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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*)

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* Invited but unable to attend :

Dr Sumiatno, Director, Pasteur Institute, Bandung, Indonesia

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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 obtained [2] the second International Standard for Streptomycin will be established.

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* 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

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[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. Phenoxymethylpenicillin

The Committee endorsed the final report [2] on the collaborative assay [3] of the proposed international standard and established this material as the International Standard for Phenoxymethylpenicillin. 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]

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[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 established [2] 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

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[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