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**REVIEW OF RECOMMENDATIONS AND GUIDELINES
FOR BIOLOGICAL SUBSTANCES USED IN
MEDICINE AND OTHER DOCUMENTS**

Dr D. Calam, Pewsey, United Kingdom

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The consolidated list of Recommendations and guidelines for biological substances used in medicine and other documents is published as an Annex in each report of ECBS. The latest version appears as Annex 7 to the 54th report of the meeting held in November 2003.

The recommendations (formerly 'requirements') and guidelines are scientific and advisory in nature but they may be adopted by a national regulatory authority as national requirements or they may be used as the basis for national requirements. These international recommendations and guidelines are also intended to provide guidance to those responsible for the production of biologicals as well as to others who may have to decide upon appropriate methods of testing, assay and control in order to ensure the quality, safety and efficacy of these products.

Although the consolidated list has been published for many years and individual documents have been revised, amended or discontinued, no comprehensive review of the items in the published list has been performed in recent years.

The purpose of this document is to propose changes to the format of the list of recommendations, guidelines and other documents and to identify individual items for revision, updating or possible discontinuation.

Because the documents listed have been published over a period of almost forty years, a further consideration is whether editorial revision of the style, format and nomenclature used in older documents should be undertaken in order to ensure consistency in presentation and interpretation.

A review of the consolidated list may help to identify other products or topics currently of importance in biological areas for which the drafting of recommendations or guidelines would be beneficial.

Finally, the publication of a single volume containing all the updated recommendations and guidelines should be considered. Such a volume would collect together into one place documents appearing in many different ECBS reports and constitute a very important resource for all those involved in the development, manufacture and regulation of biologicals.

In the tables in the succeeding pages, the title of the document, its year of publication and the action proposed or in progress are listed.

Recommendations and Guidelines:	Reference	Action proposed or in progress
Acellular pertussis component of monovalent or combined vaccines	Adopted 1996, TRS 878 (1998)	
Animal Cells, use of, as <i>in vitro</i> Substrates for the Production of Biologicals	Revised 1996, TRS 878 (1998); Addendum 2003, TRS in press	
BCG Vaccine, dried	Revised 1985, TRS 745 (1987); Amendment 1987, TRS 771 (1988)	Update in progress
Biological Products prepared by recombinant DNA technology	Adopted 1990, TRS 814 (1991)	Update needed.
Blood, Blood Components and Plasma Derivatives: collection, processing and quality control	Revised 1992, TRS 840 (1994)	Update agreed but on hold
Blood plasma products, human: viral inactivation and removal procedures	Adopted 2001, TRS 924 (2004)	
Cholera Vaccine (Inactivated, oral)	Adopted 2001, TRS 924 (2004)	
Diphtheria, Tetanus, Pertussis and Combined Vaccines	Revised 1989, TRS 800 (1990); Addendum 2003, TRS in press	Update in progress
DNA Vaccines	Adopted 1996, TRS 878 (1998)	Update in progress
<i>Haemophilus influenzae</i> Type b Conjugate Vaccines	Revised 1998, TRS 897 (2000)	
Haemorrhagic Fever with Renal Syndrome (HFRS) Vaccine (Inactivated)	Adopted 1993, TRS 848 (1994)	
Hepatitis B Vaccine prepared from Plasma	Revised 1987, TRS 771 (1988)	Review needed. If necessary, update
Hepatitis B Vaccines made by Recombinant DNA Techniques	Adopted 1988, TRS 786 (1989); Amendment 1997, TRS 889 (1999)	Update needed.
Human Interferons made by Recombinant DNA Techniques	Adopted 1987, TRS 771 (1988)	Update needed.
Human Interferons prepared from Lymphoblastoid Cells	Adopted 1988, TRS 786 (1989)	Review needed. If necessary, update
Influenza Vaccine (Inactivated)	Revised 2003. TRS in press	
Influenza Vaccine (Live)	Adopted 1978, TRS 638 (1979)	Review needed. If necessary, update. Revised document on influenza vaccine (inactivated) due for publication 2004
Japanese Encephalitis Vaccine (Inactivated) for Human Use	Adopted 1987, TRS 771 (1988)	Review needed. If necessary update. Document on live vaccine was published in 2002.
Japanese Encephalitis Vaccine (Live) for Human Use	Adopted 2000, TRS 910 (2002)	
Louse-borne Human Typhus Vaccine (Live)	Adopted 1982, TRS 687 (1983)	Review needed. If necessary update.

Recommendations and Guidelines:	Reference	Action proposed or in progress
Measles, Mumps and Rubella Vaccines and Combined Vaccine (Live)	Adopted 1992 TRS 848 (1994),	
Meningococcal Polysaccharide Vaccine	Adopted 1975, TRS 594 (1976); Addendum 1980, TRS 658 (1981), Amendment 1999, TRS 904 (2002)	This document has undergone revision and amendment. It should be reviewed and a single revised document issued
Meningococcal C conjugate vaccines	Adopted 2001, TRS 924 (2004) Addendum 2003, TRS 926 (2004)	
Monoclonal Antibodies	Adopted 1991, TRS 822 (1992)	Review and update. The European Pharmacopoeia has just adopted a monograph for monoclonal antibodies.
Pneumococcal conjugate vaccines	Adopted 2003, in press	
Poliomyelitis Vaccine (Inactivated)	Revised 2000, TRS 910 (2002); Amendment 2003, TRS 926 (2004)	
Poliomyelitis Vaccine, Oral	Revised 1999, TRS 904 (2002), Addendum 2000, TRS 910 (2002)	Update needed.
Rabies Vaccine (inactivated) for Human Use, Produced in Continuous Cell Lines	Adopted 1986, TRS 760 (1987); Amendment 1992, TRS 840 (1994)	Update in progress
Rabies Vaccine for Human Use	Revised 1980, TRS 658 (1981); Amendment 1992, TRS 840 (1994)	To be merged with updated continuous cell derived vaccine document
Rift Valley Fever Vaccine	Adopted 1981, TRS 673 (1982)	Review needed. If necessary update.
Smallpox Vaccine	Revised 2003 TRS 926 (2004)	
Sterility of Biological Substances	Revised 1973, TRS 530 (1973); Amendment 1995, TRS 872 (1998)	Update needed
Synthetic Peptide Vaccines	Adopted 1997, TRS 889 (1999)	
Thiomersal for vaccines: regulatory expectations for elimination, reduction or removal	Adopted 2003, TRS 926 (2004)	
Thromboplastins and Plasma Used to Control Oral Anticoagulant Therapy	Revised 1997, TRS 889 (1999)	
Tick-borne Encephalitis Vaccine (Inactivated)	Adopted 1997, TRS 889 (1999)	
Tuberculins	Revised 1985, TRS 745 (1987)	Review needed. If necessary update.
Typhoid Vaccine	Adopted 1966, TRS 361 (1967)	Review needed. If necessary update.
Vaccines, Clinical Evaluation: regulatory expectations	Adopted 2001, TRS 924 (2004)	
Vaccines, nonclinical evaluation	Adopted 2003, TRS 926 (2004)	
Varicella Vaccine (Live)	Revised 1993, TRS 848 (1994)	

Recommendations and Guidelines:	Reference	Action required or in progress
Vi Polysaccharide Typhoid Vaccine	Adopted 1992, TRS 840 (1994)	
Yellow Fever Vaccine	Revised 1995, TRS 872 (1998)	

Other documents:	Reference	Action proposed
Biological standardization and control: a scientific review commissioned by the UK National Biological Standards Board (1997)	Unpublished document WHO/BLG/97.1	This review was commissioned in the UK. With the passage of time, it has become less significant. Delete from list
Development of national assay services for hormones and other substances in community health care	TRS 565 (1975)	Outdated. If such a document has any value now, it should be revised as a guideline, otherwise discontinue.
Good manufacturing practices for biological products	TRS 822 (1992)	This should be a recommendation and be transferred to the first list
Guidelines for national authorities on quality assurance for biological products	TRS 822 (1992)	This should be transferred to the first list
Guidelines for the preparation, characterization and establishment of international and other standards and reference reagents for biological substances	TRS 800 (1990)	This is under revision and should be transferred to the first list
Guidelines for quality assessment of antitumour antibiotics	TRS 658 (1981)	Obsolete and no longer relevant to ECBS. Discontinue
Guidelines for the safe production and quality control of Inactivated Poliovirus manufactured from wild polioviruses	Adopted 2003, TRS 926 (2004)	Transfer to first list
Guidelines on Transmissible Spongiform Encephalopathies in relation to biological and pharmaceutical products	WHO/BCT/QSD/2003.01 unpublished	This document should be updated to reflect the current position and formally published in the first list
Laboratories approved by WHO for the production of yellow fever vaccine, revised 1995	TRS 872 (1998)	Update and retain in some way
Production and testing of WHO yellow fever virus primary seed lot 213-77 and reference batch 168-73	TRS 745 (1987)	Retain in some way
Recommendations for the assessment of binding-assay systems (including immunoassay and receptor	TRS 565 (1975)	Outdated. If such a document has any value

assay systems) for human hormones and their binding proteins. (A guide to the formulation of requirements for reagents and assay kits for the above assays and notes on cytochemical bioassay systems).		now, it should be revised as a guideline, otherwise discontinue.
Regulation and licensing of biological products in countries with newly developing regulatory authorities	TRS 858 (1987)	If such a document has any value now, it should be revised as recommendations, otherwise discontinue.
Report on the standardization and calibration of cytokine immunoassays	TRS 889 (1997)	These reports are not listed consistently. Probably best omitted. If guidelines are needed, a different document could be drafted
Standardization of interferons (reports of WHO Informal Consultations)	TRS 687 (1983) TRS 725 (1985) TRS 771 (1988)	These are reports of informal WHO consultations. Omit
Summary protocol for the batch release of virus vaccines	TRS 822 (1992)	Protocols are included in individual recommendations for vaccines. If such a document is of interest, it should be revised as a guideline, otherwise discontinue.