

WHO Expert Committee on Specifications for Pharmaceutical Preparations

Thirty-first Report

World Health Organization
Technical Report Series
790



World Health Organization, Geneva 1990

WHO Library Cataloguing in Publication Data

WHO Expert Committee on Specifications for Pharmaceutical Preparations

WHO Expert Committee on Specifications for Pharmaceutical Preparations :
thirty-first report.

(World Health Organization technical report series ; 790)

1. Drugs – standards I. Series

ISBN 92 4 120790 6

(NLM Classification: QV 771)

ISSN 0512-3054

© World Health Organization 1990

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. For rights of reproduction or translation of WHO publications, in part or *in toto*, application should be made to the Office of Publications, World Health Organization, Geneva, Switzerland. The World Health Organization welcomes such applications.

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 the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization 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.

PRINTED IN SWITZERLAND

89/8249 – Schüler SA – 6000

CONTENTS

	Page
1. Drug stability	7
2. Sampling procedures	9
3. <i>The International Pharmacopoeia</i> and basic tests	10
3.1 Quality specifications for drug substances and dosage forms	10
3.2 Dissolution test for solid oral dosage forms	10
3.3 Microbial contamination of nonsterile materials and products	13
3.4 Validation of analytical procedures	13
3.5 Simple test methodology	13
4. International Chemical Reference Substances and infrared reference spectra	14
4.1 Establishment of reference substances	14
4.2 Validation of International Chemical Reference Substances	15
4.3 Infrared reference spectra	16
5. Quality assurance of products manufactured by recombinant DNA technology	16
6. Developments in the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce	17
7. Falsely labelled, spurious, counterfeited, and substandard pharmaceutical preparations	19
8. Training of drug regulators	20
References	21
Acknowledgements	21
Annex 1. Stability of drug dosage forms	24
Annex 2. Sampling procedure for industrially manufactured pharmaceuticals	34
Annex 3. Guidance for those preparing or commenting on monographs for preparations to be included in <i>The International Pharmacopoeia</i>	48
Annex 4. List of available International Chemical Reference Substances (1988)	52
Annex 5. WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce	57
Annex 6. Guiding principles for small national drug regulatory authorities ...	64

**WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR
PHARMACEUTICAL PREPARATIONS**

Geneva, 28 November–3 December 1988

Members

Professor H.Y. Aboul-Enein, Scientist, Drug Development Laboratory, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia
Dr P. K. Gupta, Drugs Controller (India), Directorate General of Health Services, Ministry of Health, New Delhi, India (*Rapporteur*)
Professor Y. Krylov, Head, Department of Pharmacology, State Medical Stomatological Institute, Moscow, USSR
Dr T. Layloff, Director, Division of Drug Analysis, Food and Drug Administration, St Louis, MO, USA
Professor A.A. Olaniyi, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Ibadan, Ibadan, Nigeria
Dr M. Pesz, Scientific Consultant, Roussel-Uclaf SA, Romainville, France (*Chairman*)
Professor J. Richter, Director, Institute of Drugs of the German Democratic Republic, Berlin, German Democratic Republic (*Vice-Chairman*)
Professor Tu Guoshi, Scientific Adviser, Division of Pharmaceutical Chemistry, National Institute for the Control of Pharmaceutical and Biological Products, Ministry of Public Health, Beijing, China
Dr M. Uchiyama, Deputy Director-General, National Institute of Hygienic Sciences, Tokyo, Japan

Representatives of other organizations

United Nations Industrial Development Organization (UNIDO)

Mrs M. Quintero de Herglotz, Chief, Pharmaceutical Industries Unit, UNIDO, Vienna, Austria

Council of Europe

Mr R. Bontinck, Deputy Secretary, European Pharmacopoeia Commission, Council of Europe, Strasbourg, France

International Federation of Pharmaceutical Manufacturers Associations (IFPMA)

Miss M. Cone, Vice-President for Scientific Affairs, IFPMA, Geneva, Switzerland

International Pharmaceutical Federation (FIP)

Dr N. Diding, Chairman, Official Control Laboratory Section, FIP, Solna, Sweden

Secretariat

Professor J.-M. Aiache, Director, Biopharmacy Laboratory, Faculty of Pharmacy, University of Clermont-Ferrand, France (*Temporary Adviser*)

Dr J.F. Dunne, Programme Manager, Pharmaceuticals, WHO, Geneva, Switzerland
Dr A. Hunger, Head, Quality Surveillance, Ciba-Geigy Ltd, Basle, Switzerland
(*Temporary Adviser*)
Dr A. Mechkovski, Senior Pharmaceutical Officer, Pharmaceuticals, WHO, Geneva, Switzerland (*Co-Secretary*)
Mr B. Öhrner, Director, Quality Assurance, Apoteksbolaget AB, Pharmaceutical Division, Stockholm, Sweden (*Temporary Adviser*)
Miss M. Rabouhans, British Pharmacopoeia Commission, London, England
(*Temporary Adviser*)
Miss M. Schmid, Technical Officer, Pharmaceuticals, WHO, Geneva, Switzerland
Miss A. Wehrli, Senior Pharmaceutical Officer, Pharmaceuticals, WHO, Geneva, Switzerland (*Co-Secretary*)

WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Thirty-first Report

The WHO Expert Committee on Specifications for Pharmaceutical Preparations met in Geneva from 28 November to 3 December 1988. The meeting was opened on behalf of the Director-General by Dr V. Fattorusso, Adviser to Dr Hu Ching-Li, Assistant Director-General, who recalled that the supply of good-quality essential drugs—identified at the International Conference on Primary Health Care, Alma-Ata, 1978, as one of the basic prerequisites for the delivery of health care—had long been of fundamental concern to the World Health Organization. Pivotal to its efforts in this connection had been the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce. However, rigorous procedures for attesting the quality and provenance of imported products needed to be complemented, wherever possible, by the analytical facilities afforded by a national drug quality-control laboratory and, above all, by a reliable system of licensing pharmaceutical products as a prerequisite for their distribution and sale. For this reason, emphasis had been accorded within WHO's revised drug strategy to the need to prepare guiding principles for small national drug regulatory authorities. The Committee was consequently requested to consider, in addition to various important technical issues relating to quality assurance, some draft guidelines addressing this need that had been prepared as a consultative document and to submit any recommendations it might care to propose to the Director-General.

1. DRUG STABILITY

Inadequate storage and distribution of pharmaceutical products can lead to their physical deterioration and chemical decomposition, resulting in reduced activity and, occasionally, in the formation of toxic degradation products. Degradation is particularly likely to occur under tropical conditions of high ambient temperature and

humidity; and it is not widely recognized that, because of the potential for chemical interaction between the active ingredients and excipients, drug dosage forms can be more vulnerable to degradation than pure drug substances.

The stability of a specific product is thus dependent, in a large measure, on its formulation, and its expiry date should be determined on the basis of stability studies carried out by the manufacturer. Studies undertaken with a view to determining the stability of a product under temperate conditions, however, do not necessarily provide a reliable indication of its shelf-life in tropical climates. In such cases, additional proof of stability should be requested from the manufacturer, who should assume responsibility for formulating a product that is stable under the climatic conditions prevailing in the countries of destination. Relevant information should be specifically requested by the national regulatory authority in the importing country within the context of the WHO Certification Scheme (see section 6 of this report). It is obviously impossible to obtain satisfactory assurances when a product is purchased through an intermediary if its provenance is unknown to the purchaser. For domestically produced products, the regulatory authority should evaluate stability data furnished by the manufacturer. The procurement agencies and the pharmacists responsible for drug distribution should ensure that they are supplied with adequate information concerning the proper storage and handling of each product.

Annex 1, on the stability of drug dosage forms, is a comprehensive statement on both the technical aspects of the subject and the responsibilities that devolve upon the manufacturer and all agencies and individuals responsible for the product throughout the distribution chain up to the time of its administration or delivery to the patient.

Within the distribution chain, the labelled expiry date on a pharmaceutical product has a dual significance: after this date, no formal assurance is provided regarding the condition of the product; and the manufacturer may no longer have legal liability for it. The Committee agreed that the use of time-expired stock should be entertained only in the most exceptional circumstances, when to withhold the stock would have serious consequences for patients. In every instance, the proposal to release such a product must be channelled through a pharmacist or other professional experienced in quality assurance and, when appropriate, referred to the

预览已结束，完整报告链接和二维码如下：

https://www.yunbaogao.cn/report/index/report?reportId=5_30757

