World Health Organization

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Availability, safety and quality of blood products

Report by the Secretariat

1. In May 2009 the Executive Board at its 125th session considered an agenda item on the availability, quality and safety of blood products. The Board noted the report on the subject but postponed further discussion to the present session of a draft resolution submitted by several Member States.[1] This report is a revised version of the earlier report, and reflects comments made by members of the Board. Document EB126/19 Add.1 contains the draft resolution, initially considered by the Board, and additionally reflects comments and proposals made by members of the Board.

2. Blood products[2] contribute to the saving of millions of lives every year, improve dramatically life expectancy and the quality of life of patients suffering from life-threatening conditions, and support complex medical and surgical procedures. In many countries, demand outstrips supply, and blood services throughout the world face the daunting challenge of making sufficient supplies of blood products available, while also ensuring the quality and safety of these products in the face of known and emerging threats to public health. The health-related Millennium Development Goals of reducing child mortality, improving maternal health and combating HIV/AIDS, malaria and other diseases cannot be achieved unless significant attention is paid to the availability, safety and quality of blood products.

3. One of the worst treatment disasters in modern history took place in the 1980s with the widespread transmission of HIV and hepatitis viruses through infected blood products. Blood-borne transmission of pathogens has highlighted the crucial importance of effective policies, strategies, quality systems, and legislative and regulatory frameworks in the collection, testing, processing and supply of blood components, such as red cells, platelets and plasma, for clinical use. These safeguards are also crucial in the preparation of plasma for fractionation, as a raw material for the manufacturing of plasma-derived medicinal products, such as blood coagulation factor concentrates and immunoglobulins, which are on the WHO Model List of Essential Medicines.[3] Recognizing the high risk of transmission of pathogens through transfusion of contaminated blood products, the Health Assembly, in resolutions WHA28.72, on utilization and supply of human blood and blood products, and WHA58.13, on blood safety: proposal to establish World Blood Donor Day, urged Member States to promote the development of national blood services based on voluntary non-remunerated donation

[1] See document EB125/2009/REC/1, summary record of the first meeting, section 5.

[2] Blood products are defined as any therapeutic substances derived from human blood, including whole blood, labile blood components and plasma-derived medicinal products.

[3] The WHO Model List of Essential Medicines identifies individual medicines that could provide safe effective treatment for most communicable and noncommunicable diseases.

and to enact effective legislation governing their operation. These actions are complementary to the equally essential goal of improving overall good manufacturing practices.

4. Developed countries have implemented policies, strategies and procedures to ensure the availability, accessibility, safety and quality of all products derived from blood through effective blood and plasma programmes, permitting widespread access to a comprehensive range of blood products. In particular since early 1990s, regulatory oversight of the quality of blood products has become more stringent. Conversely, levels of availability, accessibility, safety and quality comparable to those in developed countries do not yet exist in most developing countries, which still face serious shortages of blood products. The risk of transmission of pathogens through transfusions has not yet been eliminated, particularly in countries where the prevalence and incidence of infections due to those pathogens is high. The failure to apply quality systems and implementation of good manufacturing practices to production activities in blood services is a major impediment to ensuring safe and sufficient supplies of blood products. The provision of blood and blood products from voluntary, non-remunerated donors must be the aim of all countries.

INCREASING NEEDS – SPECIFIC ISSUES REQUIRING ACTION

5. **Increasing needs, blood shortages and wastage of blood.** The need for safe, efficacious and secure supplies of blood products is universal. Changing population demographics and more advanced surgical and medical procedures have increased the need for blood transfusion. Globally, more than 70 countries have a blood donation rate of less than that generally considered as necessary to meet a nation's basic requirements for blood, namely 1% of the population; the requirements are higher in countries with advanced health-care systems. Ageing populations and increasingly stringent donor selection criteria have reduced the pool of eligible donors. Therefore, public awareness, donor education and voluntary, non-remunerated blood-donor programmes are needed in order to improve safety and availability of blood products. Collection of blood from unsafe and unsuitable donors, its inadequate storage and transportation, and poor stock management lead to the loss of at least five million blood units every year,[1] further limiting availability of blood products. More research is needed into new technologies for the production of blood substitutes and alternative therapies (e.g. stem cells).

6. **Wastage of plasma.** The limited availability of plasma-derived products in developing countries stems from various causes. Most plasma collected in developed countries is fractionated to meet those countries' own needs, and the potential for generating surplus products sufficient to meet the needs is therefore small. Moreover, import of such products would be prohibitively expensive. Developing countries, where feasible, should therefore provide sustainable supplies of plasma-derived products using plasma collected by their establishments from their populations, even if fractionation is done in developed countries. Currently, however, a large percentage of the plasma collected in developing countries is categorized as waste material and destroyed. This wastage occurs because appropriate technology, regulatory controls, quality systems and good manufacturing practices are all lacking, thereby rendering the plasma unsuitable for conversion into fractionated medicinal products. Unless this situation is improved, plasma from developing countries will continue to be rejected for contract fractionation programmes in a regulated environment. The facilitation of collaboration between developing and developed countries through appropriate regulatory standards and transfer of technology is a vital part of a global approach.

[1] Estimates based on Blood Safety Indicators 2007: WHO Global Database on Blood Safety.

7. **Inappropriate use of blood products.** The issues of sufficiency, availability and access cannot be considered in isolation from use of blood. National data on the use of blood products are limited, but studies suggest that these products are often inappropriately used in both developed and developing countries. Unnecessary transfusions, unsafe transfusion practices and errors (particularly at the patient's bedside) seriously compromise patient safety by exposing patients to the risk of serious adverse transfusion reactions and transfusion-transmissible infections. Unnecessary use also seriously reduces the availability of blood products for patients who are in need. Both over-transfusion and under-transfusion can result in substantial morbidity and mortality. Therefore, comprehensive monitoring and evaluation of the use of blood products and transfusion practices need to be established.

8. **Risk of transfusion-transmissible infections.** When rigorous standards for donor recruitment and selection, donation testing and processing, and clinical transfusion are not applied or fail, transfusion of blood products poses a serious risk of transmission of pathogens. Unfortunately, current systems for blood and plasma donation, processing and testing are inadequate in many developing countries. There is a pressing need to introduce and strengthen policies, strategies and quality-assurance regulations for blood products in developing countries in order to minimize these risks. More research is also needed on new technologies that reduce the risk of transfusion-transmissible infections, such as those that inactivate pathogens.

9. **Emerging and re-emerging threats.** Changes in habitat, the increasing mobility of populations, conflict and climate change all raise the threat of greater exposure to infectious agents. Pathogens such as West Nile virus and Chikungunya virus continue to emerge and may spread rapidly. The presence of known pathogens, such as those causing malaria, dengue and Chagas disease and human T-lymphotropic viruses, is of increasing concern. Climate change is expected to result in both the emergence of new diseases, some of whose causative agents may be transmissible through blood, and changes in the distribution of known diseases such as malaria in areas in which they were not previously endemic, and possibly their severity. The availability, safety and quality of blood products may also be compromised by infections that are not known to be transmissible through the products themselves, such as pandemic influenza, outbreaks of which may result in major disruptions in, and constraints on, blood donation and collection.

10. **Poor quality systems, lack of good manufacturing practices and regulation of blood products in developing countries.** The absence of quality systems in blood services is a major impediment in ensuring safe blood supplies. The quality and effectiveness of blood components depend on careful collection, testing, processing, labelling, storage and distribution. Constraints include lack of national standards, inadequate data and documentation, limited training opportunities and poor quality assessment. Developing countries recognize the need to regulate blood products and in vitro diagnostic medical devices related to blood safety. Their situation parallels that experienced by developed countries until the 1990s: before that time, blood services were largely unregulated; thereafter, they became subject to international inspection and audit, by both regulatory authorities and fractionators. Change occurred largely as a result of the requirement of regulatory authorities that fractionators be able to demonstrate effective control and traceability[1] of plasma raw material. Application of this requirement led to substantial improvements in all the activities of blood services through the adoption of good manufacturing practices for the preparation of plasma for fractionation. It can therefore be assumed that blood services in developing countries would likewise benefit from

[1] Traceability is defined as the ability to trace each individual unit of blood or derivative thereof from the donor to the patient. The term is used to describe both forward and reverse tracing.

the introduction and enforcement of the appropriate quality systems and independent and transparent quality-assurance regulations and inspection procedures.

WHO'S ACTION TO DATE

11. Recognizing the importance of the provision of safe blood products, the Director-General established a blood safety programme in the late 1980s. In 2000, safe blood was declared an Organization-wide priority and blood safety was designated the theme of World Health Day 2000. The need for safe blood products has been stressed in several resolutions adopted by regional committees, the Executive Board and the Health Assembly, giving the matter greater priority on national and global health agendas that include the achievement of the health-related Millennium Development Goals. WHO has been involved in setting evidence-based norms and standards for the quality and safety of blood products and in supporting their proper application. The Secretariat initiated a major programme to support the development of high-quality systems for all aspects of blood transfusion through the global quality management programme. It also provides guidance, support and capacity building in strengthening blood transfusion services in priority countries. WHO's blood safety activities are implemented in close collaboration with a global network of WHO collaborating centres on blood transfusion and the Expert Advisory Panel on Blood Transfusion Medicine.

12. For more than 50 years, WHO has been involved in setting quality and safety standards, elaborating guidelines and training regulators in the manufacture and quality control of biological products. The overall technical responsibility for these activities lies with the Expert Committee on Biological Standardization. International standards and biological reference preparations for use in the quality and safety control of blood products and in vitro diagnostic devices have been adopted by the Expert Committee following validation of those preparations in global coordinated studies carried out with the support of the WHO collaborating centres for blood products and biological standards.

13. The International Conference on Drug Regulatory Authorities has been instrumental in guiding WHO and regulatory authorities of Member States in determining priorities for the regulation of blood products, associated medicines and diagnostics at the national and international levels. In 2005, the WHO Blood Regulators Network was established in response to the request of both the International Conference on Drug Regulatory Authorities and the Expert Committee on Biological Standardization that WHO accept a leadership role in supporting the regulatory authorities of developing countries in order to draw up regulations for the manufacture of blood products. It is envisaged that the WHO's Blood Regulators Network will collaborate with the Expert Committee on Biological Standardization in designing and implementing an effective regulatory approach.

14. Information on blood product safety at national, regional and global levels is collected, analysed and disseminated through WHO's Global Database on Blood Safety. In order to improve blood safety, WHO has established the Global Steering Committee on Haemovigilance, which coordinates the efforts of international organizations that are providing support to countries in developing mechanisms for traceability, adverse event reporting and haemovigilance. WHO has also established the Global Collaboration for Blood Safety – a mechanism for international collaborative relationships and partnerships with organizations and institutions working for global blood safety. In resolution WHA58.13 the Health Assembly agreed to establish an annual World Blood Donor Day and requested the Director-General to work with other organizations to promote the event. Accordingly, WHO and three other agencies provide global leadership and coordination for global activities on World Blood Donor Day. The Organization also supports national voluntary blood donor programmes.

IMPROVING ACCESS TO SAFE, GOOD-QUALITY BLOOD PRODUCTS

15. Blood programmes need to be developed as an integral part of health-care systems based on the principles of primary health care. Universal and timely access to safe blood products of assured quality and efficacy and the optimal use of such products are essential for health-system strengthening and service provision. Since blood products can only be obtained from human blood, the donation of whole blood or its components is the ultimate expression of community participation in health care, which also requires effective intersectoral collaboration. The availability of safe blood products must be improved in developing countries. Achieving self-sufficiency in the supply of blood products and ensuring the security of that supply are important national goals. A safe and stable blood supply has to be built up over a long period of time; it requires a strong foundation based on voluntary, non-remunerated donation, implemented through a well-organized, coordinated and efficient national blood service.

16. Quality systems in blood services should be strengthened to ensure provision of safe blood supplies. Human resource development and training programmes to ensure a sufficiency of qualified personnel are essential to improving the quality and safety of blood transfusion services. Regulatory mechanisms need to be developed for oversight of blood systems and for assuring the availability, quality and safety of blood products. Furthermore, national blood services and medicines regulatory agencies need to be established or upgraded. Work is needed to review national legislative and regulatory frameworks for blood services. Comparable quality and safety of plasma for fractionation and plasma-derived medicinal products need to be ensured through global standardization, technology transfer, capacity building, training and implementation of regulatory standards. The quality of blood components will improve likewise. Strategies should therefore be sought for sharing the expertise, experience and technologies already generated in developed countries to improve access to safe, effective and affordable blood products worldwide.

17. Countries will need to introduce up-to-date mechanisms for implementing and enforcing quality standards for blood products and in vitro diagnostic devices related to blood safety, on the basis of international biological standards and internationally agreed guidelines. The latter should include existing WHO guidelines for the production of blood plasma for fractionation, complemented by additional guidelines to promote and support implementation of high-quality systems in blood services, including good manufacturing practices.

18. There is a growing need to strengthen blood systems in developing countries in order to minimize the risk of transfusion-transmitted infections and avoid spread of pathogens through blood products. Greater global collaboration is needed to forecast emerging risks and exchange relevant information in order to ensure patient safety. Improved systems of data collection, traceability and monitoring of adverse events are required for effective haemovigilance and pharmacovigilance. The concern expressed in the draft resolution considered by the Board in May that the increasing mobility of populations contributed to increased risk of transmission of infectious diseases worldwide was rejected by several members of the Board.[1]

19. Improving access to safe, effective and affordable blood products needs implementation of a multifaceted strategy with partners at national, regional and global levels. WHO will continue to lead an international effort that consolidates support from other international organizations, nongovernmental organizations, international professional associations and other relevant agencies.

[1] See document EB125/2009/REC/1, summary record of the first meeting, section 5.

20. The Secretariat will strengthen its work with countries in order to improve blood safety-related data management, including surveillance and reporting, to create sustainable, nationally coordinated blood and plasma programmes, based on voluntary, non-remunerated donations, and to introduce improved methods for screening and processing of blood and plasma donations, quality systems, principles of good manufacturing practices and associated regulation. These activities will contribute to the following public health benefits: (a) reduced wastage of donated blood and plasma; (b) improved safety and quality of blood products; (c) appropriate clinical use of blood products and safe transfusion practices; (d) sustainable and affordable supply of and accessibility to safe blood products; (e) reduced risk of transmission of blood-borne pathogens, both within countries and internationally; (f) improved epidemiological knowledge of infectious diseases, prevention and control of disease transmission, and monitoring the health of blood donors; (g) promotion of healthy life-styles of donor populations and social unity; (h) potential application of quality systems and principles of good manufacturing practices to other medical laboratory disciplines; and (i) representation of developing countries in the international transfusion community and plasma fractionation associations.

21. It will be important to balance the growing complexity of technology and regulatory actions with the needs of patients worldwide. Risk-benefit analysis must be used to ensure that sufficient quantities of the required products are available at a cost that does not prevent all but the wealthy from having access. The strategic goal should remain that of providing safe and effective blood products in an equitable manner.

ACTION BY THE EXECUTIVE BOARD

22. The Executive Board is requested to consider the draft resolution contained in document EB126/19 Add.1 and the financial and administrative implications for the Secretariat contained in document EB126/19 Add.2.

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