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WORLD HEALTH ORGANIZATION

TECHNICAL REPORT SERIES

No. 172

**EXPERT COMMITTEE ON  
BIOLOGICAL STANDARDIZATION**

**Twelfth Report**

WORLD HEALTH ORGANIZATION

PALAIS DES NATIONS

GENEVA

1959

## EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Geneva, 22-27 September 1958

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This report was originally issued as mimeographed document WHO/BS/450.

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## **EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION**

### **Twelfth Report \***

The Expert Committee on Biological Standardization met in Geneva from 22 to 27 September 1958.

Dr P. Dorolle, Deputy Director-General, on behalf of the Director-General of the World Health Organization, welcomed the members of the Committee. He noted that the present meeting coincided with a change in the directorship at both International Laboratories for Biological Standards, and thanked Dr W. L. M. Perry, London, and Dr O. Maaløe, Copenhagen, for the valuable assistance which they had given to the World Health Organization during the last ten years. He welcomed their successors, Dr D. G. Evans and Dr P. Krag.

The Deputy Director-General outlined the project of the World Health Organization for issuing recommended requirements for important biological substances. These requirements are intended to facilitate the exchange of preparations of these substances between different countries; to fill a great practical need for guidance; and to ensure a greater uniformity in the production of safe, reliable and potent therapeutic and prophylactic biological preparations. A number of recommended requirements have now been drafted by specialized study groups and the Deputy Director-General asked the Expert Committee to express its opinion on these drafts.

### **PHARMACOLOGICAL**

#### **ANTIBIOTICS**

The Committee considered the possibility of making reference preparations of antibiotic substances available as soon as possible after they had been shown to be clinically safe and effective. The Committee agreed that such a service would be very useful and therefore invited responsible

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

1. NOTES the twelfth 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 EB23.R37, *Off. Rec. Wld Hlth Org.*, 1959, 91, 19)

workers in the antibiotic field to submit clinical and laboratory data on new antibiotics in order to enable the Committee to decide what preparations should be included in this international service. The National Institute for Medical Research, London, would then be asked to obtain quantities of such substances for distribution as international reference preparations. This procedure would temporarily satisfy a need which, at a later date, could be met by replacement of such international reference preparations by international standards.

### 1. Streptomycin

The Committee noted that the National Institute for Medical Research, London, had completed the statistical analysis of the results of the collaborative assays on the proposed second international standard and that the participants had agreed that the unit should remain unchanged.<sup>1</sup> The Committee also noted that, in accordance with the authorization given in its eleventh report,<sup>2</sup> the second International Standard for Streptomycin has now been established, and that the International Unit is defined as the activity contained in 0.001282 milligram of the second International Standard. The International Standard thus contains 780 International Units per milligram.

### 2. Neomycin

The Committee noted that a preliminary examination had been made of the proposed international standard for neomycin and that agreement had not been obtained regarding the relative concentrations of neomycin B, neomycin C and neamine.<sup>3</sup> Nevertheless, the Committee considered that the proposed standard could serve an immediate and useful purpose and, in accordance with the opinion stated above, decided to establish this material as the International Reference Preparation of Neomycin.

Since preparations of virtually pure neomycin B are now available and are being more widely used, the Committee was of the opinion that such a preparation would be preferable as an international standard. The Committee therefore asked the National Institute for Medical Research, London, to obtain a quantity sufficient for a new proposed international standard and to proceed with collaborative assays.

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<sup>1</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/421

<sup>2</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1958, **147**, 5

<sup>3</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/428

### 3. Nystatin

The Committee noted that a batch of nystatin had been obtained<sup>1</sup> and established this material as the International Reference Preparation of Nystatin. Preliminary studies have indicated that this material would be suitable as an international standard and the Committee therefore asked the National Institute for Medical Research, London, to proceed with the organization of a collaborative assay.

### 4. Novobiocin

The Committee established the material now held by the National Institute for Medical Research, London,<sup>2</sup> as the International Reference Preparation of Novobiocin. The Committee agreed that there is now a need for an international standard for novobiocin, and asked the National Institute for Medical Research to proceed to examine whether the International Reference Preparation would be suitable to serve as an international standard and, if so, to arrange a collaborative assay.

### 5. Oleandomycin

The Committee established the material now held by the National Institute for Medical Research, London,<sup>3</sup> as the International Reference Preparation of Oleandomycin. The Committee agreed that there is now a need for an international standard for oleandomycin and asked the National Institute for Medical Research to proceed to examine whether the International Reference Preparation would be suitable to serve as an international standard and, if so, to arrange a collaborative assay.

### 6. Procaine Benzylpenicillin in Oil with Aluminium Monostearate (PAM)

The Committee noted that in a collaborative study of various preparations of PAM<sup>4</sup> a consistent correlation between the results in man and in

<sup>1</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/429

<sup>2</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/431

<sup>3</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/430

<sup>4</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/422

rabbits had not been observed in the data so far obtained. There was, however, agreement on the order in which the preparations should be ranked with respect to their property of providing a persistent concentration of penicillin in the circulating blood. The Committee therefore decided to authorize the National Institute for Medical Research, London, to establish as the International Reference Preparation of PAM the preparation found in this collaborative study to be most suitable, and it asked the National Institute for Medical Research to prepare a report incorporating the results from all participants.

#### **7. Benzathine Penicillin**

The Committee noted that the antibiotic potency of preparations of benzathine penicillin could be validly assayed against the International Standard for Penicillin. Considering that the prolonged-acting properties of benzathine penicillin were inherent in the substance itself and not, as in the case of PAM, dependent upon the vehicle, the Committee decided that there was no need for an international reference preparation for benzathine penicillin nor for a comparative study of the prolonged-acting properties of different batches.

#### **8. Kanamycin, Leucomycin, Ristocetin, Vancomycin, and Amphotericin**

The Committee considered the new antistaphylococcal antibiotics kanamycin, leucomycin, ristocetin, and vancomycin, and the new antifungal antibiotic amphotericin, and asked the National Institute for Medical Research, London, to obtain quantities of these antibiotics suitable for serving as international reference preparations.

### **HORMONES**

#### **9. Corticotrophin**

The Committee noted that a batch of corticotrophin suitable for replacing the International Standard had been obtained and that an international collaborative assay would be organized.<sup>1</sup> In view of the urgent need for a new international standard and for working standards it authorized the National Institute for Medical Research, London, to establish this material

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<sup>1</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/432

as the third International Standard for Corticotrophin and to define its unitage as soon as the agreement of the participants in the collaborative assay had been obtained. Since the production and calibration of working standards for corticotrophin require considerable effort, and since the quantity obtained is sufficiently large, the Committee agreed that part of this material could be made internationally available as a working standard.

#### **10. Human Menopausal Gonadotrophin**

The Committee noted that a quantity of human menopausal gonadotrophin had been obtained,<sup>1</sup> and on the basis of the existing data authorized the National Institute for Medical Research, London, to establish this material as the International Reference preparation of Human Menopausal Gonadotrophin.

The Committee also asked the National Institute for Medical Research to obtain and hold a sufficient amount of the current unofficial reference preparation, used by many research workers, for comparative assays against the international reference preparation should it be decided at a later date to establish an international standard.

#### **11. Prolactin**

The Committee noted that a collaborative assay of the material proposed for the replacement of the International Standard for Prolactin had been completed,<sup>2</sup> but that the results had not yet been statistically analysed. It further noted that, in accordance with the authorization given in its tenth report,<sup>3</sup> the National Institute for Medical Research, London, will establish this material as the second International Standard for Prolactin and will define its unitage, with the agreement of the participants in the collaborative assay.

#### **12. Relaxin**

The Committee considered a report by the National Institute for Medical Research, London,<sup>4</sup> on the need for an international reference preparation

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<sup>1</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/434

<sup>2</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/446

<sup>3</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1957, **127**, 16

<sup>4</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/423

of relaxin, but decided that the basic information at present available was insufficient for the establishment of such a reference preparation.

### 13. Insulin

The Committee noted that the analysis of the collaborative assay had been completed<sup>1</sup> and that, in accordance with the authorization given in its tenth report,<sup>2</sup> the fourth International Standard for Insulin had been established. The Committee defined one International Unit as the activity contained in 0.04167 milligram of the International Standard. The Standard thus contains 24 International Units per milligram. It is composed of 52% bovine and 48% porcine insulin.

The Committee considered it desirable to obtain data on the stability of the material at high temperatures and asked the National Institute for Medical Research, London, to initiate accelerated degradation tests.

### 14. Oxytocic, Vasopressor and Antidiuretic Substances

The Committee noted that a generous offer of 2 grams of a synthetic oxytocin for use as an international standard had been made by the Institute of Chemistry of the Czechoslovak Academy of Science, Prague, where further work was in progress towards establishing the purity of this material. The Committee therefore asked the National Institute for Medical Research, London, to prepare a report on the possibility of replacing the International Standard for Oxytocic, Vasopressor and Antidiuretic Substances with preparations of synthetic peptides.

## MISCELLANEOUS

### 15. Dextran Sulfate

The Committee reconsidered the need for an international standard for dextran sulfate and decided, on the basis of a report from the National Institute for Medical Research, London,<sup>3</sup> that such a standard would not serve a useful purpose at the present time, but noted that the National

<sup>1</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/427

<sup>2</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1957, **127**, 16

<sup>3</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/426

Institute for Medical Research would hold and distribute on request the material which was originally proposed for the purpose.

### 16. Heparin

The Committee noted that, in accordance with the authorization given in its tenth report,<sup>1</sup> the National Institute for Medical Research, London, had established the second International Standard for Heparin,<sup>2</sup> and that one International Unit is defined as the activity contained in 0.0077 milligram of the International Standard. The replacement of the first International Standard has involved no change in the definition of the International Unit.

### 17. Pyrogen

The Committee noted that, in accordance with the authorization given in its eleventh report,<sup>3</sup> the National Institute for Medical Research, London, had established a highly purified preparation of the O antigen of *Shigella dysenteriae* as the International Pyrogen Reference Preparation.<sup>4</sup>

## IMMUNOLOGICAL

### ANTIGENS

#### 18. Poliomyelitis Vaccine

The Committee noted that attempts in a number of laboratories to prepare dry stable preparations of poliomyelitis vaccine had not been successful but that preliminary studies made by the Institute for Poliomyelitis Prophylactics, Moscow, had indicated that a dried vaccine prepared in this Institute had retained considerable antigenic activity and was highly stable in this form.<sup>5</sup> The Committee welcomed the offer made by the

<sup>1</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1957, **127**, 17

<sup>2</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/424

<sup>3</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1958, **147**, 11

<sup>4</sup> National Institute for Medical Research, London, unpublished working document WHO/BS/425

<sup>5</sup> Institute for Poliomyelitis Prophylactics, Moscow, unpublished working document WHO/BS/449

Moscow Institute for Poliomyelitis Prophylactics, of providing a large quantity of dried trivalent vaccine for international standardization purposes if further studies now in progress confirm the preliminary findings. The Committee also noted that the National Institutes of Health, Bethesda, had set aside a large quantity of a fluid trivalent vaccine for use as a national reference preparation and that part of this material might be available for international standardization purposes.

The Committee further noted the recommendations, made in the report of a Study Group on Recommended Requirements for Poliomyelitis Vaccine,<sup>1</sup> that an international study be undertaken to investigate the various methods of testing the antigenic activity. The study would include a common reference vaccine, as well as other vaccines, and dilutions thereof, and the participating laboratories would be asked to test the vaccines by a specified chick test, a specified guinea-pig test, and a specified antibody-combining test, as well as by other methods in routine use in these laboratories.

The Committee asked the Statens Seruminstitut, Copenhagen, to arrange a collaborative study as outlined by the Study Group and to make provision to include in this study, if available, the materials prepared by the Moscow Institute for Poliomyelitis Prophylactics and by the National Institutes of Health, Bethesda.

#### 19. Smallpox Vaccine

The Committee noted that a study group would be asked to draft recommended requirements for smallpox vaccine in the near future. The Committee asked the Statens Seruminstitut, Copenhagen, to include the methods for potency determination which will be recommended by the study group in the collaborative assay of the proposed international reference preparation of smallpox vaccine.<sup>2</sup>

#### 20. Cholera Vaccine

The Committee noted that a Study Group on Recommended Requirements for Biological Substances (Yellow Fever Vaccine and Cholera Vaccine)<sup>3</sup> had suggested that an immediate collaborative study be made of the suitability of the potency tests formulated by the Study Group. The Committee asked the Statens Seruminstitut, Copenhagen, to arrange such

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<sup>1</sup> This report will be published separately.

<sup>2</sup> WHO Secretariat, unpublished working document WHO/BS/442

<sup>3</sup> The report of this study group will be published separately.

a collaborative study but recognized that the proposed study would make serious demands on the stock of the International Reference Preparations of Cholera Vaccines. The Committee also agreed with the suggestion made by the Study Group that it would be important to carry out a well-controlled field trial of different batches of cholera vaccine and to include the International Reference Preparations in such a trial, since this would be the only way of obtaining international reference preparations of proven prophylactic efficacy. The Committee therefore requested the Statens Seruminstitut to acquire, as soon as possible, quantities of monospecific cholera vaccines large enough both to replace the present International Reference Preparations and to be used in a field trial at a later date.

The Committee endorsed the opinion of the Study Group, however, that if an attempt to provide material on this scale seemed likely to delay the start of the collaborative study of the potency tests it would be preferable to initiate these studies making use of the existing International Reference Preparations.

### 21. Typhoid Vaccine

The Committee noted that no further progress had been made in obtaining the two large quantities of typhoid vaccine<sup>1</sup> which were needed for the laboratory and field studies envisaged in its eleventh report.<sup>2</sup> Since there is an urgent need for international recommendations on the control of typhoid vaccine, the Committee was of the opinion that, on the basis of present knowledge, a study group might formulate requirements which would be useful until data on the correlation between laboratory and field results were obtained.

### 22. Swine Erysipelas Vaccine

The Committee noted that the Paul-Ehrlich-Institut, Frankfurt-am-Main,<sup>3</sup> had prepared a quantity of swine erysipelas vaccine adequate to serve as an international standard. The Committee also noted the results of a collaborative assay in five laboratories arranged by the Central Veterinary Laboratory, Weybridge.<sup>4</sup> Four of these laboratories had obtained concordant results on the potency of this material relative to the existing German standard, whereas one had obtained discordant results.

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<sup>1</sup> WHO Secretariat, unpublished working document WHO/BS/441

<sup>2</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1958, **147**, 11

<sup>3</sup> Paul-Ehrlich-Institut, Frankfurt-am-Main, unpublished working document WHO/BS/436

<sup>4</sup> Central Veterinary Laboratory, Weybridge, unpublished working document WHO/BS/435

The Committee authorized the Statens Serum Institut, Copenhagen, in consultation with the Paul-Ehrlich-Institut and the Central Veterinary Laboratory, to establish this material as the international standard for swine erysipelas vaccine, subject to a satisfactory resolution of the present discrepancy, and to define its unitage with the agreement of all participants in the collaborative assay.

### 23. Newcastle Disease Vaccine

The Committee noted that the Paul-Ehrlich-Institut, Frankfurt-am-Main, will soon establish a reference preparation of Newcastle disease vaccine (inactivated) for use in Germany, and asked the Secretariat to assess whether there is a need for an international reference preparation of this vaccine.

### 24. Tetanus Toxoid, Adsorbed

The Committee considered information received by the Secretariat on the assay of tetanus toxoid in mice, and noted that adsorbed preparations of tetanus toxoid could not be assayed validly against the present International Standard for Tetanus Toxoid. The Committee, therefore, asked the Statens Serum Institut, Copenhagen, in consultation with the Secretariat, to obtain opinions of other workers on the need for an international standard for tetanus toxoid, adsorbed, and to acquire a suitable quantity of an adsorbed preparation of tetanus toxoid if the need was confirmed.

### 25. Cardioliipin

The Committee noted that the Third International Reference Preparation of Cardioliipin had been established.<sup>1</sup>

### 26. Egg Lecithin

The Committee noted that material had been obtained suitable for the replacement of the present International Reference Preparation of Egg Lecithin and that a collaborative assay had been arranged.<sup>2</sup> It authorized the Statens Serum Institut, Copenhagen, to establish this material as the

<sup>1</sup> Weis Bentzon, M. & Krag, P., unpublished working document WHO/BS/420 (WHO/VDT/SERO 85)

<sup>2</sup> Krag, P., unpublished working document WHO/BS/440

third International Reference Preparation of Egg Lecithin, subject to the agreement of the participants in the collaborative assay.

## ANTIBODIES

### 27. Antipoliomyelitis Sera

The Committee considered a report on the collaborative study of the freeze-dried type-specific antipoliomyelitis sera<sup>1</sup> which had been proposed as international reference preparations. It recognized that the value of these sera had been demonstrated, since the relative neutralizing potencies of unknown sera in terms of the proposed reference preparations obtained in different laboratories showed much less variation than the actual titres.

The Committee also considered a report<sup>2</sup> which suggested that the neutralizing potency of the sera might vary from ampoule to ampoule. This variation had not been demonstrated in the extensive collaborative study and since there is an urgent need for making such reference preparations available, the Committee decided to establish these preparations as the International Reference Preparations of Antipoliomyelitis Sera of Types 1, 2, and 3.

The Committee agreed, however, that the International Reference Sera should, in due course, be replaced by international standard sera, and asked the Statens Seruminstitut, Copenhagen, to obtain suitable material for this purpose.

### 28. Syphilitic Human Serum

The Committee considered a report<sup>3</sup> on the assay by the complement-fixation technique of the proposed international standard for syphilitic human serum against the German standard serum, and noted that agreement had been obtained on the relative potency. The Committee further noted that the International Standard for Syphilitic Human Serum has now been established and that the International Unit has been defined, with the agreement of the participants in the international collaborative study, as the activity contained in 3.617 milligrams of the International Standard. The International Unit is equivalent to the existing German unit.

The Committee noted that there is a need for an international reference serum for use in the *Treponema pallidum* immobilization test, and it asked

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<sup>1</sup> Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/444

<sup>2</sup> Perkins, F. T., unpublished working document WHO/BS/433

<sup>3</sup> Weis Bentzon, M. & Krag, P., unpublished working document WHO/BS/439 (WHO/VDT/SERO/86)

the Statens Seruminstitut, Copenhagen, to investigate whether the International Standard for Syphilitic Human Serum could be used for this purpose.

### **29. Anti-Yellow-Fever Serum**

The Committee noted that the Laboratory of the West African Council for Medical Research, Lagos, Nigeria,<sup>1</sup> had prepared from immunized monkeys a quantity of anti-yellow-fever serum adequate for serving as an international reference preparation, and that a collaborative examination of this material will be arranged by the Statens Seruminstitut, Copenhagen, in consultation with the West African Council for Medical Research.

### **30. Anti-Streptolysin O**

The Committee noted that the collaborative study of the proposed international standard for anti-streptolysin O has been completed,<sup>2</sup> and that the international standard will be established when agreement has been obtained from the participants.

### **31. Anti-Toxoplasma Human Serum**

The Committee noted that a conference on toxoplasmosis, held during the Seventh International Congress for Microbiology in Stockholm, had recommended the establishment of an international reference preparation of anti-toxoplasma serum.<sup>3</sup> The Committee also noted that steps had already been taken by the Statens Seruminstitut, Copenhagen, to obtain adequate quantities of human serum for this purpose and it asked the institute to arrange a collaborative examination of the suitability of this material as a reference serum in complement-fixation tests, Sabin-Feldman tests, and haemagglutination tests.

### **32. Anti-Leptospira Sera**

The Committee noted that the WHO/FAO International Leptospirosis Reference Laboratories had prepared several type-specific anti-leptospira

<sup>1</sup> Macnamara, F. N., unpublished working document WHO/BS/438

<sup>2</sup> Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/443

<sup>3</sup> WHO Secretariat, unpublished working document WHO/BS/447

sera which had been distributed into a large number of ampoules, and freeze-dried.<sup>1</sup> The Committee agreed that these sera would serve a useful purpose in the identification of strains of leptospira in different parts of the world, and decided to establish the following International Reference Preparations of Type-Specific Anti-Leptospira Sera on the basis of the collaborative studies already made by the International Leptospirosis Reference Laboratories :

International Reference Preparation of Anti-*Leptospira saxkoebing* Serum  
 International Reference Preparation of Anti-*Leptospira ballum* AB Serum  
 International Reference Preparation of Anti-*Leptospira canicola* Serum  
 International Reference Preparation of Anti-*Leptospira sejroe* Serum  
 International Reference Preparation of Anti-*Leptospira mini* AB Serum  
 International Reference Preparation of Anti-*Leptospira grippotyphosa* Serum  
 International Reference Preparation of Anti-*Leptospira australis* A Serum  
 International Reference Preparation of Anti-*Leptospira icterohaemorrhagiae* AB Serum  
 International Reference Preparation of Anti-*Leptospira icterohaemorrhagiae* A Serum  
 International Reference Preparation of Anti-*Leptospira hyos* Serum  
 International Reference Preparation of Anti-*Leptospira autumnalis* AB Serum  
 International Reference Preparation of Anti-*Leptospira autumnalis* A Serum  
 International Reference Preparation of Anti-*Leptospira pomona* Serum  
 International Reference Preparation of Anti-*Leptospira bataviae* Serum  
 International Reference Preparation of Anti-*Leptospira semaranga* Serum  
 International Reference Preparation of Anti-*Leptospira hebdomadis* Serum  
 International Reference Preparation of Anti-*Leptospira andamana* Serum  
 International Reference Preparation of Anti-*Leptospira javanica* Serum  
 International Reference Preparation of Anti-*Leptospira pyrogenes* Serum

The Committee noted that routine distribution of samples of these sera, together with corresponding strains of leptospira, will be undertaken by the International Leptospirosis Reference Laboratories, but that a stock of ampoules will be held by the Statens Serum Institut, Copenhagen.

### 33. Anti-Tick-Borne-Encephalitis Sera

The Committee noted that the Advisory Group on the Control of Neurotropic Diseases in Europe<sup>2</sup> had recommended that one or more international reference preparations of anti-tick-borne-encephalitis sera be established. Such preparations were needed for use in virus neutralization

<sup>1</sup> WHO Secretariat, unpublished working document WHO/BS/437

<sup>2</sup> Unpublished working document EURO-180/8 Rev.1

tests, for measuring the potency of therapeutic sera, and possibly for use in complement-fixation tests. The Committee asked the Statens Serum-institut, Copenhagen, to investigate how this recommendation could be implemented.

## RECOMMENDED REQUIREMENTS FOR BIOLOGICAL SUBSTANCES

### 34. General Requirements

The Committee studied the general requirements for manufacturing establishments and for control laboratories drafted by a study group on recommended requirements for biological substances.<sup>1</sup> It noted that these recommendations had been amended and approved by study groups on recommended requirements for poliomyelitis vaccine, yellow fever vaccine, and cholera vaccine, and it was of the opinion that the present text was a satisfactory formulation of the basic requirements which establishments manufacturing or controlling biological substances should meet.

### 35. Requirements for Poliomyelitis Vaccine

The Committee studied the requirements for poliomyelitis vaccine (inactivated) drafted by a study group on recommended requirements for poliomyelitis vaccine.<sup>2</sup> It noted that requirements for the antigenic potency of this vaccine could not, at the present time, be formulated in satisfactory detail, but that the study group had recommended the arrangement of an international investigation in order to obtain the basic information necessary for the international recommendation of definite levels of acceptance for potency.

The Committee made arrangements for such an international investigation, as outlined in section 18 of the present report (page 11).

Though a revision of this part of the recommended requirements for poliomyelitis vaccine will, therefore, become necessary when the proposed investigation has been successfully completed, the Committee was of the opinion that the present text represented an important contribution towards the effective control of poliomyelitis vaccine throughout the world.

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<sup>1</sup> The report of this study group, containing the requirements referred to, will be published separately.

<sup>2</sup> The report of this study group, containing the requirements referred to, will be published separately.

### 36. Requirements for Yellow Fever Vaccine

The Committee studied the requirements for yellow fever vaccine drafted by a study group on recommended requirements for yellow fever vaccine and cholera vaccine.<sup>1</sup> It noted that this set of requirements would apply only to yellow fever vaccine intended for use by subcutaneous injection and recommended that, for the issue of valid International Certificates of Vaccination or Revaccination against Yellow Fever, the World Health Organization approve vaccines for subcutaneous use only if they satisfy all requirements as formulated.

The Committee was of the opinion that the present text represented a satisfactory revision of the existing standards for the manufacture and control of yellow fever vaccine adopted by the Standing Technical Committee on Health of the United Nations Relief and Rehabilitation Administration in 1945.<sup>2</sup>

### 37. Requirements for Cholera Vaccine

The Committee studied the requirements for cholera vaccine drafted by a study group on recommended requirements for yellow fever vaccine and cholera vaccine.<sup>1</sup> It noted that the tests for the antigenic potency of cholera vaccine had been only provisionally formulated and that the Study Group had recommended that an immediate laboratory investigation be carried out in order to determine their suitability. The Committee made arrangements for such an international investigation as outlined in section 20 of the present report (page 12).

Though revision of this part of the recommended requirements might, therefore, become necessary when the proposed investigation has been successfully completed, the Committee was of the opinion that the present text represented an important contribution towards the effective control of cholera vaccine throughout the world.

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<sup>1</sup> The report of this study group, containing the requirements referred to, will be published separately.

<sup>2</sup> *Epidem. Inform. Bull. (UNRRA)*, 1945, 1, 365

## GENERAL

### 38. Classification

The Committee decided to make a clearer distinction between international standards and international reference preparations, and agreed upon the following description of these categories. An International Standard is a preparation to which an International Unit has been assigned on the basis of an extensive international collaborative study. An International Reference Preparation is a preparation to which an International Unit has not been assigned. The reason for this may be that the completion of a full international study, which must precede the establishment of an international standard, would delay the availability of an international reference preparation for which there is an immediate demand. The reason may also be that an international unit would not serve a useful purpose or that extensive laboratory studies have failed to provide a satisfactory assay method.

The Expert Committee on Biological Standardization takes no responsibility for biological preparations which are not included in one of these two categories. The Committee noted that experience has shown that there is no need for a separate category of "Author's Preparations".

The Committee agreed to continue the practice of attaching to its Report an annex listing all International Standards and International Reference Preparations held for distribution at the International Laboratories for Biological Standards in Copenhagen and in London. It, therefore, asked the Secretariat to revise the list which appeared as an annex to the eleventh report<sup>1</sup> in accordance with the classification now agreed upon.

The Committee agreed that it would also be useful to list proposed international standards and proposed international reference preparations which are under consideration by the Expert Committee on Biological Standardization, as well as other biological preparations which can be obtained on request from the International Laboratories for Biological Standards.

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<sup>1</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1958, 147, 19

## **Annex**

### **I. INTERNATIONAL BIOLOGICAL STANDARDS AND INTERNATIONAL BIOLOGICAL REFERENCE PREPARATIONS 1959**

The primary purpose underlying the establishment of International Biological Standards and International Biological 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 substances listed to which an International Unit has been assigned are International Biological Standards. Those listed without designation of an International Unit are International Biological Reference Preparations.

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 International Biological 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,*

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

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Antigens (contd)</b>		
Cholera antigen (Ogawa)	—	Ampoules containing approximately 100 mg of dried antigen
Cholera vaccine (Inaba)	—	Ampoules containing 20 mg of dried vaccine ( $1.6 \times 10^{10}$ organisms per ampoule)
Cholera vaccine (Ogawa)	—	Ampoules containing 20 mg of dried vaccine ( $1.6 \times 10^{10}$ organisms per ampoule)
Cardiolipin	—	Ampoules containing 4 ml, 8 ml or 16 ml of a solution of purified cardiolipin in ethanol. (6.4 mg cardiolipin per ml, as calculated from the phosphorus content).
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)
<b>ANTIBODIES</b>		
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 (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, <b>12</b> , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, <b>86</b> , 7; WHO/BS 52, 130, 167, 222, 255
<i>1st Reference Preparation 1953</i>	<i>Bull. Wld Hlth Org.</i> , 1950, <b>3</b> , 43; 1955, <b>12</b> , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, <b>86</b> , 7; WHO/BS 23, 36, 41, 52, 69, 82, 87, 87 Add.1, 107, 130, 222, 255, 342, 410; WHO/BS/IR/58
<i>1st Reference Preparation 1953</i>	<i>Bull. Wld Hlth Org.</i> , 1950, <b>3</b> , 43; 1955, <b>12</b> , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, <b>86</b> , 7; WHO/BS 23, 36, 41, 52, 69, 82, 87, 87 Add.1, 107, 130, 222, 255, 342, 410; WHO/BS/IR/58
1st Reference Preparation 1951 2nd Reference Preparation 1953 3rd Reference Preparation 1958	<i>Bull. Wld Hlth Org.</i> , 1951, <b>4</b> , 151; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, <b>56</b> , 8; 1958, <b>147</b> , 14; <i>Cardiolipin antigens</i> , 1955 (WHO Monograph No. 6); WHO/BS 72, 117, 238, 278, 278 Add.1, 305, 360, 414, 420
1st Reference Preparation 1951 2nd Reference Preparation 1953	<i>Bull. Wld Hlth Org.</i> , 1951, <b>4</b> , 151; 1955, <b>13</b> , 323; 1956, <b>14</b> , 567, 577; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, <b>56</b> , 8, <i>Cardiolipin antigens</i> , 1955 (WHO Monograph No. 6); WHO/BS 72, 238, 278, 278 Add.1, 305
1st Reference Preparation 1951 2nd Reference Preparation 1953	<i>Bull. Wld Hlth Org.</i> , 1951, <b>4</b> , 151; 1955, <b>13</b> , 323; 1956, <b>14</b> , 567, 577; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, <b>56</b> , 8; <i>Cardiolipin antigens</i> , 1955 (WHO Monograph No. 6); WHO/BS 72, 238, 278, 278 Add.1, 305
<i>1st Standard 1928</i>	<i>Bull. Wld Hlth Org.</i> , 1949, <b>2</b> , 59; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1950, <b>2</b> , 5; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 506; 1936, <b>5</b> , 702; 1938, <b>7</b> , 684, 713, 733, 739; 770, 776, 783; 1940/41, <b>9</b> , 447, 452; 1942/43, <b>10</b> , 104, 113; 1945/46, <b>12</b> , 14; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 210, 338; WHO/BS 37, 44
<i>1st Standard 1922</i>	<i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 505; 1938, <b>7</b> , 711, 853; 1945/46, <b>12</b> , 12; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 208, 324; WHO/BS 68, 77

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Antibodies (contd)</b>		
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)
Clostridium welchii (perfringens) type B antitoxin	0.0137	Ampoules containing 68.5 mg of dried hyperimmune horse serum (5000 I.U. per ampoule)
Clostridium welchii (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>vibrion 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)
Staphylococcus $\alpha$ 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)

Years of establishment (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> 1928	<i>Bull. Wld Hlth Org.</i> , 1951, <b>4</b> , 111; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 508; 1945/46, <b>12</b> , 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, <b>1</b> , 9; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, <b>108</b> , 7; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 510; 1938, <b>7</b> , 695, 802, 818; 1939, <b>8</b> , 797; 1942/43, <b>10</b> , 97; 1945/46, <b>12</b> , 22; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 209, 332; WHO/BS 281
<i>1st Standard</i> 1954	<i>Bull. Wld Hlth Org.</i> , 1956, <b>14</b> , 557; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, <b>96</b> , 6; WHO/BS 281, 283, 298, 303, 343
<i>1st Standard</i> 1954	<i>Bull. Wld Hlth Org.</i> , 1956, <b>14</b> , 557; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, <b>96</b> , 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, <b>1</b> , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 1, 13, 511; 1938, <b>7</b> , 699, 815; 1942/43, <b>10</b> , 97; 1945/46, <b>12</b> , 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, <b>68</b> , 11; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 3, 42, 511; 1942/43, <b>10</b> , 97; 1945/46, <b>12</b> , 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, <b>56</b> , 17; <i>Bull. Hlth Org. L. o. N.</i> , 1936, <b>5</b> , 576, 659; 1945/46, <b>12</b> , 21; WHO/BS 91, 131
<i>1st Standard</i> 1938	<i>Bull. Hlth Org. L. o. N.</i> , 1938, <b>7</b> , 698, 807; 1939, <b>8</b> , 856; 1945/46, <b>12</b> , 21
1st Standard 1934 (0.5000 mg) 2nd Standard 1938	<i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 6, 68, 514; 1938, <b>7</b> , 702, 845; 1945/46, <b>12</b> , 32

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Antibodies (contd)</b>		
Scarlet fever streptococcus anti-toxin	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)
Syphilitic human serum	3.617	Ampoules containing 177.4 mg of dried human serum (49 I.U. per ampoule)
Cholera agglutinating serum (Inaba)	—	Ampoules containing 0.6 ml of monospecific serum

Years of establishment (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> 1952	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, <b>68</b> , 11 ; WHO/BS 38, 60, 84, 150, 225
<i>Ist Standard</i> 1954	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, <b>96</b> , 10 ; WHO/BS 246, 297, 300
<i>Ist Standard</i> 1934	<i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 4, 48, 512
<i>Ist Standard</i> 1934	<i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 5, 65, 512
<i>Ist Standard</i> 1952	<i>Bull. Wld Hlth Org.</i> , 1950, <b>3</b> , 309 ; 1953, <b>9</b> , 385, 399 ; 1954, <b>10</b> , 927 ; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, <b>68</b> , 9 ; WHO/BS 128, 162, 223, 224, 228
<i>Ist Standard</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1955, <b>13</b> , 807 ; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, <b>86</b> , 10 ; WHO/BS 177, 230, 276, 276 Add.1, 296
<i>Ist Standard</i> 1955	<i>Bull. Wld Hlth Org.</i> , 1954, <b>10</b> , 781 ; 1955, <b>13</b> , 747, 773 ; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, <b>108</b> , 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
<i>Ist Standard</i> 1950	<i>Bull. Wld Hlth Org.</i> , 1950, <b>3</b> , 301 ; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, <b>36</b> , 10 ; WHO/BS 42, 49, 74
<i>Ist Standard</i> 1950	<i>Bull. Wld Hlth Org.</i> , 1950, <b>3</b> , 301 ; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, <b>36</b> , 10 ; WHO/BS 42, 49, 74
<i>Ist Standard</i> 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 16 ; WHO/BS 239, 289 Rev.1, 304, 341, 379, 380 Rev.1, 439
<i>Ist Reference Preparation</i> 1953	<i>Bull. Wld Hlth Org.</i> , 1955, <b>12</b> , 945 ; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, <b>86</b> , 7 ; WHO/BS 40, 98, 130, 167, 222, 255

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Antibodies (contd)</b>		
Cholera agglutinating serum (Ogawa)	—	Ampoules containing 0.6 ml of monospecific serum
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)
Antityphoid serum (provisional)	—	Ampoules containing 5 ml of hyperimmune horse serum, dried
Antipoliomyelitis serum (type 1)	—	Ampoules containing 1 ml of a 1:100 dilution of hyperimmune monkey serum in a 6% solution of dextran in distilled water, dried
Antipoliomyelitis serum (type 2)	—	Ampoules containing 1 ml of a 1:100 dilution of hyperimmune monkey serum in a 6% solution of dextran in distilled water, dried
Antipoliomyelitis serum (type 3)	—	Ampoules containing 1 ml of a 1:100 dilution of hyperimmune monkey serum in a 6% solution of dextran in distilled water, dried
Anti- <i>Leptospira saxkoebing</i> serum	—	
Anti- <i>Leptospira ballum</i> AB serum	—	
Anti- <i>Leptospira canicola</i> serum	—	
Anti- <i>Leptospira sejroe</i> serum	—	Ampoules containing 0.5 ml or 1.0 ml of hyperimmune rabbit serum, dried
Anti- <i>Leptospira mini</i> AB serum	—	
Anti- <i>Leptospira grippotyphosa</i> serum	—	
Anti- <i>Leptospira australis</i> A serum	—	

Years of establishment (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, <b>12</b> , 945; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1954, <b>86</b> , 7; WHO/BS 40, 98, 130, 167, 222, 255
1st Reference Preparation 1935 2nd Reference Preparation 1938 3rd Reference Preparation 1945 4th Reference Preparation 1956	<i>Bull. Wld Hlth Org.</i> , 1947/48, <b>1</b> , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1936, <b>5</b> , 577, 695; 1938, <b>7</b> , 712, 859; 1945/46, <b>12</b> , 12; WHO/BS 318, 359
<i>1st Reference Preparation</i> 1952	<i>Bull. Wld Hlth Org.</i> , 1954, <b>10</b> , 911; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1953, <b>68</b> , 10; WHO/BS 182, 226
<i>1st Reference Preparation</i> 1958	WHO/BS 313, 361, 363, 385, 433, 444
<i>1st Reference Preparation</i> 1958	WHO/BS 313, 361, 363, 385, 433, 444
<i>1st Reference Preparation</i> 1958	WHO/BS 313, 361, 363, 385, 433, 444
<i>1st Reference Preparation</i> 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, <b>113</b> ; WHO/BS 413, 437

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Antibodies (contd)</b>		
Anti- <i>Leptospira icterohaemorrhagiae</i> AB serum	—	Ampoules containing 0.5 ml or 1.0 ml of hyperimmune rabbit serum, dried
Anti- <i>Leptospira icterohaemorrhagiae</i> A serum	—	
Anti- <i>Leptospira hyos</i> serum	—	
Anti- <i>Leptospira autumnalis</i> AB serum	—	
Anti- <i>Leptospira autumnalis</i> A serum	—	
Anti- <i>Leptospira pomona</i> serum	—	
Anti- <i>Leptospira bataviae</i> serum	—	
Anti- <i>Leptospira semaranga</i> serum	—	
Anti- <i>Leptospira hebdomadis</i> serum	—	
Anti- <i>Leptospira andamana</i> serum	—	
Anti- <i>Leptospira javanica</i> serum	—	
Anti- <i>Leptospira pyrogenes</i> serum	—	
<b>MISCELLANEOUS</b>		
Opacity reference preparation	—	Ampoules containing 20 ml of a suspension of Pyrex-glass particles in water (10 I.U. of opacity per ml)

<p>Years of establishment (in brackets, unitage of previous standards)</p>	<p>References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)</p>
<p><i>Ist Reference Preparation 1958</i></p>	<p><i>Wld Hlth Org. techn. Rep. Ser., 1956, 113; WHO/BS 413, 437</i></p>
<p><i>Ist Reference Preparation 1953</i></p>	<p><i>Bull. Wld Hlth Org., 1955, 12, 769; Wld Hlth Org. techn. Rep. Ser., 1954, 86, 14; WHO/BS 124, 172, 198, 256</i></p>

## B. PHARMACOLOGICAL

*Held by the International Laboratory for Biological Standards,*

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>ANTIBIOTICS</b>		
Penicillin	0.0005988	Ampoules containing 30 mg of sodium benzylpenicillin (1670 I.U. per mg)
Phenoxymethylpenicillin	0.00059	Ampoules containing 75 mg of phenoxymethylpenicillin (1695 I.U. per mg)
Streptomycin	0.001282	Ampoules containing 175 mg of streptomycin sulfate (780 I.U. per mg)
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)

## SUBSTANCES

*National Institute for Medical Research, London, England*

Years of establishment (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Standard 1944 (0.0006000 mg) 2nd Standard 1952	<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
1st Standard 1957	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 127, 14; 1958, 147, 7; WHO/BS 399
1st Standard 1950 (0.001282 mg) 2nd Standard 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, 36, 9; 1958, 147, 5; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 198, 279; WHO/BS 11, 67, 76, 369, 393, 421
1st Standard 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
1st Standard 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
1st Standard 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
1st Standard 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
1st Standard 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
1st Standard 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
1st Standard 1955	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, 108, 14; WHO/BS 263, 326

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Antibodies (contd)</b>		
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
Neomycin	—	Ampoules containing 100 mg of Neomycin sulfate
Nystatin	—	Ampoules in preparation
Novobiocin	—	Ampoules in preparation
Oleandomycin	—	Ampoules in preparation
<b>HORMONES</b>		
Oxytocic, vasopressor and anti-diuretic substances (previously named : posterior pituitary lobe)	0.5	Ampoules containing 30 mg of acetone-dried powder of whole posterior pituitary gland of the ox (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 pituitary gland of the ox (approximately 100 I.U. per tablet)
Corticotrophin (previously named : adrenocorticotrophic hormone)	0.88	Ampoules containing 28 mg of crude corticotrophin from anterior pituitary gland of the pig (1.14 I.U. per mg)
Thyrotrophin	13.5	Ampoules containing ten 20-mg tablets of a blend of 1 part purified thyrotrophin from anterior pituitary gland of the ox 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)

Years of establishment (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> 1951	<i>Bull. Wld Hlth Org.</i> , 1954, <b>10</b> , 895; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1952, <b>56</b> , 11; WHO/BS 132
<i>1st Reference Preparation</i> 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 6; WHO/BS 347, 398, 428
<i>1st Reference Preparation</i> 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 8; WHO/BS 347, 429
<i>1st Reference Preparation</i> 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 6; WHO/BS/394, 431
<i>1st Reference Preparation</i> 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 8; WHO/BS 430
1st Standard 1925 (0.5 mg) 2nd Standard 1942 (0.5 mg) 3rd Standard 1957	<i>Bull. Wld Hlth Org.</i> , 1947/48, <b>1</b> , 9; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, <b>127</b> , 15; 1958, <b>147</b> , 8; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 530; 1936, <b>5</b> , 572; 1942/43, <b>10</b> , 89; 1945/46, <b>12</b> , 42; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 191, 342; WHO/BS 351, 352, 395
<i>1st Standard</i> 1939	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, <b>127</b> , 16; <i>Bull. Hlth Org. L. o. N.</i> , 1939, <b>8</b> , 901; 1942/43, <b>10</b> , 96; 1945/46, <b>12</b> , 62; WHO/BS 208, 310, 350, 405, 446
1st Standard 1950 (1.00 mg) 2nd Standard 1955	<i>Bull. Wld Hlth Org.</i> , 1956, <b>14</b> , 543; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1951, <b>36</b> , 7; 1958, <b>147</b> , 8; WHO/BS 85, 156, 158, 249, 262, 308, 356, 386, 387, 432
<i>1st Standard</i> 1954	<i>Bull. Wld Hlth Org.</i> , 1955, <b>13</b> , 917; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1955, <b>96</b> , 14; 1956, <b>108</b> , 16; WHO/BS 1955, 158, 210, 284, 309
<i>1st Standard</i> 1955	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, <b>108</b> , 16; WHO/BS 140, 158, 250, 320

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Hormones (contd)</b>		
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	0.04167	Ampoules containing 110-125 mg of purified insulin, 52% from bovine and 48% from porcine pancreas (24 I.U. per mg)
Heparin	0.0077	Ampoules containing 20 mg of sodium salt of purified active principle from bovine tissue (130 I.U. per mg)
<b>MISCELLANEOUS</b>		
Vitamin D <sub>3</sub>	0.000025	Bottles containing 10 g of a solution of vitamin D <sub>3</sub> 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)
Digitalis	76.0	Ampoules containing 2500 mg of dry powdered leaves of <i>Digitalis purpurea</i> (0.01316 I.U. per mg)
Neosphenamine	—	Ampoules containing 300 mg of neosphenamine

Years of establishment (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Standard 1939	<i>Bull. Hlth Org. L. o. N.</i> , 1939, <b>8</b> , 887, 898; 1945/46, <b>12</b> , 60; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 98, 263
1st Standard 1939	<i>Bull. Hlth Org. L. o. N.</i> , 1939, <b>8</b> , 862, 884; 1945/46, <b>12</b> , 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) 3rd Standard 1952 (0.04082 mg) 4th Standard 1958	<i>Bull. Wld Hlth Org.</i> , 1952, <b>7</b> , 445; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 525; 1936, <b>5</b> , 575, 584; 1945/46, <b>12</b> , 44; <i>Pharmacopoea Internationalis</i> , 1955, Vol. II, 130, 264; WHO/BS 89, 116, 119, 137, 138, 204, 205, 267, 311, 357, 388, 427
1st Standard 1942 (0.0077 mg) 2nd Standard 1958	<i>Bull. Wld Hlth Org.</i> , 1947/48, <b>1</b> , 9; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, <b>147</b> , 10; <i>Bull. Hlth Org. L. o. N.</i> , 1942/43, <b>10</b> , 144, 151; 1945/46, <b>12</b> , 46; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 104, 341; 1955, Vol. II, 126; WHO/BS 353, 390, 424
1st Standard 1931 (0.1 mg) [Irradiated ergosterol] 2nd Standard 1949	<i>Bull. Wld Hlth Org.</i> , 1954, <b>10</b> , 875; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1950, <b>3</b> , 7; <i>Bull. Hlth Org. L. o. N.</i> , 1940/41, <b>9</b> , 425; 1945/46, <b>12</b> , 54; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 369; WHO/BS 8
1st Standard 1955	<i>Bull. Wld Hlth Org.</i> , 1957, <b>16</b> , 291; <i>Wld Hlth Org. techn. Rep. Ser.</i> , 1956, <b>108</b> , 18; WHO/BS 78, 135, 160, 163, 232, 271, 306
1st Standard 1926 (100.0 mg) 2nd Standard 1936 (80.0 mg) 3rd Standard 1949	<i>Bull. Wld Hlth Org.</i> , 1950, <b>2</b> , 655; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 522; 1936, <b>5</b> , 574; 1945/46, <b>12</b> , 41; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 93, 357; WHO/BS 33, 51
1st Reference Preparation 1925 2nd Reference Preparation 1935 3rd Reference Preparation 1940	<i>Bull. Wld Hlth Org.</i> , 1947/48, <b>1</b> , 9; <i>Bull. Hlth Org. L. o. N.</i> , 1935, <b>4</b> , 528; 1936, <b>5</b> , 573; 1945/46, <b>12</b> , 40; <i>Pharmacopoea Internationalis</i> , 1951, Vol. I, 147, 347; WHO/BS 26

Substance	International Unit of present standard (mg)	Form in which dispensed
<b>Miscellaneous (contd)</b>		
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
Pyrogen	—	Ampoules containing 2 mg of dried purified 'O' somatic antigen of <i>Shigella dysenteriae</i>

Years of establishment (in brackets, unitage of previous standards)	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
1st Reference Preparation 1925 2nd Reference Preparation 1936 3rd Reference Preparation 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 Reference Preparation 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 Reference Preparation 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
1st Reference Preparation 1958	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, 147, 11; WHO/BS 90, 147, 206, 264, 312, 365, 400, 425

**II. PROPOSED INTERNATIONAL BIOLOGICAL STANDARDS  
AND  
INTERNATIONAL BIOLOGICAL REFERENCE PREPARATIONS**

**A. IMMUNOLOGICAL SUBSTANCES**

Substance	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
Anti-Rh <sub>0</sub> (anti-D) albumin-potentiated blood-typing serum	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1950, 2, 12; WHO/BS 46, 165, 213, 328, 366, 407
Anti-rh' (anti-C) blood-typing serum	WHO/BS 46, 165, 366, 407
Anti-rh" (anti-E) blood-typing serum	WHO/BS 46, 165, 366, 407
Antistreptolysin O	WHO/BS 402, 443
Anti-yellow-fever serum	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1957, 136, 9; WHO/BS 416, 438
Anti-toxoplasma human serum	WHO/BS 447
<i>Bothrops</i> antivenin	WHO/BS 316, 317, 333, 334, 364, 373
<i>Naja</i> antivenin	WHO/BS 316, 317, 333, 334, 364, 373
Poliomyelitis vaccine	WHO/BS 235, 260, 321, 376, 376 Annex 1, 449; WHO/BS/IR/44
Typhoid vaccine	<i>Wld Hlth Org. techn. Rep. Ser.</i> , 1958, 147, 11; WHO/BS 217, 291, 301, 340, 378, 409, 441
Rabies vaccine	WHO/BS 372, 411, 411 Annex 1
Smallpox vaccine	WHO/BS 14, 73, 105, 371, 381, 383, 417, 442; WHO/BS/IR/70
Swine erysipelas vaccine	WHO/BS 344, 377, 435, 436
Egg lecithin (3rd Int. Ref. Prep.)	WHO/BS 360, 440
Anti- <i>Leptospira mankarso</i> serum	WHO/BS 437
Anti- <i>Leptospira muenchen</i> serum	WHO/BS 437
Anti- <i>Leptospira naam</i> serum	WHO/BS 437
Anti- <i>Leptospira poi</i> serum	WHO/BS 437
Anti- <i>Leptospira sarmin</i> serum	WHO/BS 437
Anti- <i>Leptospira schüffneri</i> serum	WHO/BS 437
Anti- <i>Leptospira bangkinang</i> serum	WHO/BS 437
Anti- <i>Leptospira celledoni</i> serum	WHO/BS 437
Anti- <i>Leptospira cynopteri</i> serum	WHO/BS 437
Anti- <i>Leptospira hardjo</i> serum	WHO/BS 437
Anti- <i>Leptospira kremastos</i> serum	WHO/BS 437
Anti- <i>Leptospira wolffii</i> serum	WHO/BS 437
Anti- <i>Leptospira australis</i> B serum	WHO/BS 437
Anti- <i>Leptospira benjamin</i> serum	WHO/BS 437
Anti- <i>Leptospira djasiman</i> serum	WHO/BS 437
Anti- <i>Leptospira medanensis</i> serum	WHO/BS 437
Anti- <i>Leptospira paidjan</i> serum	WHO/BS 437
Anti- <i>Leptospira sentot</i> serum	WHO/BS 437

## B. PHARMACOLOGICAL SUBSTANCES

Substance	References (WHO/BS refers to unpublished working documents of the WHO Expert Committees on Biological Standardization)
Amphotericin	WHO/BS 450
Kanamycin	WHO/BS 450
Leucomycin	WHO/BS 450
Ristocetin	WHO/BS 450
Vancomycin	WHO/BS 450
Procaine benzylpenicillin in oil with aluminium monostearate	WHO/BS 324, 349 Rev.1, 358 Rev.1, 403, 404
Corticotrophin (3rd Int. Standard)	WHO/BS 356, 386, 387, 432
Human menopausal gonadotrophin	WHO/BS 392
Prolactin (2nd Int. Standard)	WHO/BS 350, 405, 446
Vitamin B <sub>12</sub>	WHO/BS 34, 58, 61, 118, 142, 164, 209, 268, 355, 389

## III. 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  $\beta$  Antitoxin may be obtained on request from the International Laboratory for Biological Standards, Statens Seruminstitut, Copenhagen, Denmark, by laboratories desiring to establish their own working standard for research purposes.

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

Substance	International Unit (mg)	Adopted	Discontinued
Arsphenamine	—	1925	1935
Ouabain	—	1928	1954
Provitamin A ( $\beta$ -carotene)	0.0006	1931	1956
Vitamin B (synthetic vitamin B <sub>1</sub> )	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 ( $\alpha$ -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 $\beta$ antitoxin	2.623	1952	1956
*Chloramphenicol	—	1953	1956

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