

# Contents

<b>Abbreviations</b>	xiii
<b>1. Introduction</b>	1
<b>2. General</b>	3
2.1 Current directions	3
2.1.1 Strategic directions in the regulation of medicines and other health technologies	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	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	12
2.2.3 Report from the WHO network of collaborating centres for blood products and in vitro diagnostics	13
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	16
2.4.1 Update from the WHO Expert Committee on Specifications for Pharmaceutical Preparations	16
2.4.2 WHO Global Benchmarking Tool	17
2.4.3 Development of WHO guidelines on good regulatory practices	18
2.4.4 Snake-bite envenoming	19
2.4.5 Update from the WHO Product Development for Vaccines Advisory Committee	21
2.4.6 Pilot WHO prequalification of biosimilar monoclonal antibodies	22
2.4.7 Model NRA Lot Release Certificate for prequalified vaccines	23
2.4.8 Planned proficiency testing study of a standardized method for determining total and free saccharide content of Hib liquid combined vaccines	24
2.4.9 Vaccine prequalification - establishment of the WHO-NNB	24
2.5 Strategic issues	25
2.5.1 Standards for priority pathogens for public health emergencies	25
2.5.2 International standards and reference preparations - revision of TRS 932 Annex 2	27
<b>3. International Recommendations, Guidelines and other matters related to the manufacture, quality control and evaluation of biological substances</b>	29
3.1 Biotherapeutics other than blood products	29
3.1.1 Guidelines on procedures and data requirements for changes to approved biotherapeutic products	29

3.2	Cellular and gene therapies	30	7.1.8	First WHO International Standard for anti-cytomegalovirus immunoglobulin G	56
3.2.1	Global activities in cell therapy products	30	7.1.9	First WHO International Standard for chikungunya virus RNA for NAT-based assays	57
3.3	In vitro diagnostics	31	7.1.10	First WHO International Standard for Zika virus antibodies (immunoglobulin G and immunoglobulin M) (human)	58
3.3.1	WHO IVD prequalification: update report	31	7.2	Proposed new projects and updates - in vitro diagnostics	59
3.3.2	Human immunodeficiency virus rapid diagnostic tests for professional use and/or self-testing	33	7.2.1	Proposed First WHO Reference Panel for cancer mutation detection	59
3.3.3	Establishing stability of in vitro diagnostic medical devices	34	7.2.2	Proposed Third WHO International Standard for prekallikrein activator	60
3.3.4	WHO consultation on the First WHO International Standard for anti-rubella immunoglobulin	35	7.2.3	Proposed First WHO Reference Reagent for anti-human platelet antigen 15b	60
3.4	Vaccines and related substances	36	7.2.4	Proposed First WHO International Standard for anti-cyclic citrullinated peptide antibodies	61
3.4.1	Guidelines on the quality, safety and efficacy of Ebola vaccines	36	7.2.5	Proposed Second WHO International Standard for rheumatoid factor	62
<b>4.</b>	<b>International reference materials - antibiotics</b>	<b>38</b>	7.2.6	Proposed Second WHO reference reagents for dengue virus subtypes 1 -4	63
4.1	Proposed new projects and updates - antibiotics	38	7.2.7	Proposed First WHO International Standard for cutaneous leishmaniasis; and First WHO Reference Panel for cutaneous leishmaniasis	63
4.1.1	Proposed Third WHO International Standard for erythromycin	38	7.2.8	Proposed First WHO International Standard for <i>Plasmodium vivax</i> antigens; and First WHO Reference Reagent for anti-malaria ( <i>Plasmodium vivax</i> ) serum	64
<b>5.</b>	<b>International reference materials - biotherapeutics other than blood products</b>	<b>39</b>	7.2.9	Proposed First WHO International Standard for anti-MERS-CoV serum	65
5.1	WHO International Standards and Reference Reagents - biotherapeutics other than blood products	39	7.2.10	Proposed First WHO International Standard for MERS-CoV RNA for NAT-based assays	65
5.1.1	Second WHO International Standard for parathyroid hormone 1-34 (recombinant, human)	39	7.2.11	Proposed Sixth WHO International Standard for hepatitis C virus RNA for NAT-based assays	66
5.1.2	First WHO International Standard for rituximab	40	<b>8.</b>	<b>International reference materials - vaccines and related substances</b>	<b>68</b>
5.1.3	First WHO International Standard for infliximab	41	8.1	WHO International Standards and Reference Reagents - vaccines and related substances	68
<b>6.</b>	<b>International reference materials - blood products and related substances</b>	<b>44</b>	8.1.1	First WHO international standards for oral poliomyelitis vaccines	68
6.1	WHO International Standards and Reference Reagents - blood products and related substances	44	8.1.2	Second WHO International Standard for pertussis toxin	69
6.1.1	First WHO Reference Reagent for activated blood coagulation factor X (human)	44	8.1.3	First WHO international standards for <i>Citrobacter freundii</i> and <i>Salmonella</i> Typhi Vi polysaccharides	70
6.1.2	Second WHO International Standard for activated blood coagulation factor IX (human)	45	8.1.4	First WHO International Standard for anti-typhoid capsular Vi polysaccharide immunoglobulin G (human)	72
6.1.3	First WHO International Standard for blood coagulation factor XII (plasma, human) via assignment of additional analytes to the current Second WHO International Standard for blood coagulation factor XI (plasma, human)	46	8.1.5	First WHO International Standard for antiserum to respiratory syncytial virus	73
<b>7.</b>	<b>International reference materials - in vitro diagnostics</b>	<b>48</b>	8.2	Proposed new projects and updates - vaccines and related substances	74
7.1	WHO International Standards and Reference Reagents - in vitro diagnostics	48	8.2.1	Proposed First WHO Reference Panel for <i>Vibrio cholera</i> 01 and 0139 lipopolysaccharides	74
7.1.1	First WHO Reference Reagent for lupus anti-dsDNA serum	48	8.2.2	Proposed First WHO Reference Panel for anti-Wbr/o <i>cholera</i> 01 and 0139 lipopolysaccharide serums (rabbit)	75
7.1.2	Third WHO International Standard for hepatitis A virus RNA for NAT-based assays	49	8.2.3	Proposed First WHO International Standard for <i>Vibrio cholera</i> vaccine (oral, inactivated)	76
7.1.3	Fourth WHO International Standard for HIV-1 RNA for NAT-based assays	50	8.2.4	Proposed First WHO International Standard for antibody to the influenza virus hemagglutinin stem domain	76
7.1.4	First WHO International Standard for Ebola virus antibodies (plasma, human); and First WHO Reference Panel for Ebola virus antibodies (plasma, human)	51	8.2.5	Proposed First WHO international standards for influenza virus pathogenicity for safety testing	77
7.1.5	First WHO Reference Panel for genomic KRAS codons 12 and 13 mutations	52	8.2.6	Proposed Third WHO International Standard for anti-rabies immunoglobulin (human)	78
7.1.6	First WHO International Standard for human herpes virus 6B DNA for NAT-based assays	54			
7.1.7	First WHO International Standard for <i>Plasmodium falciparum</i> antigens	55			

## **Annex 1**

WHO Recommendations, Guidelines and other documents related to the manufacture, quality control and evaluation of biological substances used in medicine 81

## **Annex 2**

Guidelines on the quality, safety and efficacy of Ebola vaccines 87

## **Annex 3**

Guidelines on procedures and data requirements for changes to approved biotherapeutic products 181

## **Annex 4**

Technical Specifications Series (TSS) for WHO Prequalification - Diagnostic Assessment 281

## **Annex 5**

Technical Guidance Series (TGS) for WHO Prequalification - Diagnostic Assessment 315

## **Annex 6**

Biological substances: WHO International Standards, Reference Reagents and Reference Panels 377