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Twelfth Report

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Geneva, 22-27 September 1958

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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

* 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.[1] The Committee also noted that, in accordance with the authorization given in its eleventh report,[2] 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.[3] 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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[1] National Institute for Medical Research, London, unpublished working document WHO/BS/421

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1958, **147**, 5

[3] 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 [1] 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,[2] 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,[3] 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 [4] a consistent correlation between the results in man and in

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[1] National Institute for Medical Research, London, unpublished working document WHO/BS/429

[2] National Institute for Medical Research, London, unpublished working document WHO/BS/431

[3] National Institute for Medical Research, London, unpublished working document WHO/BS/430

[4] 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.[1] 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

[1] National Institute for Medical Research, London, unpublished working document