

Preface: *The International Pharmacopoeia*, Twelfth Edition

2025

This is the Twelfth Edition of *The International Pharmacopoeia*, published in 2025.

The International Pharmacopoeia^[1] (Ph.Int.) is comprised of a collection of recommended procedures for analysis and specifications for the determination of "pharmaceutical substances" (active pharmaceutical ingredients), excipients and "dosage forms" (general texts and individual finished pharmaceutical products) that is intended to serve as source material for reference or adaptation by any World Health Organization (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 section below entitled "Scope and function". A summary of the history and major changes in the previous editions is provided in the folder "Background to previous editions of The International Pharmacopoeia".

The International Pharmacopoeia is based on advice and decisions from the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSP). All specifications included in this edition have been developed following the WHO consultation process and were adopted by the ECSP.

New and revised texts. New and revised texts are introduced for 11 monographs on pharmaceutical substances, 12 monographs on dosage forms, 3 methods of analysis, 2 texts for inclusion in the Supplementary information section and 1 general monograph on dosage forms.

Omitted texts. Following a decision at the Fifty-seventh meeting of the ECSP, two monographs were omitted from the Eleventh Edition. Omitted texts are further accessible on the website of *The International Pharmacopoeia* (<https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards-for-pharmaceuticals/international-pharmacopoeia>). Users of these texts may note that the documents are provided for information; they will neither be updated or revised, nor will the prescribed International Chemical Reference Substances (ICRS) be further monitored for the analytical purpose mentioned in the monograph. Users will need to ensure that the described pharmaceutical substances or specific dosage forms comply with current rules and regulations governing medicines in their respective territories.

A list of new, revised and omitted texts is provided as an annex to this preface.

International Chemical Reference Substances. ICRS are primary chemical reference substances for use in physical and chemical tests and assays described in *The International Pharmacopoeia*. More information on ICRS can be found on the following website: <https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards-for-pharmaceuticals/international-pharmacopoeia/international-chemical-reference-substances>.

Trade names of stationary phases. The selectivity of chromatographic tests may not only depend on the parameters mentioned in the methods' descriptions but also on the material of the used stationary phases. *The International Pharmacopoeia* has provided on its website (<https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards-for-pharmaceuticals/international-pharmacopoeia>) a list of trade names of the stationary phases that were found to be suitable when the monographs were being developed. This information is provided solely for the convenience of users. The mentioned suppliers are neither endorsed nor recommended by *The International Pharmacopoeia* , nor does the information imply any preference to other stationary phases of a similar nature which are not mentioned. The user should also be aware of the fact that some stationary phases can show significant batch-to-batch variations.

Scope and function. The activities related to *The International Pharmacopoeia* are an essential element in the overall quality control and assurance of pharmaceuticals contributing to the safety and efficacy of medicines.^[2]

The selection of monographs for inclusion in *The International Pharmacopoeia* recognizes the needs of specific disease programmes and the essential medicines nominated under these programmes. *The International Pharmacopoeia* specifies primarily the quality of essential medicines that are listed:

- on the WHO Model List Of Essential Medicines (EML) and on the EML for Children;

- on the invitations to manufacturers to submit an expression of interest (EOI) to the WHO Prequalification Team – Medicines (PQTm); and

- in other United Nations (UN)/WHO documents recommending the use of medicines for the treatment of specific diseases and/or for use by treatment programmes.

The work on *The International Pharmacopoeia* is carried out in collaboration with members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations as well as with specialists from regulatory authorities, from industry and from other institutions. Clearly defined steps are followed in the development of new monographs. ^[3], ^[4]

It is emphasized that pharmacopoeial specifications represent only one element of the quality assurance of medicines.

Pharmaceutical substances and dosage forms for human use, as described in a monograph of *The International Pharmacopoeia*, should be manufactured according to the current requirements of good manufacturing practices.^[5] The processes, premises, equipment and installations should also comply with the provisions of the product license or marketing authorization, relevant regulations and, in the case of products destined for export, with any binding international norms that would affect their entry onto the market. In many cases, this compliance cannot be verified by analysing a sample of the final product against a pharmacopoeial monograph. The national, regional or other competent authority will need to ensure that all relevant provisions have been met by any means at its disposal, including use of appropriate certificates, inspection of the manufacturing sites or testing of samples beyond specifications.

There is a distinction exists between pharmacopoeial standards and manufacturers' release specifications. Pharmacopoeial standards are publicly available compliance specifications and provide the means for an independent check of the quality of a product at any time during its shelf life. Release specifications should generally be aligned to pharmacopoeial specifications; they may, however, include additional tests or limits to meet regulatory requirements. Manufacturer are entitled to use other analytical methods for testing and, moreover, they may assure themselves that the requirements of the pharmacopoeia will be met by other means than routinely performing all of the tests in the monograph.

The requirements of the monographs are not framed to detect all possible impurities and contaminants. The present tests are designed to determine impurities on which attention should be focused, to fix the limits of those that are tolerable to a certain extent and to indicate methods for ensuring the absence of those that are undesirable. It is, therefore, not to be presumed that an impurity can be tolerated because it has not been precluded by the prescribed tests.

Pharmaceutical preparations (dosage forms) that are produced on a large scale and stored before use should undergo testing to show physical and chemical stability during storage over the claimed shelf life.

The degree of protection provided by pharmacopoeial standards will depend not only on their technical content but also to a great extent on how they are used. The specified tolerances and limits allow for the inherent variations that occur during production and packaging, as well as for subsequent degradation within normal handling and storage conditions and for any acceptable variance of analytical results.

When pharmacopoeial standards are used to establish the compliance of products with regulatory requirements, the following principles apply:

the interpretation of a monograph must be in accordance with all general requirements and testing methods, texts or notices pertaining to it as found in this edition; and

no further tolerances are to be applied to the limits prescribed.

Online publication. The Twelfth Edition is published online.

ANNEX

NEW TEXTS

Pharmaceutical substances

- [Linezolid](#)
- [Molnupiravir](#)
- [Nirmatrelvir](#)

Dosage forms

- [Albendazole tablets](#)
- [Estradiol valerate and norethisterone enantate injection](#)
- [Lamivudine and tenofovir disoproxil tablets](#)
- [Linezolid tablets](#)
- [Molnupiravir capsules](#)
- [Nirmatrelvir tablets](#)

Methods of analysis

- [Micro determination of water by the Karl Fischer method](#)

Supplementary information

- [Tests for diethylene glycol and ethylene glycol in liquid preparations for oral use](#)
- [Test for 1-Methyl-4-nitroso piperazine in rifampicin active pharmaceutical ingredient or rifampicin tablets / capsules by HPLC-MS/MS](#)

REVISED TEXTS

Pharmaceutical substances

- [Albendazole](#)
- [Efavirenz](#)
- [Glycerol](#)
- [Glycerol 85% m/m](#)
- [Isoniazid](#)
- [Propylene glycol](#)
- [Rifampicin](#)
- [Tenofovir disoproxil fumarate](#)

Dosage forms

- [Albendazole chewable tablets](#)
- [Dolutegravir, lamivudine and tenofovir disoproxil tablets](#)
- [Isoniazid tablets](#)
- [Paracetamol oral solution](#)
- [Pyrimethamine tablets](#)
- [Tenofovir disoproxil tablets](#)

Methods of analysis

- [Melting temperature and range](#)
- [Chromatography](#)

General monographs for dosage forms

- [Liquid preparations for oral use](#)

OMITTED TEXTS

Dosage form

- Yttrium (90Y) silicate injection
- Amodiaquine

[1] Published in accordance with World Health Assembly Resolution WHA3.10, WHO Handbook of Resolutions and Decisions, Vol. 1, 1977, p. 127. This Edition is published electronically by means of an online version.

[2] The International Pharmacopoeia: revised concepts and future perspectives. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-first report. Geneva: World Health organization, 2017: Annex 2 (WHO Technical Report Series, No. 1003; <https://apps.who.int/iris/handle/10665/258720>, assessed 05 August 2022.

[3] Procedure for the elaboration, revision and omission of monographs and other texts for The International Pharmacopoeia. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-fourth report. Geneva: World Health organization, 2020: Annex 1 (WHO Technical Report Series, No. 1025; <https://apps.who.int/iris/handle/10665/331814>, assessed 05 August 2022.

[4] Updating mechanism for the section on radiopharmaceuticals in The International Pharmacopoeia. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: Forty-ninth report. Geneva: World Health organization, 2015: Annex 2 (WHO Technical Report Series, No. 992; <https://apps.who.int/iris/handle/10665/176954>, assessed 05 August 2022.

[5] For the current WHO recommendations, consult the WHO Medicines website (https://www.who.int/health-topics/medicines#tab=tab_1).