

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

### **Report by the Secretariat**

#### **EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION**

##### **Sixty-fourth report Geneva, 21–25 October 2013<sup>2</sup>**

1. The Expert Committee on Biological Standardization reviews developments in the field of biological substances used in human medicine, including vaccines, biological therapeutics, blood products and related in vitro diagnostic devices. It coordinates activities leading to the adoption of recommendations for assuring the quality, safety and efficacy of such substances and the establishment of international reference materials.
2. The use of international reference materials for designating the activity of biological substances used in prophylaxis or therapy, or for ensuring the reliability of quality control or diagnostic procedures, allows comparability of data worldwide.

#### **Main recommendations**

3. Based on the results of international collaborative laboratory studies, the Committee established 11 new or replacement international reference materials; these are the primary calibrants against which regional or national measurement standards are benchmarked.<sup>3</sup>
4. The Committee also adopted revised written standards for production and control of **biotherapeutic products**. New WHO guidelines for regulatory evaluation of **adjuvanted vaccines** and for **typhoid conjugate vaccines** were adopted.

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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> WHO Technical Report Series, No. 987, 2014.

<sup>3</sup> An up-to-date list of WHO International Biological Reference Preparations is available at <http://www.who.int/bloodproducts/catalogue/en/> (accessed 28 February 2014).

## Significance for public health policies

5. Recommendations published by WHO provide guidance for national regulatory authorities and manufacturers on production, quality control and associated safety and regulatory issues for biological medicines. They serve as the basis for national regulations. WHO International Standards are used to calibrate regional, national or manufacturers' standards and often form the basis for licensing, routine lot release and clinical dose determination worldwide.

6. Member States have recognized that the norms and standards applicable to medicines need to be updated in the light of advances made in biotechnology and the new generation of medicines introduced as a result in order to ensure the entry into the market of medicines that are affordable, safe, efficacious, of quality and accessible in a timely and adequate fashion. Further, Member States have requested support in strengthening their capacity in the area of the health regulation of biotherapeutic products. The revised guidelines on biotherapeutic products are intended to meet these needs. Additional guidance for similar biotherapeutic products has previously been established by the Committee.<sup>1</sup>

7. Over the past decades, strategies and approaches for the development and delivery of vaccine antigens have been expanded. Some of these antigens are weakly immunogenic and require the presence of adjuvants for the induction or enhancement of an adequate immune response. Vaccines with aluminium-based adjuvants have been used extensively in immunization programmes worldwide and a significant body of safety information has accumulated for them. As the knowledge of immunology and the mechanisms of vaccine adjuvant action have developed, the number of vaccines containing novel adjuvants being evaluated in clinical trials has increased. Given the importance and the complexity of the issues, the extensive guidance on the nonclinical and preclinical testing of adjuvants and adjuvanted vaccines should allow manufacturers and regulators to proceed in an efficient manner on the critical path towards development and licensure of adjuvanted vaccines indicated for the control of diseases with important global public health impact.

8. The new guidelines on the quality, safety and efficacy of typhoid conjugate vaccines pave the way for access to these vaccines. The evidence gathered indicates that such vaccines may overcome several limitations of unconjugated Vi polysaccharide vaccines. Conjugate vaccines may demonstrate (i) greater efficacy and effectiveness; (ii) longer persistence of immunity; (iii) immunogenicity across all age groups, including infants and children younger than two years of age; (iv) perhaps some degree of herd immunity; and (v) induction of immune memory with initial dosing, leading to anamnestic responses to a subsequent dose or doses.

## Implications for the Organization's programmes

9. The Committee provides up-to-date recommendations on the quality, safety and potency of biological substances used in human medicine and ensures the availability of necessary international reference materials. Its work enables WHO to fulfil its constitutional mandate in this area. The global norms and standards defined by the Committee provide the basis for assessing the acceptability of vaccines for purchase by PAHO and other international bodies, such as UNICEF.

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<sup>1</sup> WHO Technical Report Series, No. 977, 2013.

10. The Committee's observations, conclusions and recommendations have significant implications for several of WHO's activities. In particular, they provide recommendations and reference preparations for assuring the quality, safety and efficacy of vaccines and blood products, and the provision of reference materials for standardizing essential diagnostic assays for the detection of contaminants in blood products.

11. The timely development of new WHO reference materials and standards is vital for the harnessing of scientific developments for new biologicals. At the same time, the active management of the existing inventory of reference preparations requires a carefully planned programme of work to replace established materials before the stock of containers, which comprises the standard, is exhausted. A total of 16 new reference preparation projects were endorsed by the Committee to enable the WHO standards-setting programme to continue to deliver appropriate standards at the appropriate time.

12. The Committee deferred taking a decision on a proposal requesting approval for work on WHO reference materials and reference panels for cancer diagnostics. The basis for this delay was that such an approach would represent a shift into a potentially large new area of work that needed careful consideration of the resources needed and impact on the focus of the Committee's work.

## **SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS**

### **Forty-eighth Expert Committee on Specifications for Pharmaceutical Preparations Geneva, 14–18 October 2013<sup>1</sup>**

13. The Expert Committee on Specifications for Pharmaceutical Preparations provides international standards, good practices and global regulatory tools enabling quality assurance of medicines throughout their life cycle from development to supply to patients, wherever they are in the world. The Expert Committee reviews developments and advises the Director-General and Member States in the area of quality assurance of medicines.

#### **Main recommendations**

14. Based on studies carried out in collaboration with WHO collaborating centres, the Forty-eighth Expert Committee adopted more than 20 new monographs and general texts for inclusion in *The international pharmacopoeia*. The specifications under development are internationally applicable test methodologies for anti-infective, antimalarial, antituberculosis and antiretroviral medicines, contraceptives, and medicines for children. In addition, 11 new International Chemical Reference Substances were adopted for use in testing medicines. The Expert Committee also adopted a new procedure for the development and revision of specifications for radiopharmaceuticals (see Annex).

15. The Expert Committee expressed its support for the WHO initiative, in close cooperation with national and regional pharmacopoeias, towards future convergence of pharmacopoeial requirements. It expressed its thanks to the Indian Pharmacopoeia Commission for co-hosting the related Second International Meeting of World Pharmacopoeias (New Delhi, 18–19 April 2013).

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<sup>1</sup> WHO Technical Report Series, No. 986, 2014 (in preparation).

16. The Expert Committee strongly recommended the continuation of WHO's External Quality Assurance Assessment Scheme to enable participating laboratories to demonstrate, compare and improve their performance. It further supported the continuation of the work of drafting guidance and tools that will assist national control laboratories in testing suspect spurious/false-labelled/falsified/counterfeit medicines.

17. In order to support the work of WHO's Prequalification Team–Medicines, the Expert Committee adopted the guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities (see Annex). These new guidelines will enhance synergies with and among national and regional medicines regulatory authorities in order to speed up and facilitate access to medicines and are therefore expected to have a major public health impact.

18. Taking into consideration the principles of quality risk management and trends in science, the Expert Committee adopted an update of the main principles of the WHO good manufacturing practices for pharmaceutical products.

19. The Committee actively supported the current efforts to harmonize the quality-assurance aspects of international procurement procedures for medicines with the aim of streamlining the processes and saving resources. It adopted the revised WHO model quality assurance system for procurement agencies, and related thereto the revised model inspection report, a new interagency product questionnaire, as well as the new assessment tool based on the model quality assurance system for procurement agencies: aide-memoire for inspection (see Annex).

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

20. WHO's international guidelines, good practices and physical standards developed under the aegis of this Expert Committee are designed to serve all Member States, their national and regional regulatory authorities, international organizations, and bodies of the United Nations system, and support universal health coverage by helping to ensure the good quality of the medicines that patients take. This normative work supports regional, subregional and interregional efforts towards regulatory harmonization, and underpins important initiatives, including the prequalification of medicines, the Roll Back Malaria Programme, Stop TB, and WHO's work on essential medicines and on medicines for children.

21. The advice and recommendations provided by this Expert Committee are intended to protect patients and facilitate access to medicines by assisting Member States, procurement agencies, major international bodies and institutions, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, and international organizations and bodies such as UNICEF, in their efforts to provide good quality medicines to those who need them.

22. The Expert Committee responds to the need for international quality assurance standards and regulatory tools, taking into consideration current science, new developments, and the increasingly complex international supply chains for medicines which have resulted in more complicated regulatory processes and the need for convergence and synergies among regulatory authorities.

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

23. The Expert Committee provides up-to-date norms, standards and related recommendations on the quality assurance of pharmaceutical starting materials and finished products. Its work enables

WHO to fulfil its constitutional mandate in this area and has direct or indirect implications for all WHO's programmes that deal with medicines.

24. The Expert Committee especially serves the WHO Regulatory Systems Strengthening Group and the Prequalification Team–Medicines, and adopts global regulatory standards and test specifications. This close collaboration has resulted in a significant advantage, as the Expert Committee receives immediate practical feedback whenever a clarification, a revision or additional guidance is needed.

25. Through the Expert Committee's recommendations, WHO is in a position to offer technical support on quality management issues to all those bodies that deal with the supply and procurement of medicines. It can provide tools and guidance to help to ensure that good-quality medicines reach patients and thus contributes to universal health coverage.

## ANNEX

### **The following new standards and guidelines were adopted and recommended for use**

- *The International Pharmacopoeia* – updating mechanism for the section on radiopharmaceuticals (Annex 1)
- WHO good manufacturing practices for pharmaceutical products: main principles (Annex 2)
- Model quality assurance system for procurement agencies, including appendices (model inspection report and product questionnaire) (Annex 3)
- Assessment tool based on the model quality assurance system for procurement agencies: aide-memoire for inspection (Annex 4)
- Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part (Annex 5)
- Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities (Annex 6).

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