heparin.² The Committee therefore authorized the National Institute for Medical Research, London, in consultation with the participants in these assays, to assign a unitage to this preparation and to obtain material for an international standard for dextran sulfate, which will, after collaborative assay, be given a unitage in terms of the existing Author's Preparation.

22. Hyaluronidase

The Committee noted that material suitable for an international standard for hyaluronidase had been obtained,³ and authorized the National Institute for Medical Research, London, to proceed with a collaborative examination and to establish it as the International Standard for Hyaluronidase and to define an international unit approximately equivalent to the "turbidity reducing unit" commonly used in the USA, on the basis of the results of the collaborative studies and with the approval of the participants.

23. Male Fern

The Committee considered reports⁴ on laboratory studies of specimens of male fern. No correlation was found between anthelmintic potency and filicin content. Since no evidence is available of any relationship between laboratory assays and therapeutic efficacy in man, the Committee decided that at the present time it could take no further action.

¹ Perry, W. L. M., unpublished working document WHO/BS/261

² Mussett, M. V. & Perry, W. L. M., unpublished working document WHO/BS/270

³ Reinert, H., unpublished working document WHO/BS/271

⁴ National Institute for Medical Research, Department of Biological Standards, London, unpublished working document WHO/BS/272; Tréfouël, J., unpublished working document WHO/Pharm/Ed. Sec./17

24. International Reference Preparations of Melaminyl Trypanocides

The Committee considered the results of collaborative assays of batches of three melaminyl trypanocides.^{1, 2} The Committee established International Reference Preparations of Mel B and MSb. Since Melarsen is a defined chemical substance, the sample of this material held by the National Institute for Medical Research, London, will be offered for inclusion in the collection of authentic chemical substances which the Expert Committee on the International Pharmacopoeia proposes to establish.³

25. Ouabain

The Committee noted that the supply of the International Standard for Ouabain is exhausted and agreed that there is no need to replace it, since it is a defined chemical substance.⁴ The Committee also noted that the National Institute for Medical Research, London, has a supply of ouabain which is available for inclusion in the collection of authentic chemical substances which the Expert Committee on the International Pharmacopoeia proposes to establish.³

26. Pyrogens

The Committee noted a progress report on the collaborative assays of the two preparations of pyrogen now being carried out.⁵

27. Vitamin A

The Committee noted that supplies of the International Standard for Vitamin A (pure vitamin A acetate) are exhausted. In accordance with the decision reached at the Committee's sixth session,⁶ this standard will not be replaced.

¹ "Melarsen" = di-sodium *p*-melaminylphenylarsonate; "Mel B" = melaminyl-4-phenylarseno-dithioglycerin; "MSb" = sodium *p*-melaminylphenylstibonate polymer

² Perry, W. L. M., unpublished working document WHO/BS/273

³ WHO Expert Committee on the International Pharmacopoeia, twelfth report, unpublished working document WHO/Pharm/266, pp. 13, 14

⁴ Perry, W. L. M., unpublished working document WHO/BS/269

⁵ *Wld Hlth Org. techn. Rep. Ser.* 1954, 86, 19; Perry, W. L. M., unpublished working document WHO/BS/264

⁶ See *Wld Hlth Org. techn. Rep. Ser.* 1953, 68, 15.

GENERAL

28. Author's Preparations

The Committee discussed the practicability of creating international standards or reference preparations of a number of biologically active metabolites.¹ The Committee decided that the preparations referred to, being studied at the research level exclusively, would fall within the category of Author's Preparations as defined in the Annex (see page 18).

29. Stability of International Standards

The Committee noted reports² on the stability of international standards. Previous conclusions that certain serum standards are highly stable were confirmed.

30. Biological Assay Methods for the Pharmacopoea Internationalis

The Committee, in response to a request from the Expert Committee on the International Pharmacopoeia,³ agreed to continue to give its advice on and approval of draft methods of bio-assays for the *Pharmacopoea Internationalis*.

The Committee accepted for comment drafts of a test for therapeutic potency of suramin⁴ and of a test for pyrogens,⁵ submitted by the Expert Committee on the International Pharmacopoeia.

31. International Shigella Centres

At its fourth session, the Committee had recommended the establishment of two international shigella centres.⁶ It was noted that these centres

¹ Rocha e Silva, M., unpublished working document WHO/BS/292; refers to the following substances: bradykinin, darmstoff, depressan, hypertensin (angiotonin), kallidin, kallikrein (padutin), prostglandin, renin, substance-P, vascularin, vesiglandin

² Jerne, N. K., unpublished working document WHO/BS/257, Perry, W. L. M., unpublished working document WHO/BS/265

³ WHO Expert Committee on the International Pharmacopoeia, thirteenth report, unpublished working document WHO/Pharm/282, p. 12

⁴ Unpublished working document WHO/Pharm/273 Rev. 3 Add. 1

⁵ Unpublished working document BS/8/5

⁶ See *Wld Hlth Org. techn. Rep. Ser.* 1951, 36, 14.

were established at the Central Public Health Laboratory, London, and the Communicable Disease Center, Atlanta, Ga., USA, on 1 January 1954.¹

Annex

NOTES ON AUTHOR'S PREPARATIONS

The primary purpose underlying the establishment of international standards is to provide a means of ensuring uniformity throughout the world in the designation of potency of preparations which are used in the therapy or the diagnosis of human and animal disease, and which cannot be characterized adequately by chemical and physical means. The Expert Committee on Biological Standardization recognizes, however, that there is an additional, if secondary, purpose in the provision of international standards, namely the facilitation of research work that may follow the creation of a single common point of reference. Out of such research work, indeed, clinical applications of the substances concerned may arise.

Nevertheless, there is a limit to the amount of work which can be undertaken by the Expert Committee on Biological Standardization and by the International Centres for Biological Standards in the creation of new international standards, and priority obviously must be given to those substances of recognized clinical application. The pressure of such more urgent work may thus make it impossible to create international standards for substances of interest only to research workers without considerable delay, which may greatly reduce the usefulness of the resulting standards.

It was to meet this situation that the Expert Committee on Biological Standardization introduced a class of substances known as "Author's Preparations". The principles which apply to such preparations may be summarized as follows:

- (1) The International Centres for Biological Standards are willing to hold and distribute Author's Preparations to interested workers throughout the world.
- (2) The author may offer, or he may be asked by the Expert Committee on Biological Standardization to supply, such a preparation.

¹ Unpublished working document WHO/BS/280

(3) Author's Preparations will normally be accepted only if already packaged in small quantities suitable for final distribution (e.g., in ampoules) and in sufficient quantity to serve not only for distribution to interested workers but also for the characterization of more definitive reference preparations should this prove desirable.

(4) Evidence that the preparation is reasonably stable should be supplied by the author.

(5) It will generally be advisable to assign a unitage to each Author's Preparation. Should the author already have defined a unit of convenient size and in terms of an amount of his preparation, this might be used as a basis for an international unit.

(6) The Expert Committee on Biological Standardization can take no formal responsibility for the authenticity or stability of any Author's Preparation but will undertake the storage and distribution of these preparations under the same conditions as for the International Standards, as a service to research workers.

For the information of authors who may wish to submit preparations, some of the principles governing the setting up and use of standard preparations have been discussed by Hartley.¹ In case of doubt, WHO will always be willing to advise.

¹ Hartley, P. (1935) *Pharm. J.* **2**, 625; Hartley, P. (1945) *Bull. Hlth Org. L.o.N.* **12**, 76

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