

*This report contains the collective views of an international group of experts and
does not necessarily represent the decisions or the stated policy of the World Health Organization*

WHO Technical Report Series

858

WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Forty-fifth Report



World Health Organization

Geneva 1995

WHO Library Cataloguing in Publication Data

WHO Expert Committee on Biological Standardization
WHO Expert Committee on Biological Standardization :
forty-fifth report.

(WHO technical report series ; 858)

1. Biological products – standards I. Series

ISBN 92 4 120858 9
ISSN 0512-3054

(NLM Classification: QW 800)

The World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full. Applications and enquiries should be addressed to the Office of Publications, World Health Organization, Geneva, Switzerland, which will be glad to provide the latest information on any changes made to the text, plans for new editions, and reprints and translations already available.

© World Health Organization 1995

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. All rights reserved.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

Printed in Switzerland

95/10584 – Benteli – 7000

Contents

Introduction	1
General	1
Development and distribution of International Biological Standards and Reference Reagents	1
Suitability of reference materials for use in different assay systems	3
Regulation and licensing of biological products	3
Guidelines for the inspection of manufacturers of biological products	4
Need for expert advice	4
Cytokines	5
Interferons	6
Acellular pertussis vaccines	6
Priority setting	6
Publicizing the work of the Committee	7
Requirements for biological substances	7
Requirements for hepatitis A vaccine (inactivated)	7
Requirements for hepatitis B vaccine prepared from plasma	7
Requirements for yellow fever vaccine	8
International reference materials	8
Antibiotics	8
Amphotericin B, vancomycin and spiramycin	8
Gentamicin	8
Antibodies	9
Anti-toxoplasma serum	9
Anti-rubella serum and anti-rubella immunoglobulin	9
Anti-borrelia serum	10
Anti-streptolysin O	10
Anti-parvovirus B19 serum	10
Anti-mumps serum	10
Anti-cytomegalovirus immunoglobulin	11
Antibodies to human interferon alfa and beta	11
Thyroid-stimulating antibody	11
Antigens and related substances	12
Hepatitis A vaccine (inactivated)	12
Measles vaccine (live)	12
Mumps vaccine (live)	12
Rubella vaccine (live)	13
Pertussis vaccine (whole-cell)	13
Poliomyelitis vaccine (inactivated)	13
Prostate-specific antigen	14
Blood products and related substances	14
Antithrombin, plasma	14
Factors II, IX and X concentrate	15
Factor VIII concentrate	15
Factor IXa	15

Plasma fibrinogen	16
Plasminogen activators	16
Plasminogen-activator inhibitor 1	16
Protein S in plasma	16
Tissue factor pathway inhibitor	16
Cytokines	17
Bactericidal/permeability-increasing protein	17
Epidermal growth factor	17
Insulin-like growth factor 1	17
Interferon gamma, recombinant human	18
Interleukin-2 soluble receptor	18
Interleukin-3 and interleukin-4	18
Interleukin-8	18
Stem cell factor	19
Endocrinological and related substances	19
Inhibin, recombinant human	19
Luteinizing hormone, recombinant human	19
Somatropin	19
Toxins	20
Endotoxin	20
Annex 1	
Regulation and licensing of biological products in countries with newly developing regulatory authorities	21
Annex 2	
Requirements for hepatitis A vaccine (inactivated)	36
Annex 3	
Requirements for hepatitis B vaccine prepared from plasma	61
Annex 4	
Biological substances: International Standards and Reference Reagents	93
Annex 5	
Requirements for Biological Substances and other sets of recommendations	96
Annex 6	
Corrigenda: reference materials for apolipoproteins A-1 and B and haemoglobins A ₂ and F	102

WHO Expert Committee on Biological Standardization

Geneva, 11–18 October 1994

Members

- Dr D. H. Calam, National Institute for Biological Standards and Control, Potters Bar, Herts., England (*Rapporteur*)
- Dr S. G. Drozdov, Director, Institute of Poliomyelitis and Viral Encephalitides, Moscow, Russian Federation
- Dr I. D. Gust, Research and Development Director, CSL Ltd, Parkville, Victoria, Australia (*Chairman*)
- Dr M. C. Hardegree, Director, Office of Vaccine Research and Review, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD, USA
- Mr P. E. Lemoine, formerly Head, Biological Standardization, Institute of Hygiene and Epidemiology, Brussels, Belgium (*Vice-Chairman*)
- Mr J. Lyng, Head, Laboratory of Biological Standardization, Statens Seruminstitut, Copenhagen, Denmark
- Dr F. A. Ofori, Department of Pathology, McMaster University, Hamilton, Ontario, Canada
- Dr It-Koon Tan, Division Head, Department of Pathology, Singapore General Hospital, Singapore
- Mr Zhou Hai-jun, Director, National Institute for the Control of Pharmaceutical and Biological Products, Temple of Heaven, Beijing, China

Representatives of other organizations

Council of Europe

- Mr J.-M. Spieser, Principal Scientific Officer, Biological Standardization Department, European Pharmacopoeia Commission, Council of Europe, Strasbourg, France

International Federation of Pharmaceutical Manufacturers Associations

- Dr B. Montagnon, Head, Registration, Pasteur Mérieux Sera and Vaccines, Marcy l'Etoile, France

- Dr J. Peetermans, Director, Quality Control and Regulatory Affairs, SmithKline Beecham Pharmaceuticals, Rixensart, Belgium

International Society on Thrombosis and Haemostasis

- Dr T. Barrowcliffe, National Institute for Biological Standards and Control, Potters Bar, Herts., England

Secretariat

- Dr E. Fajardo, Finlay Institute, Centre for Investigation and Production of Vaccines and Sera, Havana, Cuba (*Temporary Adviser*)
- Dr V. Grachev, Scientist, Biologicals, WHO, Geneva, Switzerland
- Dr E. Griffiths, Chief, Biologicals, WHO, Geneva, Switzerland (*Secretary*)
- Dr M. Haase, Paul Ehrlich Institute, Langen, Germany (*Temporary Adviser*)
- Dr G. Hansen, Statens Seruminstitut, Copenhagen, Denmark (*Temporary Adviser*)
- Dr A. Padilla, Scientist, Biologicals, WHO, Geneva, Switzerland

Professor W. G. van Aken, Medical Director, Central Laboratory of the Netherlands
Red Cross Blood Transfusion Service, Amsterdam, Netherlands (*Temporary
Adviser*)

Dr W. W. Wright, Senior Scientist, Drug Standards Division, United States
Pharmacopeia, Rockville, MD, USA (*Temporary Adviser*)

Dr K. Zoon, Director, Center for Biologics Evaluation and Research, Food and Drug
Administration, Rockville, MD, USA (*Temporary Adviser*)

Introduction

The WHO Expert Committee on Biological Standardization met in Geneva from 11 to 18 October 1994. The meeting was opened on behalf of the Director-General by Dr F. S. Antezana, Assistant Director-General.

Dr Antezana emphasized the contribution of WHO's biological standardization programme to health programmes in Member States through the provision of biological reference materials and the establishment of minimum requirements for biological substances. WHO was able to provide only limited financial support to the programme, but that reflected the current financial situation rather than a lack of commitment on the part of the Organization. He thanked the International Laboratories for Biological Standards and their governments for the support that they provided to the biological standardization programme. He also drew attention to the rapid and continuing developments, particularly in the fields of recombinant products, cytokines and interferons, and informed the Committee of two WHO informal consultations that had been held recently on the last two topics. He noted that the work of the Committee continued to reflect technical progress in these fields.

General

Development and distribution of International Biological Standards and Reference Reagents

The Committee was informed of the distribution of international reference materials by the International Laboratories for Biological Standards during 1993 (Table 1). It emphasized that the programme was essential for the harmonization of reference materials and requirements internationally, and to facilitate the distribution and use of biological products.

The Committee was concerned to learn of the reduction that WHO had been obliged to make in the budgets of the International Laboratories, and emphasized the continuing and increasing importance of their work. It recognized with gratitude the efforts that the International Laboratories were making, with their own resources and the support of their governments, to maintain their contribution to the biological standardization programme. Nevertheless, the growing demands made on these laboratories and requests that the programme should be expanded increased concern about funding. Possibilities that should be explored included obtaining funding from other sources for specific project areas and recovering some of the costs through more realistic charges for handling and processing requests for reference materials.

The Committee therefore requested the Secretariat to review the priorities and needs for additional standards, to obtain more detailed

**onal Biological Standards and Reference Reagents distributed in 1993 to laboratories in WHO regions by the International
ries for Biological Standards^a**

WHO	Number of items distributed by International Laboratories for Biological Standards					% of total for all regions
	Amsterdam	Copenhagen	Potters Bar	Weybridge	Total	
	25	92	66	0	183	1.4
	147	667	1 591	19	2 424	18.4
nean	16	105	107	2	230	1.7
	1 096	1 437	6 044	122	8 699	66.1
st	87	195	305	5	592	4.5
	4	191	830	14	1 039	7.9
	1 375	2 687	8 943	162	13 167	100.0

aboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, Netherlands: items distributed during the calendar year 1993. Statens
stitut, Copenhagen, Denmark: items distributed during the calendar year 1993. National Institute for Biological Standards and Control, Potters Bar, Herts.,
items distributed between 1 April 1993 and 31 March 1994. Central Veterinary Laboratory, Weybridge, Surrey, England: items distributed during the
year 1993.

预览已结束，完整报告链接和二维码如下：

https://www.yunbaogao.cn/report/index/report?reportId=5_30705

