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Blood and other medical products of human origin

Report by the Secretariat

1. In response to proposals from some Member States to call for strategic guidance on self-sufficiency in blood and blood products based on voluntary non-remunerated donations and the call at the Sixty-seventh World Health Assembly for the WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation to be applied to medical products of human origin,[1] the Secretariat has produced this report which covers both blood and other medical products of human origin.

MAIN CHALLENGES

2. Medical products of human origin are derived wholly or in part from the human body and intended for clinical application. They include blood and blood products, organs, bone marrow, cord blood, corneas and tissues. Over the years, their type and use have broadened, and many are widely used. Donors and recipients face a wide range of risks, depending on the type of product used. From donation to the follow-up of recipients, health systems face many challenges, and a global consensus is needed on some guiding principles for the donation and use of medical products of human origin, including the promotion of good and harmonized practices. Most of these principles apply to all public health interventions,[2] but have to be adapted to the particularities of medical products of human origin.[3] The main issue is the existence of a human being at the origin of these products, giving rise to high levels of complexity and responsibility for health systems and health-care providers. Launched in April 2013, the WHO initiative for medical products of human origin aims to create a global framework on common principles for the donation and use of all medical products of human origin, which recognizes the specificities of each product.[4] Three principles concern respect for human dignity, availability and safety, and good governance.

3. **Respect for human dignity.** With special attention to the protection of vulnerable groups, the respect for dignity implies that all donations are based on a voluntary and free informed decision, without coercion or undue inducement. The use of financial or disproportionate incentives and the lack of information provided to potential donors put the validity of the decision to donate at risk. Donors of

[1] See document WHA67/2014/REC/3, summary record of the twelfth meeting of Committee A of the Sixty-seventh World Health Assembly, section 9 K.

[2] See Universal Declaration on Bioethics and Human Rights, resolution 36 adopted by the General Conference of UNESCO at its 33rd session, in 2005.

[3] See for example the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin, adopted by the Council of Europe in 2002.

[4] See document A67/40, para 103, noted by the Sixty-seventh World Health Assembly (document WHA67/2014/REC/3, summary record of the twelfth meeting of Committee A, section 9 J and K).

medical products of human origin act for the benefit of others and this act of solidarity and generosity has to be respected. The use of incentives to improve the rate of donation should be avoided when this becomes an undue inducement or coercion. The confidentiality of all personal data must be ensured throughout the process of donation, and the screening of potential donors should be based on scientific evidence.

4. **Availability and safety.** In the context of universal health coverage, equitable access to safe medical products of human origin should be provided, especially in the context of life-saving support. For example, blood and blood products are included in the WHO Model List of Essential Medicines. Health systems have a special responsibility to safeguard the safety and efficiency of the donation, processing, and use of medical products of human origin, and there must be appropriate regulatory oversight. The risk-benefit ratio should be optimized at all stages, from donors to recipients, and donation incentives should not adversely affect the availability and safety of the final products.

5. **Good governance.** Mechanisms of good governance are needed at national and global levels in order to promote transparency; provide public access to information on modalities of the donation and use of medical products of human origin while protecting the confidentiality of personal data; strengthen efficiency, accountability and responsiveness; and maintain the public's trust. National health authorities are responsible for defining clear policies and strategies to ensure that safe and effective products are available to meet clinical needs within the framework of the development of their national health system, which includes a responsibility to promote voluntary donation. Medical products of human origin should be allocated in an equitable way and, when provided, should be safe and effective. Equally, inappropriate use or overuse needs to be controlled and clinical use needs, at all times, to be evidence-based.

PROGRESS MADE

Blood and blood products

6. The universal and timely access to safe blood and blood products,[1] which include blood components for transfusion and plasma-derived medicinal products, and their appropriate use are essential components of good health-care provision. Health authorities are responsible for the quality, safety, availability and equitable distribution of these products. This responsibility encompasses the establishment of an effective national blood system that is integrated into the national health system, protecting the health of blood donors and recipients, and ensuring the safety, sufficiency, security and accessibility of supply. To achieve this, countries will need to implement quality-assurance systems and good manufacturing practices in blood transfusion services, together with the enforcement of regulatory oversight for all blood products and the strengthening of the technical capacity of regulatory authorities and control laboratories. WHO's urgent appeal and actions to make convalescent blood products available as a treatment option for Ebola virus disease are a timely reminder of the urgent need to strengthen blood transfusion services and ensure their proper regulatory oversight, as these are an important component of national and international public health infrastructures.

7. The Health Assembly, through resolutions WHA28.72 and WHA58.13 in particular, urged Member States to promote the development of national blood services based on voluntary non-remunerated donation and to take other actions necessary to protect and promote the health of

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

blood donors and recipients. In resolution WHA63.12 on availability, safety and quality of blood products it urged Member States "to take all necessary steps to establish, implement and support nationally-coordinated, efficiently-managed and sustainable blood and plasma programmes according to the availability of resources, with the aim of achieving self-sufficiency, unless special circumstances preclude it". In this context, self-sufficiency means that the needs of patients for safe blood and blood products, as assessed within the framework of a given national health system, are met in a timely manner and that patients have equitable access to transfusion services and safe blood products. Regional networks provide a useful mechanism to manage intermittent shortages of plasma-derived medicinal products and differential demand for individual products. The European Union, for example, is committed to the principle of "self-sufficiency at the European level".[1]

8. Many countries are still facing challenges in making sufficient supplies of blood and blood products available in a sustainable way, while ensuring their quality and safety. Consequently, many patients who require life-saving transfusion therapy still lack access to safe blood and blood products. Ensuring sufficient supplies of safe blood for transfusion remains a big challenge, in particular in developing countries. According to data reported to WHO in 2011, the median blood donation rate per 1000 population in high-income countries was 36.8 donations, compared with 11.7 donations in middle-income countries and 3.9 donations in low-income countries, indicating the disparity in blood supply across countries.

9. An estimated 23–28 million litres of human plasma are fractionated annually in the world.[2] Large volumes of this plasma used for the manufacturing of plasma-derived medicinal products are collected from compensated or paid donors in plasma collection centres operated by commercial plasma fractionators.[3] On the other hand, large volumes of plasma recovered from whole-blood donations, mainly in low- and middle-income countries, are discarded because of quality concerns or requirements. This loss, estimated to be close to 9.3 million litres per year,[4] reveals the weakness of national regulatory systems, which are often unable to execute the effective regulatory oversight needed to ensure the implementation of quality standards. The discarding of blood represents a lack of consideration to the donor and to the act of solidarity surrounding donation. It is important to increase availability of recovered plasma for fractionation, which can provide significant benefits to national health-care systems, as well as being the key to the long-term safe and secure supply of plasma-derived medicinal products. This requires improved quality systems, including good manufacturing practices and access to plasma fractionation facilities; functioning national regulatory systems are needed to facilitate this. However, the regulatory systems for blood products are not as well-developed as those for medicines in general in most developing countries.

10. The optimal use of blood components and stable plasma derivatives is regarded as both an ethical duty, since these are scarce and precious resources, and an important means for countries to achieve self-sufficiency. Data on the use of blood products are limited, but studies suggest that blood products are often wrongly or over-prescribed in all countries. Unnecessary transfusions expose patients to the risk of serious adverse reactions and transfusion-transmissible infections, and limit the

[1] Council of Europe Committee of Ministers. Recommendation No. R (90)9 of the Committee of Ministers to member states on plasma products and European self-sufficiency (adopted by the Committee of Ministers on 29 March 1990, at the 436th meeting of the Ministers' Deputies).

[2] Burnouf T. Modern plasma fractionation. Transfusion Medicine Review, 2007, 21(2):101–117.

[3] Bertolini J, Goss N, Curling J, eds. Production of plasma proteins for therapeutic use. Hoboken, New Jersey, United States of America: John Wiley & Sons, Inc.; 2013.

[4] Access to blood products, WHO Drug Information, 2013; 27(1).

availability of blood products for patients who are really in need. Strategies to optimize use of blood and blood products include the establishment of transfusion committees in hospitals and the promotion of better clinical decision-making to improve the appropriate use of the products through an evidence-based education programme on patient blood management, and the implementation of haemovigilance systems.

11. Recently WHO has issued interim guidance[1] for national health authorities and blood transfusion services, outlining the steps required to collect convalescent whole blood or plasma from patients who have recovered from Ebola virus disease for transfusion into patients in the early stages of the disease, as an empirical treatment. WHO has also embarked on the urgent strengthening of national blood services in the countries affected by Ebola virus disease.

Human cells, tissue and organs for transplantation

12. Advances in surgery and medicine, such as the development of immunosuppressive medicines, have allowed the successful transplantation of organs, saving innumerable lives around the world. Unfortunately, as with blood products, the critical factor is the severe shortage of organs available for transplants, a scarcity that is the root cause of organ trafficking, with the related risk of exploitation of donors and important safety issues for the recipients.

13. Although kidney transplants save thousands of lives and transform the quality of life of thousands more, many people die or remain on renal replacement therapy because the supply of kidneys falls drastically short of demand. At any one moment, nearly 40 000 patients are waiting for a kidney in western Europe alone, and the number of cadaveric donors remains stable at around 5000 each year for the whole of Europe:[2] in the United States of America the gap between available organs and patients on the waiting list is comparable: more than 110 000 patients on the waiting list and around 8000 cadaveric donors each year.[3] Mortality rates for patients awaiting a heart, liver or lung transplant generally range between 15% and 30%, but rates can be higher for patients awaiting transplants of other organs.

14. The Sixty-third World Health Assembly in resolution WHA63.22 in 2010 endorsed the WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation, which include reinforcement of the principles of human dignity and solidarity, prevention of financial gain in transactions involving human body parts, including organ trafficking and transplant tourism, and the responsibility of Member States to protect the vulnerable and the poor from being exploited and to provide equitable access to safe medical products of human origin.

15. More work on implementing the Guiding Principles still needs to be done as comprehensive national programmes must also include steps to prevent or delay for example end-stage organ failure and blindness in order to reduce the need for transplantation. Educational programmes about organ donation aimed at the general public and in collaboration with the media should actively contribute to prevention, by promoting a healthy lifestyle. Early detection and prevention of illnesses leading to

[1] Use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease as an empirical treatment during outbreaks. Geneva: World Health Organization; 2014 (document WHO/HIS/SDS/2014.8, http://www.who.int/csr/resources/publications/ebola/convalescent-treatment/en/, accessed 7 November 2014).

[2] Global Observatory for Donation and Transplantation. http://www.transplant-observatory.org/Pages/home.aspx (accessed 29 October 2014).

[3] United Network for Organ Sharing. http://www.unos.org/ (accessed 29 October 2014).

end-stage organ failure, such as diabetes, cardiovascular diseases and kidney diseases, are urgently needed within a national framework that includes a regulatory oversight policy. In addition to programmes encouraging deceased donation being integrated into national health systems, strict ethical practices for living donation must exist to ensure donors' safety and the protection of their fundamental rights.

The way forward

16. The Secretariat will continue its work with Member States and the international community to enhance the availability and ensure the quality of medical products of human origin, more specifically:

- Member States and the Secretariat will build a global consensus on, and Member States will ensure the implementation of, guiding principles and standards of good governance for the safe donation and use of medical products of human origin.

- Member States and the Secretariat will further develop WHO's policy on promoting access to life-saving products of human origin (including blood and blood products), and collaborate on strengthening regulatory oversight of these products and on promoting the sharing of best practices in the context of universal health coverage.

- Member States should strengthen accountability through global systems of traceability, surveillance, vigilance and rapid alert, as well as the reporting and sharing of data on clinical outcomes and adverse events/reactions associated with medical products of human origin, and work with the Secretariat towards a global monitoring system.

- Member States and the Secretariat should facilitate the involvement of all relevant stakeholders in policy-making, in particular patients and communities.

- Member States and the Secretariat should collaborate to deal with specific issues related to the particularities of each medical product of human origin, with specific recommendations for each, including emerging therapies in the field of regenerative medicine.

17. Building and implementing a global framework on principles for the donation and use of medical products of human origin require flexibility at country level. Cultural values may need to be taken into account as well domestic laws and regulations that should be progressively harmonized with the agreed global guiding principles.

ACTION BY THE EXECUTIVE BOARD

18. The Board is invited to note this report and to provide guidance on the proposed way forward set out in paragraphs 16 and 17.

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