The International Pharmacopoeia, Fourth Edition

Volumes 1 and 2 of the Fourth Edition were published together in 2006. Volume 1 contains the *General Notices* and many of the monographs for pharmaceutical substances and Volume 2 contains the remaining monographs for pharmaceutical substances together with those for dosage forms and radiopharmaceutical preparations, the methods of analysis and the reagents section and index. The main volumes of this edition consolidated and updated the texts of the five separate volumes of the third edition and included new monographs for antiretroviral substances.

The International Pharmacopoeia comprises a collection of recommended procedures for analysis and specifications for the determination of pharmaceutical substances, excipients and dosage forms that is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements. The pharmacopoeia, or any part of it, shall have legal status, whenever a national or regional authority expressly introduces it into appropriate legislation. Further explanation of the role of *The International Pharmacopoeia* is provided in the paragraphs entitled "Scope and function" at the end of the *Preface* in Volume 1.

In accordance with WHO's consultation process for new standards and guidelines in the area of medicines quality assurance, all new specifications, all amendments relating to existing texts and all supplementary information texts have been circulated widely for comments in several working documents phases, have been through a thorough revision and validation process, and have been subsequently adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations.

In preparing this consolidated edition, the opportunity has been taken to improve certain aspects of the layout and format of the publication. In this edition all the monograph texts have been brought together in one main section and the method texts in another. Each of these major sections has been divided into appropriate subsections and the method texts have been numbered for ease of cross-reference.

General Notices. During preparation of this edition a review was carried out of the *General Notices*. Certain additions and amendments have been made in order to clarify the interpretation of the Pharmacopoeia and to facilitate application of the requirements by the user. New *General Notices* have been added for *Definition*, *Manufacture* and *Impurities*. The new notice on *Definition* serves to define dosage forms as being made with active ingredients of pharmacopoeial quality and to clarify the mandatory status of certain statements in monographs. The new notice on *Manufacture* governs the interpretation of statements included under this heading in monographs such as the general monographs for dosage forms, the monographs for the different grades of water and certain other individual monographs, for example, Bleomycin hydrochloride and Desferoxamine mesilate. The need for a notice on *Impurities* arose from the inclusion of information at the end of certain of the new monographs for antiretoviral substances. Such lists of known and potential impurities that have been shown to be controlled by the tests in a monograph are likely to be included more widely in future. Notices that have been significantly revised include those for *Labelling*, *General Requirements* and *Tests and Assays*. General methods of analysis that are commonly used in carrying out the tests and assays included in the monographs of *The International Pharmacopoeia* are described in the section on *Methods of analysis*. In some cases a specific cross-reference to the method required is provided within the monograph text. Examples include references to Spectrometry in the infrared region, High performance liquid chromatography (HPLC) and Limit test for heavy metals. In other cases, where the relevant method can be inferred from the title of the test, no explicit cross-reference is given. Examples include tests for Specific optical rotation, Sulfated ash, Loss on drying and pH value. A statement has been added to the *General notice* on *General requirements* to assist in the correct interpretation of the monograph requirements, especially in those cases where there is no cross-reference. It emphasizes that whether or not a specific cross-reference is included, the requirements of the monographs of *The International Pharmacopoeia* are to be interpreted in relation to the relevant method of analysis.

New monographs. New monographs are included for the following antiretroviral substances: Didanosine, Indinavir sulfate, Nelfinavir mesilate, Nevirapine, Ritonavir, Saquinavir and Saquinavir mesilate. These monographs have been developed as part of the WHO strategy to make quality antiretroviral medicines more widely available to HIV-positive patients. Such specifications support the joint United Nations Children's Fund (UNICEF)-WHO-United Nations (UN) Prequalification Team, managed by WHO. These monographs provide an element of choice in relation to test methods used for identification and, where possible, a titration method for assay, in line with established policy. However, in order to provide adequate control of impurities, it has been found necessary to place reliance on HPLC.

Revision. The monograph for Oral rehydration salts has been revised to conform to the modified formula as published in the 13th EML and in the Model Formulary 2004. The revised formula has a reduced sodium chloride and glucose content providing a solution with a reduced osmolarity of 245 mOsm/L. Due to the improved effectiveness of the reduced osmolarity ORS solution, especially for children with acute, non- cholera diarrhoea, WHO and UNICEF now recommend that countries use and manufacture this formulation in place of the previously recommended ORS, that is, the one published in the Third Edition of *The International Pharmacopoeia*, which had a total osmolarity of 311mOsm/L.

The general monograph for *Parenteral Preparations* has been amended to make reference to the test for bacterial endotoxins as the preferred method for ensuring the quality of preparations with respect to pyrogens. Individual monographs no longer include recommended storage temperatures where these are covered by the normal storage conditions as defined in the *General Notices* . Method texts that have been updated include, for example, the text on HPLC. This has been revised to clarify certain technical

terms and to add advice on adjustment of chromatographic conditions as recommended by the WHO Expert Committee on Specifications for Pharmaceutical Preparations.

CD-ROM. This Fourth Edition is published simultaneously both in print and on CD-ROM. The response from users of the CD-ROM of the Third Edition, published in 2004, had demonstrated the usefulness of making the publication available electronically.