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CONTENTS

Page

General 7

International standards and units for biological substances 7
Biological standards for biological and chemical reference purposes 7
Matrix standards 9
Biotechnology 10
Causes of damage to polypeptides during freeze-drying 10
Information memoranda distributed with standards 11
Veterinary biologicals produced by modern techniques 12
Human interferons 12
Potency assay of diphtheria and tetanus toxoids 12
Varicella vaccine 13

SUBSTANCES

Antibiotics

1. Erythromycin 13
2. Netilmicin 14
3. Sisomicin 14
4. Tobramycin 15
5. Kanamycin 15

Antibodies

6. *Clostridium botulinum* type B antitoxin, equine 15
7. Cholera antitoxin, goat 15

Antigens

8. House dust mite (*Dermatophagoides pteronyssinus*) extract 16

Blood products and related substances

9. Anti-C complete and anti-E complete blood typing serum 16
10. Anti-D complete blood typing sera 17
11. Anti-varicella zoster immunoglobulin 17
12. Rabies immunoglobulin 17
13. Prekallikrein activator (PKA) 18
14. Beta-thromboglobulin (β-TG) and platelet factor 4 (PF_4) 18
15. Human tissue plasminogen activator (t-PA) 19
16. $Beta_2$ microglobulin (β_2m) 19

Endocrinological and related substances

17. Insulins 20
18. Proinsulins and human insulin C-peptide 20
19. Prolactin, human, for immunoassay 20
20. Calcitonins 21
21. Growth hormone releasing factor 21

22. Alpha and beta subunits of human pituitary luteinizing hormone 22
23. Alpha and beta subunits of thyroid stimulating hormone (TSH) 22
24. Follicle stimulating hormone (FSH) 23
25. Growth hormone and growth factors 23

Miscellaneous

26. Endotoxin 24
27. Interferons 24
28. Rubella antiserum, rabbit 25
29. Human liver ferritin protein 25

REQUIREMENTS FOR BIOLOGICAL SUBSTANCES

30. Requirements for diphtheria toxoid, pertussis vaccine, tetanus toxoid, and combined vaccines 26
31. Requirements for hepatitis B vaccine prepared from plasma 26
32. Requirements for varicella vaccine (live) 27

Acknowledgements 27

ANNEXES

Annex 1. Standardization of interferons 28
Annex 2. Requirements for diphtheria toxoid, pertussis vaccine, tetanus toxoid, and combined vaccines (addendum 1984) 65
Annex 3. Requirements for hepatitis B vaccine prepared from plasma (revised 1984) 70
Annex 4. Requirements for varicella vaccine (live) 102
Annex 5. Biological substances: international standards, reference preparations, and reference reagents 134
Annex 6. Requirements for biological substances and other sets of recommendations 137

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Geneva, 12–18 June 1984

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WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Thirty-fifth Report

The WHO Expert Committee on Biological Standardization met in Geneva from 12 to 18 June 1984. The meeting was opened on behalf of the Director-General by Dr Lu Rushan, Assistant Director-General.

GENERAL

International standards and units for biological substances

The Committee was informed that, in compliance with the Constitution of the World Health Organization, a list of biological standards updated since 1973 and, for the first time, a list of international biological reference preparations had been placed before the Executive Board and the Thirty-seventh World Health Assembly.[1] The Health Assembly recommended that Member States recognize officially the international standards and reference preparations and units for biological substances enumerated in the two lists.[2] The Health Assembly was informed that in many instances the potency, in terms of international units, of each biological standard is now defined on the basis of the contents of the ampoule rather than in terms of a defined weight of the standard.

Biological standards for biological and chemical reference purposes

The Committee considered the need for reference preparations of biological substances for use in control procedures of physico-chemical tests. Such preparations may be needed for tests of purity by liquid chromatography or for tests of identity in which a map of the peptides produced by treating the test material with an

[1] *International standards and units for biological substances.* Geneva, World Health Organization, 1984 (document WHA37/1984/Rec/1, Annex 4).

[2] Resolution WHA37.27. *Handbook of resolutions and decisions of the World Health Assembly and the Executive Board. Volume II, 1985,* p. 135.

enzyme is compared with that of the reference material treated identically. For such purposes well characterized preparations of purified stable authentic substances are required; these should be free from extraneous materials that might interfere with the analyses. For certain antibiotics, the international standards themselves may be suitable for such tests, as well as serving their original purpose as standards for bioassay. Moreover, when it becomes possible to characterize a substance completely by chemical and physical means and an international standard for bioassay is no longer required, the remaining stock of the standard could be reserved for use for such physicochemical tests. Conversely, if for certain substances the international standard established for bioassay is unsuitable for physicochemical tests, there may be a need for an authentic preparation of the pure substance. Thus, a preparation of human growth hormone (form with relative molecular mass 22 000) is needed for tests of identity in connection with the product made by recombinant DNA (rDNA) methods, since the International Standard for Growth Hormone, for Bioassay, consists of a mixture of the several natural forms of the hormone (see item 25, page 23).

The Committee also considered the question of replacing biologically standardized reference preparations, (e.g., the International Standard for Erythromycin) with authentic chemical reference preparations. The Committee recognized that authentic chemical reference substances could also be used for reference purposes in biological assays or for identification purposes. The technical problems involved in confirming the purity of materials being considered for use as authentic chemical reference substances were discussed. It was recognized that although methods of analysis such as chromatography can reveal the presence of extremely small quantities of certain impurities, they may not detect certain others. The demonstration of a single chromatographic peak does not of itself provide proof of the purity of the preparation. Frequently, other chemical and physical tests, such as phase-solubility analysis, can provide strong confirmatory evidence of purity.

In the past, whenever it was concluded that an international biological reference material should be discontinued, in most instances, it was found convenient and helpful for the WHO Collaborating Centre for Chemical Reference Substances, Solna, Sweden, to establish and provide authentic chemical material for international use. Also, in some such instances, the International Pharmacopoeia specifies that the authentic chemicals may also be