Main outcomes of the meeting of the WHO Expert Committee on Biological Standardization held from 13 to 16 October 2025

The 81st meeting of the WHO Expert Committee on Biological Standardization (ECBS) was held from 13 to 16 October 2025 as a hybrid meeting. ECBS members met in person at the WHO Training Centre in Tunis, with other participants attending virtually. The ECBS discussed a broad range of current issues in relation to the quality, safety and efficacy of biological products used in medicine, and was updated on the activities of the custodian laboratories for the highly specialized WHO measurement standards used in this field. Prior to the main meeting, an open information-sharing session was held on Monday 13 October 2025 that included representatives of non-state actors, intergovernmental organizations and other entities. ECBS members, regulatory authority representatives and subject matter experts from governmental organizations then participated in the main meeting from Monday 13 October to Wednesday 15 October 2025. All ECBS decisions and recommendations regarding the establishment of new and replacement WHO measurement standards, as well as the adoption of WHO published guidance documents, were made during a closed session held on Thursday 16 October 2025 attended only by ECBS members and the WHO secretariat. At the end of the closed session, the ECBS provided its feedback and recommendations to WHO. A full meeting report will be published in the WHO Technical Report Series in 2026.

The main meeting outcomes included the ECBS recommendation to adopt the following WHO document:

- **WHO Guidelines on the replacement or removal of animal tests for the quality control of biological products**

Animal tests have long played a part in the quality control and lot release of biological products. However, their inherent variability and poor precision is increasingly rendering such tests inferior to well-designed non-animal in vitro assays for monitoring product quality and production consistency, and for assessing the potential consequences of manufacturing changes. As part of its continuing and concerted efforts in this area, WHO convened an expert drafting group to develop overarching guidance on the replacement or removal of animal tests that will now supersede the relevant recommendations provided in previously published WHO documents. This important new document has been aligned with current thinking among regulators worldwide, and reinforces WHO's commitment to support manufacturers and regulators of biological products in accelerating the implementation of non-animal in vitro alternatives to animal-based quality control approaches whenever scientifically justified.

As shown in Table 1, the ECBS also recommended the establishment of six replacement and 11 new WHO international reference standards.

Table 1. WHO international reference standards established by the ECBS in October 2025

Material	Unitage	Status
Biotherapeutics other than blood products		
Ranibizumab	1000 IU/ampoule VEGF165 neutralizing activity	First WHO International Standard

	1000 IU/ampoule VEGF165 binding activity	
Anti-drug antibodies to adalimumab for binding assays	50 000 IU/ampoule	First WHO International Standard
Anti-drug antibodies to adalimumab for neutralization assays	50 000 IU/ampoule	First WHO International Standard
Low-activity anti-drug antibodies to adalimumab; detection of	No unitage assigned	WHO International Reference Reagent
Low-affinity anti-drug antibodies to adalimumab; detection of	No unitage assigned	WHO International Reference Reagent
Blood products and related substances		
Protein C (plasma)	0.91 IU/ampoule for functional assays 0.89 IU/ampoule for antigen assays	Third WHO International Standard
Blood coagulation factor IX (concentrate)	10.6 IU/ampoule	Sixth WHO International Standard
Thromboplastin (human, recombinant, plain)	International Sensitivity Index = 1.08	Sixth WHO International Standard
Anti-A and anti-B haemagglutinins in intravenous immunoglobulin products; positive control	No unitage assigned	WHO International Reference Reagent
Anti-A and anti-B haemagglutinins in intravenous immunoglobulin products; negative control	No unitage assigned	WHO International Reference Reagent
Anti-A and anti-B haemagglutinins in intravenous immunoglobulin products; limit control	No unitage assigned	WHO International Reference Reagent
In vitro diagnostics		
Beta-2 microglobulin	103 IU/ampoule	Second WHO International Standard
Vaccines and related substances		
Antibodies to influenza A virus haemagglutinin stem domain (group 1) for binding assays	100 IU/ampoule	First WHO International Standard
Antibodies to Sudan virus for neutralization assays (human serum)	250 IU/ampoule	First WHO International Standard
Antibodies to Sudan virus for binding assays (human serum)	250 IU/ampoule anti-glycoprotein IgG	First WHO International Standard

Antiserum to respiratory syncytial virus	960 IU/ampoule (RSV/A) 690 IU/ampoule (RSV/B)	Second WHO International Standard
Vi polysaccharide of *Salmonella* Typhi	1.73 ± 0.04 mg/ampoule	Second WHO International Standard

As well as recommending the adoption of the above WHO Guidelines and the establishment of the 17 international reference standards shown in Table 1, the ECBS also discussed the following:

1. A core function enshrined in the WHO Constitution is to develop, establish and promote the use of international standards. Such standards include the international reference standards that form the basis of national regulation of vitally needed biological products and in vitro diagnostics. The Committee was updated on the progress made in revising the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards. Reflecting both the considerable technological advances made in recent years in the manufacturing and testing of biological products, and the increasing range, use and demand for the associated WHO international reference standards, the revised document will continue to be the foundational document in guiding the work of WHO, its custodian laboratories and other key stakeholders in this field. The ECBS commended the progress that had been made and looked forward to reviewing the document with a view to recommending its adoption at its next meeting in April 2026.

2. WHO Recommendations, Guidelines and other published guidance documents on biological products underpin the vital WHO prequalification process, and are an invaluable resource for product developers, manufacturers and regulators, especially in low- and middle-income countries. Faced with unprecedented demand for these highly resource-intensive but crucially needed products, WHO continues to promote transparency around the process used to prioritize their development. The ECBS reviewed the priorities presented for forthcoming WHO publications in the context of their global public health importance. Highlighted priorities included the need for published WHO guidance on new tuberculosis vaccines and on cell-based yellow fever vaccines, along with a recognized need for ECBS inputs and subsequent published WHO guidance in the coming years on the development of poliomyelitis vaccines based on virus-like particles.

3. The development of polysaccharide conjugate vaccines continues to represent a key strategy in protecting infants and young children against a range of pathogens associated with considerable public health burdens, particularly in low-and middle-income countries. With regard to the need for specific WHO guidance in this area, the ECBS noted that a number of such vaccines were now at an advanced stage of development and that work had now started on developing published WHO guidance for multivalent group B streptococcal vaccines. Although WHO guidance on bivalent *Salmonella* Typhi Vi and *Salmonella* Paratyphi A conjugate vaccines was also urgently required, its development will depend upon the outcomes of ongoing clinical studies, which include controlled human infection model data. The ECBS requested that WHO explore the possibility of updating its current guidelines on human challenge studies to support regulators, manufacturers, academia and other stakeholders working in this and other areas of clinical vaccine development. The ECBS also expressed support for a proposal to develop an overarching document on the

production and quality control of polysaccharide conjugate vaccines to be supplemented by a series of addenda to be produced as required on the nonclinical and clinical development of such vaccines against specific pathogens.

4. The ECBS also discussed the potential application of advances in artificial intelligence to the field of biological product standardization. In particular, the standardization and analysis of digital data generated by the broad range of methods typically used to evaluate such products is an area of potentially great interest and importance. The ECBS noted that meeting the specialized demands of this aspect of biological standardization would require strengthening its knowledge and expertise, including through the inviting of expert presentations to ECBS.

The next meeting of the ECBS is scheduled for 20–24 April 2026.