

Report on meetings of expert committees and study groups¹

Report by the Director-General

EVALUATION OF CERTAIN FOOD ADDITIVES

Eighty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives, virtual meeting,² 1–12 June 2020³

Main recommendations

1. The report contains the Expert Committee's evaluations of technical, toxicological, epidemiological, occurrence and dietary exposure data for six food additives (adenosine 5'-monophosphate deaminase from *Streptomyces murinus*, D-allulose 3-epimerase from *Arthrobacter globiformis* expressed in *Escherichia coli*, carbohydrate-derived fulvic acid, jagua (genipin-glycine) blue (Jagua blue), lipase from *Mucor javanicus* and phosphatidylinositol-specific phospholipase C expressed in *Pseudomonas fluorescens*). The Committee also assessed the dietary exposure for one group of food additives (sucrose esters of fatty acids and sucrose oligoesters).
2. The Committee evaluated the safety of two groups of flavouring agents and revised the specifications for 12 flavouring agents. Tentative specifications were prepared for three, as the safety evaluations for these flavouring agents had not been completed.
3. Specifications for the following food additives were revised: magnesium stearate, polyvinyl alcohol and sorbitan esters of fatty acids.
4. The assessments, recommendations and comments by the Committee will be discussed by the Codex Committee on Food Additives in order to generate recommendations to national authorities on the safe use of these food additives and to identify and recommend appropriate risk management and risk-mitigation measures to reduce human exposure, where necessary.

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. 1027 (in press).

5. 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.¹ FAO publishes summaries of the identity and purity of food additives.

Significance for public health policies

6. 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, 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).

7. 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.

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

9. 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

10. The evaluation of chemicals in food by the Committee is an ongoing activity. Two meetings on food additives of the Committee were held in the biennium 2018–2019.² One more meeting besides the eighty-ninth meeting is planned for the biennium 2020–2021.

11. 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.

12. 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.

¹ Safety evaluation of certain food additives. WHO Food Additives Series, No. 80. Toxicological monographs of the eighty-seventh meeting (in preparation).

² For more information, see https://www.who.int/foodsafety/areas_work/chemical-risks/jecfa/en/ (accessed 5 October 2020).

BIOLOGICAL STANDARDIZATION

Seventy-first report of the Expert Committee on Biological Standardization, virtual meeting,¹ 24–28 August 2020²

13. The Expert Committee on Biological Standardization reviews developments in the field of biological products used in human medicine, which include vaccines, biotherapeutics, blood products and related substances, and in vitro diagnostic reagents. It coordinates activities leading to: (a) the adoption of WHO guidelines and recommendations for ensuring the quality, safety and efficacy of such substances; and (b) the establishment of WHO international standards and other reference materials.³

14. The use of international reference materials for designating the activity of biological products used in prophylaxis or therapy, or for ensuring the reliability of quality control or diagnostic procedures, allows for the comparison of data worldwide.

15. This exceptional meeting was held in addition to the Committee's annual October meeting. The Committee focused on a number of urgent biological standardization issues relating to the coronavirus disease (COVID-19) pandemic.

Main recommendations

16. On the basis of the results of international collaborative laboratory studies, the Committee recommended the establishment of two new WHO international reference standards and one replacement WHO international reference standard. In addition, the Committee endorsed four proposals for future new or replacement reference standards, two of which were of direct relevance to the COVID-19 pandemic.

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

- Guidelines on the quality, safety and efficacy of plasmid DNA vaccines (replacement of Annex 1 of WHO Technical Report Series, No. 941); and
- Amendment to Annex 4 of WHO Technical Report Series, No. 1016, Guidelines for the safe production and quality control of poliomyelitis vaccines.

18. It is clear that additional written and measurement standards specific to COVID-19 are required. Notably, messenger RNA (mRNA) vaccines were among the first candidate vaccines to enter clinical development during the pandemic, prompting requests for regulatory guidance. Because of significant differences in the way mRNA vaccines are produced and evaluated, the Committee considered it inappropriate to incorporate such guidance into the above-mentioned WHO plasmid DNA vaccines guidelines recommended for adoption at the meeting. The Committee instead recommended that a separate document on regulatory considerations for the evaluation of mRNA vaccines should be developed, which could be updated as more scientific and clinical data become available. The

¹ Coordinated from WHO headquarters, Geneva.

² WHO Technical Report Series, No. 1028 (in press).

³ An up-to-date list of WHO international reference preparations is available at <http://www.who.int/bloodproducts/catalogue/en/> (accessed 7 October 2020).

Committee further proposed that an appendix should be included in the document to cover issues specific to mRNA vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Significance for public health policies

19. Vaccines based on the direct administration of plasmid DNA encoding an immunogen (known as plasmid DNA vaccines or DNA vaccines) are at an advanced stage of clinical development. Given the potential of this technology for rapidly responding to the emergence of priority pathogens during public health emergencies and the pressing need for candidate vaccines to address the current COVID-19 pandemic, the availability of an up-to-date WHO written standard to drive international regulatory convergence for such vaccines is a matter of urgency. The above-mentioned guidelines recommended by the Committee for adoption set out the guiding principles for ensuring the quality, safety and efficacy of plasmid DNA vaccines for human use.

20. At its meeting in 2018, the Committee recommended the adoption of the WHO Guidelines for the safe production and quality control of poliomyelitis vaccines. Following publication of these guidelines, poliomyelitis vaccine manufacturers requested that WHO consider allowing for the use of more flexible facility-specific risk-based approaches in a number of key areas. In consultation with the WHO Containment Advisory Group, the Committee subsequently recommended the amendment of the guidelines. Following detailed discussion of the interpretation and implications of the amended text for vaccine manufacturers, the proposed amendments were recommended for adoption by WHO. The amended sections of the guidelines will allow for facility-specific risk assessments, which will help to better balance the risk of reintroduction of poliovirus from a vaccine manufacturing facility into the community against the need to ensure a global poliomyelitis vaccine supply as a critical component of polio eradication.

21. The COVID-19 pandemic has had an adverse impact on the supply of blood and blood components in many countries. The Committee was updated on the latest WHO interim guidance on maintaining a safe and adequate blood supply during the pandemic, and on the safe collection of COVID-19 convalescent plasma. Evidence indicates that the treatment of patients with such plasma is a potentially effective therapy. It is essential that titres of neutralizing antibodies against SARS-CoV-2 are standardized to facilitate consistent treatment. It was the strongly held view of the Committee that SARS-CoV-2 antibody titres in COVID-19 convalescent plasma should be calibrated in International Units as soon as an appropriate WHO international standard is established (see below).

Implications for the Organization's programmes

22. The Committee was briefed on the impact of COVID-19 on WHO's work on vaccines and biological therapeutic medicines. WHO has set out the guiding principles for SARS-CoV-2 vaccine standardization on its website, explaining how current WHO written standards provide useful guidance and information on the development, production and evaluation of such vaccines, together with information on the availability of related measurement standards.

23. Following a review of the range of vaccine platforms currently being used to develop SARS-CoV-2 candidate vaccines, and of the challenges in ensuring their safety and efficacy, the Committee identified a need for both written and measurement standards to support the development and manufacturing of such vaccines. In particular, guidance was needed on the design, validation and standardized comparison of antibody assays. Guidance was also needed on the measurement and standardization of cellular immune responses, specifically with regard to safety issues. Furthermore,

there are currently no guidelines specifically on ensuring the quality, safety and efficacy of SARS-CoV-2 vaccines or more generally any vaccine based on an RNA platform.

24. Proposals for the development of two international standards for use in public health emergencies were also endorsed at the meeting – the First WHO International Standard for SARS-CoV-2 RNA for NAT-based assays¹ and the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin. The first is urgently needed to standardize diagnostic assays, which are essential both for clinical treatment and for containing outbreaks. The second is essential for: (a) the standardization of assays used to measure antibody responses elicited by vaccination; (b) diagnosing previous exposure to SARS-CoV-2; and (c) standardizing SARS-CoV-2 antibody content in COVID-19 convalescent plasma.

25. High-throughput sequencing technology is proving to be increasingly important for supplementing or replacing the currently recommended assays for detecting adventitious viruses in biological products. Two proposals were presented to the Committee for the development of reference standards for adventitious virus detection in biological products using high-throughput sequencing. These proposals demonstrate how the rapid evolution of highly sophisticated assay technologies is increasingly having an impact on the work of this Committee and thus of WHO.

TOBACCO PRODUCT REGULATION

Report of the tenth meeting of the WHO Study Group on Tobacco Product Regulation, virtual meeting,² 28 September–2 October 2020³

26. The WHO Study Group on Tobacco Product Regulation publishes a series of reports to provide a scientific basis for tobacco product regulation. This is a global public health good and is in line with resolutions WHA54.18 (2001), WHA53.17 (2000) and WHA53.8 (2000). In line with Articles 9 and 10 of the WHO Framework Convention on Tobacco Control,⁴ as well as the relevant decisions of the Conference of the Parties to the WHO Framework Convention on Tobacco Control^{5,6} and relevant WHO reports submitted to the Conference of the Parties,^{7,8} these reports of the Study Group identify evidence-based approaches to regulating nicotine and tobacco products, including new and emerging products such as electronic nicotine delivery systems, electronic non-nicotine delivery systems and heated tobacco products.

¹ NAT: nucleic acid amplification technique.

² Coordinated from WHO headquarters, Geneva.

³ WHO Technical Report Series, No. 1029 (in preparation).

⁴ For the text of the WHO Framework Convention on Tobacco Control, see <https://apps.who.int/iris/handle/10665/42811> (accessed 2 November 2020).

⁵ Decision FCTC/COP7(9) (2016) (https://www.who.int/fctc/cop/cop7/FCTC_COP7_9_EN.pdf, accessed 2 November 2020).

⁶ Decision FCTC/COP6(9) (2014) ([https://apps.who.int/gb/fctc/PDF/cop6/FCTC_COP6\(9\)-en.pdf](https://apps.who.int/gb/fctc/PDF/cop6/FCTC_COP6(9)-en.pdf), accessed 2 November 2020).

⁷ Document FCTC/COP/7/11 (2016) (https://www.who.int/fctc/cop/cop7/FCTC_COP_7_11_EN.pdf, accessed 2 November 2020).

⁸ Document FCTC/COP/6/10 Rev.1 (https://apps.who.int/gb/fctc/PDF/cop6/FCTC_COP6_10Rev1-en.pdf, accessed 2 November 2020).

27. The tenth meeting of the Study Group discussed nine background papers on the following areas: toxicants in heated tobacco products: exposure, health effects and examination of the claims of reduced risk; the attractiveness and addictive potential of heated tobacco products: effects on perception and use and associated effects; variability of heated tobacco products: considerations and implications; regulatory mapping of heated tobacco products, including country approaches, barriers to regulation and regulatory considerations; exploration of the methods available for the quantification of individual health risk and application of these methods to electronic nicotine delivery systems, evaluation of population health impact and implications for regulation; estimation of nicotine exposure from use of electronic nicotine delivery systems compared with that from conventional cigarettes; flavours in novel and emerging nicotine and tobacco products and traditional products; use of heated tobacco products: switching and dual and poly use of tobacco products; and global landscape of novel and emerging nicotine and tobacco products marketing, promotion and associated impacts. In addition, the Study Group discussed two horizon scanning papers on: nicotine forms in the tobacco plant, chemical modifications and implications for electronic nicotine delivery systems; and e-cigarette, or vaping, product use associated lung injury. The information from these papers will update knowledge and advance nicotine and tobacco product regulation in order to inform policy at global level.

28. The Study Group examined the requests made to WHO, via the Convention Secretariat, in decision FCTC/COP8/(22) on novel and emerging tobacco products by the Conference of the Parties at its eighth session in 2018.¹ This decision, as well as other emerging issues in tobacco product regulation, informed the development of the content of the background papers on heated tobacco products, specified in paragraph 27. Member States have requested technical support on these areas to inform national policy development. The WHO Secretariat for the Study Group, in consultation with members of the Study Group, invited subject-matter experts, who, in addition to contributing to discussions, provided the most up-to-date empirical data on nicotine and tobacco product regulation in their background papers. The report of the Study Group's tenth meeting (which will be the eighth report of the Study Group on the scientific basis of tobacco product regulation) will help to guide Member States in achieving the most effective and evidence-based means to bridge regulatory gaps in tobacco control and aid the development of coordinated regulatory frameworks for tobacco products. Additionally, future areas of work are identified in the report, focusing on the regulatory needs of countries, thus providing a strategy for ensuring continued technical support to Member States.

Main recommendations

29. The main recommendations to policy-makers and all other interested parties include, but are not limited to, the following:

- (a) to maintain focus on evidence-based measures to reduce tobacco use as outlined in the WHO Framework Convention on Tobacco Control and seek to avoid being distracted from these actions by the promotion of novel tobacco products such as heated tobacco products;
- (b) to use existing regulations for tobacco products to regulate heated tobacco products (including the device) and consider broadening the scope of the existing regulations, where regulatory loopholes may be exploited by the tobacco industry, including in countries in which these tobacco products are currently not legally available;

¹ Decision FCTC/COP8(22) (2018) ([https://www.who.int/fctc/cop/sessions/cop8/FCTC__COP8\(22\).pdf](https://www.who.int/fctc/cop/sessions/cop8/FCTC__COP8(22).pdf), accessed 2 November 2020).

- (c) to apply the most restrictive tobacco control regulations to heated tobacco products (including the device), as appropriate within national laws, taking into account the need for a high level of protection for human health;
- (d) to prohibit all manufacturers and associated groups from making claims about reduced harm of heated tobacco products, compared with other products, or portraying heated tobacco products as an appropriate approach for cessation of any tobacco product and ban their use in public spaces unless robust independent evidence emerges to support a change in policy;
- (e) to ensure that the public is well informed about the risks associated with use of heated tobacco products, including the risks of dual use with conventional cigarettes and other smoked tobacco products, and also their use during pregnancy; to correct false perceptions, counter misinformation and clarify that reduced exposure does not necessarily mean reduced harm;
- (f) to rely on independent data and to support continuing independent research on the public health impact of heated tobacco products, along with critically analysing and interpreting tobacco industry-funded data, including but not limited to research data pertaining to emissions and toxicity of heated tobacco products and associated exposures and effects in users and non-users;
- (g) to require tobacco manufacturers to disclose all product information – including product design, chemical profile, total nicotine content, nicotine forms, toxicity, other findings of product testing and testing methods – to appropriate regulatory agencies at least once a year; any modifications to products should require an updated report;
- (h) to ban all activities related to the commercial marketing of electronic nicotine delivery systems, electronic non-nicotine delivery systems and heated tobacco products, including in social media and through organizations funded by and associated with the tobacco industry;
- (i) to prohibit electronic nicotine delivery systems and electronic non-nicotine delivery systems over which the user can control device features and liquid ingredients (that is, open systems);
- (j) to prohibit the sale of electronic nicotine delivery systems that have a higher abuse liability than conventional cigarettes, for example by restricting the emission rate or/flux of nicotine; and
- (k) to prohibit the addition of pharmacologically active substances (in jurisdictions where they are legal) other than nicotine in electronic nicotine delivery systems, such as cannabis and tetrahydrocannabinol to electronic nicotine delivery systems and electronic non-nicotine delivery systems.

Significance for public health policies

30. The Study Group's report provides helpful guidance in understanding research and evidence on novel and emerging nicotine and tobacco products, in particular, electronic nicotine delivery systems, electronic non-nicotine delivery systems and heated tobacco products. It highlights the public health impact of these products and/or features on users and non-users, including: their addictive potential, perception and use, attractiveness, potential role in initiating and stopping tobacco use; marketing, including promotional strategies and impacts; claims of reduced harm; variability of products; quantification of risk to the health of individuals and populations; regulatory mapping and experience of selected countries; impact on tobacco control efforts; and research gaps. The Study Group's

recommendations, outlined above, directly tackle some of the unique regulatory challenges faced by Member States due to the penetration of these products into several markets. Further, the report will help Member States to update their knowledge on novel and emerging nicotine and tobacco products and aid the formulation of effective regulatory strategies for nicotine and tobacco products.

31. The Study Group, because of its unique composition of regulatory, technical and scientific experts, navigates and distills complex data and research and synthesizes them into policy recommendations, which inform policy development at country, regional and global levels. Such recommendations promote international coordination of regulatory efforts and the adoption of best practices in product regulation, strengthen product regulation capacity-building across all WHO regions, provide a ready resource to Member States based on sound science and support the implementation of the WHO Framework Convention on Tobacco Control by its States Parties.

Implications for the Organization's programmes

32. The report fulfils the mandate of the WHO Study Group on Tobacco Product Regulation to provide the Director-General with scientifically sound, evidence-based recommendations for Member States about tobacco product regulation,¹ which is a highly technical area of tobacco control in which Member States face complex regulatory challenges. The outcomes of the Study Group's deliberations and main recommendations will improve Member States' understanding of electronic nicotine delivery systems, electronic non-nicotine delivery systems and heated tobacco products. The report's contribution to the body of knowledge on product regulation will play a critical role in informing the work of the tobacco programme within WHO's Department of Health Promotion, especially in providing technical support to Member States. It will also contribute to updating Member States, as well as regulators, through meetings of the WHO Global Tobacco Regulators' Forum and information sharing via the EZCollab network of the Global Tobacco Regulators' Forum. States Parties to the WHO Framework Convention on Tobacco Control will be updated through a comprehensive report on research and evidence on novel and emerging tobacco products, which was requested by the Conference of the Parties at its eighth session.² The comprehensive report will include the key messages and recommendations of the eighth report of the Study Group. All of these will contribute to meeting target 3.a of the Sustainable Development Goals (that is, strengthening the implementation of the WHO Framework Convention on Tobacco Control).

ACTION BY THE EXECUTIVE BOARD

33. The Board is invited to note the report.

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¹ In November 2003, the Director-General formalized the status of the former Scientific Advisory Committee on Tobacco Product Regulation from a scientific advisory committee to a study group.

² See decision FCTC/COP8(22), paragraph 2(a).