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International Nonproprietary Names for Pharmaceutical Substances

World Health Organization

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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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)

55th Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) meeting

1. Summary and recommendations

The World Health Organization (WHO) Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) advises the Director-General of WHO in the area of medicines quality assurance. It oversees the maintenance of *The International Pharmacopoeia* and provides guidance for use by relevant WHO units and regulatory authorities in WHO Member States to ensure that medicines meet unified standards of quality, safety and efficacy. The ECSPP's guidance texts are developed through a broad consensus-building process, including iterative public consultation. Representatives from international organizations, State actors, non-State actors, pharmacopoeias and relevant WHO departments are invited to the ECSPP's annual meetings, to provide updates and input to the Expert Committee's discussions.

At its Fifty-fifth meeting, held virtually from 12 to 19 October 2020, the ECSPP received updates on cross-cutting issues from other WHO bodies, including the Prequalification team, the Regulatory Systems Strengthening unit and the International Nonproprietary Names team. Updates were also provided by partner organizations, including the International Meeting of World Pharmacopoeias (IMWPs), the International Atomic Energy Agency (IAEA) and the United Nations Population Fund (UNFPA), on collaborative projects. The ECSPP was further updated on the latest efforts to ensure manufacturers and inspectors tackle antimicrobial resistance.

The European Directorate for the Quality of Medicines & HealthCare (EDQM) updated the ECSPP on its activities as the custodial centre in charge of international chemical reference substances (ICRS) for use with monographs of *The International Pharmacopoeia*. Results from the latest phase of the External Quality Assurance Assessment Scheme (EQAAS), which is organized by WHO with the assistance of EDQM, were also shared with the ECSPP.

The ECSPP reviewed new and revised specifications and general texts for quality control testing of medicines for inclusion in *The International Pharmacopoeia*. The Expert Committee adopted 17 pharmacopoeial texts (4 general chapters, 11 new and revised monographs, including 10 subject to a final review by a subgroup (*), and 2 corrections); and confirmed the release of 2 new ICRS established by the custodial centre for use in connection with *The International Pharmacopoeia*.

The ECSPP reviewed proposals for new and updated quality assurance and regulatory guidance, adopting 10 new guidance texts. In line with last year's recommendations, the ECSPP updated the WHO Biowaiver List as an annex to its report. Moreover, it agreed to annex *a consolidated list of all current guidelines and guidance texts adopted by the ECSPP* to date to the report (Annex 1).

Following an update from the Regulatory Systems Strengthening unit and further discussion therein, the Expert Committee adopted a definition for WHO-listed authorities (WLAs).

The sections that follow summarize the specific decisions and recommendations made by the ECSPP during its Fifty-fifth meeting in 2020.

1.1. Guidelines and decisions adopted and recommended for use

The following guidelines and decisions were adopted and recommended for use:

- *Points to consider when including Health Based Exposure Limits (HBELs) in cleaning validation* (Annex 2)
- *Good manufacturing practices: water for pharmaceutical use* (Annex 3)
- *WHO Guideline on data integrity* (Annex 4)
- *UNFPA/WHO Recommendations for condom storage and shipping* (Annex 5)
- *UNFPA/WHO Guidance on testing of male latex condoms* (Annex 6)
- *UNFPA/WHO Guidance on conducting post-market surveillance of condoms* (Annex 7)
- *WHO Biowaiver List* (Annex 8)
- *WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce* (Annex 9)
- *Good reliance practices in the regulation of medical products: high level principles and considerations* (Annex 10)
- *Good regulatory practices for regulation of medical products* (Annex 11)

1.2. Texts adopted for inclusion in *The International Pharmacopoeia*

The ECSPP adopted a series of texts, chapters and monograph, as listed below.

1.2.1. General chapters

- Dissolution test for solid oral dosage forms (revision)
- General identification tests (revision)

1.2.2. Monographs

General monographs for dosage forms

- Powders for inhalation (new)
- Liquid preparations for oral use (revision)

COVID-19 therapeutics

- dexamethasone sodium phosphate (correction)
- dexamethasone phosphate injection (correction)
- remdesivir (new)*
- remdesivir intravenous infusion (new)*

Antiviral medicines, including antiretrovirals

- dolutegravir sodium (new) *
- dolutegravir tablets (new) *
- zanamivir (new) *
- zanamivir powder for inhalation, pre-metered (new) *

Medicines for tropical diseases

- albendazole chewable tablets (revision) *
- ivermectin tablets (revision)

Excipients

- sodium starch glycolate (new) *
- sodium laurilsulfate (new) *
- hydroxypropylcellulose, low-substituted (new) *

1.2.3. Omissions

The ECSPP agreed to omit the following texts from *The International Pharmacopoeia*:

- test for histamine-like substances (vasodepressor substances), including the whole of Chapter 3.6 and all reference to vasodepressor substances in the monographs on bleomycin sulfate, spectinomycin hydrochloride and streptomycin sulfate.

1.2.4. International chemical reference substances

The ECSPP confirmed the release of the following ICRS that have been newly characterized by the custodial centre, EDQM:

- estradiol valerate ICRS, batch 1; and
- moxifloxacin hydrochloride ICRS, batch 1.

1.3. Recommendations

The ECSPP made a series of recommendations related to quality assurance, as listed below. Progress on the suggested actions will be reported to the ECSPP at its Fifty-sixth meeting in October 2021.

The Expert Committee recommended that the WHO Secretariat, in collaboration with experts as appropriate, should take the actions listed next.

1.3.1. *The International Pharmacopoeia*

- Continue the development of monographs, general methods and texts and general supplementary information, including IAEA/WHO specifications for radiopharmaceuticals, in accordance with the 2020–2021 workplan and as decided at the meeting.
- Develop a concept for future work on excipient monographs in *The International Pharmacopoeia*, considering the need for such monographs from a public health perspective, addressing known quality deficiencies, and exploring ways to harmonize specifications with other pharmacopoeias.

1.3.2. Quality control – national laboratories

- Continue the EQAAS in support of national and regional Pharmaceutical Quality Control Laboratories (PQCLs), including continuing the post-assessment assistance programme.

1.3.3. Good manufacturing practices and related areas

- Continue collaborating with the European Union (EU), European Medicines Agency (EMA) and Pharmaceutical Inspection Co-operation Scheme (PIC/S) to harmonize guidance on sterile products and, if feasible, present such guidance for possible adoption at its next meeting in 2021.
- Continue the development of a new good manufacturing practices (GMP) text for radiopharmaceuticals for investigational use.
- Open the existing WHO guideline on cleaning validation to review and update it in accordance with the latest good practices, including the newly adopted *Points to consider when including Health Based Exposure Limits (HBELs) in cleaning validation.*
- Publish results of the survey of pharmaceutical manufacturers engaging in synthesis and/or production of antimicrobials on their waste and wastewater management practices in a regulatory journal.
- Assist national inspectorates and manufacturers towards implementing recommendations made in the *Points to Consider for manufacturers and inspectors: environmental aspects of manufacturing practices for the prevention of antimicrobial resistance.*

- Update the *WHO GMP for investigational pharmaceutical products for clinical trials in humans.*
- Explore the need for updated *WHO guidelines on transfer of technology in pharmaceutical manufacturing.*
- Explore the need for a new guideline to address good practices during the research and development of medicinal products

1.3.4. Distribution and supply chain

- Encourage WHO colleagues involved in procurement to support implementation of *Points to consider for setting the remaining shelf life of medical products upon delivery.*
- Circulate for public consultation the proposed amendment to consider emergency health kits for use in humanitarian emergency response as an additional example to the *Points to consider for setting the remaining shelf life of medical products upon delivery* guideline.

1.3.5. Regulatory mechanisms

- Start the next phase of the WHO Biowaiver Project (Cycle IV) to continue the Biopharmaceutics Classification System (BCS)-based classification of ten further active pharmaceutical ingredients (APIs): dexamethasone, doxycycline, ethambutol, isoniazid, hydroxycholoroquine, lamivudine, levonorgestrel, nifurtimox and proguanil.
- Undertake a pilot expansion study in Cycle IV of the WHO Biowaiver Project to consider API stability under pH conditions representative of stomach and small intestine.
- Promote the results of the WHO Biowaiver Project through publication, advocacy, engagement and partnership.
- Explore the feasibility of presenting the WHO Prequalification of Medicines team's product-specific guidance texts on how to design bioequivalence studies to the ECSPP with a view to making them more generally available to regulators.
- Continue efforts to update the *WHO List of International Comparator Products*