1003

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Fifty-first report



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 disease 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.

An annual subscription to this series, comprising about four to six such reports, costs CHF 150.00/US\$ 180.00 (CHF 105.00/US\$ 126.00 in developing countries). For further information, please contact: WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel. +41 22 791 3264; fax: +41 22 791 4857; e-mail: bookorders@who.int; order on line: http://www.who.int/bookorders).

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Fifty-first 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



WHO Library Cataloguing-in-Publication Data

Fifty-first report of the WHO Expert Committee on specifications for pharmaceutical preparations.

(WHO technical report series; no. 1003)

ISBN 978 92 4 121003 4 ISBN 978 92 4 069643 3 (PDF) ISSN 0512-3054

© World Health Organization 2017

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. Fifty-first report of the WHO Expert Committee on specifications for pharmaceutical preparations. Geneva: World Health Organization; 2017 (WHO technical report series; no. 1003). 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 the World Health Organization.

Contents

| Introduction | | |
|--------------|--|--|
| 1. | General policy | 3 |
| | 1.1 Cross-cutting pharmaceutical quality assurance issues1.2 International collaboration | 3 6 |
| 2. | Quality control – specifications and tests | 8 |
| | 2.1 The International Pharmacopoeia 2.1.1 Updates 2.1.2 Workplan 2016–2017 2.2 Specifications for medicines, including children's medicines and | 8 8 8 |
| | radiopharmaceuticals 2.2.1 Maternal, newborn, child and adolescent health medicines 2.2.2 Antituberculosis medicines 2.2.3 Antiviral medicines 2.2.4 Medicines for tropical diseases 2.2.5 Other anti-infective medicines 2.2.6 Other medicines 2.2.7 Radiopharmaceuticals 2.3 General monographs for dosage forms and associated method texts 2.4 General policy | 10 10 11 12 12 13 14 14 15 |
| 3. | Quality control – International Reference Materials (Internation | |
| | Chemical Reference Substances and Infrared Reference Spectra | |
| 4. | Quality control – national laboratories | 21 |
| | 4.1 External Quality Assurance Assessment Scheme (EQAAS) 4.2 Guidance on testing of "suspect" substandard/spurious/falsely-labelled/falsecounterfeit medicines | 21 |
| | 4.3 Recommendations from the meeting on regulatory guidance for multisour products | ce 22 |
| 5. | Prequalification of quality control laboratories | 23 |
| | 5.1 Update on the prequalification of quality control laboratories 5.2 Update on WHO quality monitoring projects 5.3 Revision of the procedure for assessment of quality control laboratories | 23 23 24 |
| 6. | Quality assurance – collaboration initiatives | 25 |
| | 6.1 International meetings of world pharmacopoeias 6.2 Good pharmacopoeial practices 6.3 Inspection guidelines and good practices | 25 25 26 |
| 7. | Quality assurance – good manufacturing practices | |
| | 7.1 Update of WHO good manufacturing practices: validation 7.2 Heating, ventilation and air-conditioning (HVAC) 7.3 Update and recommendations from the inspectors' meeting | 27 27 28 |
| 8. | Regulatory frameworks | 29 |
| | 8.1 Local manufacturing of essential medicines8.2 WHO Global Model Regulatory Framework for Medical Devices | 29 30 |

| 9. | Regulatory guidance | 31 |
|-----|--|----------|
| | 9.1 Biowaiver list based on the WHO List of Essential Medicines9.2 International Comparator Products List for equivalence assessment of | 31 |
| | interchangeable multisource (generic) products | 31 |
| | 9.3 Good regulatory practices | 32 |
| | 9.4 Collaborative procedure for stringent regulatory authority-approved medicines 9.5 Recommendations from the meeting on regulatory guidance for multisource | 32 |
| | products | 33 |
| 10. | Prequalification of priority essential medicines and active | |
| | pharmaceutical ingredients | 37 |
| | 10.1 Update on the prequalification of medicines | 37 |
| | 10.2 Update on the prequalification of APIs | 37 |
| 11. | Nomenclature, terminology and databases | 39 |
| | 11.1 Quality assurance terminology | 39 |
| | 11.2 International Nonproprietary Names (INN) for pharmaceutical substances | 39 |
| | 11.3 Revision of guidance on representation of graphic formulae | 39 |
| 12. | Closing remarks | 41 |
| 13. | Summary and recommendations | 42 |
| Ack | nowledgements | 48 |
| Ann | nex 1 | |
| | WHO guidelines for selecting marker substances of herbal origin for quality control of herbal medicines | 71 |
| Ann | nex 2 | |
| | The International Pharmacopoeia: revised concepts and future perspectives | 87 |
| Ann | nex 3 | |
| | Prequalification of quality control laboratories: procedure for assessing the acceptability in principle, of quality control laboratories for use by United Nations agencies | /, 91 |
| Ann | nex 4 | |
| | WHO Global Model Regulatory Framework for Medical Devices including in vitro diagnostic medical devices | 103 |
| Ann | nex 5 | |
| | General background notes on the list of international comparator pharmaceutical products | 179 |
| Ann | nex 6 | |
| | Equilibrium solubility experiments for the purpose of classification of active pharmaceutical ingredients according to the Biopharmaceutics Classification System, as an appendix to the WHO guidelines on <i>Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability</i> (Annex 7, WHO Technical Report Series, No. 992, 2015) | 181 |

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Geneva, 17-21 October 2016

Members¹

Professor Erwin Adams, Leuven, Belgium

Professor Saleh A. Bawazir, Riyadh, Saudi Arabia

Professor Shaohong Jin, Beijing, People's Republic of China

Ms Gugu N. Mahlangu, Harare, Zimbabwe (*Chairperson*)

Dr Justina A. Molzon, Bethesda, MD, USA (Rapporteur)

Mrs Lynda Paleshnuik, Arnprior, Ontario, Canada

Dr Jitka Sabartova, Prague, Czech Republic (Rapporteur)

Dr Budiono Santoso, Yogyakarta, Indonesia

Dr Daisaku Sato, Chiodaku, Tokyo, Japan (Co-Chairperson)

Dr Gyanendra Nath Singh, Raj Nagar, Ghaziabad, India

Dr Varley Dias Sousa, Brasília, Brazil

Dr Adriaan J. van Zyl, Cape Town, South Africa

Temporary advisers²

Dr Nazeeh Sh Alothmany, Riyadh, Saudi Arabia

Dr Raymond Boudet-Dalbin, Paris, France

Dr Marius Brits, Potchefstroom, South Africa

Dr John Gordon, Wolfville, Nova Scotia, Canada

Dr Joey Gouws, Pretoria, South Africa

Professor Jos Hoogmartens, Leuven, Belgium

Dr Agnes Sitta Kijo, Dar es Salaam, United Republic of Tanzania

Dr John Miller, Ayr, Scotland

Dr Baoming Ning (observer), Beijing, People's Republic of China

Dr Lembit Rägo, Geneva, Switzerland

¹ Unable to attend: Dr Luisa Stoppa, Rome, Italy.

Unable to attend: Dr Lucette Cargill, Kingston, Jamaica; Professor Theo G. Dekker, Potchefstroom, South Africa; Dr Alexandre Lemgruber, Pan American Health Organization; Dr C. Michelle Limoli, Silver Spring, MD, USA; Professor Gerhard Scriba, Jena, Germany; Mr John Wilkinson, London, England.

Representation from international organizations³

Council of Europe

Dr Andrea Lodi, Head, Laboratory Department, European Directorate for the Quality of Medicines & HealthCare (EDQM), Strasbourg, France

European Medicines Agency (EMA)

Mr Andrei Spinei, Scientific Administrator, Manufacturing and Quality Compliance, Compliance and Inspections Department, London, England

International Atomic Energy Agency (IAEA)

Dr Uday Bonsle, Radiopharmaceutical Scientist, Radioisotope Products and Radiation Technology Section, Division of Physical and Chemical Sciences, Department of Nuclear Sciences, Vienna, Austria

United Nations Children's Fund (UNICEF)

Dr Peter Svarrer Jakobsen, Quality Assurance Specialist, UNICEF Supply Division, Copenhagen, Denmark

United Nations Industrial Development Organization (UNIDO)

Dr Alistair West, Vienna, Austria

Dr Kay Weyer, Vienna, Austria

World Trade Organization (WTO)

Mr Devin McDaniels, Economic Affairs Officer, Trade and Environment Division, WTO, Geneva, Switzerland

Mr Camilo Vicaria Angel, Trade and Environment Division, WTO, Geneva, Switzerland

Representation from non-state actors⁴

Global Fund to Fight AIDS, Tuberculosis and Malaria

Dr Alain Prat, Geneva

International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)

Dr Valérie Faillat-Proux, Senior Director, Regulatory Affairs and Malaria Programme, Sanofi, Geneva, Switzerland

003, 201

预览已结束,完整报告链接和1

https://www.yunbaogao.cn/report/index/report?re