World Health Organization

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Availability, safety and quality of blood products

Report by the Secretariat

1. Blood products[1] 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. Blood services throughout the world are facing the daunting challenge of making sufficient supplies of blood products available to meet the needs of patients, while also ensuring the quality and safety of those 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.

2. One of the worst treatment disasters in modern history took place in the 1980s with the widespread transmission through infected blood products of viral pathogens, in particular HIV and hepatitis B and C viruses. Blood-borne transmission of pathogens has highlighted the crucial importance of effective policies, quality systems, and legislative and regulatory frameworks in the collection, processing and supply of blood products such as red cells, platelets and plasma for clinical use, and in the preparation of plasma for fractionation, as a raw material for the manufacturing of plasma-derived medicinal products, such as clotting factor concentrates and immunoglobulins, which are on the WHO Model List of Essential Medicines.[2] Recognizing the high risk of transmission of pathogens through transfusion of contaminated blood products, the Health Assembly, in resolution WHA58.13, urged Member States to promote the development of national blood services based on voluntary non-remunerated donation and to enact effective legislation governing their operation.

3. Since then, developed countries have implemented policies, strategies and procedures to ensure the availability, safety and quality of all products derived from blood, permitting widespread access to a comprehensive range of safe blood products. In particular, regulatory oversight of the quality of blood products has become more stringent. Conversely, comparable levels of availability, safety and quality do not yet exist in most developing countries, which still face serious blood shortages and the fact that the risk associated with transfusion-transmissible infections has not yet been eliminated, particularly in countries where the prevalence and incidence of those infections are high. In recent years, unchecked and unsafe practices in blood and plasma collection have, in some countries, led to

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

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

donors being infected by HIV and other pathogens in epidemic proportions. The absence of quality systems in blood services is a major impediment to ensuring safe blood supplies. 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

4. **Increasing needs, blood shortages and wastage of blood.** The need for safe and quality blood products is universal. Changing population demographics and more advanced surgical and medical procedures have further increased the need for transfusion support. Globally, more than 70 countries have a blood donation rate of less than 1% of the population. WHO estimates that donation by 1% of the population is generally the minimum needed to meet a nation's most basic requirements for blood; the requirements are higher in countries with more advanced health-care systems. Ageing populations and increasingly stringent donor selection criteria are further reducing the pool of eligible donors. Inadequate storage and transportation, blood collection from unsafe and unsuitable donors, and poor blood stock management leads to the loss of over two million blood units every year, further limiting availability.

5. **Wastage of plasma.** The limited availability of blood-derived products in developing countries stems from various different 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 of developing countries is therefore small. Moreover, products made available in this manner would be prohibitively expensive for such countries. Developing countries thus have to create their own sustainable supplies of blood-derived products using blood plasma collected by their own establishments and from their own populations, even if fractionation is done in developed countries. Currently, however, a large percentage of the plasma collected in developing countries is categorized as a waste material and destroyed. This wastage occurs because lack of appropriate technology, controls and Good Manufacturing Practice render the plasma unsuitable for conversion into fractionated medicinal products.

6. **Inappropriate use of blood products.** The issues of sufficiency, availability and access cannot be considered in isolation from use of blood. Data on the use of blood products are limited, but studies suggest that blood products are often overprescribed in both developed and developing countries. Unnecessary transfusions and unsafe transfusion practices at the patient's bedside seriously compromise, respectively, availability and safety; they also expose patients to the risk of serious adverse transfusion reactions and transfusion-transmissible infections. Unnecessary use also seriously affects the availability of blood products for patients who are in need. Comprehensive monitoring and regulation of the whole blood chain – from blood collection to use of blood products – needs to be established.

7. **Risk of transfusion-transmitted diseases.** When rigorous standards for donor selection, donation processing and testing are not applied or fail, blood transfusions and blood products constitute potent vectors for transmission of pathogens. Unfortunately, current systems for blood and plasma donation, processing and testing are inadequate in a vast number of developing countries. In addition, the increasing international mobility of populations and the globalization of the blood industry render even more pressing the need to introduce and strengthen policies and systems for quality assurance and regulations in developing countries in order to minimize these risks and avoid the international spread of infectious diseases through blood products.

8. **Emerging and re-emerging threats.** The risk of wider spread of infection is increasing as a result of changes in habitat, the increasing mobility of populations, conflict and climate change. Pathogens such as West Nile virus, variant Creutzfeldt-Jakob disease agent and Chikungunya virus continue to emerge and may spread rapidly. The presence of known pathogens, such as human T-lymphotropic virus and those causing malaria and Chagas disease, is of increasing concern in regions where these diseases are not endemic. Climate change is expected to result both in the emergence of new diseases, some of which may be capable of transmission through blood, and in changes in the distribution and severity of known diseases such as malaria in areas in which they were not previously endemic. 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 severe acute respiratory syndrome and pandemic influenza, outbreaks of which may result in major disruptions in, and constraints on, blood donation and collection.

9. **Poor quality systems and regulation of blood products in developing countries.** The absence of basic quality systems in blood services is a major impediment in ensuring safe blood supplies. Constraints include lack of national standards, inadequate data and documentation, limited training opportunities and poor quality assessment. Developing countries also recognize the need to regulate blood products and blood safety related to in vitro diagnostic devices. Their situation parallels that experienced by developed countries until the 1990s: before that time, blood establishments were largely unregulated; thereafter, they became subject to international inspection and audit, by both national 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. This led to substantial improvements in all the activities of blood establishments. It can therefore be assumed that blood establishments in developing countries would likewise benefit from the introduction and enforcement of the appropriate independent and transparent quality-assurance regulations and inspection procedures; the lessons learnt and rewards gained are likely to parallel those observed in developed countries.

WHO'S ACTION TO DATE

10. 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 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.

[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.

11. 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.

12. The International Conference on Drug Regulatory Authorities provides regulatory authorities of Member States with a forum to discuss ways to strengthen collaboration. The Conference has been instrumental in guiding WHO and interested stakeholders 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 to develop regulations for the manufacture of blood products. WHO's Blood Regulators Network could foster international consensus on an effective regulatory approach. It is envisaged that the Network will collaborate with the Expert Committee on Biological Standardization in designing and implementing such an approach.

13. 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 collaborative relationships and partnerships with organizations and institutions working for global blood safety. Resolution WHA58.13 established 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

14. 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. 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.

15. The availability of safe blood products must be improved in developing countries. Member States should be alerted to the risk of inadequate regulation of blood products, and should benefit from guidance and technical support in establishing regulatory oversight of blood systems. Work is needed to review national legislative and regulatory frameworks for blood products. Furthermore, national blood services and medicines regulatory agencies need to be established or upgraded. Comparable quality and safety of blood products need to be ensured through global standardization and

implementation of regulatory standards. Strategies should therefore be sought for sharing the expertise and experience already generated in developed countries and for improving access to safe, effective and affordable blood products worldwide.

16. 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 Practice.

17. In view of the increasing international mobility of populations, together with globalization, there is a growing need to strengthen blood systems in developing countries in order to minimize the risk of transfusion-transmitted infections and avoid the international spread of infections through blood products. Greater global collaboration is needed to forecast emerging risks and exchange the 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.

18. 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 which consolidates support from other international organizations, nongovernmental organizations, international professional associations and other relevant agencies.

19. Working with countries to create sustainable blood and plasma programmes with appropriate regulatory systems will contribute to the following public health benefits: (a) optimal use of donated blood and plasma; (b) safer blood products; (c) appropriate clinical use of blood products; (d) sustainable and affordable supply of safe blood products; (e) less transmission of blood-borne pathogens, both within countries and internationally; (f) improved quality and safety of all products from blood services through the implementation of standards and quality systems; (g) improved epidemiological knowledge of infectious diseases, prevention and control of disease transmission, and monitoring the health of blood donors, all of which contribute substantially to national and regional public health programmes; (h) potential application of quality systems and principles of Good Manufacturing Practice to other medical laboratory disciplines; and (i) inclusion of developing countries in the international transfusion community and associated plasma fractionation industry.

20. 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

21. The Executive Board is requested to take note of this report and provide further guidance.

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