



AIDE MEMOIRE

Quality and safety of blood products and related substances:

Blood products and related substances used as biological medicines and *in vitro* diagnostics in human medicine have historically played a paramount role in improving world health. These products constitute a key health concern in both the developing and the developed world, requiring specialized expertise of National Regulatory Authorities (NRAs) and coordination across national boundaries for their control. The World Health Organization (WHO), in accordance with its constitutional obligation to develop, establish and promote international standards for all biological products is the lead agency globally in this field, coordinating collaboration and consensus on key issues related to the safety and quality of these products.

WHO has a major role for continued support to NRAs of Member States to protect global public health. This document describes the tools provided by WHO which can be used by NRAs and manufacturers of Member States as measures for assuring the quality, safety and efficacy of blood products and related biologicals used in human medicine. The relevant elements to enhance development of appropriate regulations in this area are described in greater detail overleaf:

- WHO International Biological Reference Materials (IBRM);
- WHO Recommendations and Guidelines
- Technical assistance to National Regulatory Authorities (NRAs) and National Control Laboratories (NCLs)

Words of advice

- Establish a National Regulatory Authority (NRA) with a statutory mandate to ensure that manufacturers adhere to approved standards of quality assurance and good manufacturing practice.
- NRA responsibilities should include the establishment and implementation of effective national regulations, standard setting and controls, based on the WHO Guidelines for national regulatory authorities on quality assurance of biological products.
- The NRA should have access to independent laboratory facilities and recourse to relevant scientific and medical expertise specific to its mandate, making use of expert committees in the countries.

☑ Norms & Standards

WHO International Biological Reference Materials

- ☐ Define an internationally agreed Unit of biological activity for blood derived medicinal products and diagnostic reagents
- ☐ The international Unit forms the basis for the establishment of clinical dosing and licensing
- ☐ Biological activity of those products used in diagnostics, prophylaxis or therapy worldwide can be directly traceable to the WHO primary standard

WHO Recommendations and Guidelines

- ☐ Authoritative international consensus on procedures and criteria needed to assure safety and effectiveness of blood derived medicinal products
- ☐ Applied to the evaluation and control of technologies and quality and safety of blood products and related biologicals.
- ☐ NRAs adopt WHO Recommendations and Guidelines as a basis for their national regulations

Technical assistance to NRAs/NCLs

- ☐ Assistance in acquiring necessary skills and competencies for the evaluation and control of blood products and related biologicals.
- ☐ Technical advice and guidance on use and interpretation of validated technologies for the evaluation and control of those products
- ☐ Advice and assist Member States in the establishment and functioning of structures for national control laboratories

Key elements / WHO Role

National Regulatory Authorities and Control Laboratories

National regulatory authorities have the duty to ensure that available pharmaceutical/biological products, whether imported or manufactured locally, are of good quality, safe and efficacious. The evaluation and control of the quality, safety and consistency of production of blood products and related biologicals involve the evaluation of starting materials, production processes and test methods to characterize batches of the product and this requires specialized expertise by the NRAs. WHO has a major role to upgrade the technical expertise of NRAs in developing countries as requested by Member States at the WHA Resolution 50.20 of May 1997. Priority is given to upgrading the expertise of NRAs from countries where manufacture of blood products and other related biologicals exist. WHO has a number of activities related to the quality assurance of blood products and related biologicals used for the diagnosis, prevention and treatment of diseases. These include:

- Development and establishment of WHO International Biological Reference Materials (IBRMs)
- Development and adoption of WHO Recommendations and Guidelines
- Promotion of the appropriate use of these Guidelines for adoption of regulations by Member States

The responsibility for adopting WHO Recommendations and Guidelines for all the biological substances used in medicine and for establishing WHO International Standards and Reference Materials rests with the WHO Expert Committee on Biological Standardization. WHO provides in this way the standardization and quality control guidance needed at the global level.

International Biological Reference Materials	WHO Recommendations And Guidelines	Technical assistance to NRAs/NCLs
<p>IBRMs are essential tools for the standardization of biological measurements of medicinal blood products and related biologicals. These materials are primary standards, defining an internationally agreed unitage of biological activity, established on the basis of wide international WHO collaborative studies. IBRMs are used in the calibration of national, regional or working reference materials applied routinely by manufacturers and NCAs.</p> <p>Activities developed by WHO:</p> <ul style="list-style-type: none"> ■ Catalytic role to influence the development of new technologies with relevant impact in public health ■ Source donations of appropriate biological materials to WHO for the production of IBRMs. ■ Coordinate WHO international collaborative studies ■ Evaluation of collaborative studies by WHO ECBS to support the establishment of IBRMs ■ Ensure timely replacement of depleted IBRMs to maintain the continuity of the defined international Unit ■ Promote the adoption of international Units for the development of national/ regional materials ■ Provide advice on the preparation of regional and/or national reference materials 	<p>The content of WHO Recommendations and Guidelines should reconcile the needs of manufacturers and NRAs in countries with limited resources, with the principles of countries with an advanced regulatory system. A unique standard will be promoted in terms of quality and safety. As developing countries become involved in production systems, a further demand of support arises in this area of quality and safety of products requiring international standards.</p> <p>Activities developed by WHO:</p> <ul style="list-style-type: none"> ■ Guidance for NRAs and manufacturers on validated and robust quality control procedures, good manufacturing practices and criteria for assuring the quality and safety of specific products or group of products ■ Assessment of relevant technologies and methods for the standardization and control of blood products and related biologicals ■ Facilitate understanding and implementation of WHO Guidelines and Recommendations as a basis for national regulations of Member States through educational Multicountry Regional workshops ■ Enhance the technical capacities of less advanced countries, by including educational and training elements 	<p>WHO provides a forum for NRAs - to converge on quality assurance and safety issues that are generally applicable to Member States worldwide. Main objectives within this forum are to promote regional and international collaboration of regulatory authorities regarding quality and safety to protect consumers from unsafe and ineffective medicinal and diagnostic blood derived products and other biologicals.</p> <p>Activities developed by WHO:</p> <ul style="list-style-type: none"> ■ Promote harmonization of international standardization processes ■ Promote coordination with other standard setting institutions ■ Promote and facilitate regional collaboration and intercountries information exchange ■ Promote appropriate dissemination of appropriate technologies, regulatory decisions on key issues related to quality and safety ■ Appropriate dissemination of information for access and appropriate use of IBRMs ■ Promote appropriate dissemination of the information to relate normative functions to operational functions

