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WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Seventeenth Report

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WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Geneva, 28 September - 3 October 1964

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Representative of the Food and Agriculture Organization of the United Nations :

Mr H. I. Field, Director, Central Veterinary Laboratories and Veterinary Investigation Services, Weybridge, Surrey, England

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Mr E. C. Hulse, Director, Department of Biological Standards, Central Veterinary Laboratory, Weybridge, Surrey, England (*Consultant*)

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WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Seventeenth Report

The WHO Expert Committee on Biological Standardization met in Geneva from 28 September to 3 October 1964.

Dr P. Dorolle, Deputy Director-General, on behalf of the Director-General, welcomed members of the Committee. He also welcomed the representative of the Food and Agriculture Organization of the United Nations, who is also the Director of the Veterinary Laboratory and Investigation Services at Weybridge where one of the three International Laboratories for Biological Standards is located.

Reviewing briefly the agenda before the Committee, the Deputy Director-General noted that the task of biological standardization is an endless one and that WHO would need committees such as this one as long as it exists. He cited some of the more important substances for which standards were to be considered in relation to the other projects within the programme of WHO activity and also referred to the increasing responsibility of the Committee for adopting international requirements for biological substances.

GENERAL

The question of including biological diagnostic reagents in the collection of international biological substances has been considered on a number of occasions by the Committee. Such reagents are distinct from the international standards and reference preparations, which are materials designed to serve in the quantitative assay of the activity of biological products. Diagnostic reagents on the other hand are used for such purposes as the identification of micro-organisms and should therefore have a high specificity for the organism concerned. Further, the performance of the international collaborative quantitative assays prerequisite to the adoption of international standards and certain reference preparations is not the type of study generally required for diagnostic reagents. The same strict attention should however be given to ensuring the stability of diagnostic reagents as

is given to international standards and reference preparations. The Committee, in extension of the views expressed in its thirteenth report,[1] agreed that a useful purpose would be served if diagnostic reagents were included in the collection of international biological substances and were held for reference purposes by an International Laboratory for Biological Standards. By this means they would serve for verification or replacement of diagnostic reagents.

The Committee therefore decided that a new category of international substances should be established, to be called *international biological reference reagents*.[2] This new category could include, in the first instance, the anti-leptospira sera now classified as international reference preparations. In addition, several specific antisera used for the identification of viruses and antisera specific for other micro-organisms, toxins or antigens could be included. The Committee agreed that reference reagents should be fully documented as regards their method of preparation, specificity and stability, together with relevant information on their use, before they could be considered as international reference reagents. In some instances, the studies necessary to characterize the materials intended to serve as reference reagents would be arranged under the supervision of an International Laboratory for Biological Standards. In such cases the International Laboratory would both hold and distribute the reagents, as in the case of international standards of reference preparations. In other instances, the International Laboratory for Biological Standards would act only as custodian of part of the materials, while other arrangements would be made for distribution of the reagents.

Since 1959, a number of international requirements for some of the more important biological products have been formulated. The aim of these requirements is to facilitate exchange of biological products between countries, to help control authorities and manufacturers to achieve an acceptable degree of safety and potency of their products, and to give guidance on points where diversity of opinion exists. The establishment of international requirements has undoubtedly revealed many problems concerning manufacture and control procedures and moreover has stimulated research in these problems.

Since those requirements that have been published to date have proved useful in the manufacture and control of a number of products, the Committee stressed that formulation of international requirements should be continued for further products and that requirements already established should be regularly revised on the basis of new scientific information. This work should continue to be a major responsibility of the Committee.

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[1] *Wld Hlth Org. techn. Rep. Ser.*, 1960, **187**.

[2] Unpublished working document WHO/BS/720.

PHARMACOLOGICAL

ANTIBIOTICS

1. Ristocetins

The Committee noted [1] that in accordance with the request in its sixteenth report [2] the preparation of ristocetin B had been examined and found suitable to serve as an international reference preparation. The Committee therefore established the material as the International Reference Preparation of Ristocetin B.

The Committee requested the National Institute for Medical Research, London, to arrange a collaborative assay of the International Reference Preparation of Ristocetin with a view to defining an international unit for ristocetin.

2. Oleandomycin

The Committee noted [3] that the collaborative assay of the proposed international standard had been completed and that in accordance with the authorization in its thirteenth report [4] the International Standard for Oleandomycin had been established and the International Unit for Oleandomycin had been defined as the activity contained in 0.001176 mg of the International Standard for Oleandomycin.

3. Nystatin

The Committee was informed that the stability studies of the International Standard for Nystatin requested in its sixteenth report [2] were in progress.

4. Gramicidin

The Committee noted [5] that in accordance with the request in its thirteenth report [4] the National Institute for Medical Research, London, had obtained a sample of gramicidin suitable to serve as an international reference preparation and that a collaborative assay was in progress. The Committee also noted [5] that the material consisted of a mixture of grami-

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[1] Unpublished working document WHO/BS/686.

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1964, **274**.

[3] Unpublished working document WHO/BS/714.

[4] *Wld Hlth Org. techn. Rep. Ser.*, 1960, **187**.

[5] Unpublished working document WHO/BS/682.

cidins comparable with gramicidin preparations used clinically. It authorized the National Institute for Medical Research to establish the material as the International Reference Preparation of Gramicidin on the basis of the results of the collaborative assay and to define the international unit with the agreement of the participants.

5. Spiramycin

The Committee noted [1] that studies had been made of the International Reference Preparation of Spiramycin and defined the International Unit for Spiramycin as the activity contained in 0.0003125 mg of the International Reference Preparation of Spiramycin.

6. Bacitracin

The Committee noted [2] that in accordance with the authorization in its fifteenth report [3] the second International Standard for Bacitracin had been established and that with the agreement of the participants in the collaborative assay the International Unit for Bacitracin had been defined as the activity contained in 0.01351 mg of the International Standard for Bacitracin.

7. Viomycin

The Committee noted [4] that in accordance with the request in its sixteenth report [5] the National Institute for Medical Research, London, had obtained material suitable to serve as an international standard to replace the International Reference Preparation of Viomycin and that a collaborative assay was in progress.

8. Kanamycin

The Committee noted [6] that in accordance with the request in its sixteenth report [5] studies had been made of the International Reference Preparation of Kanamycin which showed that it contained less than 1% of kanamycins other than kanamycin A.

The Committee also noted [6] that the National Institute for Medical Research, London, had obtained a preparation of kanamycin B which was

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[1] Unpublished working document WHO/BS/692.
[2] Unpublished working document WHO/BS/681.
[3] *Wld Hlth Org. techn. Rep. Ser.*, 1963, **259**.
[4] Unpublished working document WHO/BS/683.
[5] *Wld Hlth Org. techn. Rep. Ser.*, 1964, **274**.