

# WHO Expert Committee on Specifications for Pharmaceutical Preparations

---

Fifty-fifth report



World Health  
Organization

The World Health Organization was established in 1948 as a specialized agency of the United Nations serving as the directing and coordinating authority for international health matters and public health. One of WHO's constitutional functions is to provide objective and reliable information and advice in the field of human health, a responsibility that it fulfils in part through its extensive programme of publications.

The Organization seeks through its publications to support national health strategies and address the most pressing public health concerns of populations around the world. To respond to the needs of Member States at all levels of development, WHO publishes practical manuals, handbooks and training material for specific categories of health workers; internationally applicable guidelines and standards; reviews and analyses of health policies, programmes and research; and state-of-the-art consensus reports that offer technical advice and recommendations for decision-makers. These books are closely tied to the Organization's priority activities, encompassing diseases prevention and control, the development of equitable health systems based on primary health care, and health promotion for individuals and communities. Progress towards better health for all also demands the global dissemination and exchange of information that draws on the knowledge and experience of all WHO's Member countries and the collaboration of world leaders in public health and the biomedical sciences. To ensure the widest possible availability of authoritative information and guidance on health matters, WHO secures the broad international distribution of its publications and encourages their translation and adaption. By helping to promote and protect health and prevent and control disease throughout the world, WHO's books contribute to achieving the Organization's principal objective – the attainment by all people of the highest possible level of health.

The *WHO Technical Report Series* makes available the findings of various international groups of experts that provide WHO with the latest scientific and technical advice on a broad range of medical and public health subjects. Members of such expert groups serve without remuneration in their personal capacities rather than as representatives of governments or other bodies; their views do not necessarily reflect the decisions or the stated policy of WHO. To purchase WHO publications, please contact: WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel. +41 22 791 3264; fax: +41 22 791 4857; email: [bookorders@who.int](mailto:bookorders@who.int); <http://www.who.int/bookorders>).

W H O T e c h n i c a l R e p o r t S e r i e s  
1 0 3 3

# WHO Expert Committee on Specifications for Pharmaceutical Preparations

---

Fifty-fifth report

*This report contains the views of an international group of experts and  
does not necessarily represent the decisions or the stated policy of the World Health Organization*



**World Health  
Organization**

WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-fifth report

(WHO Technical Report Series, No. 1033)

ISBN 978-92-4-002090-0 (electronic version)

ISBN 978-92-4-002091-7 (print version)

ISSN 0512-3054

© World Health Organization 2021

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization.

**Suggested citation.** WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-fifth report. Geneva: World Health Organization; 2021 (WHO Technical Report Series, No. 1033). Licence: CC BY-NC-SA 3.0 IGO.

**Cataloguing-in-Publication (CIP) data.** CIP data are available at <http://apps.who.int/iris>.

**Sales, rights and licensing.** To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <http://www.who.int/about/licensing>.

**Third-party materials.** If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

**General disclaimers.** The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

This publication contains the collective views of an international group of experts and does not necessarily represent the decisions or the policies of WHO.

# Contents

<b>Abbreviations</b>	vi
<b>WHO Expert Committee on Specifications for Pharmaceutical Preparations</b>	x
<b>Declarations of interest</b>	xvi
<b>OPEN SESSION</b>	1
Introduction and welcome	1
I. Expert Committee on Specifications for Pharmaceutical Preparations processes and procedures	1
II. Update on new guidelines, norms and standards	2
III. Technical agenda topics of the Fifty-fifth Expert Committee on Specifications for Pharmaceutical Preparations	2
IV. Points of discussion	3
<b>PRIVATE AND CLOSED SESSIONS</b>	5
Opening	5
<b>1. General policy</b>	7
1.1 Process for development of WHO norms and standards	7
<b>2. Quality assurance: collaboration initiatives</b>	8
2.1 International Meeting of World Pharmacopoeias	8
<b>3. Nomenclature, terminology and databases</b>	9
3.1 International nonproprietary names for pharmaceutical substances	9
3.2 Quality assurance terminology	10
3.3 Guidelines and guidance texts adopted by the Expert Committee on Specifications for Pharmaceutical Preparations	10
<b>4. Quality control – national laboratories</b>	11
4.1 External Quality Assurance Assessment Scheme	11
4.1.1 Final report on phase 9	11
4.1.2 Update on phase 10	12
<b>5. Quality control – specifications and tests</b>	13
5.1 <i>The International Pharmacopoeia</i>	13
5.2 General chapters	13
5.2.1 Dissolution test for oral dosage forms	13
5.2.2 General identification tests	14
5.2.3 Test for histamine-like substances	14
5.3 General monographs for dosage forms	15
5.3.1 Powders for inhalation	15
5.3.2 Liquid preparations for oral use	15
5.4 Specifications and draft monographs for medicines, including paediatric medicines, and candidate medicines for COVID-19	16
5.4.1 COVID-19 therapeutics	16

5.4.2	Antiviral medicines, including antiretrovirals	17
5.4.3	Medicines for tropical diseases	18
5.4.4	Medicines for maternal, newborn, child and adolescent health	19
5.4.5	Excipients	20
5.5	Update on the virtual informal consultation on Screening Technologies, Laboratory Tools and Pharmacopoeial Specifications for Medicines	20
<b>6.</b>	<b>Quality control: international reference materials</b>	<b>22</b>
6.1	Update on International Chemical Reference Substances	22
<b>7.</b>	<b>Quality assurance: good manufacturing practice and inspection</b>	<b>23</b>
7.1	Inspection guidelines and good practices with partner organizations	23
7.1.1	Revision of good manufacturing practices for sterile products	23
7.1.2	Good manufacturing practices for radiopharmaceuticals for investigational use	23
7.2	Approaches to carryover limits in cleaning validation	24
7.3	Water for pharmaceutical use	25
7.4	Guideline on data integrity	26
7.5	Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance	27
7.6	Recommendations from the virtual consultation on good practices for health products and inspection	29
<b>8.</b>	<b>Quality assurance: distribution and supply chain</b>	<b>30</b>
8.1	Shelf life for supply and procurement of medical products	30
8.1.1	Revision to the guideline on remaining shelf life	30
8.2	Updated and new WHO guidance, procedures and operational documents for pharmaceutical procurement	31
8.2.1	World Health Organization/United Nations Population Fund prequalification guidance on condoms	31
<b>9.</b>	<b>Regulatory guidance and model schemes</b>	<b>33</b>
9.1	Proposal to waive in vivo bioequivalence requirements for medicines on the <i>WHO Model List of Essential Medicines</i>	33
9.2	WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce	36
9.3	Good practices in regulatory decision-making	38
9.3.1	Good reliance practices in the regulation of medical products	38
9.3.2	Good regulatory practices in the regulation of medical products	39
9.4	Update on WHO-listed authorities	40
9.5	Recommendations from the virtual consultation on Regulatory Guidance for Multisource Products	41
<b>10.</b>	<b>Miscellaneous: update on activities related to COVID-19</b>	<b>43</b>
10.1	Oxygen specifications	43
10.2	Therapeutic specifications	43
10.3	Existing guidance	44
10.4	New activities	44
<b>11.</b>	<b>Closing remarks</b>	<b>45</b>

<b>12. Summary and recommendations</b>	46
12.1 Guidelines and decisions adopted and recommended for use	47
12.2 Texts adopted for inclusion in <i>The International Pharmacopoeia</i>	47
12.3 Recommendations	49
<b>Acknowledgements</b>	52
<b>References</b>	71
<b>Annex 1</b>	
Guidelines and guidance texts adopted by the Expert Committee on Specifications for Pharmaceutical Preparations	75
<b>Annex 2</b>	
Points to consider when including Health-Based Exposure Limits (HBELs) in cleaning validation	93
<b>Annex 3</b>	
Good manufacturing practices: water for pharmaceutical use	111
<b>Annex 4</b>	
Guideline on data integrity	135
<b>Annex 5</b>	
World Health Organization/United Nations Population Fund Recommendations for condom storage and shipping temperatures	161
<b>Annex 6</b>	
World Health Organization/United Nations Population Fund Guidance on testing of male latex condoms	167
<b>Annex 7</b>	
World Health Organization/United Nations Population Fund guidance on conducting post-market surveillance of condoms	189
<b>Annex 8</b>	
WHO "Biowaiver List": proposal to waive in vivo bioequivalence requirements for <i>WHO Model List of Essential Medicines</i> immediate-release, solid oral dosage forms	197
<b>Annex 9</b>	
Guidelines on the implementation of the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce	205
<b>Annex 10</b>	
Good reliance practices in the regulation of medical products: high level principles and considerations	237
<b>Annex 11</b>	
Good regulatory practices in the regulation of medical products	269

# Abbreviations

ACT	Access to COVID-19 Tools
ALCOA	attributable, legible, contemporaneous, original and accurate
AMR	antimicrobial resistance
API	active pharmaceutical ingredient
AQL	acceptance quality level
AUC	area under the curve
BCS	Biopharmaceutics Classification System
BE	bioequivalence
BMDL	benchmark dose level
BPW	bulk purified water
BWFI	bulk water for injection
CAPA	corrective and preventive action
CpK	process capability ( <i>also saved under P</i> )
CPP	certificate of a pharmaceutical product
DABT	Diplomate of the American Board of Toxicology
DIRA	data integrity risk assessment
EAP	WHO Expert Advisory Panel on <i>The International Pharmacopoeia</i> and Pharmaceutical Preparations
ECSP	Expert Committee on Specifications for Pharmaceutical Preparations

预览已结束，完整报告链接和

<https://www.yunbaogao.cn/report/index/repor>