Main outcomes of the meeting of the WHO Expert Committee on Biological Standardization held from 7 to 11 October 2024

The 80th meeting of the WHO Expert Committee on Biological Standardization (ECBS) was held from 7 to 11 October 2024 as a hybrid meeting, with ECBS members meeting in person in Geneva and other participants attending virtually. ECBS members, regulatory authority representatives and subject matter experts from governmental organizations participated in the meeting from Monday 7 October to Thursday 10 October 2024. An open information-sharing session involving a broader range of participants, including non-state actors, was held on Monday 7 October 2024. After receiving updates on the activities of other WHO committees and groups, and on the scientific issues identified by the custodian laboratories of WHO biological standards, the ECBS went on to discuss a range of current issues in the field. All ECBS decisions and recommendations regarding the adoption of WHO guidance documents and the establishment of physical WHO laboratory measurement standards were made during a closed session held on Friday 11 October 2024 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 the range of issues that had been discussed. A full meeting report will be published in the WHO Technical Report Series in 2025.

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

- **Nonclinical and clinical evaluation of RSV monoclonal antibodies and related products intended for the prevention of respiratory syncytial virus disease**

  Respiratory syncytial virus (RSV) is a major cause of severe morbidity and mortality in infants, the elderly and immunocompromised individuals, and is a common cause of death in low-income countries that lack effective treatment options. Administering prophylactic RSV monoclonal antibody products to infants and young children offers immediate protection against severe disease, and several such products have now been approved. Following the adoption in 2023 of the WHO Guidelines on the nonclinical and clinical evaluation of monoclonal antibodies and related products intended for the prevention or treatment of infectious diseases, the above document now provides RSV-specific guidance on the nonclinical and clinical evaluation of these emerging products.

- **Recommendations to assure the quality, safety and efficacy of rotavirus vaccines**

  Rotaviruses are a major cause of severe dehydrating gastroenteritis in children under the age of 5 years worldwide. However, fatality rates are significantly higher in countries with poor access to health care, particularly rehydration therapy, reinforcing the crucial importance of infant vaccination. Since the publication of the WHO Guidelines to assure the quality, safety and efficacy of live attenuated rotavirus vaccines (oral), numerous technical advances have been made and considerable experience gained in the use of such vaccines. The above comprehensively revised Recommendations now reflect current manufacturing and quality control practices for live attenuated rotavirus vaccines, while its nonclinical and clinical recommendations are now more broadly applicable to any type of rotavirus vaccine, including prospective non-replicating viral-vectored products. It is envisaged that as the development and use of non-replicating rotavirus vaccines advance further, specific complementary guidance on this class of vaccine will also be provided.

- **Good practices for blood establishments**

  A key strategic objective of the WHO Action Framework to advance universal access to safe, effective and quality-assured blood products 2020–2023 is the establishment of functioning and efficiently managed blood services. However, a lack of knowledge in implementing and maintaining good practices in blood establishments has been identified as a common barrier to ensuring good quality systems. Following significant technological advances in this field, the above document has been developed to replace the 2011 WHO Guidelines on GMP for blood establishments. The revised document now reflects a broad range of developments in key administrative procedures, quality assurance and regulatory compliance. Aligned with existing international guidance and regulations, this document is intended to provide material support to the increasing efforts now under way to improve global blood donation processes, promote universal access to safe blood and blood components for transfusion, and to develop vitally needed plasma-derived medicinal products.

As shown in Table 1, the ECBS also recommended the establishment of one replacement and seven new WHO international reference materials. The ECBS also endorsed seven proposals to establish future such materials.

Table 1. WHO international reference materials established by the ECBS in October 2024

Material	Unitage	Status
In vitro diagnostics		
Epidermal growth factor receptor variant T790M (c.2369C>T) genomic DNA	Variant allele frequency = 100%	WHO International Reference Reagent
Epidermal growth factor receptor variant L858R (c.2573T>G) genomic DNA	Variant allele frequency = 100%	WHO International Reference Reagent
Epidermal growth factor receptor variant p.E746_A750del (c.2235_2249del) genomic DNA	Variant allele frequency = 100%	WHO International Reference Reagent
Serum amyloid A	56 µg per ampoule	Second WHO International Standard
Thyroglobulin antibodies (human serum)	735 IU/ampoule	First WHO International Standard
Tissue transglutaminase autoantibodies (human serum)	200 IU/vial anti-tTG IgA 100 IU/vial anti-tTG IgG	First WHO International Standard
Vaccines and related substances		
Marburg virus antibodies for binding assays (human serum)	250 IU/ampoule anti-glycoprotein IgG	First WHO International Standard
SARS-CoV-1 antibodies for neutralization assays (human immunoglobulin)	250 IU/ampoule	First WHO International Standard

The ECBS also recommended the discontinuation of two existing WHO international reference materials (Table 2) and confirmed its agreement with a decision not to proceed with a project to develop a First WHO International Standard for antibodies to influenza A(H7N9) virus.

Table 2. WHO international reference materials discontinued from October 2024

Material	Rationale	Discontinuation pathway
First WHO International Standard for calcitonin, ASU 1–7 eel calcitonin analogue (elcatonin) **NIBSC code 84/614**	Low, and highly geographically restricted, demand	Managed distribution of remaining stocks until depletion in around 2 years
First WHO International Standard for human C-reactive protein **NIBSC code 85/506**	Low demand as a result of limited adoption of the assigned IU	Managed distribution of remaining stocks until depletion in around 2 years

As well as recommending the adoption of the above three WHO documents, the establishment of the eight international reference materials shown in Table 1 and the discontinuations listed in Table 2, the following topics were discussed in detail by the ECBS:

1. A key objective of laboratory medicine is to accurately guide potentially life-saving patient treatment decisions regardless of the different assays used in different laboratories. However, many assays give different results for the exact same clinical sample, and as clinical decisions are based on assay results, this can dramatically impact on the treatment and well-being of patients. The Committee discussed at length the paramount importance of ensuring that the biological standards recommended for establishment by WHO are fit for purpose when used to harmonize clinically critical assays worldwide.

2. WHO documents on the production, quality assessment, and nonclinical and clinical evaluation of biological products are vital resources for both manufacturers and regulators worldwide. In addition to serving as the basis for setting national regulatory requirements, they also underpin the WHO prequalification process. Faced with an unprecedented level of demand for new or revised guidance documents in this field, a number of considerations were presented in prioritizing document development to ensure that WHO will continue to address the global need for guidance on biological products of assured quality, efficacy and safety. The ECBS welcomed the efforts being made to further increase the transparency of decision-making in this important area.

3. Animal testing approaches have long been used for the quality control and lot release of vaccines and biotherapeutics. However, animal-based assays are inherently variable and hugely time consuming, often delaying access to vitally needed medicinal products. In light of ongoing technological developments and following an independent review of WHO documents that include the use of animals, the ECBS was updated on the development of overarching WHO guidance on replacing animal assays used in quality control testing with increasingly sophisticated non-animal alternatives. Acknowledging that such a shift must be driven and guided by rigorous scientific principles, the ECBS welcomed this initiative and looked forward to reviewing the document for potential adoption at its next meeting.

The next meeting of the ECBS is scheduled for 13-17 October 2025.