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Reports on meetings of expert committees and study groups[1]

Report by the Director-General

DRUG DEPENDENCE

Forty-third report of the Expert Committee on Drug Dependence, virtual meeting,[2] 12–16 October 2020[3]

1. 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

2. The Committee convened at its forty-third meeting from 12 to 16 October 2020 to consider whether 11 new psychoactive substances present significant harms to public health that would warrant their placement under international control.

3. The Committee recommended that eight new psychoactive substances be placed under international control. The substance include isotonitazene, a powerful synthetic opioid that has recently emerged on the illicit drug market that has been associated with a high number of opioid overdose deaths. The Committee also recommended that three synthetic benzodiazepine drugs, clonazolam, flubromazolam and diclazepam, be placed under international control as psychotropic substances. These three benzodiazepines are sometimes sold as falsified benzodiazepines and have been associated with deaths; they have also sometimes been used in drug-facilitated sexual assault cases. These substances do not have any recognized therapeutic uses.

[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. 1034 (in press).

4. The Committee further recommended that three new psychoactive substances be placed under WHO surveillance to facilitate continued monitoring and data reporting by countries regarding the harms pertaining to their use.

5. The Committee's recommendations were communicated to the United Nations Secretary-General by the Director-General and considered by the 64th session of the United Nations Commission on Narcotic Drugs in April 2021. The Commission voted to accept all recommendations made by WHO.

Significance for public health policies

6. The Committee's recommendations ensure that psychoactive substances are available for medical and scientific purposes, while preventing them from being diverted and causing harm to health. The Committee's recommendations to place psychoactive substances under international control or to change their level of control mean that countries should enforce restrictions on import, export and possession of these controlled substances.

7. New psychoactive substances, such as the synthetic drugs considered for review by the Committee, have no therapeutic use and have contributed to substantial numbers of deaths by overdose, in addition to other significant harms to public health. The Committee's recommendations would place these substances under international control to restrict their use, and Member States would implement national control for these substances to prevent their misuse and abuse and to protect public health.

Implications for the Organization's programmes

8. Novel synthetic benzodiazepine drugs, such as those reviewed by the Committee, are falsely sold as medicines and may have fatal effects. WHO's work in this area, including the WHO Global Surveillance and Monitoring System for substandard and falsified medical products, should facilitate detection of these dangerous substances and falsified medicines.

9. To ensure that essential medicines placed under international control, such as opioids, are available for legitimate use where they are needed, the Secretariat of the Committee works closely 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 information is shared on the appropriate use of controlled medicines for various conditions, including the management of pain and palliative care.

10. The Secretariat of the Committee also works closely with technical departments across the Secretariat towards the promotion of universal health coverage policies and to ensure that health is central in addressing the world drug problem.

11. The recommendations of the Committee present broad implications for partnership work within WHO regional and country offices. These include raising awareness of public health risks of psychoactive substances, and promoting the use of guidelines for improving access to and safe use of controlled medicines and those for the prevention and treatment of drug disorders at country level.

SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Fifty-fifth report of the Expert Committee on Specifications for Pharmaceutical Preparations, virtual meeting,[1] 12–19 October 2020[2]

12. The Expert Committee on Specifications for Pharmaceutical Preparations advises the Director-General in the area of medicines' quality assurance and provides regulatory tools for medical products. Its advice is developed through a broad consensus-building process based on worldwide public consultation, following an established process, and covers all areas of quality assurance of medicines throughout their life cycle and across supply chains from development to distribution to patients.

Main recommendations

13. The Committee adopted 10 guidelines and 17 pharmacopoeial texts for inclusion in *The International Pharmacopoeia* and confirmed the release of two International Chemical Reference Substances established by the custodian centre.

14. The following guidelines and guidance texts were adopted:

(a) Points to consider when including Health-Based Exposure Limits (HBELs) in cleaning validation;

(b) Good manufacturing practices: water for pharmaceutical use;

(c) Guideline on data integrity;

(d) World Health Organization/United Nations Population Fund recommendations for condom storage and shipping temperatures;

(e) World Health Organization/United Nations Population Fund guidance on testing of male latex condoms;

(f) World Health Organization/United Nations Population Fund guidance on conducting post-market surveillance of condoms;

(g) WHO "Biowaiver List": proposal to waive in vivo bioequivalence requirements for *WHO Model List of Essential Medicines* immediate-release, solid oral dosage forms;

(h) Guidelines on the implementation of the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce;

(i) Good reliance practices in the regulation of medical products: high-level principles and considerations; and

(j) Good regulatory practices in the regulation of medical products.

[1] Coordinated from WHO headquarters, Geneva.

[2] WHO Technical Report Series, No. 1033, 2021.

15. It was recommended to continue the External Quality Assurance Assessment Scheme to build the capacity of quality-control laboratories and to ensure speedy implementation by the Secretariat of the revised WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce with the active participation of Member States.

16. A number of recommendations were made by the Committee on norms and standards for pharmaceuticals to be presented at the fifty-sixth meeting of the Expert Committee, on: collaboration with partners and international organizations; ongoing activities, such as the organization of the international meeting of world pharmacopoeias and developing specifications for medicines for inclusion in *The International Pharmacopoeia*; the WHO Biowaiver Project; good manufacturing practices for investigational pharmaceutical products; and activities enhancing the implementation of guidance texts.

Significance for public health policies

17. At a time when access to essential medicines is a pressing issue on the sustainable development agenda, the Committee's standard-setting work makes a unique and critical contribution towards more equitable access to much-needed medicines of assured quality.

18. The Committee's technical guidance on medicines' quality is designed to serve regulatory authorities of all Member States, as well as organizations in the United Nations system and other major international bodies. Much of the Committee's work is aimed at increasing convergence in the areas of quality assurance and regulatory guidance in order to facilitate synergies among and within the respective authorities and pharmacopoeias, and to reduce duplication of effort and, thus, costs.

19. The Committee recommends regulatory guidelines of importance to multisource medicines designed to be used globally, be it in hot and humid climates, small or large countries, or well- or less-developed settings. The outcome is intended to protect patients and facilitate access to high-quality medicines as a response to the new global agenda, articulated in the 2030 Agenda for Sustainable Development, prioritizing inter alia universal health coverage. This Committee actively contributes to bringing about access to good quality essential medicines and health products for all.

Implications for the Organization's programmes

20. The first meeting of this Committee was convened in 1947 and its recommendations continue to be relevant for all those in WHO dealing with medicines, from country and regional offices to other expert committees and partnerships. As its decisions affect the quality of widely used medicines, the Committee serves not only WHO Member States but also many programmes within WHO and other international organizations.

21. The Committee especially serves the WHO Prequalification Unit – Medicines and Regulatory Systems Strengthening teams, as well as the disease-specific programmes. In return, practical feedback, for example on pressing needs for new texts and updates, is provided directly to the Committee by those who implement the comprehensive set of currently more than 130 guidelines, 600 specifications and 250 International Chemical Reference Substances.

22. The Committee's work provides international norms and standards – developed through a global consultation process – for medicines' quality assurance and regulatory tools. They are globally applicable, help to ensure that good quality medicines reach patients and are of relevance for all involved with medicines within WHO.

EVALUATION OF CERTAIN CONTAMINANTS IN FOOD

Ninetieth report of the Joint FAO/WHO Expert Committee on Food Additives, virtual meeting,[1] 26 October–6 November 2020[2,3]

23. The report contains the Expert Committee's evaluations of 18 substances that may occur as previous cargoes and the trichothecenes T-2 and HT-2. The tasks before the Committee were: to elaborate principles governing the evaluation of the acceptability of previous cargoes in order to undertake toxicological evaluations and dietary exposure assessments in relation to contaminants in food.

Main recommendations

24. The Committee concluded that 16 of the 18 assessed substances that may occur as previous cargoes meet the criteria for acceptability as previous cargoes.

25. It became apparent during the meeting that the time limitations precluded the toxicological evaluation of the trichothecenes T-2 and HT-2. The toxicological evaluation and overall risk assessment will therefore be considered at a future meeting.

26. The assessments, recommendations and comments by the Committee will be discussed by the Codex Committee on Fats and Oils and the Codex Committee on Contaminants in Food in order to provide recommendations to national authorities on health concerns regarding the previous cargoes and contaminants, and to identify and recommend appropriate risk management and risk-mitigation measures to reduce human exposure, where necessary.

27. WHO will publish detailed monographs in the WHO Food Additives Series with the toxicological and other related information upon which the safety assessments of the compounds were based.[4] FAO publishes summaries of the identity and purity of previous cargoes and contaminants.

Significance for public health policies

28. The Committee identifies and, where possible, quantifies the public health significance of exposure to chemicals in food – in these cases, contaminants in food – through scientific risk assessment based on international consensus. When a health concern is identified, clear recommendations are issued for action by national governments or through the Joint FAO/WHO Food Standards Programme (the Codex Alimentarius Commission and its subsidiary bodies).

29. The Committee's recommendations are used by the Codex Alimentarius Commission in the development of international food safety standards and other guidance and recommendations. Such standards are science-based and are established only for substances that have been evaluated by the Committee. This ensures that food commodities that are traded internationally meet strict safety standards to protect the health of the consumer and ensure fair practices in food trade.

[1] Coordinated from WHO headquarters, Geneva.

[2] With an additional day for approval of the report on 24 November 2020.

[3] WHO Technical Report Series, No. 1032 (in press).

[4] Safety evaluation of certain contaminants in food. WHO Food Additives Series, No. 81. Toxicological monographs of the ninetieth meeting (in preparation).

30. The advice provided by the Committee is also considered by Member States directly when national or regional food safety standards are being established.

31. The Committee's work, in its complexity and in reaching an international scientific consensus on the evaluation of these compounds, is unique in its importance for and impact on global public health decisions related to food safety.

Implications for the Organization's programmes

32. The evaluation of chemicals in food by the Committee is an ongoing activity. Two meetings of the Committee on food additives and one on contaminants in food were held in the biennium 2019–2020.[1] One more meeting on food additives and another one on contaminants in food are planned for 2021.

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

34. The Committee's evaluations are also used by Heads of WHO offices in countries, territories and areas and by regional offices when advice is provided to Member States on food safety issues.

BIOLOGICAL STANDARDIZATION

Seventy-second and seventy-third reports of the Expert Committee on Biological Standardization, virtual meetings,[2] 19–23 October 2020 and 9–10 December 2020[3]

35. The Expert Committee on Biological Standardization reviews developments in the field of biological products used in human medicine. Such products include vaccines, biotherapeutics, cellular and gene therapies, blood products and in vitro diagnostics. The Committee coordinates activities leading to: the adoption of WHO recommendations, guidelines and other guidance documents (written standards) on ensuring the quality, safety and efficacy of such products; and the establishment of WHO international reference standards (measurement standards).

36. The adoption and publication of WHO written standards and the establishment and use of WHO measurement standards to designate the activity of biological products used for the diagnosis, prevention or treatment of disease allows for the comparison of non-clinical and clinical data worldwide. Ensuring the comparable quality, safety and efficacy of biological products is a critical step in promoting their equitable global availability.

37. Following its full annual meeting in October 2020, the Committee also held an exceptional meeting in December in order to focus on a number of urgent biological standardization issues relating to the coronavirus disease (COVID-19) pandemic.

[1] For more information, see https://www.who.int/foodsafety/areas_work/chemical-risks/jecfa/en/ (accessed 23 April 2021).

[2] Coordinated from WHO headquarters, Geneva.

[3] WHO Technical Report Series, No. 1030 (in press).

Main recommendations

38. On the basis of the results of international collaborative laboratory studies, the Committee recommended the establishment of 16 new WHO measurement standards and three replacement WHO measurement standards. In addition, the Committee endorsed 14 proposals to develop new or replacement WHO measurement standards.

39. The Committee also recommended the adoption of three WHO written standards:

(a) Recommendations to assure the quality, safety and efficacy of typhoid conjugate vaccines;

(b) Recommendations to assure the quality, safety and efficacy of enterovirus 71 vaccines (inactivated); and

(c) Collaborative procedure between the World Health Organization and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified in vitro diagnostics.

40. The Committee also highlighted the urgent need for comprehensive WHO guidance on the development and clinical evaluation of monoclonal antibody products for use against infectious diseases, including COVID-19. Numerous such products for treating and preventing infectious diseases are now in development due to their short development time, rapid clinical effect and established safety profile. The Committee expressed its support for a proposal to develop a WHO guidance document broadly applicable to all monoclonal antibodies intended for use against infectious diseases, with disease-specific supplements to be drafted as required.

41. The Committee indicated its support for a review of the current scientific evidence and experience gained in the regulatory evaluation of similar biotherapeutic products to inform the updating and revision of the 2009 WHO Guidelines on evaluation of similar biotherapeutic products. It is anticipated that the increasing availability of such products worldwide will improve access to these medicines by increasing competition and bringing down prices. The Committee also supported a related proposal to systematically review and update all WHO written standards on this subject published since 2009 given the significant advances made in this field over the past decade.

42. Following discussion of recent developments in the production and quality control of oral poliomyelitis vaccines, the Committee expressed its support for the extensive revision of the 2012 WHO Recommendations to assure the quality, safety and efficacy of poliomyelitis vaccines (oral, live, attenuated).

43. Following the identification of a number of issues and new developments in the way in which yellow fever vaccines were currently manufactured and evaluated, the Committee agreed that there was now a need to amend the 2010 WHO Recommendations to assure the quality, safety and efficacy of live attenuated yellow fever vaccines.

44. The Committee noted that updated guidance was now required on the temporary deferral of blood donors following vaccination against COVID-19 and expressed its support for the updating of the 2020 WHO interim guidance on maintaining a safe and adequate blood supply during the COVID-19 pandemic and on the collection of convalescent plasma. The updated guidance should take into account the latest scientific evidence on the clinical use of convalescent plasma to treat COVID-19.

Significance for public health policies

45. Typhoid fever continues to be endemic in many low- and middle-income countries, particularly where access to safe water and basic sanitation is limited. The WHO Recommendations to assure the quality, safety and efficacy of typhoid conjugate vaccines will significantly support the manufacture, quality control and regulatory evaluation of such vaccines.

46. Enterovirus 71 is associated with hand, foot and mouth disease throughout the world and has caused epidemics in Asia, Europe and North America. Manifestations of the disease range from asymptomatic infection to severe central nervous system complications and cardiopulmonary failure. In severe cases mortality rates can be high, especially in children. The WHO Recommendations to assure the quality, safety and efficacy of enterovirus 71 vaccines (inactivated) will provide recommendations to regulators, vaccine developers and manufacturers on the manufacture, quality control and regulatory evaluation of such vaccines.

47. The assessment of applications for the approval and registration of in vitro diagnostics by national regulatory authorities is an essential step in ensuring their quality, safety and performance before they come to market. The collaborative procedure between WHO and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified in vitro diagnostics provides a pragmatic approach for accelerating the national assessment and registration of WHO-prequalified in vitro diagnostics by taking into consideration the WHO prequalification dossier assessment, performance evaluation and manufacturing site inspection reports. The procedure will benefit all parties by accelerating registration timelines thus helping to ensure the broader and timely availability of in vitro diagnostics.

48. The establishment of two WHO measurement standards for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies will support the serological surveillance of COVID-19 cases and will strengthen current efforts to develop and evaluate candidate COVID-19 vaccines. These same standards will also allow for standardization of SARS-CoV-2 neutralizing antibody titres in COVID-19 convalescent plasma thus facilitating consistent treatment and more rigorous assessment of this potential therapeutic approach. In addition, the availability of the newly established WHO measurement standard for SARS-CoV-2 RNA will result in greater comparability and harmonization of global SARS-CoV-2 RNA diagnostic assays.

Implications for the Organization's programmes

49. The development and provision of global measurement standards is a core normative WHO activity and their timely availability is crucial in harnessing the benefits of scientific advances in the production and evaluation of biological products. The 19 WHO measurement standards recommended by the Committee for establishment represent the continuation of this core activity across a broad range of priority global public health issues.

50. The Committee also endorsed a total of 13 proposals to develop new or replacement WHO measurement standards. The scheduled establishment of these international reference standards will ensure that existing standards are replaced in a timely manner and new standards developed in response to emerging priorities.

51. The establishment of the above-mentioned WHO measurement standards for SARS-CoV-2 antibodies and SARS-CoV-2 RNA will have immediate implications for a wide range of WHO collaborative surveillance, diagnostic, and therapeutic and vaccine development efforts now under way in response to the COVID-19 pandemic.

52. The support of the Committee for the above-mentioned development or revision of WHO written standards on the evaluation of monoclonal antibodies used in the prevention or treatment of infectious diseases and on the regulatory evaluation of similar biotherapeutic products will result in strengthened and up-to-date WHO guidance in both of these increasingly important areas. In addition, support was expressed for the development of WHO guidance on the regulatory evaluation of messenger RNA vaccines to address the current lack of WHO guidance in this emerging field.

53. The establishment of the first WHO measurement standards for use in high-throughput sequencing technologies reflects the continuing rapid evolution of these and other highly sophisticated assay technologies. It is likely that the need to evaluate measurement standards for these advanced technologies, and for other advanced technologies such as cellular and gene therapies, will increasingly have an impact on the work of this Committee and thus of WHO.

ACTION BY THE EXECUTIVE BOARD

54. The Board is invited to note the report.

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