Main outcomes of the meeting of the WHO Expert Committee on Biological Standardization held from 16 to 19 October 2023

The 78th meeting of the WHO Expert Committee on Biological Standardization (ECBS) was held from 16 to 19 October 2023 as a hybrid meeting, with ECBS members meeting in person in Geneva and other participants attending virtually. In addition to ongoing work arising from the COVID-19 pandemic, the ECBS also discussed a range of other biological standardization issues, and was updated on the work of custodian laboratories for WHO biological standards. ECBS members, regulatory authority representatives and subject matter experts from governmental organizations participated in the meeting from Monday 16 October to Wednesday 18 October 2023. A short open information-sharing session involving all participants, including non-state actors, was held on Monday 16 October 2023. All ECBS decisions and recommendations regarding the adoption of WHO written standards and the establishment of WHO measurement standards were made during a closed session held on Thursday 19 October 2023 attended only by ECBS members and WHO staff. At the end of the closed session, the ECBS provided its feedback and recommendations to WHO on a number of current issues in biological standardization. A full meeting report will be published in the WHO Technical Report Series in 2024.

The main meeting outcomes included the recommended adoption of the following WHO document:

- **Guidelines on preparedness for regulatory oversight of vaccines used in pandemics in importing countries**

  Large-scale disease outbreaks can result in a severe disease burden, claiming millions of lives and causing economic hardship worldwide. The implementation of strategies to shorten the time between the emergence of a pathogen and the availability of safe and effective vaccines is crucial in strengthening global health security. At its meeting in October 2016, the ECBS recommended the adoption of the WHO Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine-producing countries. Since then, several Ebola outbreaks and the COVID-19 pandemic have highlighted the need to broaden the scope of this document to include other vaccines used in pandemics and other public health emergencies. The revised Guidelines provide guidance to NRAs of importing countries on the regulatory oversight of such vaccines, including authorization and post-authorization activities. The document emphasizes the role of regulatory reliance and the importance of risk-based decision-making in ensuring the approval and timely availability of life-saving vaccines during a public health emergency.

As shown in Table 1, the ECBS also recommended the establishment of six new and five replacement WHO international reference materials. In addition, the ECBS endorsed seven proposals to establish future such materials. The ECBS also noted the proposed managed discontinuation of the WHO International Standard for C-reactive protein established in 1986 (NIBSC code 85/506). Following limited adoption of the assigned IU, it was proposed that this material would not be replaced when stocks are exhausted in approximately 3 years. The ECBS was also updated on the intention not to proceed with a previously endorsed series of standards for oral polio vaccines following recent developments in the field that would significantly reduce their utility.

Table 1
WHO international reference materials established by the ECBS in October 2023

Material	Unitage	Status
Biotherapeutics other than blood products		
Alpha-fetoprotein (human)	7800 IU/ampoule	Second WHO International Standard
Follicle-stimulating hormone and luteinizing hormone for bioassay (human, urinary)	177 IU/ampoule FSH 170 IU/ampoule LH	Sixth WHO International Standard
Thyroid-stimulating hormone (human, pituitary)	11.7 mIU/ampoule	Fourth WHO International Standard
Blood products and related substances		
Thrombin activatable fibrinolysis inhibitor (plasma)	Activity: 0.87 IU/ampoule Antigen: 0.92 IU/ampoule Antigen: 7.43 µg/ampoule (expanded uncertainty limits = 7.05–7.82 with k=2 taken to correspond to a 95% level of confidence)	First WHO International Standard
In vitro diagnostics		
Protein S (plasma)	0.71 IU/ampoule activity 0.83 IU/ampoule free antigen 0.88 IU/ampoule total antigen	Third WHO International Standard
Q fever (*Coxiella burnetii*) antibodies (human plasma)	100 U/ampoule for Phase I antigens 16 U/ampoule for Phase II antigens	WHO International Reference Reagent
Standards for use in high-throughput sequencing technologies		
Gut microbiome DNA extraction (whole cell)	No unitage assigned	WHO International Reference Reagent
Standards for use in public health emergencies		
SARS-CoV-2 RNA for NAT-based assays	7.50 $\log_{10}$ IU/ampoule	Second WHO International Standard
Vaccines and related substances		
Nipah virus antibodies for use in binding assays (human serum)	250 IU/ampoule anti-glycoprotein IgG	First WHO International Standard
Nipah virus antibodies for use in neutralization assays (human serum)	250 IU/ampoule	First WHO International Standard

Ross River virus antibodies for use in neutralization assays (human plasma)	500 U/vial	WHO International Reference Reagent

In addition to recommending the adoption of the above WHO document and the establishment of the 11 reference materials shown in Table 1, the ECBS also discussed the following:

1. The ECBS discussed a number of issues in relation to the COVID-19 pandemic. Following recommendations made at its two previous meetings, WHO guidelines had been adopted on: (a) the production and quality control of monoclonal antibodies (mAbs) intended for medicinal use; and (b) the nonclinical and clinical evaluation of mAbs intended for the prevention and treatment of infectious diseases. At the current meeting, the ECBS was updated on progress in developing a prospective addendum to the second of these documents specifically covering mAbs for use against COVID-19. Several mAbs against COVID-19 have now been licensed or approved for emergency use, with many more currently in development. The ECBS was also updated on recent reviews of studies of the efficacy of high-titre convalescent plasma or hyperimmune immunoglobulin in treating SARS-CoV-2 infection. Although considered safe, uncertainty remains concerning the efficacy of such products, including in immunocompromised patients.

2. Animal testing approaches have long been used for the quality control and lot release of many vaccines and biotherapeutics. However, animal-based assays are inherently variable and highly time consuming, potentially causing delays in the availability of life-saving products. In light of recent significant advances in the implementation of non-animal technologies for the quality control of biological medicines, WHO had commissioned an independent review of the animal-based methods currently recommended in its written standards for biologicals. This review had been conducted by the National Centre for the 3Rs in the United Kingdom and its final report and associated proposals were presented to the ECBS. Acknowledging the quality and comprehensiveness of the work undertaken during the review, the ECBS recommended that a working group be established to build upon its findings and to develop further WHO guidance in this area.

3. This was the first face-to-face meeting of the ECBS since the start of the COVID-19 pandemic and included several new committee members. There was broad recognition of the immense value of meeting in person, and of how this had allowed for a rich exchange of knowledge, experience and ideas. Looking ahead, the ECBS expressed strong support for the proposal to hold two meetings each year, with one to be held virtually during the first quarter, followed by an October meeting held in the same hybrid format as the current meeting. It was envisaged that the earlier meeting would allow for the more timely and responsive establishment of measurement standards that would otherwise have to wait until October, while the October meeting would allow for a fuller and broader agenda, which would also include, for example, consideration of the cross-cutting activities of other WHO groups and committees, and feedback from custodian laboratories.

The next meeting of the ECBS is scheduled for 11–15 March 2024.