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WHO Drug Information

WHO Drug Information provides an overview of topics relating to medicines development, regulation, quality and safety. The journal also publishes and reports on guidance documents and includes lists of International Nonproprietary Names for Pharmaceutical Substances (INN), ATC/DDD classification and monographs for The International Pharmacopoeia. It presents and describes WHO policies and activities while reflecting on technical and pharmaceutical topics of international and regional interest.

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International Nonproprietary Names (INN)

Abbreviations and websites

CHMP	Committee for Medicinal Products for Human Use (EMA)
EMA	European Medicines Agency (www.ema.europa.eu)
EU	European Union
FDA	U.S. Food and Drug Administration (www.fda.gov)
Health Canada	Federal department responsible for health product regulation in Canada (www.hc-sc.gc.ca)
HPRA	Health Products Regulatory Authority, Ireland (www.hpra.ie)
HSA	Health Sciences Authority, Singapore (www.hsa.gov.sg)
ICDRA	International Conference of Drug Regulatory Authorities
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (www.ich.org)
IGDRP	International Generic Drug Regulators Programme (https://www.igdrp.com)
MHLW	Ministry of Health, Labour and Welfare, Japan
MHRA	Medicines and Healthcare Products Regulatory Agency, United Kingdom (www.mhra.gov.uk)
Medsafe	New Zealand Medicines and Medical Devices Safety Authority (www.medsafe.govt.nz)
Ph. Int	*The International Pharmacopoeia* (http://apps.who.int/phint/)
PMDA	Pharmaceuticals and Medical Devices Agency, Japan (www.pmda.go.jp/english/index.htm)
Swissmedic	Swiss Agency for Therapeutic Products (www.swissmedic.ch)
TGA	Therapeutic Goods Administration, Australia (www.tga.gov.au)
WHO	World Health Organization (www.who.int)
WHO MHP	WHO Access to Medicines and Health Products Division (www.who.int/medicines/en/)
WHO RPQ	WHO Regulation and Prequalification Department
WHO PQT	WHO Prequalification Unit (https://www.who.int/topics/prequalification/en/)
WHO HPS	WHO Health Product Policy and Standards Department

Note: The online version of this issue is available at www.who.int/medicines/publications/druginformation)

White Paper for the WHO International Meeting of World Pharmacopoeias

Value of Pharmacopoeial Standards for Access to Quality Medicines

Introduction

In healthcare systems around the world, medicines play an important role in treating illness, preventing disease, and ultimately, saving lives. In a broader sense, medicines are valuable to society as tools to protect the public health. Nowadays, medicines are complex products made from numerous ingredients sourced through the global supply chain. The quality of medicines is ensured by the control of many factors such as the quality of their components. While quality medicines are safe and effective, substandard and falsified medicines can be ineffective and even harmful.

Medicine Quality Standards: The Pharmacopoeias

Because medicine quality is so important to society, standards for medicine quality have been developed and published in countries around the world. In some countries, the standards have been compiled and placed in a valuable resource called a pharmacopoeia for decades and, in some cases, for centuries. A pharmacopoeia is an official collection of quality standards and specifications for medicines and their ingredients. This information is publicly available, shared, and used by parties concerned about the quality of medicines. These different parties, known as stakeholders, include medicine manufacturers, analytical laboratories, raw material suppliers, policy makers, regulatory agencies, pharmacies and other interested groups. Traditionally, a pharmacopoeia was only contained in a book, now an increasing number of pharmacopoeias are also available online. The Pharmacopoeias constantly work to improve access to the information and enhance the user's ability to benefit from the full range of standards, best practices, and guidance provided.

A pharmacopoeia contains detailed, descriptive information about quality attributes of medicines and their ingredients in the form of quality standards. The information encompasses procedures for how the medicine should be tested for identity, purity, potency, and other aspects of quality before it reaches the market and throughout its shelf life. Indeed, potential impurities that need to be kept under the maximum allowable level are controlled by the quality standard. In addition to these binding quality standards, the pharmacopoeia also provides useful guidance and recommendations for laboratories and production facilities. This guidance typically describes best practices, such as the preferred techniques and procedures to use in testing the medicines, and may be in the form of non-binding chapters or other means.

The core purpose of a pharmacopoeia is to help ensure that medicines and their ingredients are safe, effective, and of appropriate quality. The standards define the specifications that pharmaceutical ingredients and products on the market must fulfill throughout their shelf life. As such, the quality standards in the pharmacopoeia serve as a benchmark for quality, underpinning the overall safety of medicines and making a vital contribution to protecting public health. Quality standards also provide a common, or shared, understanding of appropriate quality characteristics for medicines and their ingredients. This common understanding helps streamline communications between manufacturers and regulatory authorities, saving time and resources while also building confidence in medicine quality among healthcare professionals and patients.

Transparent, Unbiased Public Process

Pharmacopoeias and the standards they contain are the end result of a unique collaborative effort by a range of stakeholders who work collectively to protect public health. These stakeholders are individual scientific experts who come together from regulatory agencies, academia, healthcare practice, industry, and other related areas to serve as members of pharmacopoeial committees and advisory groups. Their expertise is critical to the scientific development, review, evaluation, and approval of quality standards. Clear rules for identifying and managing potential conflicts of interest are therefore crucial. This ensures that the scientific experts on the pharmacopoeial committees are functioning as independent, impartial individuals, driven by science and acting in the best interests of public health.

The rules for ensuring that the experts are impartial are crucial to the integrity and credibility of the pharmacopoeia. Equally critical is the transparent, well-defined public process used for developing quality standards. One aspect of transparency is that stakeholders are informed in advance of possible upcoming changes to quality standards. This ensures that a stakeholder who may have concerns about a certain quality standard will have time to provide input and participate in the standard-setting process. This practice of transparency includes opportunities to comment on proposals made about the standards. Input from stakeholders is carefully considered and may be incorporated by the pharmacopoeia's committees of scientific experts before a standard is finalized. The process to develop quality standards is publicly available, open, and held to account, enabling stakeholders to have confidence in pharmacopoeial standards.

Data-driven and Grounded in Science

Given their critical role in healthcare and public health, pharmacopoeial standards must be based on robust data and sound scientific principles. Data are mainly submitted by stakeholders who seek to support the development of a new standard. These data, from a variety of sources, are gathered and used to construct the quality standard. All the evidence is evaluated carefully by experts from multiple scientific disciplines, allowing for thorough, productive scientific discussions and decision making.

After the new standard has been finalized and published, relevant data and evidence continue to be used throughout the lifecycle of the standard to ensure that it remains fit-for-purpose and reflective of the current state of the science, resulting, where necessary, in frequent revisions of standards. The standard must continue to reflect the expected quality of the specific medicine or its ingredients over time. Robust pharmacopoeial standards are supported by appropriate validation data that confirm that the analytical procedures are suitable for the intended purpose. Feedback and input from stakeholders are collected on an ongoing basis to ensure that the standards remain appropriate and applicable to all stakeholders, most specifically the regulatory agencies or pharmaceutical industry.

Responsive to Public Health Needs

Over time, the number and complexity of medicines on the market is growing. Simultaneously, quality control strategies and manufacturing paradigms are becoming more diverse. In this complex environment, quality standards are playing an increasingly relevant role in protecting public health. As part of a broader health and social care system, quality standards can help maintain a stable, affordable, accessible supply of essential medicines while also facilitating the development of new medicines[1].

[1] For example, a very recent US study [1] shows that pharmacopoeial standards facilitate patients' access to quality medicines while at the same time saving the healthcare system billions (USD) annually. Additionally, findings of a new survey [2] suggest that the use of pharmacopoeial standards also reduces time and costs associated with product development for manufacturers of high-quality generic medicines. Moreover, survey respondents' perceptions are that usage of the standards decreases the risk of rejection of the marketing approval application by the regulators, in this case FDA. While the results found are valid for the United States, it is likely that similar benefits would exist in other countries.

In this way, quality standards represent a critical element in the safety net that protects the public's supply of safe, effective, and affordable medicines. At the same time, the emerging public health needs of society can stimulate beneficial changes in current pharmacopoeial standards. These changes allow the standards to better reflect and respond to public health priorities as they evolve. Examples of these evolving public health priorities include addressing antimicrobial resistance, substandard or falsified medicines, and fostering access to safe, quality medicines for all[2].

Whilst this article was finalized following the 10th IMWP in February 2020, the IMWP felt it was important that it address the role of the pharmacopoeias in the global healthcare response to the COVID-19 pandemic. In early March 2020, the IMWP met as a result of the initiation of the Pharmacopeial alert system with the specific goal to share knowledge and experience with regards the role that pharmacopeias can play in assuring the continued supply of quality medicines during the pandemic. Through regular communications, the IMWP has shared information with regards to maintaining operations in developing and distributing standards, engaged on strategies for the development of pharmacopeial standards for critical COVID-19 treatments, and established a public dashboard on monograph availability of COVID-19 investigated drugs in world pharmacopeias. The pharmacopoeias are resolute in their commitment to supporting the healthcare response to COVID-19 and will continue to reflect on the lessons learnt from the pandemic to improve their ability to meet public health needs.

Continuous Updates Reflect Scientific Advances

The world is changing rapidly, particularly in the realm of science and technology. These changes affect many aspects of society, including quality standards for medicines. It is important to note that a pharmacopoeia must be updated continuously, as it cannot remain stagnant while technology evolves around it. Instead, pharmacopoeial standards adapt over time to better support the changing needs of users and to keep pace with technology. One example is the replacement of legacy technologies with contemporary techniques, as was the transition from thin-layer chromatography to liquid chromatography for the test for related substances. This shift in technique is just one example that illustrates how quality standards can and do respond to advances in technology and science. Therefore, scientific progress and an evolving regulatory environment are driving forces behind the need to constantly revise a pharmacopoeial standard so it can remain relevant and effective.

[2] For example, Antimicrobial resistance (3), Substandard and falsified medical products (4), the Universal Health Coverage (5) and the related Sustainable Development Goals "SDGs" (6).

Global Collaboration on Quality Standards

The utility of pharmacopoeial standards relies heavily on their continued alignment with public health priorities and current, practical scientific approaches to quality. To help ensure positive outcomes, the organizations that develop pharmacopoeias collaborate with each other, industry, and regulators around the world. These stakeholders work together to ensure public health by ensuring the quality of medicines by assembling the appropriate expertise and proposing viable solutions to address public health issues related to medicines quality, including during times of public health emergencies, such as with the adulteration of heparin and glycerol with toxic contaminants, as well as the current concerns with nitrosamine impurities in sartans and other pharmaceutical products. In addition, pharmacopoeias from around the globe through a meeting hosted by WHO called the International Meeting of World Pharmacopoeias worked to develop the first ever guideline on Good Pharmacopoeial Practices (7), which was developed through a collaborative effort and based on feed back during a global consultation.

Supportive of Making Medicines Available to All

Pharmacopoeias have another important function and role. Their quality standards facilitate the development, manufacture, authorization, and post-market surveillance of medicines in countries around the world. In this way, pharmacopoeias help support making medicines widely available to patients around the world. When pharmaceutical companies are developing innovative medicines to treat diseases, their scientists typically refer to the relevant quality standards in the pharmacopoeia. The awareness and understanding of standards enable the development of quality medicines and facilitates approval from regulatory agencies. Indeed, meeting the regulatory expectations for quality is critical when a company seeks approval to manufacture and market a medicine.

Moreover, when there are multiple manufacturers making the same ingredient or product for the market, the existence of common standards helps to assist all companies to achieve the expected quality. Every time a pharmacopoeial standard for a given product becomes available, it creates a level playing field for all manufacturers making the product, helping them to meet the same benchmark. Ultimately, this plays a key role in protecting patients and in assuring healthcare professionals that the medicines they prescribe or dispense are reliable, effective, and safe.