

Annex 2

The International Pharmacopoeia: revised concepts and future perspectives

General context and overview

WHO Constitution and World Health Assembly

The quality of pharmaceuticals has been a concern of the World Health Organization (WHO) since its inception. The setting of global standards is requested in Article 2 of the WHO Constitution, which cites as one of the Organization's functions that it should "develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products". The World Health Assembly has adopted many resolutions requesting the Organization to develop international standards, recommendations and instruments to assure the quality of medicines, whether produced and traded nationally or internationally. In addition, many national governments financially support the activities of WHO collaborating centres.

Expert Committee and activities related to *The International Pharmacopoeia*

In response to the World Health Assembly resolutions, the WHO Expert Committee on Specifications for Pharmaceutical Preparations, which was originally established to prepare *The International Pharmacopoeia* (Ph.Int.), has made numerous recommendations relevant to quality assurance and quality control of medicines.¹

The activities related to Ph.Int. are an essential element in overall quality control of pharmaceuticals, contributing to the safety and efficacy of medicines. In contrast to other pharmacopoeias, priority has been given for many years to medicines included in the WHO Model List of Essential Medicines, to those important for WHO health programmes and to those that are not included in other pharmacopoeias, e.g. new antimalarials. Since the inception of the WHO Prequalification of Medicines Team (PQT) in 2001 the Ph.Int. workplans also focus on medicines that are included in the PQT's invitations to submit an Expression of Interest for product evaluation. These first focused on

¹ See, for example, *Quality assurance of pharmaceuticals: WHO guidelines, good practices, related regulatory guidance and GXP training materials*, 2016 (CD-ROM, regularly updated).

antiretrovirals and medicines used in the treatment of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), tuberculosis (TB) and malaria, and were later expanded to other groups of products.

The quality control specifications published in the Ph.Int. are developed independently in accordance with an international consultative procedure. The official procedure for the development of monographs and other texts for *The International Pharmacopoeia* was developed and adopted by the Expert Committee on Specifications for Pharmaceutical Preparations and is updated regularly. The policy is to use state-of-the-art analytical procedures. However, the needs of developing countries are taken into account and, whenever possible, simpler, appropriate alternative methods are also included.

The Ph.Int. undoubtedly strengthens the scientific credibility of WHO.

Revised concepts and future perspectives

The first volume of the first edition of the Ph.Int. was published in 1951 with the aim of harmonizing quality requirements for pharmaceutical substances worldwide. After 65 years of existence, and in the light of new international efforts towards pharmacopoeial harmonization and synergy, it would seem appropriate to propose revised concepts and perspectives for the Ph.Int. This will be realized through WHO's observer status to the Pharmacopoeial Discussion Group (PDG) and the initiation of regular international meetings of world pharmacopoeias with the objectives of preparing guidelines on good pharmacopoeial practices and convergence of methodology and specifications. A more global approach and exploitation of new opportunities for synergies in the area of quality control of pharmaceuticals will contribute to the reduction of costs and thus increase the access to affordable quality medicines worldwide.

Targets and priorities

The ultimate goals are the promotion of good quality pharmaceutical products and the development of quality control methods so as to assure the safety and efficacy of medical treatments worldwide. The Ph.Int. thus supports programmes for the eradication or control of WHO priority diseases, e.g. HIV/AIDS, malaria and TB, by development of appropriate monographs. In addition, monographs for newly developed antimicrobials will be needed to help combat microbial resistance.

The Ph.Int. provides international standards for the identification, content, purity and quality of active ingredients, pharmaceutical products and excipients moving in international commerce. Each monograph must be interpreted in accordance with all the general requirements and testing methods, texts or notices pertaining to it. A product is not of pharmacopoeial quality unless it complies with all the applicable requirements. Moreover, the

underlying principle of a pharmacopoeia is that pharmaceutical substances and products intended for medical use should be manufactured according to good manufacturing practices since quality cannot be tested into a product. The development of monographs in the context of WHO's prequalification activities is a priority. Priority will also be given to those active pharmaceutical ingredients and finished pharmaceutical products that are not covered by any other pharmacopoeia.

Implementation of the guidance on good pharmacopoeial practices and further collaboration with other pharmacopoeias are targeted, for example, through:

- adoption or adaptation of existing standards (with due reference to the source of the text);
- development of a new standard through coordinated consideration (prospective harmonization);
- revision or creation of a standard between two or more pharmacopoeias (bilateral or multilateral harmonization), e.g. through a harmonization initiative of the PDG.

Monographs in the Ph.Int. together with related general methods and notices have an added value as discussed above and can also be used as references in the development of national quality standards as well as for the assessment of registration dossiers.

Setting of specifications and validation of methods

The independence of WHO in setting specifications is of fundamental importance.

Validation of analytical methods is a prerequisite for the publication of monographs and WHO is actively assisted in this task by numerous WHO collaborating centres worldwide.

International Chemical Reference Substances

The establishment of International Chemical Reference Substances (ICRS) is an essential part of quality control. This major task is performed by the custodian centre located in the Council of Europe. This work must be fully supported to ensure the supply of ICRS and thus the success of WHO programmes.

List of priorities

In the context of medicines quality control, the priorities are as follows:

- continuation of the development of international standards for testing pharmaceuticals;

- promotion of global synergy and harmonization in the quality control of pharmaceuticals by strengthening cooperation with world pharmacopoeias, e.g. PDG, agreements, and making use of the opportunities provided by their international meetings;
- increasing the availability of documents and information on WHO activities in quality assurance;
- providing advice to WHO priority programmes on quality assurance matters;
- providing information to WHO Member States on the harmonization process and on collaboration;
- promotion of external quality assurance assessment schemes to improve the performance and recognition of laboratories.