

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES

No. 147

**EXPERT COMMITTEE ON
BIOLOGICAL STANDARDIZATION**

Eleventh Report

WORLD HEALTH ORGANIZATION

PALAIS DES NATIONS

GENEVA

1958

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION *

Geneva, 16-21 September 1957

Members :

Dr N. H. Fisek, Head, Biologics Control Division, Central Institute of Hygiene, Ankara, Turkey

Dr E. Grasset, Professeur d'Hygiène, Directeur de l'Institut d'Hygiène, Université de Genève, Geneva, Switzerland

Dr O. Maaløe, Chief, Department of Biological Standardization, Statens Seruminstitut, Copenhagen, Denmark (*Rapporteur*)

Dr R. Murray, Director, Division of Biologics Standards, National Institutes of Health (Public Health Service), Bethesda, Md., USA (*Chairman*)

Dr A. S. Outschoorn, Head, Division of Pharmacology, Medical Research Institute, Colombo, Ceylon

Dr W. L. M. Perry, Director, Department of Biological Standards, National Institute for Medical Research, London, England

Professor R. Prigge, Director, Paul-Ehrlich-Institut, Staatliche Anstalt für experimentelle Therapie, Frankfurt-on-Main, Federal Republic of Germany (*Vice-Chairman*)

Dr H. Welch, Director, Division of Antibiotics, Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C., USA

Secretariat :

Dr N. K. Jerne, Chief, Biological Standardization Section, WHO (*Secretary*)

* Invited but unable to attend :

Dr Sumiatno, Director, Pasteur Institute, Bandung, Indonesia

This report was originally issued in mimeographed form as document WHO/BS/418.

CONTENTS

PHARMACOLOGICAL

Antibiotics	Page
1. Streptomycin	5
2. Tetracycline	6
3. Erythromycin	6
4. Neomycin	6
5. Novobiocin	6
6. Phenoxymethylpenicillin	7
7. Procaine benzylpenicillin in oil with aluminium monostearate (PAM)	7
8. Nystatin, oleandomycin, and other antibiotics	8
Hormones	
9. Oxytocic, vasopressor, and antidiuretic substances	8
10. Corticotrophin	8
11. Human menopausal gonadotrophin	9
12. Prolactin	9
13. Relaxin	9
14. Insulin	9
Miscellaneous	
15. Dextran sulfate	10
16. Heparin	10
17. Vitamin B ₁₂	10
18. Pyrogens	11

IMMUNOLOGICAL

Antigens	
19. Pertussis vaccine	11
20. Typhoid vaccines	11
21. Cholera vaccine	12
22. Rabies vaccine	12
23. Smallpox vaccine	13
24. Swine erysipelas vaccine	13
25. Poliomyelitis vaccine	13
26. Japanese B encephalitis vaccine	14
27. Leptospirosis vaccines	14
28. Cardioliipin	14

Antibodies	Page
29. Gas gangrene antitoxin (<i>vibrion septique</i>)	15
30. Anti-streptolysin O	15
31. Blood-typing sera	15
32. Poliomyelitis sera	16
33. Typhoid and paratyphoid agglutinating sera	16
34. Syphilitic human serum	16
35. Leptospirosis sera	17
36. Yellow fever immune serum	17

GENERAL

37. Recommended requirements for biological substances	18
38. Stability of biological standards	18
39. List of International Biological Standards	18

ANNEX

I. International Biological Standards and Reference Preparations, 1958	19
II. Proposed International Biological Standards	36
III. Author's Preparations	37
IV. Discontinued International Biological Standards	38

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Eleventh Report *

The Expert Committee on Biological Standardization met in Geneva from 16 to 21 September 1957.

The Assistant Director-General, Central Technical Services, on behalf of the Director-General of the World Health Organization, welcomed the members of the Committee.

PHARMACOLOGICAL

ANTIBIOTICS

1. Streptomycin

The Committee noted that the National Institute for Medical Research, London, has completed the statistical analysis of the results of the collaborative assays,¹ and that as soon as agreement of the participants has been obtained² the second International Standard for Streptomycin will be established.

* The Executive Board, at its twenty-first session, adopted the following resolution :
The Executive Board

1. NOTES the eleventh 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 EB21.R2, *Off. Rec. Wld Hlth Org.*, 1958, 83, 6).

¹ National Institute for Medical Research, London, unpublished working document WHO/BS/393

² Participants : Biologics Control Laboratory, Department of National Health and Welfare, Ottawa, Canada ; Hindustan Antibiotics Ltd, Pimpri, near Poona, India ; Istituto Superiore di Sanità, Rome, Italy ; Department of Viral and Rickettsial Diseases, National Institute of Health, Tokyo, Japan ; Distillers Company (Biochemicals) Ltd, Great Burgh, Epsom, United Kingdom ; Glaxo Laboratories, Greenford, United Kingdom ; National Institute for Medical Research, London, United Kingdom ; Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C., USA

2. Tetracycline

The Committee noted that, in accordance with the authorization given in its tenth report,¹ the International Standard for Tetracycline has been established^{2, 3} and that one International Unit is defined as the activity contained in 0.00101 milligram of the International Standard. The standard thus contains 990 units per milligram; one International Unit may be regarded as equivalent to one microgram of pure tetracycline hydrochloride.

3. Erythromycin

The Committee noted that, in accordance with the authorization given in its tenth report,¹ the International Standard for Erythromycin has been established^{4, 5} and that one International Unit is defined as the activity contained in 0.001053 milligram of the International Standard. The standard thus contains 950 units per milligram; one International Unit may be regarded as equivalent to one microgram of pure erythromycin base.

4. Neomycin

The Committee noted that the active material constituting the proposed international standard for neomycin is a mixture of approximately 80% of neomycin B and 20% of neomycin C.⁶ Since this composition is also characteristic of most commercial products and of the standard used by the Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C., the Committee considered the material suitable and asked the National Institute for Medical Research, London, to proceed with the collaborative assay.

5. Novobiocin

The Committee decided that there was no need for an international standard for novobiocin at the present time. It noted that, in case such a

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1957, 127, 13

² National Institute for Medical Research, London, unpublished working document WHO/BS/396

³ Humphrey, J. H., Lightbown, J. W. & Mussett, M. V., unpublished working document WHO/BS/396, Annex 1

⁴ National Institute for Medical Research, London, unpublished working document WHO/BS/397

⁵ Humphrey, J. H., Lightbown, J. W. & Mussett, M. V., unpublished working document WHO/BS/397, Annex 1

⁶ National Institute for Medical Research, London, unpublished working document WHO/BS/398

need should arise, the quantity of novobiocin now held by the National Institute for Medical Research, London,¹ would suffice for the establishment of an international standard.

6. Phenoxyethylpenicillin

The Committee endorsed the final report² on the collaborative assay³ of the proposed international standard and established this material as the International Standard for Phenoxyethylpenicillin. The International Unit is defined as the activity contained in 0.00059 milligram of the International Standard. The International Standard thus contains 1695 International Units per milligram.

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

The Committee noted that preliminary studies of an assay method for PAM in terms of a reference preparation of PAM had been completed. The National Institute for Medical Research, London, had obtained several batches of PAM believed to possess different characteristics with respect to the production, after intramuscular injection, of persistent concentrations of penicillin in circulating blood, but only two of these were available in sufficient quantity to serve as international reference preparations.⁴ In view of the continued use of this drug in mass campaigns against treponematoses, the Committee requested the National Institute for Medical Research to proceed with its plan for collaborative studies in man and in rabbits; the Committee emphasized that an adequate number of tests in man should be included.

The Committee also noted the final report describing an assay method for the determination of small concentrations of penicillin in blood serum.⁵

¹ National Institute for Medical Research, London, unpublished working document WHO/BS/394

² National Institute for Medical Research, London, unpublished working document WHO/BS/399

³ Participants: "Biochemie" G.m.b.H., Kundl, Tyrol, Austria; Laboratory of Hygiene, Department of National Health and Welfare, Ottawa, Canada; Statens Serum-institut, Copenhagen, Denmark; Institut Pasteur, Paris, France; Antibiotics Department, Institute of Hygiene, Warsaw, Poland; Distillers Company (Biochemicals) Ltd, Great Burgh, Epsom, United Kingdom; National Institute for Medical Research, London, United Kingdom; Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C., USA

⁴ National Institute for Medical Research, London, unpublished working document WHO/BS/403

⁵ National Institute for Medical Research, London, unpublished working document WHO/BS/404

8. Nystatin, Oleandomycin, and Other Antibiotics

The Committee agreed that it may become necessary in the future to establish international standards for nystatin and oleandomycin, and it asked the National Institute for Medical Research, London, to obtain adequate quantities of these substances and to carry out preliminary studies of their suitability as international standards. The Committee also agreed that no steps should be taken at this time to set up international standards for other antibiotics.

HORMONES

9. Oxytocic, Vasopressor, and Antidiuretic Substances

The Committee noted that, in accordance with the authorization given in its tenth report,¹ the International Standard for Oxytocic, Vasopressor, and Antidiuretic Substances has now been established² and that one International Unit of each substance is defined as the activity contained in 0.5 milligram of the International Standard. The establishment of the third International Standard in place of the second has involved no change in the size of the International Units.

10. Corticotrophin

The Committee noted that the International Conference on Corticotrophin, which met in London in July 1957 under the auspices of the Medical Research Council, had recommended replacement of the International Standard for Corticotrophin with a preparation consisting of corticotrophin purified by adsorption on oxycellulose.³ The Committee agreed with this proposal and asked the National Institute for Medical Research, London, to obtain material of pig origin and to proceed with its characterization in terms of the existing standard. The Committee recognized that the assay of the new standard in terms of the existing one would be complicated by the fact that the potency as determined by subcutaneous assay would probably be higher than the potency as determined by intravenous assay. Since most commercial preparations are administered subcutaneously, it was agreed that the definition of the unit should be based entirely

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1957, 127, 15

² National Institute for Medical Research, London, unpublished working document WHO/BS/395

³ National Institute for Medical Research, London, unpublished working document WHO/BS/386

upon the results of subcutaneous assays, thereby ensuring clinical continuity of dosage.

The Committee noted that the Conference had recommended that the new international standard should be available for use as a working standard, but also recognized that there were great difficulties in handling an amount of material large enough to serve as a working standard for international use without running the risk of inhomogeneity.¹ It recommended that the National Institute for Medical Research should try to obtain a large batch of material, part of which would be used as the international standard; the remainder could then be made available, in bulk, for the setting up of national working standards about which an *a priori* assumption of equivalence with the international standard could be made.

11. Human Menopausal Gonadotrophin

The Committee noted a request by the International Federation of Gynecology and Obstetrics for the establishment of an international standard for human menopausal gonadotrophin. A quantity of human menopausal gonadotrophin has been offered to the National Institute for Medical Research, London,² and when received it will be examined for its suitability as an international reference preparation.

12. Prolactin

The Committee noted the progress made by the National Institute for Medical Research, London,³ with the preparation of the proposed second international standard for prolactin.

13. Relaxin

The Committee noted a suggestion that an international standard for relaxin be established. It asked the National Institute for Medical Research, London, to assess the need for such a standard and to investigate whether suitable material could be obtained.

14. Insulin

The Committee noted that the statistical analysis of the results of the international collaborative assay of the proposed fourth international

¹ National Institute for Medical Research, London, unpublished working document WHO/BS/387

² National Institute for Medical Research, London, unpublished working document WHO/BS/392

³ National Institute for Medical Research, London, unpublished working document WHO/BS/405

standard for insulin is progressing,¹ and recommended that high priority need not be given to the time-consuming calculations involved, since adequate supplies of the present International Standard are still available.

MISCELLANEOUS

15. Dextran Sulfate

The Committee noted that satisfactory progress² is being made towards the establishment of an international standard for dextran sulfate.

16. Heparin

The Committee noted that satisfactory progress³ is being made towards the establishment of the second international standard for heparin.

17. Vitamin B₁₂

The Committee noted that the collaborative assay⁴ of the proposed international standard for vitamin B₁₂ is now complete,⁵ and that the standard will be established and the international unit defined as soon as agreement of the participants has been obtained.

The Committee recognized that, although vitamin B₁₂ can be fully characterized by chemical and physical means, the standard is needed for potency determinations in biological assays.

¹ National Institute for Medical Research, London, unpublished working document WHO/BS/388

² National Institute for Medical Research, London, unpublished working document WHO/BS/391

³ National Institute for Medical Research, London, unpublished working document WHO/BS/390

⁴ Participants : Biochemisches Laboratorium, Stockstadt am Main, Federal Republic of Germany ; N.V. Organon, Oss, Netherlands ; Statens Institut for Folkhälsan, Tomtebodavägen, Sweden ; Glaxo Laboratories, Greenford, United Kingdom ; National Institute for Medical Research, London, United Kingdom ; National Institute for Research in Dairying, Shinfield, Reading, United Kingdom ; Department of Scientific and Industrial Research, National Physical Laboratory, Teddington, United Kingdom ; Lederle Laboratories, American Cyanamid Company, Pearl River, N.Y., USA ; Merck & Co. (Analytical Department), Rahway, N.J., USA ; Chas. Pfizer & Co., Inc., New York, N.Y., USA ; E. R. Squibb & Sons (Product Specifications Department), New Brunswick, N.J., USA

⁵ National Institute for Medical Research, London, unpublished working document WHO/BS/389

18. Pyrogens

The Committee considered the report¹ on the study carried out by the National Institute for Medical Research, London, on a highly purified preparation of the O somatic antigen of *Shigella dysenteriae* which produces threshold pyrogenic responses in rabbits after intravenous injection of about 0.003 microgram per kilogram of body-weight. The Committee noted that, in the opinion of the participants in the previous collaborative assay, any of a number of pyrogenic substances of bacterial origin would be suitable as a reference preparation; it therefore authorized the National Institute for Medical Research to establish the new material as the International Reference Preparation of Pyrogen, without further collaborative studies.

IMMUNOLOGICAL

ANTIGENS

19. Pertussis Vaccine

The Committee noted that, in accordance with the authorization given in its tenth report,² the International Standard for Pertussis Vaccine has been established,³ and it defined the International Unit as the activity contained in 1.5 milligrams of the International Standard, this activity being equivalent to the protective unit used by the National Institutes of Health, Bethesda, Md., USA. The Committee emphasized that, in view of the fact that current assay methods yield inexact estimates, great care should be taken to avoid giving a false impression of accuracy when stating the immunizing potency of a vaccine.⁴

20. Typhoid Vaccines

The Committee noted the progress made⁵ towards obtaining two stable typhoid vaccines in quantities sufficient for one or two future field trials, for extensive laboratory studies, and for the possible establishment of an

¹ National Institute for Medical Research, London, unpublished working document WHO/BS/400

² *Wld Hlth Org. techn. Rep. Ser.*, 1957, **127**, 5

³ Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/408

⁴ Perry, W. L. M., Evans, D. G. & Standfast, A. F. B., unpublished working document WHO/BS/401

⁵ WHO Secretariat, unpublished working document WHO/BS/409

international standard for typhoid vaccine. The two lots will be prepared from the same strain of *Salmonella typhosa*; one will be acetone-dried, the other heat-killed and freeze-dried. The Committee, recognizing that it may be some time before a field trial is possible and considering that it is essential that the materials used in the field and for laboratory study be identical, recommended that the bulk of these preparations, intended for field trials, should not be handled differently from the portions set aside for use as standard preparations. The Committee asked the Statens Serum-institut, Copenhagen, to initiate laboratory studies of a variety of assay methods¹ as soon as the dried vaccines become available.

21. Cholera Vaccine

The Committee considered the problem of standardizing cholera vaccine.²

Most studies so far undertaken have indicated that vaccination against cholera confers a degree of protection in man; assay methods are in use which appear to give consistent results in some, but not in all, laboratories. Despite these facts, there is still no evidence that a vaccine which would be considered good on the basis of laboratory results would also be a good vaccine for prophylactic use in man. Such evidence can be obtained only by concurrent field and laboratory studies in which the potency of a number of available cholera vaccines, as evaluated by laboratory methods, is compared with their prophylactic efficacy in man.

The Committee therefore recommended that a careful and detailed survey be made in an endemic area in order to determine whether a combined field and laboratory investigation can be carried out on a sufficiently large scale.

For several years to come, the control of cholera vaccines will continue to depend on determination of the bacteriological and immunological characteristics of the seed cultures and on animal tests of the antigenic properties of the vaccine. The Committee noted that the Study Group on Recommended Requirements for Biological Substances might consider this aspect of the problem.³

22. Rabies Vaccine

The Committee noted that the proposed international standard for rabies vaccine is available in insufficient quantity and that its stability is

¹ Prigge, R. & Günther, O., unpublished working document WHO/BS/378

² Maaløe, O., unpublished working document WHO/BS/410

³ The report of this study group, which met in Geneva from 7 to 12 October 1957, has been issued as mimeographed document WHO/BS/IR/27.

questionable.¹ It recommended that a larger quantity of dried rabies vaccine be provided as soon as possible and that it be studied for stability and for suitability in assay.

23. Smallpox Vaccine

The Committee noted that arrangements had been made for a collaborative study of the behaviour, in various assay methods, of different freeze-dried smallpox vaccines, including the proposed international reference preparation.² It stressed the need for concurrent studies on the efficiency of the vaccines in producing specific skin lesions in man.

The Committee noted reports on an improved design for assay of the potency of smallpox vaccine by intracutaneous injection into rabbits,³ and on the use of tissue-culture methods for the determination of the virus content⁴ of such vaccines.

24. Swine Erysipelas Vaccine

The Committee noted that the type B swine erysipelas vaccine which has been examined by the Paul-Ehrlich-Institut, Frankfurt-on-Main, and the Central Veterinary Laboratory, Weybridge, while possessing the qualities required of an international standard, is not available in sufficient quantity for this purpose. The Committee therefore asked the Paul-Ehrlich-Institut to make available a larger quantity of similar material, with a view to establishing it as the International Standard for Swine Erysipelas Vaccine.

Preliminary studies⁵ in mice inoculated with type B vaccine have shown that satisfactory assays can be performed, provided *Erysipelothrix rhusiopathiae*, type B or N, is used for challenge. It is not known whether the proposed standard would be suitable in the assay of type A vaccines.

25. Poliomyelitis Vaccine

The Committee noted that efforts were being made in several countries to obtain a stable dried vaccine for use as a reference preparation. The determination of stability is complicated by the fact that existing tests cannot demonstrate small changes in potency unless large numbers of animals are employed. The Committee considered that this was a proper

¹ WHO Secretariat, unpublished working document WHO/BS/411

² Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/383

³ Fisek, N. H., unpublished working document WHO/BS/381

⁴ Cutchins, E. & Warren, J., unpublished working document WHO/BS/417

⁵ Prigge, R. & Eissner, G., unpublished working document WHO/BS/377

field for international collaboration since national resources might be inadequate for proper evaluation of the stability of dried vaccines.

It was understood that preliminary studies had suggested that certain dried preparations of poliomyelitis vaccine might be stable. The Statens Seruminstitut, Copenhagen, was asked to try to obtain supplies of such preparations and to compile a list of laboratories willing to take part in collaborative stability studies. It was agreed that at present the aim must be to obtain a trivalent standard vaccine in order to minimize the number of animals required in the determination of potency.

The Committee recommended that the stability study be regarded as a matter of urgency and not postponed until better assay methods for potency became available, since the development of improved methods of potency testing might be greatly facilitated by the provision of a stable standard.¹

26. Japanese B Encephalitis Vaccine

The Committee noted that the WHO Secretariat had investigated the need for an international reference preparation of Japanese B encephalitis vaccine,² and decided that it would be premature to attempt to standardize this vaccine.

27. Leptospirosis Vaccines

The Committee noted that the WHO Secretariat had investigated the need for international reference preparations of leptospirosis vaccines,³ and decided that there would be little advantage in setting up international reference preparations, in view of the fact that the antigenic composition of the vaccines used in different parts of the world varied according to the prevalent strains of *Leptospira*.

28. Cardiolipin

The Committee considered a report⁴ on the collaborative study⁵ of the material intended for replacement of the present International Reference Preparation of Cardiolipin, and noted that this material would be established as the third International Reference Preparation of Cardiolipin when the agreement of participants had been obtained.

¹ Prigge, R. & Bonin, O., unpublished working document WHO/BS/376, Annex 1

² WHO Secretariat, unpublished working document WHO/BS/412

³ WHO Secretariat, unpublished working document WHO/BS/413

⁴ Weis Bentzon, M. & Krag, P., unpublished working document WHO/BS/414

⁵ Participants: Serodiagnostic Department, Statens Seruminstitut, Copenhagen, Denmark; Laboratoire de Sérologie, Faculté de Médecine et de Pharmacie de l'Université de Bordeaux, Bordeaux, France; Venereal Disease Research Laboratory, Communicable Disease Center, Chamblee, Ga., USA; Division of Laboratories and Research, New York State Department of Health, Albany, N.Y., USA

ANTIBODIES

29. Gas Gangrene Antitoxin (*Vibrion Septique*)

The Committee noted that, in accordance with the authorization given in its tenth report,¹ the third International Standard for Gas Gangrene Antitoxin (*vibrion septique*) has been established² and that one International Unit is defined as the activity contained in 0.118 milligram of the International Standard.

30. Anti-Streptolysin O

The Committee noted that a quantity of human anti-streptolysin O of satisfactory stability had been obtained,³ and authorized the Statens Seruminstitut, Copenhagen, to establish this material as the International Standard for Anti-Streptolysin O when the collaborative study had been completed and agreement obtained from the participants. It decided that the International Unit should be equated to the unit used by the Statens Seruminstitut.

31. Blood-Typing Sera

The Committee noted that a collaborative study of albumin-potentiated anti-Rh₀ (anti-D) blood-typing serum has been completed.⁴ It authorized the Statens Seruminstitut, Copenhagen, in consultation with the International Blood Group Reference Laboratory, London, to establish this material as the International Standard for Albumin-Potentiated Anti-Rh₀ (anti-D) Blood-Typing Serum and to define the International Unit when agreement had been obtained from participants in the collaborative study.⁵

The Committee noted that there is a need for establishing international standards for agglutinating ("saline-agglutinating") anti-Rh₀ (anti-D)

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1957, **127**, 9

² Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/384

³ Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/402

⁴ International Blood Group Reference Laboratory, London, unpublished working document WHO/BS/407

⁵ Participants: Dr V. Friedenreich, Statens Seruminstitut, Copenhagen, Denmark; Dr J. Moullec, Centre national de Transfusion sanguine, Paris, France; Dr J. Gurevitch, Hadassah Medical School, The Hebrew University, Jerusalem, Israel; Dr J. J. van Loghem, Blood Transfusion Service, Amsterdam, Netherlands; Dr O. Hartmann, States Institutt for Folkehelse, Oslo, Norway; Professor B. Broman, Statens Rattskemiska Laboratorium, Stockholm, Sweden; Dr A. Hässig, Blood Donor Service, Berne, Switzerland; Dr F. Stratton, Regional Transfusion Centre, Manchester, United Kingdom; Dr J. Wallace, Blood Transfusion Service, Law Hospital, Carlisle, United Kingdom

blood-typing serum, as well as for anti-rh' (anti-C) and anti-rh'' (anti-E) blood-typing sera, but that continuing difficulties in obtaining adequate quantities of these sera to serve as standards have not been overcome.

32. Poliomyelitis Sera

The Committee noted that the Statens Seruminstitut, Copenhagen, had obtained supplies, sufficient for a collaborative laboratory study, of freeze-dried preparations of human, monkey, guinea-pig, and horse immune sera.¹ Comparative titrations of these sera in terms of the proposed international reference preparations will be made in order to determine whether the international reference preparations are suitable for use in tests of the virus-neutralizing potency of sera from different animals. The Committee authorized the Statens Seruminstitut, with the agreement of the participants in the collaborative study, to establish the International Reference Preparations of Poliomyelitis Sera of Types 1, 2, and 3, and to assign unitages to them. The Committee emphasized the urgent need for these reference sera.

33. Typhoid and Paratyphoid Agglutinating Sera

The Committee noted that the opinions expressed by the participants in the collaborative assay of the proposed international reference sera for the Widal test were divergent as to the value of this test as well as to the usefulness of the sera.² It was therefore decided that these sera would be held by the Statens Seruminstitut, Copenhagen, as Author's Preparations.

34. Syphilitic Human Serum

The Committee considered the final report³ from the WHO Serological Reference Centre, Copenhagen, on the results of the collaborative investigation of the proposed international reference preparation of syphilitic human serum, and noted that this serum, which is a pool of reactive human sera, was of satisfactory stability and had proved useful for the detection of differences in sensitivity between assay methods.

While this investigation was in progress, a national reference preparation of syphilitic human serum and a national unit were established by the Paul-Ehrlich-Institut, Frankfurt-on-Main.⁴ Comparative studies had

¹ Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/385

² WHO Secretariat, unpublished working document WHO/BS/415

³ Krag, P. & Weis Bentzon, M., unpublished working document WHO/BS/380 Rev.1

⁴ Prigge, R. & Heymann, G., unpublished working document WHO/BS/379

revealed that the potency of the German reference serum in terms of the proposed international reference serum was higher when assayed by complement-fixation methods than when assayed by flocculation methods. It was decided that the equation of the international unit to the existing German unit should be based on the results of complement-fixation tests, such as had been carried out in the Paul-Ehrlich-Institut. The Committee authorized the Statens Seruminstitut, Copenhagen, to establish the International Reference Preparation of Syphilitic Human Serum and to define its unitage when agreement had been obtained from the participants in the international collaborative study.¹

35. Leptospirosis Sera

The Committee considered that leptospirosis reference sera are required mainly for typing purposes, and noted that such sera are now being prepared by WHO/FAO Leptospirosis Reference Laboratories.² The Committee considered that there is no need at the present time for international standard sera for assay purposes.

36. Yellow Fever Immune Serum

The Committee noted that the Expert Committee on Yellow Fever Vaccine has recommended the establishment of international reference preparations of yellow fever immune serum and of serum non-immune to yellow fever virus.³ It noted that steps have been taken to produce sufficient quantities of immune serum for the establishment of an international reference preparation,⁴ and asked the Statens Seruminstitut, Copenhagen, in consultation with the West African Council for Medical Research, Lagos, Nigeria, to arrange a collaborative examination of this material for its suitability in mouse protection assays.

The Committee considered that it would not be appropriate to establish an international reference preparation of non-immune (normal human) serum. It noted that, since normal human serum is used as a reagent in

¹ Participants : Laboratory of Hygiene, Department of National Health and Welfare, Ottawa, Canada ; Serodiagnostic Department, Statens Seruminstitut, Copenhagen, Denmark ; Laboratoire de Sérologie, Faculté de Médecine et de Pharmacie de l'Université de Bordeaux, Bordeaux, France ; School of Tropical Medicine, Calcutta, India ; Gades Institutt, University of Bergen, Bergen, Norway ; Venereal Disease Research Laboratory, Communicable Disease Center, Chamblee, Ga., USA ; Division of Laboratories and Research, New York State Department of Health, Albany, N.Y., USA ; Bellevue Medical Center, New York University, New York, N.Y., USA

² WHO Secretariat, unpublished working document WHO/BS/413

³ *Wld Hlth Org. techn. Rep. Ser.*, 1957, 136, 9

⁴ WHO Secretariat, unpublished working document WHO/BS/416

the assay of yellow fever immune serum, the Statens Seruminstitut would hold and distribute such normal serum.

GENERAL

37. Recommended Requirements for Biological Substances

The Committee noted that WHO will convene a study group this year which will consider the problem of making recommendations on assay methods and on requirements for biological substances.¹ The Committee welcomed the fact that an attempt is now being made to deal with these complex matters and agreed that the Expert Committee on Biological Standardization could offer assistance or comments at a later stage, when the study group has drafted definitive proposals.

38. Stability of Biological Standards

The Committee noted a report² on the stability of preparations of cardiolipin and lecithins. It also noted³ that the International Standard for Tetanus Toxoid is stable after reconstitution if held at about 5°C.

39. List of International Biological Standards

The Committee was of the opinion that the list of International Biological Standards and Reference Preparations, included as an annex to the tenth report of the Committee,⁴ had enhanced the value of this report. The bibliographical information contained in the list facilitates access to available information about international standards. The Committee asked the WHO Secretariat to prepare an up-to-date list as an annex to the present report (see Annex, page 19).

The Committee recognized that the names of several international standards no longer conform to accepted international nomenclature and asked the WHO Secretariat to review the present names and to propose changes which would bring them into agreement with modern usage.

¹ The report of this study group, which met in Geneva from 7 to 12 October 1957, has been issued as mimeographed document WHO/BS/IR/27.

² WHO Serological Reference Centre & Statistical Department, Statens Seruminstitut, Copenhagen, unpublished working document WHO/VDT/Sero/65

³ Fisek, N. H., unpublished working document WHO/BS/382

⁴ *Wld Hlth Org. techn. Rep. Ser.*, 1957, 127, 21

Annex

**I. INTERNATIONAL BIOLOGICAL STANDARDS
AND REFERENCE PREPARATIONS**

1958

The primary purpose underlying the establishment of International Biological Standards and Reference Preparations is to provide a means of ensuring uniformity throughout the world in the designation of potency of preparations which are used in the prophylaxis, therapy, or diagnosis of human and animal disease, and which cannot be characterized adequately by chemical and physical means. A secondary purpose in the provision of International Biological Standards is the facilitation of research work out of which clinical application may arise.

The International Laboratories for Biological Standards at the Statens Seruminstitut, Copenhagen, Denmark, and at the National Institute for Medical Research, London, England, are custodians of all International Biological Standards and Reference Preparations, and distribute samples of these preparations, free of charge, to national laboratories for biological standards in all countries.

A. IMMUNOLOGICAL

Held by the International Laboratory for Biological Standards,

Substances	International Unit of present standard (mg)	Form in which dispensed
ANTIGENS		
Old tuberculin	0.0100	Ampoules containing 2 ml of Old tuberculin (100 000 International Units (I.U.) per ml)
Purified protein derivative of mammalian tuberculin	0.0000280	Ampoules containing 10 mg of PPD plus 4 mg of salts (500 000 I.U. per ampoule)
Purified protein derivative of avian tuberculin	0.0000726	Ampoules containing 10 mg of PPD plus 26.3 mg of salts (500 000 I.U. per ampoule)
Tetanus toxoid	0.03	Ampoules containing 25 mg (420 Lf) of alcohol purified tetanus toxoid plus glycine (833 I.U. per ampoule)
Diphtheria toxoid, plain	0.50	Ampoules containing 50 mg (1730 Lf) of alcohol purified diphtheria toxoid plus glycine (100 I.U. per ampoule)
Diphtheria toxoid, adsorbed	0.75	Ampoules containing 80 mg (50 Lf) of diphtheria toxoid adsorbed to aluminium hydroxide, dried, plus lactose (107 I.U. per ampoule)
Schick test toxin (diphtheria)	0.0042	Ampoules containing 0.005 mg (0.9 Lf) of purified diphtheria toxin plus 1 mg of bovine albumin and 2.74 mg of phosphate buffer salts (900 I.U. per ampoule)
Pertussis vaccine	1.5	Ampoules containing 52 mg of dried vaccine (34.7 I.U. per ampoule)
Cholera antigen (Inaba)	—	Ampoules containing approximately 100 mg of dried antigen

SUBSTANCES

Statens Seruminstitut, Copenhagen, Denmark

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Standard 1931 (0.0100 mg) 2nd Standard 1935	<i>Off. Rec. Wld Hlth Org.</i> , 1948, 11 , 10; <i>Bull. Wld Hlth Org.</i> , 1952, 7 , 171; 1954, 10 , 989; 1955, 12 , 179; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 475, 514; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 257, 354; WHO/BS 3, 16, 28, 64, 120
1st Standard 1951	<i>Bull. Wld Hlth Org.</i> , 1952, 7 , 171; 1954, 10 , 989; 1955, 12 , 179; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 6; WHO/BS 3, 16, 28, 64, 106, 120, 127, 173, 181
1st Standard 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96 , 11; WHO/BS 126, 181, 227, 293, 293 Add. 1 and 2
1st Standard 1951	<i>Bull. Wld Hlth Org.</i> , 1953, 9 , 837, 843; 1955, 12 , 761; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 5; WHO/BS 25, 37, 48, 68, 83, 92, 125, 192, 194, 214, 382
1st Standard 1951	<i>Bull. Wld Hlth Org.</i> , 1949, 2 , 49; 1953, 9 , 829, 843; 1955, 12 , 751; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 4; 1953, 61 , 1; WHO/BS 4, 13, 19, 32, 48, 68, 79, 83, 86, 102, 108, 113, 191, 193, 214, 215, 248, 288, 330, 331
1st Standard 1955	<i>Bull. Wld Hlth Org.</i> , 1949, 2 , 49; 1953, 9 , 829, 843; 1954, 10 , 951, 983; 1955, 12 , 751; 1955, 13 , 473; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, 61 , 1; 1956, 108 , 8; WHO/BS 4, 13, 19, 32, 48, 68, 79, 83, 86, 102, 108, 113, 191, 193, 214, 215, 248, 288, 330, 331
1st Standard 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96 , 7; WHO/BS 229, 247, 274, 275, 275 Add. 1 and 2
1st Standard 1957	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 127 , 5; 1958, 147 , 11; WHO/BS 5, 54, 62, 81, 88, 96, 123, 203, 216, 251, 259, 282, 287, 302, 338, 401, 408
1st Reference Preparation 1953	<i>Bull. Wld Hlth Org.</i> , 1955, 12 , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 7; WHO/BS 52, 130, 167, 222, 255

Substances	International Unit of present standard (mg)	Form in which dispensed
Antigens (cont.)		
Cholera antigen (Ogawa)	—	Ampoules containing approximately 100 mg of dried antigen
Cholera vaccine (Inaba)	—	Ampoules containing 20 mg of dried vaccine (1.6×10^{10} organisms per ampoule)
Cholera vaccine (Ogawa)	—	Ampoules containing 20 mg of dried vaccine (1.6×10^{10} organisms per ampoule)
Cardiolipin	—	Bottles containing 10 ml of a solution of purified sodium cardiolipin in ethanol (8.57 mg of cardiolipin per ml)
Lecithin (beef heart)	—	Bottles containing 30 ml of a solution of purified beef heart lecithin in ethanol (30.3 mg of lecithin per ml)
Lecithin (egg)	—	Bottles containing 30 ml of a solution of purified egg lecithin in ethanol (33.7 mg of lecithin per ml)
ANTIBODIES		
Tetanus antitoxin	0.3094	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (5 I.U. per ml)
Diphtheria antitoxin	0.0628	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (10 I.U. per ml)

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<i>1st Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1955, 12 , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 7; WHO/BS 52, 130, 167, 222, 255
<i>1st Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1950, 3 , 43; 1955, 12 , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 7; WHO/BS 23, 36, 41, 52, 69, 82, 87, 87 Add.1, 107, 130, 222, 255, 342, 410
<i>1st Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1950, 3 , 43; 1955, 12 , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 7; WHO/BS 23, 36, 41, 52, 69, 82, 87, 87 Add.1, 107, 130, 222, 255, 342, 410
1st Reference Preparation 1951 <i>2nd Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1951, 4 , 151; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 8; <i>Cardiolipin antigens</i> , 1955 (WHO Monograph No. 6); WHO/BS 72, 117, 238, 278, 278 Add.1, 305, 414
1st Reference Preparation 1951 <i>2nd Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1951, 4 , 151; 1955, 13 , 323; 1956, 14 , 567, 577; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 8; <i>Cardiolipin antigens</i> , 1955 (WHO Monograph No. 6); WHO/BS 72, 238, 278, 278 Add.1, 305
1st Reference Preparation 1951 <i>2nd Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1951, 4 , 151; 1955, 13 , 323; 1956, 14 , 567, 577; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 8; <i>Cardiolipin antigens</i> , 1955 (WHO Monograph No. 6); WHO/BS 72, 238, 278, 278 Add.1, 305
<i>1st Standard</i> 1928	<i>Bull. Wld Hlth Org.</i> , 1949, 2 , 59; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1950, 2 , 5; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 506; 1936, 5 , 702; 1938, 7 , 684, 713, 733, 739, 770, 776, 783; 1940/41, 9 , 447, 452; 1942/43, 10 , 104, 113; 1945/46, 12 , 14; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 210, 338; WHO/BS 37, 44
<i>1st Standard</i> 1922	<i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 505; 1938, 7 , 711, 853; 1945/46, 12 , 12; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 208, 324; WHO/BS 68, 77

Substances	International Unit of present standard (mg)	Form in which dispensed
Antibodies (cont.)		
Diphtheria antitoxin for flocculation test	—	Bottles containing 10 ml of a dilution of hyperimmune horse serum in phosphate buffered saline, containing 0.01% w/v of thiomersal (500 I.U. per ml)
Antidysentery serum (Shiga)	0.05	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (200 I.U. per ml)
Gas gangrene antitoxin (perfringens) (<i>Clostridium welchii</i> type A antitoxin)	0.1132	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (20 I.U. per ml)
<i>Clostridium welchii</i> (perfringens) type B antitoxin	0.0137	Ampoules containing 68.5 mg of dried hyperimmune horse serum (5000 I.U. per ampoule)
<i>Clostridium welchii</i> (perfringens) type D antitoxin	0.0657	Ampoules containing 65.7 mg of dried hyperimmune horse serum (1000 I.U. per ampoule)
Gas-gangrene antitoxin (<i>vibrio septique</i>)	0.118	Ampoules containing 59 mg of a dried 1:3 dilution of hyperimmune horse serum in phosphate buffered saline (500 I.U. per ampoule)
Gas-gangrene antitoxin (oedematiens)	0.1135	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (20 I.U. per ml)
Gas-gangrene antitoxin (histolyticus)	0.2	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (20 I.U. per ml)
Gas-gangrene antitoxin (Sordelli)	0.1334	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (20 I.U. per ml)

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Standard 1935 2nd Standard 1938 3rd Standard 1945 4th Standard 1956	<i>Bull. Wld Hlth Org.</i> , 1947/48, 1 , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1936, 5 , 577, 695; 1938, 7 , 712, 859; 1945/46, 12 , 12; WHO/BS 318, 359
1st Standard 1928	<i>Bull. Wld Hlth Org.</i> , 1951, 4 , 111; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 508; 1945/46, 12 , 20
1st Standard 1931 (0.3220 mg) 2nd Standard 1935 (0.2660 mg) 3rd Standard 1943 (0.3477 mg) 4th Standard 1953	<i>Bull. Wld Hlth Org.</i> , 1947/48, 1 , 9; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108 , 7; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 510; 1938, 7 , 695, 802, 818; 1939, 8 , 797; 1942/43, 10 , 97; 1945/46, 12 , 22; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 209, 332; WHO/BS 281
1st Reference Preparation 1954	<i>Bull. Wld Hlth Org.</i> , 1956, 14 , 557; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96 , 6; WHO/BS 281, 283, 298, 303, 343
1st Reference Preparation 1954	<i>Bull. Wld Hlth Org.</i> , 1956, 14 , 557; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96 , 6; WHO/BS 281, 283, 298, 303, 343
1st Standard 1934 (0.2377 mg) 2nd Standard 1947 (0.0974 mg) 3rd Standard 1957	<i>Bull. Wld Hlth Org.</i> , 1947/48, 1 , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 1, 13, 511; 1938, 7 , 699, 815; 1942/43, 10 , 97; 1945/46, 12 , 26; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 210, 334; WHO/BS 318, 367, 384
1st Standard 1934 (0.2681 mg) 2nd Standard 1952	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, 68 , 11; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 3, 42, 511; 1942/43, 10 , 97; 1945/46, 12 , 26; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 209, 328
1st Standard 1935 (0.3575 mg) 2nd Standard 1951	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 17; <i>Bull. Hlth Org. L. o. N.</i> , 1936, 5 , 576, 659; 1945/46, 12 , 21; WHO/BS 91, 131
1st Standard 1938	<i>Bull. Hlth Org. L. o. N.</i> , 1938, 7 , 698, 807; 1939, 8 , 856; 1945/46, 12 , 21

Substances	International Unit of present standard (mg)	Form in which dispensed
Antibodies (cont.)		
Staphylococcus α antitoxin	0.2376	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in phosphate buffered saline, containing 0.01% w/v of thiomersal (20 I.U. per ml)
Scarlet fever streptococcus antitoxin	0.049	Ampoules containing 490 mg of dried hyperimmune horse serum (10 000 I.U. per ampoule)
Swine erysipelas serum (anti-N)	0.14	Ampoules containing 87.9 mg of dried hyperimmune horse serum (628 I.U. per ampoule)
Antipneumococcus serum (type 1)	0.0886	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (200 I.U. per ml)
Antipneumococcus serum (type 2)	0.0894	Bottles containing 10 ml of a solution of dried hyperimmune horse serum in saline, containing 66% v/v of glycerol (200 I.U. per ml)
Anti- <i>Brucella abortus</i> serum	0.091	Ampoules containing 91 mg of dried bovine serum (1000 I.U. per ampoule)
Anti-Q-fever serum	0.1017	Ampoules containing 101.7 mg of dried bovine serum (1000 I.U. per ampoule)
Antirabies serum	1.0	Ampoules containing 86.6 mg of dried hyperimmune horse serum (86.6 I.U. per ampoule)
Anti-A blood-typing serum	0.3465	Ampoules containing 88.7 mg of dried human serum (256 I.U. per ampoule)
Anti-B blood-typing serum	0.3520	Ampoules containing 90.1 mg of dried human serum (256 I.U. per ampoule)
Antityphoid serum (provisional)	—	Ampoules containing 5 ml of hyperimmune horse serum, dried

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Standard 1934 (0.5000 mg) 2nd Standard 1938	<i>Bull. Hlth Org. L. o. N.</i> , 1935, 4, 6, 68, 514; 1938, 7, 702, 845; 1945, 46, 12, 32
1st Standard 1952	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, 68, 11; WHO/BS 38, 60, 84, 150, 225
1st Standard 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96, 10; WHO/BS 246, 297, 300
1st Standard 1934	<i>Bull. Hlth Org. L. o. N.</i> , 1935, 4, 4, 48, 512
1st Standard 1934	<i>Bull. Hlth Org. L. o. N.</i> , 1935, 4, 5, 65, 512
1st Standard 1952	<i>Bull. Wld Hlth Org.</i> , 1950, 3, 309; 1953, 9, 385, 399; 1954, 10, 927; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, 68, 9; WHO/BS 128, 162, 223, 224, 228
1st Standard 1953	<i>Bull. Wld Hlth Org.</i> , 1955, 13, 807; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86, 10; WHO/BS 177, 230, 276, 276 Add.1, 296
1st Standard 1955	<i>Bull. Wld Hlth Org.</i> , 1954, 10, 781; 1955, 13, 747, 773; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108, 11; <i>Laboratory techniques in rabies</i> , 1954 (WHO Monograph No. 23); WHO/BS 231, 277, 277 Add.1, 294, 295, 329, 329 Add.1, 375
1st Standard 1950	<i>Bull. Wld Hlth Org.</i> , 1950, 3, 301; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, 36, 10; WHO/BS 42, 49, 74
1st Standard 1950	<i>Bull. Wld Hlth Org.</i> , 1950, 3, 301; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, 36, 10; WHO/BS 42, 49, 74
1st Standard 1952	<i>Bull. Wld Hlth Org.</i> , 1954, 10, 911; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, 68, 10; WHO/BS 182, 226

Substances	International Unit of present standard (mg)	Form in which dispensed
Antibodies (cont.)		
Cholera agglutinating serum (Inaba)	—	Ampoules containing 0.6 ml of monospecific serum
Cholera agglutinating serum (Ogawa)	—	Ampoules containing 0.6 ml of monospecific serum
MISCELLANEOUS		
Opacity reference preparation	—	Ampoules containing 20 ml of a suspension of Pyrex-glass particles in water (10 I.U. of opacity per ml)

B. PHARMACOLOGICAL

Held by the International Laboratory for Biological Standards,

Substances	International Unit of present Standard (mg)	Form in which dispensed
ANTIBIOTICS		
Penicillin	0.0005988	Ampoules containing 30 mg of sodium benzylpenicillin (1670 I.U. per mg)
Penicillin K	—	Ampoules containing 20 mg of 89.9% pure sodium <i>n</i> -heptylpenicillin, with 9.6% penicillin dihydro F and 0.5% penicillin F
Phenoxymethylpenicillin	0.00059	Ampoules containing 75 mg of phenoxymethylpenicillin (1695 I.U. per mg)
Streptomycin	0.001282	Ampoules containing 25 mg of streptomycin sulfate (780 I.U. per mg)

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<i>1st Reference Preparation 1953</i>	<i>Bull. Wld Hlth Org.</i> , 1955, 12 , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 7; WHO/BS 40, 98, 130, 167, 222, 255
<i>1st Reference Preparation 1953</i>	<i>Bull. Wld Hlth Org.</i> , 1955, 12 , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 7; WHO/BS 40, 98, 130, 167, 222, 255
<i>1st Reference Preparation 1953</i>	<i>Bull. Wld Hlth Org.</i> , 1955, 12 , 769; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 14; WHO/BS 124, 172, 198, 256

SUBSTANCES

National Institute for Medical Research, London, England

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<i>1st Standard 1944 (0.0006000 mg)</i> <i>2nd Standard 1952</i>	<i>Bull. Wld Hlth Org.</i> , 1953, 9 , 15; <i>Bull. Hlth Org. L. o. N.</i> , 1945/46, 12 , 181; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 23, 277; WHO/BS 10, 15, 67, 94, 121, 170, 349 Rev.1, 404
<i>1st Reference Preparation 1951</i>	<i>Bull. Wld Hlth Org.</i> , 1954, 10 , 895; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56 , 11; WHO/BS 132
<i>1st Standard 1957</i>	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 127 , 14; 1958, 147 , 7; WHO/BS 399
<i>1st Standard 1950</i>	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, 36 , 9; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 198, 279; WHO/BS 11, 67, 76, 369, 393

Substances	International Unit of present standard (mg)	Form in which dispensed
Antibiotics (cont.)		
Dihydrostreptomycin	0.001316	Ampoules containing 70 mg of dihydrostreptomycin sulfate (760 I.U. per mg)
Bacitracin	0.0182	Ampoules containing 50 mg of bacitracin (55 I.U. per mg)
Tetracycline	0.00101	Ampoules containing 200 mg of tetracycline hydrochloride (990 I.U. per mg)
Chlortetracycline	0.001	Ampoules containing 60 mg of chlortetracycline hydrochloride (1000 I.U. per mg)
Oxytetracycline	0.00111	Ampoules containing 100 mg of oxytetracycline base dihydrate (900 I.U. per mg)
Erythromycin	0.001053	Ampoules containing 200 mg of erythromycin dihydrate (950 I.U. per mg)
Polymyxin B	0.000127	Ampoules containing 19 mg of purified polymyxin B sulfate (7874 I.U. per mg)
HORMONES		
Oxytocic, vasopressor and anti-diuretic substances (previously named: posterior pituitary lobe)	0.5	Ampoules containing 30 mg of acetone dried powder of whole posterior ox pituitary gland (2 oxytocic, 2 vasopressor, and 2 antidiuretic I.U. per mg)
Prolactin	0.1	Ampoules containing ten 10-mg tablets of dried active principle from anterior ox pituitary gland (approximately 100 I.U. per tablet)
Corticotrophin (previously named: adrenocorticotrophic hormone)	0.88	Ampoules containing 28 mg of crude corticotrophin from anterior pig pituitary gland (1.14 I.U. per mg)

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<i>Ist Standard</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1954, 10 , 901; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 15; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 89, 277; WHO/BS 122, 146, 241, 242
<i>Ist Standard</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1953, 9 , 861; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 15; WHO/BS 122, 144, 236
<i>Ist Standard</i> 1957	<i>Bull. Wld Hlth Org.</i> , 1957, 17 , 521; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 127 , 13; 1958, 147 , 6; WHO/BS 323, 370, 396, 396 Annex 1
<i>Ist Standard</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1953, 9 , 851; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, 86 , 14; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 37, 276; WHO/BS 122, 143, 245
<i>Ist Standard</i> 1955	<i>Bull. Wld Hlth Org.</i> , 1955, 13 , 903; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108 , 14; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 179; WHO/BS 122, 145, 211, 285, 307
<i>Ist Standard</i> 1957	<i>Bull. Wld Hlth Org.</i> , 1957, 17 , 527; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 127 , 13; 1958, 147 , 6; WHO/BS 322, 368, 397, 397 Annex 1
<i>Ist Standard</i> 1955	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108 , 14; WHO/BS 263, 326
<i>Ist Standard</i> 1925 (0.5 mg) <i>2nd Standard</i> 1942 (0.5 mg) <i>3rd Standard</i> 1957	<i>Bull. Wld Hlth Org.</i> , 1947/48, 1 , 9; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 127 , 15; 1958, 147 , 8; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 530; 1936, 5 , 572; 1942/43, 10 , 89; 1945/46, 12 , 42; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 191, 342; WHO/BS 351, 352, 395
<i>Ist Standard</i> 1939	<i>Bull. Hlth Org. L. o. N.</i> , 1939, 8 , 901; 1942/43, 10 , 96; 1945/46, 12 , 62; WHO/BS 208, 310, 350, 405
<i>Ist Standard</i> 1950 (1.00 mg) <i>2nd Standard</i> 1955	<i>Bull. Wld Hlth Org.</i> , 1956, 14 , 543; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, 36 , 7; WHO/BS 85, 156, 158, 249, 262, 308, 356, 386, 387

Substances	International Unit of present standard (mg)	Form in which dispensed
Hormones (cont.)		
Thyrotrophin	13.5	Ampoules containing ten 20-mg tablets of a blend of 1 part purified thyrotrophin from anterior ox pituitary gland and 19 parts lactose (approximately 1.48 I.U. per tablet)
Growth hormone	1.0	Ampoules containing 30 mg of dried active principle from anterior pituitary gland (1 I.U. per mg)
Serum gonadotrophin	0.25	Ampoules containing ten 25-mg tablets of dried active principle from serum of pregnant mares, diluted with lactose (approximately 100 I.U. per tablet)
Chorionic gonadotrophin	0.1	Ampoules containing twenty-five 10-mg tablets of dried active principle from human urine of pregnancy, diluted with lactose (approximately 100 I.U. per tablet)
Insulin	0.04082	Ampoules containing 20 mg of purified insulin, largely from the ox (24.5 I.U. per mg)
Heparin	0.0077	Ampoules containing 50 mg of sodium salt of purified active principle from bovine tissue (130 I.U. per mg)
VITAMINS, ENZYMES		
Vitamin D ₃	0.000025	Bottles containing 10 g of a solution of vitamin D ₃ in vegetable oil (1000 I.U. per g)
Hyaluronidase	0.1	Ampoules containing ten 20-mg tablets of dried bovine testicular hyaluronidase diluted with lactose (approximately 200 I.U. per tablet)
MISCELLANEOUS		
Digitalis	76.0	Ampoules containing 2500 mg of dry powdered leaves of <i>Digitalis purpurea</i> (0.01316 I.U. per mg)

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<i>1st Standard</i> 1954	<i>Bull. Wld Hlth Org.</i> , 1955, 13 , 917; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96 , 14; 1956, 108 , 16; WHO/BS 155, 158, 210, 284, 309
<i>1st Standard</i> 1955	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108 , 16; WHO/BS 140, 158, 250, 320
<i>1st Standard</i> 1939	<i>Bull. Hlth Org. L. o. N.</i> , 1939, 8 , 887, 898; 1945/46, 12 , 60; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 98, 263
<i>1st Standard</i> 1939	<i>Bull. Hlth Org. L. o. N.</i> , 1939, 8 , 862, 884; 1945/46, 12 , 60; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 98, 261; WHO/BS 93, 141
1st Standard 1925 (0.12500 mg) 2nd Standard 1935 (0.04550 mg) <i>3rd Standard</i> 1952	<i>Bull. Wld Hlth Org.</i> , 1952, 7 , 445; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 525; 1936, 5 , 575, 584; 1945/46, 12 , 44; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 130, 264; WHO/BS 89, 116, 119, 137, 138, 204, 205, 267, 311, 357, 388
<i>1st Standard</i> 1942	<i>Bull. Wld Hlth Org.</i> , 1947/48, 1 , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1942/43, 10 , 144, 151; 1945/46, 12 , 46; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 104, 341; 1955, Vol. II, 126; WHO/BS 353, 390
1st Standard 1931 (0.1 mg) [Irradiated ergosterol] <i>2nd Standard</i> 1949	<i>Bull. Wld Hlth Org.</i> , 1954, 10 , 875; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1950, 3 , 7; <i>Bull. Hlth Org. L. o. N.</i> , 1940/41, 9 , 425; 1945/46, 12 , 54; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 369; WHO/BS 8
<i>1st Standard</i> 1955	<i>Bull. Wld Hlth Org.</i> , 1957, 16 , 291; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108 , 18; WHO/BS 78, 135, 160, 163, 232, 271, 306
1st Standard 1926 (100.0 mg) 2nd Standard 1936 (80.0 mg) <i>3rd Standard</i> 1949	<i>Bull. Wld Hlth Org.</i> , 1950, 2 , 655; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4 , 522; 1936, 5 , 574; 1945/46, 12 , 41; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 93, 357; WHO/BS 33, 51

Substances	International Unit of present standard (mg)	Form in which dispensed
Miscellaneous (cont.)		
Neoarsphenamine	—	Ampoules containing 300 mg of neoarsphenamine
Sulfarsphenamine	—	Ampoules containing 300 mg of sulfarsphenamine
Oxophenarsine	—	Sets of three ampoules containing (a) 120 mg of oxophenarsine hydrochloride, (b) 100 mg of anhydrous sodium carbonate, and (c) 500 mg of anhydrous sucrose
Mel B	—	Ampoules containing 100 mg of melaminyl-4-phenylarseno-dithioglycerol
MSb	—	Ampoules containing 500 mg of sodium <i>p</i> -melaminylphenylstibonate polymer
Dimercaprol	—	Ampoules containing 2 ml of 2,3-dimercaptopropanol
Protamine	—	Ampoules containing 60 mg of protamine

Years of establishment of standards (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Standard 1925 2nd Standard 1935 3rd Standard 1940	<i>Bull. Wld Hlth Org.</i> , 1947/48, 1, 9; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4, 528; 1936, 5, 573; 1945/46, 12, 40; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 147, 347; WHO/BS 26
1st Standard 1925 2nd Standard 1936 3rd Standard 1951	<i>Bull. Wld Hlth Org.</i> , 1951, 4, 563; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56, 17; <i>Bull. Hlth Org. L. o. N.</i> , 1935, 4, 528; 1936, 5, 573; 1945/46, 12, 40; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 234, 351; WHO/BS 110
1st Standard 1951	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, 56, 7; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 176; WHO/BS 133, 174
1st Reference Preparation 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96, 16; WHO/BS 134, 148, 202, 273
1st Reference Preparation 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96, 16; WHO/BS 134, 148, 202, 273
1st Standard 1952	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, 68, 18; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 91, 122, 280; WHO/BS 159
1st Reference Preparation 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, 96, 14; WHO/BS 261

II. PROPOSED INTERNATIONAL BIOLOGICAL STANDARDS

International Standards or Reference Preparations have been proposed for the following substances. The international collaborative studies of those listed under C and L are now so far advanced that the International Laboratories for Biological Standards at the Statens Serum Institut, Copenhagen, and at the National Institute for Medical Research, London, respectively, have been authorized to establish these standards and to define the international units. Preparations of those listed under S are at present being studied for their stability and suitability to serve as international standards or reference preparations, whereas preliminary efforts are being made for obtaining and examining suitable quantities of the substances listed under P for international standardization purposes.

Substances	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<p style="text-align: center;">C</p> <p>Syphilitic human serum</p> <p>Anti-poliomyelitis serum (type 1) Anti-poliomyelitis serum (type 2) Anti-poliomyelitis serum (type 3) Anti-Rh₀ (anti-D) albumin-potentiated blood-typing serum</p> <p>Antistreptolysin O Cardiolipin (3rd Int. Ref. Prep.)</p>	<p>WHO/BS 239, 289 Rev.1, 304, 341, 379, 380 Rev.1</p> <p>WHO/BS 313, 361, 363, 385</p> <p><i>Wld Hlth Org. techn. Rep. Ser.</i>, 1950, 2, 12; WHO/BS 46, 165, 213, 328, 366, 407</p> <p>WHO/BS 402 WHO/BS 360, 414</p>
<p style="text-align: center;">L</p> <p>Dextran sulfate</p> <p>Vitamin B₁₂</p> <p>Pyrogen</p> <p>Prolactin (2nd Int. Standard) Insulin (4th Int. Standard) Heparin (2nd Int. Standard) Streptomycin (2nd Int. Standard)</p>	<p><i>Wld Hlth Org. techn. Rep. Ser.</i>, 1953, 68, 18; 1955, 96, 15; 1956, 108, 18; WHO/BS 151, 207, 220, 270, 354, 391</p> <p>WHO/BS 34, 58, 61, 118, 142, 164, 209, 268, 355, 389</p> <p>WHO/BS 90, 147, 206, 264, 312, 365, 400</p> <p>WHO/BS 350, 405 WHO/BS 357, 388 WHO/BS 353, 390 WHO/BS 369, 393</p>

Substances	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
<p style="text-align: center;">S</p> Smallpox vaccine Swine erysipelas vaccine Egg lecithin (3rd Int. Ref. Prep.) Neomycin Procaine benzylpenicillin in oil with aluminium monostearate Human menopausal gonadotrophin	WHO/BS 14, 73, 105, 371, 381, 383, 417 WHO/BS 344, 377 WHO/BS 360 WHO/BS 398 WHO/BS 324, 349 Rev.1, 358 Rev.1, 403, 404 WHO/BS 392
<p style="text-align: center;">P</p> Rabies vaccine Typhoid vaccine Poliomyelitis vaccine Anti-yellow-fever serum <i>Bothrops</i> antivenin } <i>Naja</i> antivenin } Anti-rh' (anti-C) blood-typing serum } Anti-rh'' (anti-E) blood-typing serum } Corticotrophin (3rd Int. Standard) Nystatin Oleandomycin	WHO/BS 372, 411, 411 Annex 1 WHO/BS 217, 291, 301, 340, 378, 409 WHO/BS 235, 260, 321, 376, 376 Annex 1 WHO/BS 416 WHO/BS 316, 317, 333, 334, 364, 373 WHO/BS 46, 165, 366, 407 WHO/BS 356, 386, 387

III. AUTHOR'S PREPARATIONS

This class of substances was introduced in order to meet situations in which the pressure of more urgent work may make it impossible to create international standards without considerable delay, but in which further research work may be facilitated by the provision of common points of reference. The Expert Committees on Biological Standardization can take no responsibility for the authenticity or stability of any Author's Preparations, but the storage and distribution of these preparations will be undertaken under the same conditions as for the International Standards, as a service to research workers. (*Wld Hlth Org. techn. Rep. Ser.*, 1955, 96, 18)

The following hyperimmune horse sera were prepared by the late Dr A. Felix to serve as reference preparations for use in the serodiagnosis of typhoid and paratyphoid infections. Samples of these Author's Preparations are available on request from the International Laboratory for

Biological Standards, Statens Serum Institut, Copenhagen, Denmark. (References: *Bull. Wld Hlth Org.*, 1950, **2**, 643; 1954, **10**, 919; *Wld Hlth Org. techn. Rep. Ser.*, 1953, **68**, 10; 1957, **127**, 11; 1958, **147**, 16; WHO/BS 53, 104, 218, 279, 346, 415)

Anti-*Salmonella typhi* H serum
 Anti-*Salmonella typhi* O serum
 Anti-*Salmonella typhi* Vi serum
 Anti-*Salmonella paratyphi A* H serum
 Anti-*Salmonella paratyphi B* H serum
 Anti-*Salmonella paratyphi B* non-specific H serum
 Anti-*Salmonella paratyphi B* O serum

IV. DISCONTINUED INTERNATIONAL BIOLOGICAL STANDARDS

The International Biological Standards for the following substances which can either now be characterized completely by chemical or physical tests, or for which there has been little demand, have been discontinued. (References: *Wld Hlth Org. techn. Rep. Ser.*, 1952, **56**, 14; 1953, **68**, 25; 1957, **127**, 9, 19)

Samples of the remaining stock of Staphylococcus β Antitoxin may be obtained on request from the International Laboratory for Biological Standards, Statens Serum Institut, Copenhagen, Denmark, by laboratories desiring to establish their own working standards for research purposes.

Samples of the substances marked with an asterisk are now available at the WHO Centre for Authentic Chemical Substances, Apotekens Kontrollaboratorium, 128 Lindhagensgatan, Stockholm, Sweden.

Substances	International Unit (mg)	Adopted	Discontinued
Arsphenamine	—	1925	1935
Ouabain	—	1928	1954
Provitamin A (β -carotene)	0.0006	1931	1956
Vitamin B (synthetic vitamin B ₁)	0.003	1931	1956
*Oestrone	0.0001	1932	1949
Vitamin C	0.05	1934	1956
Oestradiol monobenzoate	0.0001	1935	1949
Androsterone	0.1	1935	1950
*Progesterone	1.0	1935	1955
Vitamin E (α -tocopheryl acetate)	1.0	1941	1956
*Vitamin A (vitamin A acetate)	0.000344	1949	1954
*Tubocurarine (<i>d</i> -tubocurarine chloride)	1.0	1951	1955
Staphylococcus β antitoxin	2.623	1952	1956
*Chloramphenicol	—	1953	1956

WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES

	Price		
	s.d.	S	Sw. fr.
<i>Recent and forthcoming reports :</i>			
No. 133 Expert Committee on Health Statistics Fifth report	1/9	0.30	1.—
No. 134 The Psychiatric Hospital as a Centre for Pre- ventive Work in Mental Health Fifth report of the Expert Committee on Mental Health	1/9	0.30	1.—
No. 135 Joint ILO/WHO Committee on Occupational Health Third report	1/9	0.30	1.—
No. 136 Expert Committee on Yellow Fever Vaccine First report	1/9	0.30	1.—
No. 137 Measurement of Levels of Health Report of a study group	1/9	0.30	1.—
No. 138 Use of Specifications for Pharmaceutical Preparations Report of a study group	1/9	0.30	1.—
No. 139 African Conference on Bilharziasis, Brazzaville, French Equatorial Africa, 26 November- 8 December 1956 Report	1/9	0.30	1.—
No. 140 Conference on Public Health Training of General Practitioners, Geneva, 29 October- 2 November 1956 Report	1/9	0.30	1.—
No. 141 Chemotherapy and Chemoprophylaxis in Tuber- culosis Control Report of a study group	1/9	0.30	1.—
No. 142 Expert Committee on Addiction-Producing Drugs Eighth report	1/9	0.30	1.—
No. 143 Classification of Atherosclerotic Lesions Report of a study group	1/9	0.30	1.—
No. 144 Procedures for the Testing of Intentional Food Additives to Establish their Safety for Use Second report of the Joint FAO/WHO Expert Committee on Food Additives	1/9	0.30	1.—
No. 145 Expert Committee on Poliomyelitis Second report	<i>In preparation</i>		
No. 146 Expert Committee on Water Fluoridation First report			
No. 147 Expert Committee on Biological Standardization Eleventh report	1/9	0.30	1.—
No. 148 Joint FAO/WHO Expert Committee on Bru- cellosis Third report	<i>In preparation</i>		
No. 149 Joint FAO/WHO Expert Committee on Nutri- tion Fifth report			
No. 150 The Agreement of Brussels, 1924, respecting Facilities to be given to Merchant Seamen for the Treatment of Venereal Diseases Report of a study group	3/6	0.60	2.—

THERAPEUTIC AND DIAGNOSTIC SUBSTANCES

Introduction

International Standard for Tetracycline—*J. H. Humphrey, J. W. Lightbown & Marjorie V. Mussett*

International Standard for Erythromycin—*J. H. Humphrey, J. W. Lightbown & Marjorie V. Mussett*

The assay of diphtheria toxin—*Julia Gerwing, D.A. Long & Marjorie V. Mussett*

The assay of penicillin in blood-serum using *Sarcina lutea*—*J. W. Lightbown & D. Sulitzeanu*

Synthetic substances with morphine-like effect. Clinical experience: potency, side-effects, addiction liability—*Nathan B. Eddy, H. Halbach & Olav J. Braenden*

BULLETIN OF THE WORLD HEALTH ORGANIZATION

Vol. 17, No. 4-5, 1957; 348 pages

Price: £1; \$4.00; Sw. fr. 12.—