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Fifteenth Report

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Geneva, 10-15 December 1962

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Fifteenth Report

The Expert Committee on Biological Standardization met in Geneva from 10 to 15 December 1962.

Dr O. V. Baroyan, Assistant Director-General, on behalf of the Director-General, welcomed the members of the Committee, as well as the representative of the Food and Agriculture Organization of the United Nations. He stated that with the co-operation and concurrence of that Organization and of the Ministry of Agriculture, Fisheries and Food of Great Britain, a third International Laboratory for Biological Standards had now been designated at the Central Veterinary Laboratory, Weybridge, England. This International Laboratory would co-operate in the work of the existing international laboratories for biological standards at Copenhagen and London, but would devote its particular attention to the development of international biological standards that are primarily of veterinary importance.

The Assistant Director-General recalled the origins and growth of the work of the World Health Organization in establishing the many international biological standards now available. This work had been supervised by the fourteen Expert Committees that had met so far and had entailed the collaboration of several hundred participating laboratories throughout the world. In reviewing the extensive agenda before the present meeting he expressed his confidence that the Expert Committee would continue to maintain the high standard of work that had been established over the years.

GENERAL

In view of the increasing rate at which new prophylactic, therapeutic, and diagnostic biological substances are introduced in human and veterinary medicine, the Committee reconsidered its traditional procedures for establishing and distributing International Standards and International Reference Preparations, and for designating International Units of potency.

The expansion of the work supervised by the Committee in the veterinary field has now led to the nomination by WHO and FAO of a third International Laboratory for Biological Standards at the Central Veterinary Laboratory, Weybridge, England. In spite of this, the existing three Inter-

national Laboratories are not able to cope unaided with the work involved in elaborating and distributing all the International Standards and Reference Preparations that are being established and held under the auspices of the Committee. Thus, for example, it had already been necessary to solicit the aid of well-known laboratories in special fields for conducting collaborative assays of new preparations, such as snake-antivenins. For arrangements preceding the establishment of many other preparations the Committee depended on collaboration with the WHO Secretariat and with networks of designated WHO Reference Laboratories, as, for example, in the case of type-specific Leptospiral and Viral Sera. It was understood that, whenever it is expedient to adopt arrangements of this sort, the existing International Laboratories for Biological Standards should continue to be involved, at least in the sense that small quantities of the reference materials should be in the custody of those laboratories to ensure continuity when replacement of preparations becomes necessary.

Another aspect of the increasing rate and volume of the work of the Committee is the necessity of making standards or reference preparations of many substances available as soon as possible after such substances have been introduced into widespread use. If the establishment of International Units had to await the outcome and analysis of extensive collaborative assays there was a risk that an international unit-notation for expressing potencies would not be used universally—for example, in the case of new antibiotics, anti-poliovirus and anti-measles sera. During the years required to bring such assays to a successful completion, extensive work might already have been undertaken in many laboratories of the world and a practice of potency designation which differed from the later international one might already have become firmly entrenched.

The Committee considered that in cases where a sufficient quantity of a representative preparation of a substance had been obtained, it would be reasonable and expedient to designate international units of potency forthwith, and that the assignment of such international units might precede an extensive collaborative assay of the material. This procedure could be adopted in all cases where the Committee had reason to feel confident that the material collected was satisfactory and where a delay in introducing an international unit notation should be avoided.

The Committee upheld the distinction, described in its twelfth report,[1] between International Standards and International Reference Preparations, with the new proviso, following from the above reasoning, that an international unit can be assigned not only to an International Standard, but also to an International Reference Preparation, in spite of the fact that a preparation in the latter category might not at the time of its establishment have been extensively studied.

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[1] *Wld Hlth Org. techn. Rep. Ser.*, 1959, **172**

PHARMACOLOGICAL

ANTIBIOTICS

1. Neomycins

The Committee noted that the National Institute for Medical Research, London,[1] had been unable to obtain pure material to serve as an international standard for neomycin B, since all the samples examined contained variable amounts of other neomycins. In view of the fact that preparations of neomycin used clinically are mixtures of different neomycins, and that the existing International Reference Preparation of Neomycin was a representative sample of such preparations, the Committee considered that there was no need for an international standard for neomycin B. Instead, the Committee defined the International Unit for Neomycin as the activity contained in 0.00147 milligrams of the present International Reference Preparation of Neomycin.

2. Novobiocin

The Committee noted that the participants in the collaborative study of the International Reference Preparation of Novobiocin had not agreed on its suitability to serve as an international standard because of the wide discrepancy in the results of the assay between laboratories,[2] and that the National Institute for Medical Research, London, had therefore obtained a sample of purer material, a collaborative study of which was being arranged.

3. Ristocetins

The Committee noted[1] that these antibiotics had only limited use, and that the preparations that are used clinically are mixtures of different ristocetins. An examination of the present International Reference Preparation of Ristocetin had shown that it consisted predominantly of ristocetin B. The Committee therefore asked the National Institute for Medical Research, London, to ascertain whether this international reference preparation was suitable to serve as an international standard for mixed ristocetin preparations and if not, to obtain a more representative sample for this purpose.

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[1] Unpublished working document WHO/BS/592

[2] Unpublished working document WHO/BS/595

4. Nystatin

The Committee noted that the collaborative assay of the International Reference Preparation of Nystatin had been completed [1] and that this material would be established as the International Standard for Nystatin and the international unit defined by the National Institute for Medical Research, London, with the agreement of the participants in the assay, in accordance with the authorization in the fourteenth report of the Committee.[2]

5. Gramicidin S

The Committee noted [3] that a sample of gramicidin S had been received by the National Institute for Medical Research, London, from the Institute of Antibiotics, Academy of Medical Sciences, Moscow. The Committee decided, on the basis of the information provided by the Russian workers, to establish this material as the International Reference Preparation of Gramicidin S.

6. Gramicidin B

The Committee was informed that in accordance with the request made in its thirteenth report [4] the National Institute for Medical Research, London, was trying to acquire a sample of gramicidin B to serve as an international standard, but that so far it had not obtained sufficiently pure material.

7. Spiramycin

The Committee noted that the National Institute for Medical Research, London,[5] had obtained a sample of Spiramycin which, on the basis of the information received, was considered suitable to serve as an international reference preparation. The Committee therefore established this material as the International Reference Preparation of Spiramycin.

8. Bacitracin

The Committee noted that in accordance with the request made in its thirteenth report,[4] the National Institute for Medical Research, London,

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[1] Unpublished working document WHO/BS/580
[2] *Wld Hlth Org. techn. Rep. Ser.*, 1961, 222
[3] Unpublished working document WHO/BS/594
[4] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 187