

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Fifty-third 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 adaptation. 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; <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 1 9

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Fifty-third 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-third report

(WHO Technical Report Series, No. 1019)

ISBN 978-92-4-121028-7

ISSN 0512-3054

© World Health Organization 2019

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-third report. Geneva: World Health Organization; 2019 (WHO Technical Report Series, No. 1019). 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.

Printed in Italy

Contents

Abbreviations	vii
WHO Expert Committee on Specifications for Pharmaceutical Preparations	ix
Introduction	1
1. General policy	4
1.1 Process for the development of WHO norms and standards	4
1.2 Participation in meetings of the Expert Committee on Specifications for Pharmaceutical Preparations	5
1.3 Open session	6
1.3.1 Introduction and welcome	6
2. General updates and matters for information	8
2.1 Cross-cutting pharmaceutical quality assurance issues	8
2.1.1 Local manufacturing	8
2.1.2 Member State mechanism	9
2.1.3 Expert Committee on Biological Standardization	9
2.1.4 Expert Committee – selection and use of the <i>WHO Model List of Essential Medicines</i>	10
2.1.5 Antimicrobial resistance	11
2.1.6 International Conference of Drug Regulatory Authorities	12
2.2 International collaboration	12
2.2.1 International Atomic Energy Agency	12
2.2.2 Pharmacopoeial Discussion Group	13
2.2.3 United Nations Children’s Fund	13
3. Quality assurance – collaboration initiatives	15
3.1 International meetings of world pharmacopoeias	15
3.2 Inspection guidelines and good practices	15
3.2.1 Revision of <i>WHO good manufacturing practices for sterile pharmaceutical products</i>	15
3.2.2 <i>Good manufacturing practices for biotherapeutic products</i>	16
4. Nomenclature, terminology and databases	18
4.1 International Nonproprietary Names for pharmaceutical substances	18
4.2 Quality assurance terminology	18
4.3 Guidelines and guidance texts adopted by the Expert Committee	18
5. Prequalification of priority essential medicines and active pharmaceutical ingredients	20
5.1 Update on the prequalification of medicines	20
5.2 Update on the prequalification of active pharmaceutical ingredients	20
6. Quality control – prequalification and WHO monitoring projects	22
6.1 Update on the prequalification of quality control laboratories	22
6.2 Update on WHO quality monitoring projects	22

7. Quality control – national laboratories	23
7.1 External Quality Assurance Assessment Scheme	23
8. Quality control – specifications and tests: <i>The International Pharmacopoeia</i>	24
8.1 Update	24
8.2 Workplan 2018–2019	24
8.3 Procedure for the development, revision and omission of monographs and other texts for <i>The International Pharmacopoeia</i>	26
8.4 General policy – transition from microbiological to physicochemical assays in monographs on capreomycin active pharmaceutical ingredient and products	27
8.5 General chapters	27
8.5.1 Limit test for heavy metals	27
8.5.2 Polymorphism	28
8.5.3 Dissolution test for solid oral dosage forms	29
8.5.4 General notice: solubility	29
8.6 Specifications and draft monographs for medicines, including paediatric and radiopharmaceutical medicines	29
8.6.1 Medicines for maternal, newborn, child and adolescent health	29
8.6.2 Antimalarial medicines	31
8.6.3 Antituberculosis medicines	31
8.6.4 Antiviral medicines including antiretrovirals	32
8.6.5 Medicines for tropical diseases	33
8.6.6 Ophthalmological and dermatological medicines	34
9. Quality control – international reference materials	35
9.1 Update on International Chemical Reference Substances, including the report of the custodial centre of the dedicated ECSPP subgroup on the International Chemical Reference Substances	35
10. General policy – chemistry	36
10.1 Revision of guidance on representation of graphic formulae	36
11. Quality assurance – good manufacturing practices and inspection	37
11.1 Interpretation of <i>Guidelines on good manufacturing practices for heating, ventilation and air-conditioning systems</i>	37
11.2 Good manufacturing practices for validation	38
11.2.1 General main text	38
11.2.2 Analytical procedure validation	39
11.2.3 Validation of computerized systems	40
11.2.4 Qualification	40
11.3 Update on review of existing WHO inspection guidance, including <i>Guidelines for inspection of drug distribution channels and Quality system requirements for national good manufacturing practice inspectorates</i>	41
11.3.1 Guidelines for inspection of drug distribution channels	42
11.3.2 Quality system requirements for national good manufacturing practice inspectorates	42
11.4 Update and recommendations from inspectors' meeting, including on good manufacturing practices and environmental issues	42

11.5	Inquiry regarding production of “water for injection”	43
11.6	Proposal for good chromatography practices	44
12.	Quality assurance – distribution and supply chain	45
12.1	Guidelines on import procedures for medical products	45
12.2	Update on review of existing WHO guidance, procedures and operational documents for pharmaceutical procurement	45
12.2.1	New guidance on shelf-life for supply and procurement of medicines	45
12.2.2	Update of listing of stability conditions for WHO Member States	46
13.	Regulatory guidance and model schemes	47
13.1	Proposal to waive in vivo bioequivalence requirements for medicines included in the <i>WHO Model List of Essential Medicines</i>	47
13.1.1	Experimental pathway	48
13.1.2	Regulatory pathway	49
13.1.3	Prioritization exercise	49
13.2	WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce	50
13.3	Good practice guidance document on implementing the collaborative procedures	51
13.4	Guidance document to support and facilitate the implementation of quality management systems for national regulatory authorities	52
13.5	Good regulatory practices	52
14.	Miscellaneous	53
14.1	Update of WHO/UNFPA prequalification guidance for contraceptive devices and condoms	53
15.	Closing remarks	54
16.	Summary and recommendations	55
	Acknowledgements	60
	References	83
	Annex 1	
	Procedure for the development of World Health Organization medicines quality assurance guidelines	87
	Annex 2	
	Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products	
	Part 2: Interpretation of <i>Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products</i>	93
	Annex 3	
	Good manufacturing practices: guidelines on validation	119
	Appendix 1 Validation of heating, ventilation and air-conditioning systems	135
	Appendix 2 Validation of water systems for pharmaceutical use	136
	Appendix 3 Cleaning validation	137
	Appendix 4 Analytical procedure validation	148

Appendix 5 Validation of computerized systems	160
Appendix 6 Guidelines on qualification	181
Appendix 7 Non sterile process validation	190
Annex 4	
Protocol to conduct equilibrium solubility experiments for the purpose of Biopharmaceutics Classification System-based classification of active pharmaceutical ingredients for biowaiver	203
Annex 5	
Guidelines on import procedures for medical products	219
Annex 6	
Good practices of national regulatory authorities in implementing the collaborative registration procedures for medical products	233
Appendix 1 An example of information to applicants for registration via the WHO collaborative registration procedure	257
Appendix 2 Verification for product submitted under the WHO collaborative procedure	259
Appendix 3 Abridged/abbreviated review for product submitted under the WHO collaborative procedure	263
Appendix 4 Additional information to be included in the screening checklist	279
Appendix 5 Example of a national regulatory authority reliance model approach: information, documentary evidence and assessment activity	281
Appendix 6 Model acknowledgement or approval letter for variations of products registered through the WHO collaborative procedure	283

预览已结束，完整报告链接和

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