

## **Report on meetings of expert committees and study groups<sup>1</sup>**

### **Report by the Director-General**

#### **DRUG DEPENDENCE**

#### **Forty-fourth report of the Expert Committee on Drug Dependence, virtual meeting,<sup>2</sup> 11–15 October 2021<sup>3</sup>**

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 its forty-fourth meeting from 11 to 15 October 2021 to consider whether five new psychoactive substances present significant harms to public health that would warrant their placement under international control. The Committee also carried out preliminary assessments of the psychoactive plant kratom and its main psychoactive components mitragynine and 7-hydroxymitragynine, and the medicine phenibut.

3. The Committee recommended that three new psychoactive substances be placed under international control. The synthetic opioids buprenorphine and metonitazene should be placed under international control as narcotic drugs and the synthetic cathinone eutylone should be placed under international control as a psychotropic substance. These substances do not have any recognized therapeutic uses and deaths associated with the use of these substances have been reported.

4. The Committee further recommended that four psychoactive substances be placed under WHO surveillance to facilitate continued monitoring and data reporting by countries regarding the harms pertaining to their use. They include kratom, which has as its main psychoactive components mitragynine and 7-hydroxymitragynine, and phenibut.

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<sup>1</sup> 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.

<sup>2</sup> Coordinated from WHO headquarters, Geneva.

<sup>3</sup> WHO Technical Report Series, No. 1038.

5. The Committee's recommendations were considered for a vote by the 65th session of the United Nations Commission on Narcotic Drugs in March 2022. The Commission voted to accept all recommendations made by the Committee, thereby placing three harmful substances under international control.

### **Significance for public health policies**

6. The new psychoactive substances assessed 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 effectively place three of these substances under international control to restrict their use, and Member States will implement national control for these substances to prevent their misuse and abuse and to protect public health.

7. The Committee recommended continued surveillance of the plant kratom, which is used in traditional medicine, as well as its main psychoactive components mitragynine and 7-hydroxymitragynine. The Committee also recommended continued surveillance of phenibut, which is licensed as a medicine in some countries. Continued surveillance will facilitate data collection on the abuse and dependence potential of these substances with recognized therapeutic use.

### **Implications for the Organization's programmes**

8. Novel synthetic opioid drugs, such as those reviewed by the Committee, are falsely sold as medicines, 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 under international control, such as many 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 for controlled medicines, information is shared on their appropriate use 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 WHO Secretariat towards the promotion of universal health coverage policies for controlled medicines 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 at country level, including those for pain and palliative care and for the prevention and treatment of drug use disorders

## BIOLOGICAL STANDARDIZATION

### **Seventy-fourth report of the Expert Committee on Biological Standardization, virtual meeting,<sup>1</sup> 18–22 October 2021<sup>2</sup>**

12. The Expert Committee on Biological Standardization reviews developments in the field of biological products used in human medicine. Such products include vaccines, biotherapeutics, blood products, cell and gene therapy 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).

13. The adoption and publication of WHO written standards and the establishment and use of WHO measurement standards designating the activity of biological products used for the diagnosis, prevention or treatment of disease allow for the comparison of nonclinical and clinical data worldwide. Ensuring the comparable quality, safety and efficacy of biological products is a vital step in facilitating their equitable global availability and thus contributes towards the attainment of the key strategic WHO goal of universal health coverage.

14. During the meeting, the Committee focused on a broad range of recent WHO activities, including a number of urgent biological standardization activities relating to the coronavirus disease (COVID-19) pandemic.

#### **Main recommendations**

15. Following careful consideration of the results of international collaborative laboratory studies, the Committee recommended the establishment of five new WHO measurement standards and four replacement WHO measurement standards. In addition, the Committee endorsed 10 proposals to develop new or replacement WHO measurement standards.

16. The Committee also recommended the adoption of two WHO written standards:

- (a) Amendment to the WHO Recommendations to assure the quality, safety and efficacy of live attenuated yellow fever vaccines; and
- (b) Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations.

17. The Committee was updated on recent developments in relation to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). After being informed that unprecedented demand for the recently established First WHO International Standard for anti-SARS-CoV-2 immunoglobulin had resulted in its rapid depletion, the Committee endorsed a proposal to urgently develop a replacement standard. The Committee also endorsed a proposal to develop a First WHO International Reference Panel for antibodies to SARS-CoV-2 variants of concern that could be expanded should new variants emerge.

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<sup>1</sup> Coordinated from WHO headquarters, Geneva.

<sup>2</sup> WHO Technical Report Series, No. 1039.

18. The Committee agreed that there is currently little evidence to support the use of COVID-19 convalescent plasma in the treatment of moderate to severe COVID-19, with uncertainty also existing regarding its potential utility in treating mild or asymptomatic COVID-19 cases. In the light of the conclusions of a recently published Cochrane living systematic review on convalescent plasma or hyperimmune immunoglobulin for people with COVID-19, the Committee further concurred that this was a developing field with many studies still continuing and that firm conclusions on the efficacy of this approach in different patient subgroups had yet to be reached.

19. The Committee expressed its support for a number of recent WHO initiatives in the area of blood products and related substances, including the newly established WHO Advisory Group on Blood Regulation, Availability and Safety. This advisory group will provide a suitable diversity of expertise and experience from all six WHO regions to support the delivery of the WHO Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023.

20. The Committee welcomed the development of a WHO document setting out a regulatory framework for cell, tissue and gene therapy products, and urged WHO senior management to consider expanding the expertise of the Committee and the WHO Secretariat to provide the specialist knowledge needed to address the formidable regulatory and other challenges associated with this complex class of biological product.

21. The Committee recognized the essential work undertaken by the National Institute for Biological Standards and Control of the United Kingdom of Great Britain and Northern Ireland. The Institute is the foremost WHO collaborating centre in the development of WHO international reference materials for biological products and its activities are pivotal not only to the work of the Committee but also to the advancement of regulatory science worldwide. The contribution made by the Institute in improving access to vital medicines in some of the poorest countries in the world is important for achieving many of internationally agreed goals and targets including the Sustainable Development Goals. The Committee called for the WHO Secretariat to advocate for the adequate resourcing of the Institute to enable it to continue this essential work.

### **Significance for public health policies**

22. Yellow fever is a viral haemorrhagic fever endemic to countries in Africa, and Central and South America. Safe and highly effective live attenuated yellow fever vaccines derived from virus strain 17D have been in use since the late 1930s. However, rare serious adverse reactions associated with their use include neurological and viscerotropic disease. It is therefore crucially important to assess the levels of neurotropism and viscerotropism exhibited by new vaccine batches compared with those exhibited by vaccines shown to be clinically safe. The Amendment to the 2010 WHO Recommendations to assure the quality, safety and efficacy of live attenuated yellow fever vaccines adopted on the recommendation of the Committee will clarify and harmonize the testing procedures to be used.

23. Recent advances in the manufacture of messenger RNA (mRNA) have established the approach as an important vaccine technology and the speed with which candidate mRNA vaccines can be developed makes them eminently suitable for use during public health emergencies. The unprecedented pace of development and evaluation of candidate COVID-19 mRNA vaccines has highlighted an urgent need for WHO guidance in this area. The WHO regulatory considerations document on evaluating the quality, safety and efficacy of mRNA vaccines for the prevention of infectious diseases adopted on the recommendation of the Committee sets out the principles underlying the evaluation and licensing of such vaccines.

24. The proposed replacement of the rapidly depleted First WHO International Standard for anti-SARS-CoV-2 immunoglobulin will ensure continuity in the serological surveillance of COVID-19 cases and in efforts to develop and evaluate candidate COVID-19 vaccines. This same standard also allows for standardization of SARS-CoV-2 neutralizing antibody titres in COVID-19 convalescent plasma thus facilitating assessment of this potential therapeutic approach. In addition, the availability of the proposed First WHO International Reference Panel for antibodies to SARS-CoV-2 variants of concern will facilitate the development and harmonization of serological assays used for the prompt detection of such variants and for the development of appropriately updated vaccines and therapeutic strategies.

25. The estimated number of people worldwide with anaemia and/or micronutrient deficiency represents approximately a third of the global population. Among the recent WHO initiatives in the area of blood products and related substances commended by the Committee was the development of a WHO policy brief on the implementation of patient blood management to optimize the clinical practice of transfusion, and the proposed development of WHO guidelines to support the implementation of the optimized practice in countries.

26. The development of the WHO document on a regulatory framework for cell, tissue and gene therapy products is expected to facilitate regulatory convergence and stimulate dialogue between countries on appropriate measures to improve worldwide access to this class of product.

### **Implications for the Organization's programmes**

27. The development, establishment and promotion 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 nine 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.

28. The development of the 10 new or replacement WHO measurement standards endorsed by the Committee will ensure that much needed standards will be available to respond to the emerging priorities of WHO, and that existing WHO international reference standards will be replaced in a timely manner.

29. The efforts under way to support the regulatory evaluation of cell, tissue and gene therapy products, and thus promote their broader and more equitable availability, reflect the inevitable proliferation of these complex and challenging products. It is anticipated that developments in this field will increasingly have an impact on the work of the Committee and thus of WHO, and additional specialized expertise will be required to provide WHO with fully informed guidance

### **ACTION BY THE EXECUTIVE BOARD**

30. The Board is invited to note the report.

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