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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Tenth Report

WORLD HEALTH ORGANIZATION

PALAIS DES NATIONS

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1957

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Tenth Session *

Geneva, 8-13 October 1956

Members :

Lieutenant-Colonel M. L. Ahuja, Medical Adviser to the High Commissioner for India, London, England

Dr A. do Amaral, Director, Instituto Butantan, São Paulo, Brazil (*Vice-Chairman*)

Dr E. Grasset, Professor of Hygiene ; Director, Institute of Hygiene, University of Geneva, Switzerland

Dr J. H. Humphrey, Department of Biological Standards, National Institute for Medical Research, Mill Hill, London, England (*Rapporteur*)

Dr M. Kitaoka, Director, Department of Viral and Rickettsial Diseases, National Institute of Health, Tokyo, Japan

Dr O. Maaløe, Chief, Department of Biological Standardization, Statens Seruminstitut, Copenhagen, Denmark (*Chairman*)

Dr A. A. Miles, Director, Lister Institute of Preventive Medicine, London, England

Dr G. Penso, Chief, Laboratory of Microbiology, Istituto Superiore di Sanità, Rome, Italy

Temporary adviser :

Dr R. Murray, Director, Division of Biological Standards, National Institutes of Health (Public Health Service), Bethesda, Md., USA

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

Sir Thomas Dalling, Chief Veterinary Consultant, Animal Production Branch, Agriculture Division, FAO

Dr A. W. Stableforth, Director, Central Veterinary Laboratory, Ministry of Agriculture, Fisheries and Food, Weybridge, Surrey, England

Secretariat :

Dr W. Aeg. Timmerman, Director, Division of Therapeutic Substances, WHO

Dr N. K. Jerne, Acting Chief, Biological Standardization Section, WHO (*Secretary*)

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* Invited but unable to attend :

Dr E. Dussert, Jefe del Departamento de Control y Laboratorios, Instituto Bacteriológico de Chile, Santiago, Chile

Dr P. Lépine, Chef du Service des Virus, Institut Pasteur, Paris, France

Dr E. A. North, Deputy Director (Research), Department of Health, Commonwealth Serum Laboratories, Parkville, Victoria, Australia

Dr R. Prigge, Director, Paul-Ehrlich-Institut, Staatliche Anstalt für Experimentelle Therapie, Frankfurt-on-Main, Germany

Dr H. Welch, Director, Division of Antibiotics, Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C., USA

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Tenth report *

The tenth session of the Expert Committee on Biological standardization was held in Geneva from 8 to 13 October 1956.

The Deputy Director-General, on behalf of the Director-General of the World Health Organization, welcomed the members of the Committee, the temporary adviser and the representatives of the Food and Agriculture Organization of the United Nations.

IMMUNOLOGICAL

ANTIGENS

1. Pertussis Vaccine

The Committee noted that, as a result of field trials, there is now evidence that the protective value of pertussis vaccines in man is indicated by their potencies as determined in mice by the intracerebral challenge method.[1] The proposed international standard preparation has been extensively compared in the laboratory [2] (*a*) with the British Reference Vaccine which has been proved to be effective in man, and (*b*) with the

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

The Executive Board

1. NOTES the tenth 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 EB19.R5, *Off. Rec. Wld Hlth Org.*, 1957, **76**, 3)

[1] See *Brit. med. J.*, 1956, **2**, 454 (Report to the Whooping-Cough Immunization Committee of the Medical Research Council).

[2] Participants: Institut Pasteur, Paris, France; Rijks Instituut voor de Volksgezondheid, Netherlands; Michigan Department of Health, USA; Biological Standards Control Laboratory, England; Department of National Health and Welfare, Canada; Statens Seruminstitut, Denmark; Commonwealth Serum Laboratories, Australia; National Institutes of Health, USA; Lister Institute of Preventive Medicine, England

Reference Vaccine of the National Institutes of Health, Bethesda, Md.[1] Accelerated degradation tests have shown that the proposed international standard preparation is highly stable.[1] The Committee accordingly authorized the Statens Seruminstitut, Copenhagen, with the agreement of the participants, to define the unitage on the basis of the results of the collaborative assay, so that the International Unit for pertussis vaccine is equivalent to the protective unit used by the National Institutes of Health, and to establish the material as the International Standard for Pertussis Vaccine.

2. Typhoid Vaccines

The Committee considered the outcome of the field trial of both phenolized and alcoholized vaccines in Yugoslavia, and of the tests of these preparations carried out in several laboratories. Within the restricted circumstances of the field trial, only the phenolized vaccine could be shown to confer significant protection to man, a result which could not have been predicted from laboratory tests of antigenic potency; in the laboratory, the alcoholized vaccine proved the more effective in inducing the formation of Vi-agglutinins, and was at least as effective as the phenolized vaccine in active and passive protection tests.[2]

The Committee agreed that further research was needed on laboratory assay methods and on other types of vaccine, where possible in terms of a standard. Because of the relative instability of liquid vaccines, the Committee requested the Statens Seruminstitut, Copenhagen, to obtain a quantity of a stable, acetone-dried typhoid vaccine and to initiate studies of this material in collaboration with other interested organizations and laboratories. The Committee noted that sufficient quantities of the vaccines used in the Yugoslav field trials are still available for such collaborative studies.

3. Cholera Vaccines

The Committee noted that cholera vaccination has been widely practised during the past 50 years[3] and that the practice is increasing; but that laboratory tests of the protective value of cholera vaccines do not give results reproducible in different laboratories. The Committee also noted the report of the Committee on International Quarantine which " stressed the need for international standardization of anticholera vaccines

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[1] Maaløe, O., unpublished working document WHO/BS/338

[2] Maaløe, O., unpublished working document WHO/BS/340

[3] WHO Secretariat, unpublished working document WHO/BS/342

and expressed the wish that the Expert Committee on Biological Standardization and other experts concerned would continue to study the matter ".[1] The Committee emphasized the urgent need for further study of improved methods of testing cholera vaccines, and recommended the Secretariat to encourage and assist work directed to this end.

4. Rabies Vaccine

The Committee noted that studies of the proposed international reference preparation of rabies vaccine have shown that the material appears to be suitable,[2] and it endorsed the recommendation by the Secretariat to the Expert Committee on Rabies that a collaborative examination of its stability and suitability in assay should be arranged.

5. Smallpox Vaccine

The Committee noted that a sample of a very stable freeze-dried smallpox vaccine (sheep lymph) [3] has been offered by the Lister Institute of Preventive Medicine, London, for an international reference preparation, and asked the Statens Seruminstitut, Copenhagen, to arrange a collaborative examination of this material.

6. Swine Erysipelas Vaccine

The Committee noted the progress made by the Central Veterinary Laboratory, Weybridge, Surrey, in examining an adsorbed, freeze-dried preparation of swine erysipelas vaccine,[4] and asked the Laboratory, in conjunction with the Paul-Ehrlich-Institut, Frankfurt-on-Main, to arrange for a collaborative examination of the material for stability and suitability in assay, with a view to its establishment as the International Standard for Swine Erysipelas Vaccine.

7. Japanese B Encephalitis Vaccine

The Committee asked the Secretariat to assess the need for an international reference preparation of Japanese B encephalitis vaccine.

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[1] *Off. Rec. Wld Hlth Org.*, 1956, **72**, 36

[2] Kaplan, M., unpublished working document WHO/BS/372

[3] Cockburn, W. C. et al., unpublished working document WHO/BS/371

[4] Central Veterinary Laboratory, Standards Department, Weybridge, unpublished working document WHO/BS/344

8. Leptospirosis Vaccines

The Committee asked the Secretariat to assess the need for international reference preparations of leptospirosis vaccines.

9. Cardiolipin

The Committee noted that the collaborative study of the material for replacement of the present International Reference Preparation of Cardiolipin is nearly completed,[1] and authorized the Statens Seruminstitut, Copenhagen, with the agreement of the participants, to establish the material as the third International Reference Preparation of Cardiolipin.

10. Lecithins

The Committee noted that stocks of the International Reference Preparations of Egg and Beef Heart Lecithin are adequate for at least two years and that, since the general use of beef heart lecithin is decreasing, replacement of the corresponding International Reference Preparation will probably be unnecessary.[1] The Committee asked the Statens Seruminstitut, Copenhagen, to collect material for eventual replacement of the International Reference Preparation of Egg Lecithin.

ANTIBODIES

11. Diphtheria Antitoxin for Flocculation Test

The Committee endorsed the establishment by the Statens Seruminstitut, Copenhagen, of the fourth International Standard for Diphtheria Antitoxin for the Flocculation Test.[2]

12. Clostridium welchii (Perfringens) Antitoxins

The Committee noted the progress made by the Central Veterinary Laboratory, Weybridge, Surrey,[3] in demonstrating that, when highly

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[1] International Serological Reference Laboratory, Statens Seruminstitut, Denmark, unpublished working document WHO/BS/360

[2] Statens Seruminstitut, Denmark, unpublished working document WHO/BS/359

[3] Central Veterinary Laboratory, Standards Department, Weybridge, unpublished working document WHO/BS/343