World Health Organization

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# Matters for information: report on meetings of expert committees and study groups[1]

## Report by the Director-General

### SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

### Fifty-seventh report of the Expert Committee on Specifications for Pharmaceutical Preparations, hybrid meeting,[2] 9–13 October 2023[3]

1. The Expert Committee on Specifications for Pharmaceutical Preparations advises the Director-General on quality assurance of medicines; oversees maintenance of *The International Pharmacopoeia;* and provides guidance for medicines to meet unified standards of quality, safety and efficacy.

### Main recommendations

2. Regarding quality control and testing of medicines, the Committee adopted 21 new and revised specifications and general texts for inclusion in *The International Pharmacopoeia* and eight International Chemical Reference Substances established by a custodian centre. The Committee advised continuing the External Quality Assurance Assessment Scheme for quality control laboratories, including continuing the post-assessment assistance programme. Regarding manufacturing and quality control, the Committee adopted the following revised guidelines:

(a) WHO good manufacturing practices for excipients used in pharmaceutical products; and

(b) WHO good practices for pharmaceutical quality control laboratories.

In addition, the guideline IAEA/WHO good manufacturing practices for in-house cold kits for radiopharmaceutical preparations, developed with IAEA, was adopted.

3. Regarding reproductive health, the Committee adopted the WHO/UNFPA female condom generic specification, developed with UNFPA.

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[1] The Regulations for Expert Advisory Panels and Committees provide that the Director-General shall submit to the Executive Board a report on meetings of expert committees containing observations on the implications of the expert committee reports and recommendations on the follow-up action to be taken.

[2] Coordinated from WHO headquarters, Geneva.

[3] WHO Technical Report Series, No. 1052, 2024.

4. To facilitate development of affordable generic medicines of good quality, the Committee adopted WHO guideline on Biopharmaceutics Classification System-based biowaivers and amended the Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. The Committee updated the WHO Biowaiver List: proposal to waive in vivo bioequivalence requirements for WHO Model List of Essential Medicines immediate-release, solid oral dosage forms. The Biowaiver List now includes eight new essential medicines, bringing the total to 42.

5. The Committee noted the updated WHO list of international comparator products.

### Significance for public health policies

6. The Committee provides standards to enable medicines to be tested for quality from development to distribution to patients. It recommends regulatory guidelines for multisource medicines designed to be used globally, in diverse settings. The outcome is intended to protect patients and facilitate access to good-quality medicines. Much of the Committee's work aims to increase convergence in quality assurance and regulatory guidance, facilitating efficiencies among authorities and pharmacopoeias. The quality standards and guidelines are designed to serve all Member States, the United Nations system, and regional harmonization efforts, and underpin public health initiatives, including the prequalification and procurement by international organizations.

### Implications for the Organization's programmes

7. This Committee assists WHO in fulfilling its normative role. It especially benefits WHO teams dealing with prequalification of medicines and regulatory systems strengthening. In return, practical feedback is provided to the Committee through its link to those who implement guidelines, standards and specifications.

## BIOLOGICAL STANDARDIZATION

### Seventy-eighth report of the Expert Committee on Biological Standardization, hybrid meeting, 16–19 October 2023[1]

8. The Expert Committee on Biological Standardization reviews developments in the field of biological products used in human medicine, including vaccines, biotherapeutics, blood products, cell, tissue and gene therapy products, and in vitro diagnostics. The Committee coordinates activities for the adoption of WHO recommendations, guidelines and guidance documents (written standards) that promote quality, safety and efficacy of such products, as well as to the establishment of WHO international reference standards (measurement standards) required for the global harmonization of associated laboratory data.

9. WHO written standards and WHO measurement standards allow for the comparison of nonclinical and clinical data worldwide. Ensuring the comparable quality, safety and efficacy of biological products facilitates their equitable global availability.

10. During its seventy-eighth meeting, the Committee discussed a range of WHO activities, including biological standardization activities relating to coronavirus disease (COVID-19).

[1] WHO Technical Report Series, No. 1054 (in press).

## Main recommendations

11. The Committee recommended the adoption of the WHO Guidelines on regulatory preparedness for the oversight of pandemic or other emergency use vaccines in importing countries.

12. Following consideration of international collaborative laboratory studies, the Committee recommended the establishment of 11 new or replacement WHO measurement standards. It also endorsed seven proposals to develop new or replacement WHO measurement standards.

13. In relation to COVID-19, the Committee supported development of a proposed addendum to the WHO Guidelines on the nonclinical and clinical evaluation of monoclonal antibodies and related products intended for the prevention or treatment of infectious diseases. This addendum would address the evaluation of such products for use against COVID-19 and would be considered by the Committee for adoption in March 2024. The Committee was updated on recent reviews of studies of the efficacy of high-titre convalescent plasma or hyperimmune immunoglobulin in treating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and await further updates prior to making recommendations.

14. Animal testing approaches for the quality control and lot release of many vaccines and biotherapeutics are inherently variable and time consuming, potentially delaying the availability of life-saving products. With support from the Committee, WHO had commissioned an independent review of the animal-based methods described in its recommendations, guidelines and guidance documents on biological products. The Committee recommended establishing a working group to build on the report's findings, including through the development of WHO guidance in this area.

15. The Committee advised on priorities for new and revised WHO written standards for biological products. It requested WHO to explore ways in which the process by which written standards were prioritized for development could be more widely communicated in order to increase transparency and ensure the early involvement of stakeholders.

## Significance for public health policies

16. The WHO Guidelines on regulatory preparedness for the oversight of pandemic or other emergency use vaccines in importing countries provide up-to-date guidance to national regulatory authorities on strategies that could shorten the time between the emergence of a pathogen with pandemic potential and the availability of safe and effective vaccines.

17. The recommendation for a working group to build on the findings of the review on minimizing the use of animals in research provides an opportunity for WHO to update its guidance in this fast-moving field, and strengthen its advice on the quality control and lot release testing of biological products.

18. Timely availability of measurement standards remains crucial for harnessing the benefits of scientific advances in the production and evaluation of vital biological products. The 11 new or replacement WHO measurement standards will facilitate the more equitable availability of such products.

## Implications for the Organization's programmes

19. The Committee's advice on WHO priorities for the development of new and revised WHO written standards is important for ensuring that WHO guidance on the development, manufacture and regulation of biological products remains relevant and up to date.

20. The development, establishment and promotion of globally required biological measurement standards remain core normative activities of WHO. The decision to recommend the establishment of 11 new or replacement WHO measurement standards and endorsement of the future development of seven new or replacement WHO measurement standards will support WHO programmes addressing existing and emerging global health priorities.

21. The recommendations of the Committee have implications for the regulation and quality control of biological products and are thus relevant to stakeholders that rely on vaccines, biotherapeutics, blood products, cell, tissue and gene therapy products, in vitro diagnostics and other biological products.

# DRUG DEPENDENCE

## Forty-sixth report of the Expert Committee on Drug Dependence, Geneva, 16–19 October 2023[1]

22. WHO is mandated by *The International Drug Control Conventions* to evaluate the scientific evidence related to dependence, abuse and harm to health of psychoactive substances and their therapeutic use and make recommendations on whether psychoactive substances should be placed under international control. These recommendations are made through the Expert Committee on Drug Dependence and are the result of rigorous, evidence-driven procedures.

## Main recommendations

23. The Committee convened its forty-sixth meeting to consider whether six novel synthetic psychoactive substances present significant harms to public health that would warrant their placement under international control.

24. The Committee recommended that one novel synthetic psychoactive substance be placed under international control under the Single Convention on Narcotic Drugs of 1961: butonitazene. This synthetic opioid does not have any recognized therapeutic use and is likely to cause substantial harm.

25. The Committee further recommended that four novel synthetic psychoactive substances be placed under international control under the Convention on Psychotropic Substances of 1971. These substances comprised the cathinone and/or stimulants 3-CMC and dipentylone, the dissociative-type substance 2-fluorodeschloroketamine and the benzodiazepine bromazolam. An additional benzodiazepine, flubromazepam, was recommended for continued monitoring and surveillance by WHO. The Committee also carried out preliminary assessments of the medicines nitrous oxide and carisoprodol. It recommended that carisoprodol be subject to a future critical review and that nitrous oxide be placed under surveillance by WHO to facilitate continued monitoring and data reporting by countries regarding the harms pertaining to its non-medical use.

[1] WHO Technical Report Series, No. 1057 (in press).

26. The Committee's recommendations were considered for a vote and accepted by the 67th session of the United Nations Commission on Narcotic Drugs in March 2024.

## Significance for public health policies

27. The new psychoactive substances recommended for international control have no therapeutic use and contributed to substantial numbers of deaths by overdose, in addition to other significant harms to public health. The placement under international control will restrict their availability and support Member States to control these substances.

28. WHO's mandate ensures that a science-driven methodology informs the international control of psychoactive substances. WHO's mandate within *The International Drug Control Conventions* ensures that psychoactive substances that cause harms to public health are appropriately regulated, and that excessive drug control measures are not placed on substances that have recognized therapeutic use.

## Implications for the Organization's programmes

29. Novel synthetic drugs are falsely sold as medicines, and may pose threats to health. WHO's work to address substandard and falsified medical products, including the WHO Global Surveillance and Monitoring System for substandard and falsified medical products, should facilitate detection of these dangerous substances.

30. To ensure that essential medicines under international control due to their psychoactive properties are available for legitimate use, the secretariat of the Committee works with the Expert Committee on the Selection and Use of Essential Medicines, which is responsible for the WHO Model List of Essential Medicines. This is to ensure that for controlled medicines, information is shared on their appropriate use, including the management of pain and palliative care.

31. The secretariat of the Committee works with technical departments across WHO to promote appropriate universal health coverage policies for controlled medicines.

32. The Committee's recommendations raise awareness of public health risks of psychoactive substances and promote the use of guidelines for access to and safe use of controlled medicines at country level, including those for pain and palliative care, neurological and mental health diseases and the prevention and treatment of drug use disorders.

## EVALUATION OF CERTAIN FOOD ADDITIVES

### Ninety-seventh report of the Joint FAO/WHO Expert Committee on Food Additives, Rome, 31 October–9 November 2023[1]

### Main recommendations

33. The report contains the Joint FAO/WHO Expert Committee on Food Additives' evaluations of technical, toxicological and epidemiological data, including the occurrence of and dietary exposure to the food additive titanium dioxide.

34. The Committee assessed dietary exposure to three groups of flavouring agents: four aliphatic primary alcohols, aldehydes, carboxylic acids, acetals and esters containing additional oxygenated functional groups; nine linear and branched-chain aliphatic, unsaturated and unconjugated alcohols, aldehydes, acids and related esters; and eight saturated aliphatic acyclic linear primary alcohols, aldehydes and acids.

35. The assessments, recommendations and comments by the Committee will be discussed by the Codex Committee on Food Additives to generate recommendations to national authorities on risk-management and risk-mitigation measures to reduce human exposure.

36. WHO will publish detailed monographs in the WHO Food Additives Series with the toxicological and other related information on which the safety assessments of the compounds were based.[2] FAO publishes summaries of the identity and purity of food additives.

### Significance for public health policies

37. The Committee identifies and, where possible, quantifies the public health significance of exposure to chemicals in food – in these cases, food additives including flavouring agents – through scientific risk assessment based on international consensus. When a health concern is identified, recommendations are issued for action by national governments or through the Joint FAO/WHO Food Standards Programme.

38. The Committee's recommendations are used by the Codex Alimentarius Commission in the development of international food safety standards and other guidance. Such standards are science based and are established only for substances evaluated by the Committee. This promotes compliance with strict safety standards and ensures fair practices in international food trade.

39. The Committee's advice is also considered by Member States directly.

40. The Committee's work, in its complexity and in reaching an international scientific consensus on the evaluation of these compounds, contributes unique value to global decisions related to food safety.

[1] WHO Technical Report Series, No. 1051 (in press).

[2] Safety evaluation of certain food additives. WHO Food Additives Series, No. 88. Toxicological monographs of the ninety-seventh meeting (in preparation).

## Implications for the Organization's programmes

41. Five meetings of the Committee on food additives were held in the biennium 2022–2023.[1] Three focused on evaluating the safety of food additives, one on contaminants in food and one on residues of veterinary drugs in food.

42. WHO is a partner in the Joint FAO/WHO Food Standards Programme, whose principal organ is the Codex Alimentarius Commission. By assuring the sound scientific basis for international standards and recommendations on food additives, contaminants in food and veterinary drug residues in food, the Committee is crucial to the work of the Codex Alimentarius Commission.

43. The Committee's evaluations are also used by WHO offices when advising Member States on food safety issues.

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[1] For more information, see https://www.who.int/groups/joint-fao-who-expert-committee-on-food-additives-(jecfa) (accessed 12 February 2024).