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Ninth Report

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Ninth Session

Geneva, 10-15 October 1955

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Dr E. M. Lourie, Chief, Biological Standardization Section, WHO

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* Was unable to attend.

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Ninth Report *

The ninth session of the Expert Committee on Biological Standardization was held in Geneva from 10 to 15 October 1955.

The Assistant Director-General, Central Technical Services, on behalf of the Director-General of the World Health Organization, welcomed the members of the Committee and the representative of the Food and Agriculture Organization of the United Nations.

IMMUNOLOGICAL

1. Antivenins

The Committee noted reports on the standardization of antivenins [1] and discussed the complex problems involved. The Committee agreed that further studies on the venoms themselves should be made before proceeding with work on the standardization of antivenins. It decided therefore to begin by studying the venom of *Bothrops jararaca*, a properly prepared supply of which was offered by the Instituto Butantan, São Paulo, Brazil. The Committee agreed to ask the Instituto Butantan to arrange for the dispensing of this venom in a form acceptable for use as

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* The Executive Board, at its seventeenth session, adopted the following resolution :
The Executive Board

1. NOTES the ninth 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 EB17.R4, *Off. Rec. Wld Hlth Org.*, 1956, **68**, 2)

[1] Grasset, E., unpublished working document WHO/BS/316 (to be published in the *Bulletin of the World Health Organization*) ; Maaløe, O., unpublished working document WHO/BS/317 ; Jerne, N. K., unpublished working document WHO/BS/333 ; Christensen, P. A., unpublished working document WHO/BS/334

the working preparation, and to distribute it to interested laboratories for collaborative study of its suitability as an international reference preparation. The Committee considered that this would probably constitute appropriate material for such a study. It suggested that the investigation should include at least:

(1) an initial study of the toxicity of the venom, both freshly harvested and after storage at different temperatures;

(2) a study in several laboratories of the toxicity and thermostability of freeze-dried venom; and

(3) a collaborative study of the immunological relationship between this material and venoms from closely and distantly related congeneric snakes. Venoms and homologous antivenins for this part of the investigation will also be made available from the Instituto Butantan.

The Committee recommended that descriptions of the methods of selecting snakes from representative ecological niches and of collecting and preserving venoms, as developed in the Instituto Butantan, be made available to laboratories in other parts of the world with a view to deciding in each area whether batches of venom from the important species of snakes of the area might be obtained, which could be considered equally suitable for use in biological standardization.

The Committee recommended that laboratories producing antivenins in these geographical regions should arrange for the collection and examination of such venoms. It was suggested that the venom of *Naja flava* would be suitable material for further studies; it is understood that the South African Institute for Medical Research, Johannesburg, may be able to supply material in due course.

2. Blood-Typing Sera [1]

The Committee noted that the proposed international standard for anti-Rh_0 (anti-D) blood-typing-serum (for the characterization of saline-agglutinating sera) has been distributed for collaborative investigation.

The Committee noted further that a large batch of " incomplete " or albumin-agglutinating anti-D serum has also been collected which will likewise be submitted to a collaborative investigation of its suitability as a standard.[2]

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[1] Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/328

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1955, **96**, 5

3. Clostridium Antitoxins

3.1 *Clostridium welchii (perfringens) antitoxins*

The Committee noted that the International Standard for Gas-Gangrene Antitoxin (*perfringens*), which is a type-A antitoxin, and the newly established International Reference Preparations of *Clostridium welchii* Antitoxins of types B and D [1] have been compared, and that their contents of antitoxin against the *Clostridium welchii* toxin types A, B, and D have been determined as given in the following tabulation : [2]

Type of standard or reference serum	*One antitoxic unit is contained in the following weight (mg) of types*		
	A	*B*	*D*
A	0.1132	negligible activity	negligible activity
B	0.2293	0.0137	negligible activity
D	0.6876	negligible activity	0.0657

The Committee welcomed a suggestion that the Paul-Ehrlich-Institut, Frankfurt-on-Main, and the Veterinary Laboratory, Weybridge, Surrey, in co-operation undertake to determine the relative potencies of several antitoxins in terms of the International Reference Preparations of *Clostridium welchii* Antitoxin of types B and D, using for this purpose a series of differently prepared types B and D test-toxins.

3.2 *Clostridium septicum antitoxin*

The Committee asked the Statens Seruminstitut, Copenhagen, to arrange for replacement of the International Standard for Gas Gangrene Antitoxin (*vibrion septique*), since the stock of the existing standard is low.[3]

The Committee discussed various methods of dispensing and distributing the international serum standards. It recommended that the collaborative study of the replacement for the International Standard for Gas Gangrene Antitoxin (*vibrion septique*) should include an examination of freeze-dried serum, both undiluted and diluted, in parallel with the liquid

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[1] *Wld Hlth Org. techn. Rep. Ser.*, 1955, **96**, 6

[2] Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/281; Barr, M. & Hulse, E. C., unpublished working document WHO/BS/298 ; Skulberg, A. & Heyningen, W. E. van (1956) *Bull. Wld Hlth Org.*, **14**, 557

[3] Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/318

serum itself. Subject to the results of this investigation, the standard should, if possible, be issued in a freeze-dried diluted form and should be sent to users on request rather than as a routine issue of a solution in glycerol every six months.

The Committee also asked the Statens Seruminstitut, Copenhagen, to investigate the question of adopting this form of distribution for other serum standards in the future.

4. Diphtheria Toxoids and Antitoxin

4.1 *International Standards for Diphtheria Toxoid, Adsorbed, and for Diphtheria Toxoid, Plain*

The Committee noted reports from the Paul-Ehrlich-Institut, Frankfurt-on-Main,[1] and the Statens Seruminstitut, Copenhagen,[2] on the stability of the proposed international standard for diphtheria toxoid, adsorbed, and on its assay in terms of the existing German national standard.[3] The Committee established the material as the International Standard for Diphtheria Toxoid, Adsorbed, and, following its usual practice of equating the International Unit as far as possible with an existing national unit, defined one International Unit as the activity contained in 0.75 mg of the standard preparation, this quantity being the equivalent of one *Schutzeinheit* (protective unit).

The Committee also defined the International Unit of Diphtheria Toxoid, Plain, as the activity contained in 0.5 mg of the existing International Standard. This assignment of unitage is arbitrary since there is no national unit for preparations of diphtheria toxoid, plain.

4.2 *Diphtheria antitoxin for flocculation test*

The Committee asked the Statens Seruminstitut, Copenhagen, to arrange for replacement of the International Standard for Diphtheria Antitoxin for the Flocculation Test, since the stock of the existing standard is low.[4]

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[1] Prigge, R., unpublished working document WHO/BS/330

[2] Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/331

[3] Participants in the collaborative study: Greenberg, L., Laboratory of Hygiene, Ottawa, Canada; Ikić, K., Central Institute of Hygiene, Yugoslavia; Jerne, N. K., Maaløe, O. & Scheibel, I., Statens Seruminstitut, Denmark; Prigge, R., Paul-Ehrlich-Institut, Germany

[4] Statens Seruminstitut, Copenhagen, unpublished working document WHO/BS/318