

New global norms and standards for the quality, safety and efficacy of biologicals

Outcome of the 2008 World Health Organization Expert Committee on Biological Standardization

Introduction

Biological medical products such as vaccines, blood products, biotherapeutics and associated diagnostics save lives, reduce suffering and improve health, but only if these products and technologies are of good quality, are safe, effective, available, affordable and properly used. The World Health Organization (WHO) is working with its Member States towards the goal of using only biological medicines of assured quality in national health systems. The WHO Expert Committee on Biological Standardization (ECBS) establishes global norms and standards that help define products of assured quality. The ECBS meetings are held annually and the most recent one was held in Geneva, Switzerland from 13 to 17 October 2008. During the meeting, 57 agenda items were considered. This was accomplished, as in previous years, by running two parallel tracks, one dedicated to vaccines and selected other biological medicines; one dedicated to blood products and related *in vitro* diagnostic devices.

Highlights of the 2008 ECBS meeting

The most important outcomes of the 2008 ECBS meeting are as follows¹:

- A new written standard for **Production, Control and Regulation of snake antivenoms immunoglobulins** was established. Snake antivenom immunoglobulins (antivenoms) are the only therapeutic products for the treatment of envenomings due to snakebites. The unavailability of effective snake anti-venom immunoglobulins to treat the specific types of envenomings encountered in various regions of the world has become a critical health issue at global level. The crisis has reached its greatest intensity in sub-Saharan Africa, but other regions, such as South-East Asia, are also suffering from a lack of effective and affordable products. The complexity of the production of efficient antivenoms, in particular the importance of preparing appropriate snake venom mixtures for the production of hyperimmune plasma (source of antivenom immunoglobulins), the decreasing number of producers and the fragility of the production systems in developing countries further jeopardize the availability of efficient antivenoms in Asia, Africa, the Middle East, and South America. Most of the remaining current producers are located in countries where the application of quality and safety standards needs to be improved. The new Guidelines cover all the steps involved into the production, control and regulation of venoms and antivenoms. It is hoped that this document, by covering comprehensively the current existing experience in the manufacture, control, and preclinical and clinical assessment of these products will serve as a guide to national control authorities and manufacturers to support worldwide production of these essential medicines.
- An amendment to the written standard for **yellow fever vaccine** was also established. This requires that the expression of potency of such vaccines be in International Units

¹ The outcomes from the 2008 ECBS will be published in full in the WHO Technical Report Series.

(IU) per dose. The dose recommended for use in humans shall not be less than 3.0 log₁₀ IU. This new expression of potency should be approved by National Control Authorities, and will also be used as the standard for WHO prequalification of yellow fever vaccines.

- The Expert Committee also discussed a proposal to establish an "**Abbreviated licensing pathways for certain biological therapeutic products**". Control of chronic diseases is a major challenge for public health systems in WHO member states. Innovative biological medicines developed by modern molecular biological approaches have been successful in treating many life-threatening diseases and the market for these products is rapidly growing. However, such innovative biological medicines are expensive which has limited their use, particularly in developing countries. The expiration of the patents on key biological drugs such as recombinant insulin, human growth hormone and erythropoietin is opening the door for copies of these drugs to be made by developing country manufacturers. This may contribute to a substantial increase in their availability at affordable price. Generic versions of chemical drugs with expired patents are well known. However, copy biological medicines are far more complicated products for which the generic regulatory pathway is unsuitable. Nevertheless it is essential to ensure that there is appropriate regulatory oversight in place. The regulatory oversight should not be, on the one hand, too lax so that ineffective or dangerous products are allowed into the market place or, on the other hand, too restrictive so that safe and effective products face hurdles that are too high. The ECBS affirmed that reduced data packages may be suitable to provide sufficient assurance about the quality, safety and efficacy of certain products, but it recommended that WHO and countries move forward cautiously. Based on the outcome of the discussions, and consideration by the Committee, the ECBS therefore recommended that the current document be strengthened and some issues further clarified, and requested that a revised version be re-submitted to the Committee in 2009.
- A total of 18 new or replacement global reference preparations were established. These are the primary calibrant against which regional or national measurement standards are benchmarked. An updated list is available from the website <http://www.who.int/biologicals/en/> for reference.

About the WHO Expert Committee on Biological Standardization

Established in 1947, the Expert Committee on Biological Standardization (ECBS) is one of the longest standing WHO committees and has overall responsibility for setting written standards and establishing reference preparation materials. Standards developed through the ECBS relate to the production and quality control of safe and effective products. They provide guidance for national regulatory authorities and manufacturers and serve as the standard for prequalification of vaccines for supply to countries through international agencies. Reference preparation materials are available from designated WHO

laboratories and provide the basis for comparison of materials used in biologicals worldwide.

Members of the ECBS are scientists from national control agencies, academia, research institutes, and public health bodies. These scientists act as individual experts and not as representatives of their respective organizations or employers. The decisions and recommendations of the ECBS are based entirely on scientific principles and public health considerations.

The ECBS reports to the Director-General. These reports are also submitted to the WHO Executive Board. The outcome of each ECBS meeting is subsequently published in a technical report. This report provides updated information on standards for assuring the quality, safety and efficacy of biological products as well as on the establishment of new or updated WHO international standards for designating the activity of biological substances. To view previous ECBS technical reports, visit: <http://www.who.int/biologicals/publications/trs/en/index.html>

For more information on the ECBS, visit: http://www.who.int/biologicals/expert_committee/en/ or contact Dr David Wood, Secretary, ECBS, Immunizations, Vaccines and Biologicals Department, Family and Community Health Cluster, World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland (woodd@who.int).

Related Links

Biologicals: <http://www.who.int/biologicals/en/>

Blood products and related biologicals: <http://www.who.int/bloodproducts/en/index.html>

Immunization, Vaccines and Biologicals: <http://www.who.int/immunization/en/>