

Contents

Abbreviations	xiii
1. Introduction	1
2. General	4
2.1 Current directions	4
2.1.1 Strategic directions in biological standardization: WHO priorities	4
2.1.2 Vaccines and biotherapeutics: recent and planned activities in biological standardization	5
2.1.3 Therapeutic biological medicines: current developments and challenges	7
2.1.4 Blood products and related in vitro diagnostics: recent and planned activities in biological standardization	8
2.1.5 Overview of the international response to the Ebola epidemic, including accelerated development of vaccines and novel therapies	10
2.2 Reports	11
2.2.1 Report from the WHO Blood Regulators Network	11
2.2.2 Report from the WHO collaborating centres for biological standards	13
2.3 Feedback from custodian laboratories	14
2.3.1 Developments and scientific issues highlighted by custodians of WHO biological reference preparations	14
2.4 Cross-cutting activities of other WHO committees and groups	17
2.4.1 Proposed WHO Guidelines on good review practices	17
2.4.2 Proposed technical supplements to WHO guidance on the storage and transport of time- and temperature-sensitive pharmaceutical products	18
2.4.3 Proposed WHO Guidelines on good regulatory practices	18
2.4.4 Collaborative procedure for facilitating the licensing of WHO-prequalified medicinal products	19
2.4.5 Update of matters arising from the Expert Group on International Nonproprietary Names	19
2.4.6 Proposal to revise the procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies	20
2.4.7 A WHO and EDQM collaborative study on the determination of saccharide content of the <i>Haemophilus influenzae</i> type b component in liquid vaccine presentations	21
2.4.8 Update on the WHO global action plan to minimize poliovirus facility-associated risk	21
3. International Recommendations, Guidelines and other matters related to the manufacture and quality control of biological substances	23
3.1 Vaccines and related substances	23
3.1.1 Scientific principles for regulatory risk evaluation on finding an adventitious agent in a marketed vaccine	23
3.1.2 Recommendation to assure the quality, safety and efficacy of poliomyelitis vaccines (inactivated)	24
3.1.3 Guidelines on procedures and data requirements for changes to approved vaccines	25
3.1.4 Regulatory written standards pipeline	26

3.1.5	Clinical evaluation of dengue vaccines	27
3.1.6	Biotherapeutic products including similar biotherapeutic products	27
3.1.7	Multilateral activities relating to biotherapeutic products including similar biotherapeutic products	28
3.2	Blood products and related substances	28
3.2.1	Strengthening production capacity for blood components including plasma for fractionation	28
3.2.2	Shortage of anti-diphtheria and other specific immunoglobulins	30
3.2.3	MERS coronavirus serum panel	30
3.2.4	Use of convalescent sera to respond to emerging infectious disease threats	31
3.2.5	Overview of the biological standards endorsed by the ISTH for WHO approval	32
4.	International reference materials – antibiotics	33
4.1	WHO International Standards and Reference Reagents – antibiotics	33
4.1.1	Second WHO International Standard for bleomycin complex A2/B2	33
4.2	Proposed new projects and updates – antibiotics	33
4.2.1	Proposed Third WHO International Standard for amphotericin B	33
5.	International reference materials – biotherapeutics other than blood products	35
5.1	WHO International Standards and Reference Reagents – biotherapeutics other than blood products	35
5.1.1	Third WHO International Standard for luteinizing hormone (human pituitary)	35
5.1.2	First WHO International Standard for proinsulin (human)	36
5.2	Proposed new projects and updates – biotherapeutics other than blood products	36
5.2.1	Proposed First WHO Reference Reagent for Rituximab for use in complement-dependent cytotoxicity assays	36
5.2.2	Proposed First WHO Reference Reagent for Batroxobin	37
6.	International reference materials – blood products and related substances	39
6.1	WHO International Standards and Reference Reagents – blood products and related substances	39
6.1.1	First WHO International Standard for activated blood coagulation factor XI	39
6.1.2	First WHO Reference Panel for lupus anticoagulant	40
6.1.3	First WHO International Standard for A Disintegrin And Metalloprotease with Thrombospondin type 1 motifs 13 (ADAMTS13)	41
6.1.4	Fourth WHO International Standard for plasmin	41
6.2	Proposed new projects and updates – blood products and related substances	42
6.2.1	Proposed Second WHO International Standard for blood coagulation factor XI	42
6.2.2	Proposed Second WHO International Standard for activated blood coagulation factor IX	43
6.2.3	Proposed second WHO reference reagents for anti-A and anti-B in intravenous immunoglobulin	43
7.	International reference materials – In vitro diagnostic device reagents	44
7.1	WHO International Standards and Reference Reagents – in vitro diagnostic device reagents	44
7.1.1	Third WHO International Standard for hepatitis B virus surface antigen	44

7.1.2	First WHO International Standard for <i>Toxoplasma gondii</i> DNA for NAT-based assays	45
7.1.3	First WHO International Standard for hepatitis C virus core antigen	45
7.2	Proposed new projects and updates – in vitro diagnostic device reagents	46
7.2.1	Proposed First WHO Reference Panel for vCJD	46
7.2.2	Proposed first WHO international standards for herpes simplex virus DNA type 1 and 2	47
7.2.3	Proposed replacement WHO international standards for prostate-specific antigen (free) and prostate-specific antigen (90:10)	48
7.2.4	Proposed First WHO International Standard for anti-Müllerian hormone	48
7.2.5	Proposal to assign a holotranscobalamin value to the First WHO International Standard for vitamin B12 and folate in human serum	49
8.	International reference materials – vaccines and related substances	50
8.1	WHO International Standards and Reference Reagents – vaccines and related substances	50
8.1.1	First WHO Reference Reagent for anti-malaria (<i>Plasmodium falciparum</i>) human serum	50
8.1.2	Second WHO International Standard for <i>Haemophilus influenzae</i> type b capsular polysaccharide	51
8.1.3	First WHO International Standard for anti-typhoid capsular Vi polysaccharide immunoglobulin G (human)	52
8.2	Proposed new projects and updates – vaccines and related substances	53
8.2.1	Proposed Second WHO International Standard for <i>Bordetella pertussis</i> toxin	53
8.2.2	Proposed Third WHO International Standard for tetanus toxoid for use in flocculation test	54
8.2.3	Proposed Seventh WHO International Standard for rabies vaccine	55
8.2.4	Proposed First WHO International Standard for meningococcal serogroup X polysaccharide	55
8.2.5	Proposed First WHO International Standard for antibody to A(H7N9) influenza virus	56
Annex 1	WHO Recommendations, Guidelines and other documents related to the manufacture and quality control of biological substances used in medicine	57
Annex 2	Scientific principles for regulatory risk evaluation on finding an adventitious agent in a marketed vaccine	63
Annex 3	Recommendations to assure the quality, safety and efficacy of poliomyelitis vaccines (inactivated) Replacement of Annex 2 of WHO Technical Report Series, No. 910	89
Annex 4	Guidelines on procedures and data requirements for changes to approved vaccines	175
Annex 5	Biological substances: WHO International Standards, Reference Reagents and Reference Panels	261