

Contents

Abbreviations	xii
1. Introduction	1
2. General	3
2.1 Current directions	3
2.1.1 Strategic directions in the regulation of medicines and other health technologies: WHO priorities	3
2.1.2 Vaccines and biotherapeutics: recent and planned activities in biological standardization	5
2.1.3 Blood products and in vitro diagnostics: recent and planned activities in biological standardization	7
2.1.4 WHO comprehensive plan for the blood programme	8
2.2 Reports	10
2.2.1 Report from the WHO Blood Regulators Network	10
2.2.2 Report from the WHO network of collaborating centres on standardization and regulatory evaluation of vaccines	11
2.3 Feedback from custodian laboratories	13
2.3.1 Developments and scientific issues highlighted by custodians of WHO biological reference preparations	13
2.4 Cross-cutting activities of other WHO committees and groups	19
2.4.1 Update from the WHO Expert Committee on Specifications for Pharmaceutical Preparations	19
2.4.2 Report of the 67th WHO International Nonproprietary Names Consultation: update on nomenclature for advanced therapies	19
2.4.3 Update from the WHO National Control Laboratory Network for Biologicals	20
2.4.4 Update from the WHO Product Development for Vaccines Advisory Committee	21
2.4.5 Update on immunization policy from the Strategic Advisory Group of Experts on Immunization	22
2.4.6 Progress report on the WHO pilot procedure for the prequalification of biotherapeutic products and SBPs	24
2.4.7 WHO Global model regulatory framework for medical devices including in vitro diagnostic medical devices	26
2.4.8 First meeting of the Strategic Advisory Group of Experts on In Vitro Diagnostics	27
3. International Recommendations, Guidelines and other matters related to the manufacture, quality control and evaluation of biological substances	29
3.1 General	29
3.1.1 Revision of the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards	29
3.1.2 WHO Vero reference cell bank 10-87	30
3.1.3 Deletion of the innocuity/abnormal toxicity test for biological products	32

3.2	Biotherapeutics other than blood products	33
3.2.1	WHO Questions and Answers: similar biotherapeutic products	33
3.3	Cellular and gene therapies	34
3.3.1	Update on cellular and gene therapies	34
3.4	Vaccines and related substances	35
3.4.1	Recommendations to assure the quality, safety and efficacy of recombinant hepatitis E vaccines	35
3.4.2	Guidelines for the safe development and production of vaccines to human pandemic influenza viruses and influenza viruses with pandemic potential	37
3.4.3	Guidelines for the safe production and quality control of poliomyelitis vaccines	38
3.4.4	Revision of the WHO Recommendations to assure the quality, safety and efficacy of poliomyelitis vaccines (inactivated)	40
3.4.5	International collaborative study to assess the utility of deep sequencing of virus stocks used in the manufacture of oral poliomyelitis vaccine	41
3.4.6	Revision of the WHO Generic protocol for the calibration of seasonal and pandemic influenza antigen working reagents by WHO essential regulatory laboratories	43
4.	International reference materials – antibiotics	45
4.1	WHO International Standards and Reference Reagents – antibiotics	45
4.1.1	Third WHO International Standard for erythromycin	45
5.	International reference materials – blood products and related substances	47
5.1	WHO International Standards and Reference Reagents – blood products and related substances	47
5.1.1	Second WHO International Standard for blood coagulation factor V (plasma, human)	47
5.1.2	Third WHO International Standard for anti-D immunoglobulin (human)	48
5.2	Proposed new projects and updates – blood products and related substances	49
5.2.1	Proposed First WHO International Standard for unfractionated heparin for molecular weight calibration	49
5.2.2	Proposed Third WHO International Standard for von Willebrand factor concentrate	50
5.2.3	Update on the WHO snakebite antivenom project	51
6.	International reference materials – cellular and gene therapies	53
6.1	Proposed new projects and updates – cellular and gene therapies	53
6.1.1	Proposed First WHO International Reference Reagent for mesenchymal stromal cell identity for flow cytometry	53
7.	International reference materials – in vitro diagnostics	55
7.1	WHO International Standards and Reference Reagents – in vitro diagnostics	55
7.1.1	First WHO International Reference Reagent for CD4+ T-cells (human)	55
7.1.2	First WHO International Reference Panel for HIV-1 p24 antigen and First WHO International Reference Reagent for HIV-2 p26 antigen	57
7.1.3	First WHO International Reference Reagent for von Willebrand factor (plasma) binding to recombinant glycoprotein Ib	58

7.1.4	Second WHO International Standard for prostate specific antigen (free) and Second WHO International Standard for prostate specific antigen (human) (total: PSA-ACT + free PSA)	60
7.1.5	Second WHO International Standard for HIV-2 RNA for NAT-based assays	61
7.1.6	First WHO International Standard for adenovirus DNA for NAT-based assays	62
7.2	Proposed new projects and updates – in vitro diagnostics	64
7.2.1	Proposed additional WHO international reference reagents for blood group genotyping	64
7.2.2	Proposed First WHO international standards for (cell line name) cancer genomes	65
7.2.3	Proposed First WHO international standards for <i>PIK3CA</i> variants	66
7.2.4	Proposed Second WHO International Standard for insulin-like growth factor-1 (human, recombinant)	67
7.2.5	Proposed WHO international standards for enterovirus RNA for NAT-based assays	68
7.2.6	Proposed Fourth WHO International Standard for ferritin (human, recombinant)	69
7.2.7	Proposed First WHO International Reference Panel for microsatellite instability	70
7.2.8	Proposed First WHO International Standard for <i>Mycobacterium tuberculosis</i> DNA for NAT-based assays	71
7.2.9	Proposed First WHO International Standard for anti-thyroid peroxidase antibodies	72
7.2.10	Proposed extension of the First WHO International Reference Panel for HIV-1 circulating recombinant forms RNA for NAT-based assays	73
7.2.11	Proposed First WHO international standards for circulating tumour DNA	74
7.2.12	Proposed First WHO Reference Reagent for <i>Babesia microti</i> DNA for NAT-based assays	75
7.2.13	Update on the development of WHO international reference preparations for <i>Plasmodium vivax</i>	76
8.	International reference materials – standards for use in public health emergencies	78
8.1	WHO International Standards and Reference Reagents – standards for use in public health emergencies	78
8.1.1	First WHO International Standard for anti-Asian lineage Zika virus antibody (human)	78
8.2	Proposed new projects and updates – standards for use in public health emergencies	79
8.2.1	Proposed First WHO International Reference Reagent for MERS-CoV	79
8.2.2	Proposed WHO international standards for emerging and re-emerging viruses with epidemic potential	81
9.	International reference materials – vaccines and related substances	84
9.1	WHO International Standards and Reference Reagents – vaccines and related substances	84
9.1.1	Second WHO International Reference Cell Bank of MRC-5 cells	84
9.1.2	Seventh WHO International Standard for rabies vaccine	84
9.1.3	First WHO international standards for meningococcal serogroups W and Y polysaccharides	86

9.1.4	First WHO International Standard for Sabin inactivated poliomyelitis vaccine	87
9.2	Proposed new projects and updates – vaccines and related substances	89
9.2.1	Update on the development of influenza virus pathogenicity standards	89
9.2.2	Update on the development of the proposed First WHO International Standard for antibody to the influenza virus haemagglutinin stem domain	90
9.2.3	Proposed universal reagents for potency testing of inactivated poliomyelitis vaccines	91
9.2.4	Proposed First WHO International Standard for anti EV-D68 serum	92
Annex 1		
	WHO Recommendations, Guidelines and other documents related to the manufacture, quality control and evaluation of biological substances used in medicine	95
Annex 2		
	Recommendations to assure the quality, safety and efficacy of recombinant hepatitis E vaccines	101
Annex 3		
	Guidelines for the safe development and production of vaccines to human pandemic influenza viruses and influenza viruses with pandemic potential Replacement of Annex 5 of WHO Technical Report Series, No. 941; and the WHO 2009 A(H1N1) update; and the WHO 2013 A(H7N9) update	165
Annex 4		
	Guidelines for the safe production and quality control of poliomyelitis vaccines Replacement of Annex 2 of WHO Technical Report Series, No. 926	209
Annex 5		
	Biological substances: WHO International Standards, Reference Reagents and Reference Panels	249