Towards Self-Sufficiency in Safe Blood and Blood Products based on Voluntary Non-Remunerated Donation

Global Status 2013

World Health Organization

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(Limited Print-Run)

Printed in Italy.

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Acronyms

AFR	WHO African Region
AMR	WHO Region of the Americas
BCT	Blood components for transfusion
BTS	Blood transfusion service
CJD	Creutzfeldt-Jakob disease
EMR	WHO Eastern Mediterranean Region
EUR	WHO European Region
GDBS	Global Database on Blood Safety
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
IFRC	International Federation of Red Cross and Red Crescent Societies
PDMP	Plasma-derived medicinal products
PFF	Plasma for fractionation
S/D plasma	Solvent/detergent treated pooled human plasma
SEAR	WHO South-East Asia Region
TTI	Transfusion-transmissible infection(s)
UNAIDS	Joint United Nations Programme on HIV/AIDS
United Kingdom	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
vCJD	Variant Creutzfeldt-Jakob disease
VNRD	Voluntary non-remunerated donation
WHO	World Health Organization
WPR	WHO Western Pacific Region

1 Context

1.1 Access to safe blood and blood products for universal health coverage

Sound, efficient health systems that provide effective disease prevention and treatment to all people, no matter who they are or where they live, are fundamental to the attainment of the highest possible level of health. Everyone should have access to the health services they need. Currently, there are wide variations in the coverage of essential health services both between and within countries. To address gaps in the coverage and delivery of essential health services, universal health coverage has become a major goal for health reforms in many countries and is also a priority objective of the World Health Organization (WHO). Universal health coverage is defined as ensuring that all people have access to needed health promotion, preventive, curative and rehabilitative health services, of sufficient quality to be effective, while also ensuring that people do not suffer financial hardship when paying for these services (*1*).

Access to sufficient, secure supplies of safe blood and blood products[1] provided within a national blood system is a vital component in achieving universal health coverage. It is the responsibility of every government to provide effective leadership and governance in developing a national blood system that is fully integrated into the health-care system, consisting of all the organizations, institutions, and financial and human resources whose primary purpose is to meet the transfusion needs of all patients within the country.

As therapeutic substances of human origin which can be obtained only from human donors, blood and blood products are a precious national resource that will remain limited by nature. Governments are accountable for the establishment of effective national blood systems that can ensure the safety, sufficiency, security and accessibility of safe blood and blood products. The management of this national resource requires a long-term perspective and systematic approach aimed at ensuring the safety, continuity, sustainability and security of the supply, and a strong foundation provided by an adequate number of regular, voluntary, non-remunerated blood donors as the most robust and safe blood systems globally are based on voluntary non-remunerated donation (VNRD).2 Furthermore, in their stewardship role of managing national supplies of donated blood and the blood products derived from it, governments are also responsible for protecting the health of blood donors and recipients. At the same time,

[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] Voluntary non-remunerated donation in this context includes the donation of blood, plasma and cellular blood components.

government are responsible for implementing measures that will improve the general health of the population – thereby reducing the demand for blood and blood products – and the appropriate use of such products.

1.2 WHO strategy for blood safety and availability

The risk of transmission of serious infections, including HIV and hepatitis, through unsafe blood and chronic blood shortages brought global attention to the importance of blood safety and availability. With the goal of ensuring universal access to safe blood and blood products, WHO has been at the forefront of the movement to improve blood safety and availability, and recommends the following integrated strategy for blood safety and availability to its Member States.

1 Establishment of a national blood system with well-organized and coordinated blood transfusion services, effective evidence-based and ethical national blood policies with the goal of achieving self-sufficiency, and legislation and regulation, that can provide sufficient and timely supplies of safe blood and blood products to meet the transfusion needs of all patients.

2 Collection of blood, plasma and other blood components from low-risk, regular, voluntary-non-remunerated donors through the strengthening of systems for VNRD, the phasing out of family/replacement donation, the elimination of paid donation, and effective donor management, including care and counselling.

3 Quality-assured screening of all donated blood for transfusion-transmissible infections (TTI), including HIV, hepatitis B, hepatitis C and syphilis, confirmatory testing of the results of all donors screen-reactive for infection markers, blood grouping and compatibility testing, and systems for processing blood into blood products (blood components for transfusion and plasma derived-medicinal products), as appropriate, to meet health care needs.

4 Rational use of blood and blood products to reduce unnecessary transfusions and minimize the risks associated with transfusion, the use of alternatives to transfusion, where possible, and safe and good clinical transfusion practices, including patient blood management.

5 Step-wise implementation of effective quality systems, including quality management, standards, good manufacturing practices, documentation, training of all staff and quality assessment.

This strategy for blood safety and availability has evolved out of successive resolutions adopted by the World Health Assembly, WHO Executive Board and WHO Regional Committees, as supreme decision-making bodies for WHO (*2*). In 2010, the Sixty-Third World Health Assembly adopted resolution WHA63.12 "Availability, safety and quality of blood products" (*3*) which recognizes that achieving self-sufficiency in the supply of safe blood and blood products based on voluntary, non-remunerated blood donation and the security of that supply are important national goals to prevent blood shortages and meet the transfusion requirements of the patient population.

This document *Towards Self-Sufficiency in Safe Blood and Blood Products based on Voluntary Non-Remunerated Donation: Global Status 2013* provides an overview of

the current status of the global supply of blood components for transfusion (BCT) and plasma-derived medicinal products (PDMP). Initiatives by international organizations are described and country examples are also provided to illustrate different strategies and mechanisms for working towards self-sufficiency based on VNRD. The primary source of information for this document is the data reported by 165 countries to the WHO Global Database on Blood Safety (GDBS) for the year 2011. To give a more complete overview of the global situation, GDBS data for the year 2010 were used from 14 countries, where 2011 data were not available.

1.3 Self-sufficiency in safe blood and blood products based on VNRD

The development of national blood systems around the world has gone through successive evolutionary phases over a period of time. The main factors driving these changes have been the widespread transmission of serious infections in the 1980s through unsafe blood, particularly HIV and hepatitis, and health system reforms and developments in technologies. National blood systems in general follow a stepwise progression, based on three recognizable developmental stages: the first stage is the provision of whole blood for patients requiring transfusion; the second stage is the provision of different blood components for the management of patients, also known as blood component therapy; this is followed by the third stage when, in addition to the blood components for transfusion, national blood systems are also able to provide patients with plasma-derived medicinal products (PDMP) obtained from plasma collected within the country through plasma fractionation either within or outside the country, as currently seen in many developed blood systems.

Factors such as the stage of development of a country's health system, the formulation of policies and standards, the implementation of legislative and regulatory frameworks and quality systems, the availability of human resources, infrastructure and financial resources influence the rate of development of a national blood system. The timelines for achieving self-sufficiency vary and cannot be set or standardized at a global level as each country has different health care priorities related to the level of development of its health system. It is therefore important that countries explore different mechanisms and options to work towards self-sufficiency in safe blood and blood products based on VNRD.

With the adoption of World Health Assembly resolution WHA63.12 "Availability, safety and quality of blood products" (*3*) in 2010, working towards self-sufficiency in safe blood and blood products based on voluntary non-remunerated donation is a policy direction already agreed upon by WHO Member States. However, self-sufficiency is not yet a reality in many countries with inadequate supplies of blood and blood products from voluntary non-remunerated donors, and dependence on family/replacement donation systems and payment to blood and plasma donors to fill the gaps between supply and demand. The increasing global demands for blood and blood products, the complex nature of systems to supply these products, the inability of many national health systems to meet these urgent needs and the impact of globalization have also resulted in a rapid expansion of international commercial activities in relation to the provision of blood and blood products, as shown by increasing global markets in commercial plasma collection.

Definition

Many countries and international organizations have included national self-sufficiency based on VNRD as a policy direction since the adoption of World Health Assembly resolution WHA28.72 "Utilization and supply of human blood and blood products" (*4*) in 1975. The term "self-sufficiency" in relation to the blood supply has been subjected to various interpretations and there have been several attempts to define the concept (*5,6*). Taking these into account, the following definition of self-sufficiency in safe blood and blood products based on VNRD was developed during the "WHO Expert consultation on achieving self-sufficiency in safe blood and blood products, based on VNRD" held in 2011.

> Self-sufficiency in safe blood and blood products based on VNRD is defined as the national needs of patients for safe blood and blood products, as assessed within the framework of the national health system, are met in a timely manner, that patients have equitable access to transfusion services and blood products, and that these products are obtained from VNRD of national, and where needed, of regional origin, such as from neighbouring countries (*7*).

This definition identifies six blood products that will most likely form the drivers for the number of donations of blood, plasma and cellular blood components needed in each country. The need for each of these blood product drivers usually matches the stepwise progression in blood system strengthening within the national health system.

1 Whole blood and red blood cells, either recovered from whole blood or collected by apheresis.

2 Platelets, either recovered from whole blood or collected by apheresis.

3 Plasma for transfusion, either recovered from whole blood or collected by apheresis and prepared by any production method.

4 Plasma-derived coagulation factor VIII prepared by any production method.

5 Polyvalent human (H) immunoglobulin (intravenous immunoglobulin or subcutaneous immunoglobulin).

6 Human albumin solutions for transfusion.

Concept of "self"

Every country needs to meet its requirements for safe blood and blood products and ensure that blood supplies are free from HIV, hepatitis viruses and other serious infections that can be transmitted through unsafe transfusion, and that these supplies are sufficient to meet the health-care needs of its patient population. Blood and blood products are special in nature, being of human origin and donated blood (and other blood components) is a precious national resource. The concept of "self" in the definition is to be interpreted that each governments is responsible and accountable for meeting the need for a safe and sufficient supply of blood and blood products from blood, plasma and other blood components donated by its own population.

Working towards self-sufficiency is also rooted in the ethical principle of justice and the right to health care; it requires governments to recognize all requirements for transfusion

(both blood components for transfusion and plasma-derived medicinal products) as important and that all patients requiring transfusion have a right to equitable access to safe blood and blood products, when needed, without distinction of race, religion, political belief, economic and social status and geographical situation. Similarly, it requires that the responsibility for blood donation does not fall disproportionately on a particular group of population but is shared by all members of the population.

The concept of self-sufficiency also includes exploring and putting in place mechanisms of cooperation and collaboration with neighbouring countries at regional/international levels for regional sufficiency in safe blood and blood products. Large volumes of plasma recovered from whole blood donations based on VNRD, mainly in low- and middle-income countries, are currently not used and are discarded due to concerns that quality requirements are not being met for plasma for fractionation for the manufacture of PDMP. Regional cooperative mechanisms among governments may support improvements in quality systems and the establishment of facilities for small-scale plasma fractionation for regional self-sufficiency in PDMP, starting with regionally-recovered and source plasma from VNRD. Improving the supply of safe blood and blood products through self-sufficiency does not necessarily exclude the importation of required blood products to meet patient needs.

Self-sufficiency and voluntary non-remunerated donation

The supply of blood from voluntary non-remunerated donors originated during World War II as an expression of the civilian population's solidarity and support for the fight for a free society. After the war, VNRD continued to be one of the basic principles for the development of civilian blood services in most of the industrialized countries. In the 1970s, many national blood systems around the world were influenced by the work of Titmuss (*8*) in comparing voluntary blood donation systems with systems in which the blood supply is remunerated on a regular market. Titmuss shows that a voluntary donation system contributes to blood safety and a stable, sufficient blood supply and at the same time promotes social cohesion. He contends that a commercial supply of blood and blood products from paid donors discourages altruistic, voluntary donation, hence leading to supply shortfalls – the so-called "crowding out" effect[3] – and increasing costs. Payment for blood is inherently unsafe because financial incentives tend to encourage people in populations at high-risk for transfusion-transmissible infections to lie about their status to obtain money. Paying donors invariably draws the most economically challenged members of a community into an exploitative relationship because of economic necessity as opposed to a gift-based negotiation with the blood collection agency (*9*). Titmuss raises the concern that "If blood is considered in theory, in law, and is treated in practice as a trading commodity then ultimately human hearts, kidneys, eyes and other organs of the body may also come to be treated as commodities to be bought and sold in the marketplace". Since then, altruism has been promulgated as the ethical basis for blood donation.

[3] A crowding-out effect would mean that donation rates actually decrease after the introduction of payment. This would be due to the fact that altruistic donors feel cheated by payment for donation, or feel their altruism is no longer needed, and turn away from donating.

Meeting patients' needs: the paradigm of need, demand and use

The need for safe blood and blood products is growing every year around the world. This is due to a variety of factors including changes in population demographics and disease patterns, advances in the diagnostic, medical and surgical fields, and developments in health technologies leading to improved treatment options for many conditions in which blood and blood products are required to save patients' lives, support their recovery or maintain their health.

Meeting patients' needs remains the principal aim in working towards self-sufficiency for safe blood and blood products based on VNRD. It is therefore crucial that national requirements for blood and blood products are assessed appropriately by accountable health-care systems. Each country needs to establish a National Transfusion Committee, with relevant clinical expertise in disciplines such as transfusion medicine, haematology, surgery, anaesthesiology, paediatrics, obstetrics and gynaecology to advise the government on trends in demand and clinical use, including shortages and unmet patient needs, and on priority measures to ensure timely and sufficient supplies of blood and blood products. The committee should also address the safe and rational clinical use of blood and blood products including the use of transfusion alternatives, patient blood management and cost-effectiveness. It is important for this committee to avoid any conflicts of interest and to be independent and responsible for proper advice at public health level, based on best local clinical practice.

WHO has developed the following definitions to explain the paradigms of need, demand and use of blood.

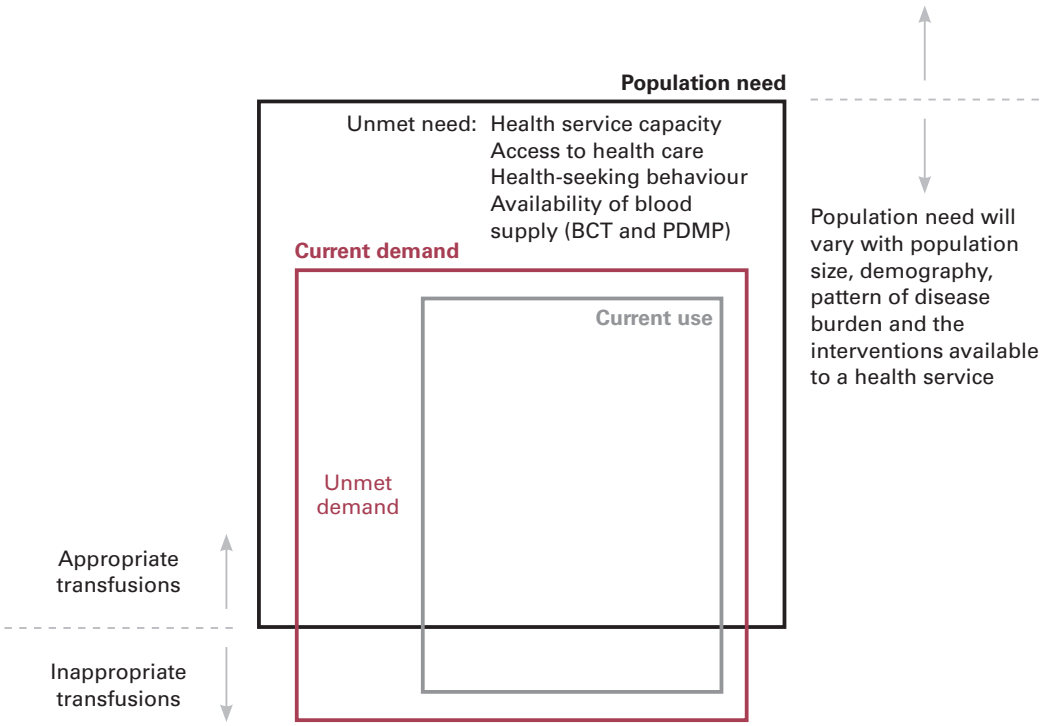
Need: An estimation of the amount of blood needed to meet the transfusion requirements of the patient population according to current policies, clinical guidelines and best practices.

Demand: The amount of blood that would be transfused if all prescriptions for blood were met. Demand may reflect appropriate or inappropriate indications and practices.

Use: The actual amount of blood currently transfused; use may be appropriate or inappropriate.

These definitions and Figure 1.1 (*10*) below summarize current concepts on the need, demand and use of blood. Many factors influence the requirements for blood to meet the health-care needs of a population, as with other treatment modalities. These include income and level and rate of development of the health care system as well as accessibility to health-care facilities by the public. The need, demand and use of blood in a country could be affected by geography, population migration and epidemiology of diseases for which blood is needed.

Figure 1.1: The paradigm of need, demand and use of blood



Assessing the need and demand for blood

Estimations of blood requirements can be based on 1) patterns of usage; 2) the capacity of the health-care system, such as the number of hospital beds plus average usage per bed; and/or 3) population size and average number of units of blood donated per person annually. Method 1 is the most practical where there is a constant supply of blood (or PDMP) and historical data are readily available. Methods 2 and 3 can be useful where no blood use data are available or when there are significant changes in population and/or health-care system capacity.

There are major differences in the estimation of blood requirements in countries which currently have an adequate blood supply compared to those which do not. In countries with mature and developed blood transfusion services, current requirements for blood are largely met (current demand and population need are closely matched) and forecasting future requirements involves making adjustments to that baseline figure. Blood transfusion services in developed countries use detailed historical blood supply data to predict incremental increases in demand (time series analysis). This "top-down" approach may be complemented by the "bottom-up" approach where facilities are canvassed for their views on changes in blood use. A further approach to estimating current demand, as defined above, is to use blood bank data on blood requests. A potential disadvantage of this approach is that the number of blood transfusion requests received by blood banks (and the amount of blood requested) may not be an accurate reflection of true demand or need, particularly where the blood supply has actually been, or has been perceived to be, insufficient.

Demographic change is likely to be one of the main drivers of long-term increases in blood requirements in developed countries (*11,12*). This can be modelled by describing current blood use by age and applying this to predictions of future population size and structure. The development of new medical interventions may also impact on future blood requirements in developing countries but these are harder to predict and may in fact serve to reduce the need for blood transfusion as well as potentially increase it.

Clinical use of blood and blood products

The issues of sufficiency, availability and access cannot be considered in isolation from the clinical use of blood. Understanding current patterns of clinical use of blood is important for blood transfusion services for demand planning.

The clinical use of blood for transfusion is characterized by variations in practice, which is well described in many journals. One of the first and most frequently quoted studies on variations in the use of blood was reported by the Sanguis Study Group in 1994 (*13*). The researchers evaluated the use of blood components for elective surgery in multiple European hospitals and reported large differences between hospitals and clinical teams in the use of red cell transfusion for the same surgical procedures, with no clear explanation based on patient and clinical factors such as age, preoperative haemoglobin or perioperative blood loss. While a degree of variation in practice is to be expected in all health-care systems, evidence of variations in practice outside an explicit set of criteria or evidence-based guidelines requires specific scrutiny.

National data on the use of blood and blood products are limited; however, studies suggest that these products are often inappropriately used in both developed and developing countries. Measures need to be taken to monitor blood demand and clinical use in order to optimize use and reduce unnecessary transfusions, make realistic forecasts of needs and efficiently manage available supplies of blood and blood products to meet patients' needs.

There is concern in some countries about the future ageing of recipient and donor populations; however, the implementation of programmes for the optimal clinical use of blood have greatly diminished inappropriate blood transfusions and the demand for blood components, mainly red blood cells, in several European Union countries (*14*). The strategies employed include rational transfusion triggers and indications, improved patient blood management and the use of surgical and anaesthetic techniques with less bleeding while at the same time reducing the use of blood.

1.4 Voluntary non-remunerated, family/replacement and paid donation systems

Voluntary non-remunerated donation is defined as that a person gives blood, plasma or cellular components of his/her own free will and receives no payment for it, either in the form of cash, or in kind which could be considered a substitute for money. This would include time off work other than that reasonably needed for the donation and travel. Small tokens, refreshments and reimbursements of direct travel costs are compatible with voluntary non-remunerated donation.

This definition has already been endorsed by the World Health Organization, the Council of Europe, the International Federation of Red Cross and Red Crescent Societies, the International Society of Blood Transfusion and the International Federation of Blood Donor Organizations.

Voluntary non-remunerated donation has been shown to be the cornerstone of a safe and sufficient blood supply and is the first line of defence against the transmission of infectious diseases through transfusion. Informed and regular, voluntary, non-remunerated blood donors from low-risk populations have been demonstrated to be at lower risks of HIV and other transfusion-transmissible infections than paid and family/replacement donors.

A number of studies have reported a significantly lower prevalence of transfusion-transmissible infections among voluntary non-remunerated donors than other types of donors. It has been observed that establishing systems to increase VNRD not only improves the safety but also the supply of blood (*9,15–17*). Lessons learned from the transmission of infections including HIV, hepatitis B and C, syphilis, variant Creutzfeldt–Jakob disease and West Nile virus through blood and PDMP have led to major blood system reforms in many countries to secure national blood supplies through voluntary, non-remunerated donation and self-sufficiency in meeting national blood needs (*18–26*).

Family/replacement donation is defined as a blood donation intended to replace or directly contribute to a transfusion needed for a relative or friend. In this situation, without the "replacement" of donations by the patient's family or friend, the treatment or intervention needed for a given patient cannot take place. In many countries, particularly in Asia and Africa, family/replacement systems of blood donation evolved when blood banks started developing as part of hospitals and national blood systems had not yet been established.

While it has been recognized that the most robust and safe blood systems are based on VNRD, it is a reality that family/replacement donation is still practised in many countries and regions in order to meet clinical needs that cannot be fully met by VNRD. The weakness of family/replacement donation is that it puts the responsibility for the provision of blood on individuals rather than on the national health system, and therefore may lead to coercion and hidden payment which often cause undue risks and harm to the donors. Some studies report that blood collected from family/replacement donors poses higher risks of the transmission of infections to recipients than the blood given by VNRD (*27,28*).

As health systems in developing countries are strengthened and more blood and blood products are needed, family/replacement donation systems will be unable to provide safe, sufficient and sustainable national blood supplies, employing both component preparation and apheresis donations, to ensure equitable access for all patients. Family/replacement donation will inevitably act as a barrier to enabling national blood systems to develop appropriately alongside countries' overall health systems (*7*). Efforts to convert suitable family/replacement donors to voluntary non-remunerated donors will contribute to a more reliable and safe national blood supply in the long term.

Paid donation is defined as monetary payment for a donation of blood, plasma or other blood components. Monetary payment includes cash, in any amount, or items

that are readily convertible to cash, regardless of where payment comes from, such as the blood centre or the sponsoring organization (*29*). Paying people to give blood or blood components undermines the principle of voluntary non-remunerated donation. Where systems of paid and voluntary donation co-exist, people who might otherwise donate voluntarily may opt to receive payment for their blood, thus weakening the voluntary blood donor programme (*30,31*). Paying some people to donate blood while others donate on a voluntary basis has been shown to crowd out altruistic donors (*32*). Sufficient safe donations and sustainable supply, availability and access to blood and blood products based on VNRD may be compromised through the presence of parallel systems of paid donation (*7*).

The prevention of the commercialization of donation and exploitation of donors are important ethical principles on which a national blood system should be based (*7*). Payment for the donation of blood not only threatens blood safety, it also erodes community solidarity and social cohesion which result through the act of voluntary non-remunerated donation. By providing under-privileged populations in need of money with financial incentives to donate, the commercial collection of blood, plasma and cellular blood components may exploit the poor and vulnerable, which may leads to undue risks and harm to these donors. The Oviedo Convention on Human Rights and Biomedicine of 1997 explicitly prohibits any financial gain from the human body and its parts (*33*). The right to equal opportunity in access to blood and blood products of uniform and high quality based on the patients' needs is rooted in social justice and the social right to health care.

The "for-profit" plasma industry uses financial incentives to procure source material and evidence, despite the opacity, demonstrates that it targets a vulnerable subset of the population, often locating plasma collection centres in economically disadvantaged areas (*34*). Advocates of the use of paid plasma donations (source plasma) for PDMP in parallel with the use of VNRD for blood components for transfusion, in general prefer the term "compensated donation" over "paid donation" (*35,36*). According to the requirements of the United States Food and Drugs Administration, such donations would be labelled as "paid donations" (*37*).

There is a lack of access to data on the prevalence of transfusion-transmissible infections in first-time plasma sellers. However, the United States General Accounting Office Testimony "Blood safety: enhancing safeguards would strengthen the nation's blood supply" in 1997 (*38*) showed that test-positive rates for commercial plasma donors were substantially higher than those of voluntary whole blood donors, ranging from about two to 20 times higher on the different tests. The report also noted that monetary incentives such as those offered by commercial plasma-collection centres may be tantalizing to some of those who are known to be at risk for infectious diseases. As was shown by Volkow et al (*39*) in two Mexican-United States border cities, injection drug users hardly donated in Mexico where payment for donations is banned, but they cross-border to the United States where payment is allowed, while denying their risk behaviour.

1.5 Evolution of WHO policy on self-sufficiency in safe blood and blood products based on VNRD

Utilization and Supply of Human Blood and Blood Products, WHA28.72 (1975)

Historically, the industrial production of plasma-derived products expanded exponentially from the mid-1960s onwards and, by the 1970s, an international blood market had developed with a number of companies engaging in large-scale industrial production of plasma-derived medicinal products. A huge number of plasma donations were needed to manufacture PDMP, and such companies were prepared to pay individuals for their plasma in order to ensure a sufficient supply (*40,41*).

At around the same time in the early 1970s, WHO started to receive reports from the League of Red Cross Societies and members of WHO Expert Advisory Panels on the extent of activities of commercial firms in obtaining blood or plasma from paid donors in developing countries in order to produce blood derivatives for sale in their own countries or for export. It appeared that the practice started in South and Central America and was spreading to Africa and Asia with a risk that it could lead to possible dangers to the health of donors and transfusion recipients. WHO later confirmed the existence of these activities in five countries, noting its concerns that they were deleterious to blood donors and recipients as well as undermining efforts by countries to develop blood transfusion services based on VNRD (*42*).

These concerns led to the adoption by the World Health Assembly of resolution WHA28.72 on "Utilization and supply of human blood and blood products" in 1975 urging Member States to promote the development of national blood services based on voluntary non-remunerated donation and to enact effective legislation governing their operation (*4,43*). Recognizing the increasing use of blood and blood products, the resolution noted the extensive and increasing activities of private firms in trying to establish commercial blood collection and plasmapheresis projects in developing countries and expressed serious concern that such activities may interfere with efforts to establish efficient national blood transfusion services based on voluntary non-remunerated donation. It also highlighted the higher risk of transmitting diseases when blood products have been obtained from paid rather than voluntary donors and the harmful consequences to the health of donors of too frequent donations, one of the causes being remuneration.

This World Health Assembly resolution is often referred to as the defining resolution on self-sufficiency and voluntary non-remunerated donation and is still pertinent to this day. The availability of safe blood and blood products is integral to the WHO plan to accelerate the prevention of HIV infection and to the achievement of the health-related Millennium Development Goals to reduce child mortality, improve maternal health, combat HIV and other infections (*51,52*). Global blood safety and availability (which includes timely access and the rational use of safe, secure, cost-effective, affordable, sustainable, adequate supplies of quality blood and blood products for all patients requiring transfusion) is one of the strategic areas of the work of the WHO.

Blood Safety: Proposal to establish World Blood Donor Day, WHA58.13 (2005)

In 2005, the Fifty-Eighth World Health Assembly adopted resolution WHA58.13 to establish World Blood Donor Day (*53*) in response to the ongoing chronic shortage of safe blood and blood products, particularly in low- and medium-income countries. This resolution recognized voluntary non-remunerated donation as the cornerstone of a safe and adequate national blood supply and called for the introduction of legislation to eliminate paid blood donation (except in limited circumstances of medical necessity and in such cases to require informed assent of the transfusion recipient), and agreed to the establishment of an annual World Blood Donor Day (WBDD), to be celebrated on 14 June each year.

This resolution pulled together much of the earlier guidance and addressed most aspects of a national blood system. It laid out the fundamentals of a well-organized, nationally-coordinated and sustainable blood programme, including government commitment and support, a national blood policy, legislative framework and national blood plan, quality management systems, organizational management, suitable infrastructure and adequate resources. The resolution highlighted the importance of equitable access to blood and blood products, voluntary non-remunerated blood donors from low-risk populations, appropriate testing and processing of all donated blood and blood products and the appropriate clinical use of blood and blood products while urging Member States to support the full implementation of national blood programmes with appropriate regulatory systems.

The Melbourne Declaration, 2009

Following the establishment of World Blood Donor Day as an annual event, a WHO Global Consultation (*54*) was held in Melbourne, Australia, in 2009 to review barriers to achieving a safe global blood supply based on VNRD and identifying strategies to overcome them. This resulted in the development of the "Melbourne Declaration on 100% voluntary non-remunerated donation of blood and blood components" (*46*). This declaration was a call for action to all governments to achieve 100% voluntary non-remunerated donation by 2020 as the cornerstone of their blood policies, in accordance with World Health Assembly Resolutions WHA28.72 and WHA58.13. It also called on them to appreciate and protect all voluntary non-remunerated blood donors and recommended the development of national strategies for a stepwise progression from whole blood to labile components to ensuring that all recovered plasma is used for fractionation thereby fully utilizing every voluntary non-remunerated blood donation. The Declaration reaffirmed the achievement of self-sufficiency in blood and blood products based on VNRD as the important national policy direction for ensuring a safe, secure and sufficient supply of blood and blood products.

Availability, Safety and Quality of Blood Products, WHA63.12 (2010)

In 2010, the Sixty-Third World Health Assembly deliberated on challenges to the availability, safety and quality of blood products (*55*) and adopted resolution WHA63.12 (*3*) which urges Member States "to take all the 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".

WHA63.12 addresses the management of plasma programmes and plasma-derived medicinal products as well as blood components for transfusion, noting that assuring the suitability of plasma for fractionation requires the establishment of a nationally-coordinated and sustainable plasma programme within a properly organized, legally established and regulated national blood programme. It recognizes that, as the capacity to collect plasma is limited and would not suffice to produce sufficient PDMP to cover global needs, it is essential that all countries have local capacity to collect plasma of acceptable quality and safety from voluntary and unpaid donations in order to meet their needs. It also notes that fractionation should be set up as close to the source as possible, and that, where national plasma fractionation capacities are lacking, there should be an option for supply of fractionation capacity in other countries, ensuring that the supply of plasma-derived medicinal products can be made available to meet local needs in the country of the plasma supplier.

The resolution also raises a number of related issues and challenges in improving access to essential blood products for patients in developing countries, the lack of quality systems that make plasma unacceptable for fractionation with resultant wastage in a number of countries, the increasing movement of blood products across boundaries, and the excessive and unnecessary use of transfusions and PDMP, unsafe transfusion practices and errors that may seriously compromise patient safety.

WHO Expert Consensus Statement on Self-Sufficiency, 2011

Recognizing that self-sufficiency is not yet a reality in many countries, WHO convened an "Expert Consultation on Achieving Self-sufficiency in Safe Blood and Blood Products based on VNRBD" in 2011 in Geneva, Switzerland. The consultation addressed the urgent need to establish strategies and mechanisms for achieving self-sufficiency in safe blood and blood products, based on VNRD, which includes blood components for transfusion as well as plasma-derived medicinal products. Information on the current situation, and country perspectives and experiences were shared. Factors influencing the global implementation of self-sufficiency, including safety, ethics, security and sustainability of supply, trade and its potential impact on public health, availability and access for patients, were analyzed to define strategies and mechanisms and provide practical guidance on achieving self-sufficiency.

The consultation concluded with the development of an "Expert Consensus Statement" (*7*) outlining the rationale and definition of self-sufficiency in safe blood and blood products based on VNRD and made recommendations to national health authorities and WHO. The recommendations to WHO included the provision of policy guidance and technical support to countries in establishing and implementing nationally-coordinated, efficiently-managed and sustainable blood and plasma programmes to move towards self-sufficiency in safe blood and blood products; the development of a report on the global status of self-sufficiency in safe blood and blood products based on VNRD, and the establishment of global governance mechanisms to support the implementation of self-sufficiency based on VNRD.

2 Global supply of blood and blood products: current status

The objective of this chapter is to provide an overview of the current status and trends in blood supply, safety, sufficiency and usage globally. The chapter is primarily based on data for the year 2011 which were reported by 165 countries to the WHO Global Database on Blood Safety. To give a more complete overview of the global situation, data for the year 2010 have been used from 12 countries from which 2011 data are not available. These 177 countries account for a total population of 6.8 billion, representing 98.6% of the global population.

The WHO Global Database on Blood Safety was established in 1998 to provide data about the availability, safety and accessibility of blood for transfusion. The main objective of the survey is to collect and analyse data on national blood systems from all countries as the basis for effective action to improve access to safe blood and blood products and transfusion practices globally. The WHO Blood Transfusion Safety programme has undertaken surveys on the safety and availability of blood in Member States since 1998. GDBS data are collected using a standardized tool which is sent to national health authorities for completion. Web-based tools were used for 2011 data collection.

Data submitted by national health authorities have not been independently verified. While many countries report comprehensive national data on blood availability and safety, others provide limited information on the activities of a subset of blood centres. Efforts have been made to validate GDBS data by comparing them with data available from other published sources (see Annex 1). Where GDBS data are available from a relatively small number of countries only and no similar data are available in other published literature, caution is needed to generalize the findings to other countries.

2.1 Collection and supply of blood components for transfusion

Blood donations

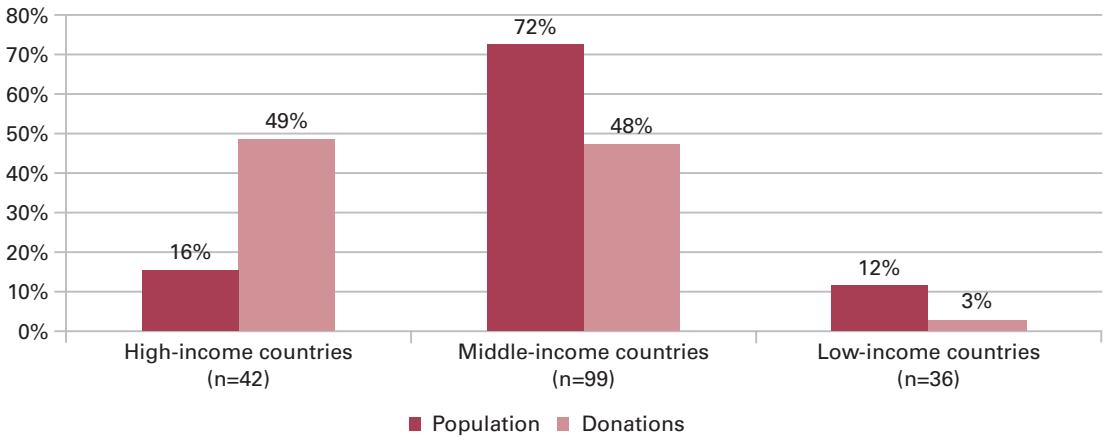
A total of 177 countries provided data for 2011[4] to the WHO Global Database on Blood Safety, reporting a total collection of 107.8 million blood donations: 96.4 million whole blood donations and 11.4 million apheresis donations. The total number of whole blood donations represents an increase of around 20% on the 80.7 million whole blood donations estimated to have been collected in 2004. These donations were collected from all types of blood donor (voluntary non-remunerated, family/replacement and paid).

The collection of these blood donations needs to be interpreted in the context of regional and country populations. Almost 50% of the total 107.8 million whole blood and apheresis donations were collected in high-income countries, home to about 16% of the world's population (Figure 2.1). In contrast, middle-income countries with 72% of the

[4] Includes 2010 data from 12 countries which did not report data for 2011.

world's population collected only 48% of the total donations and low-income countries with 12% of the global population collected 3% of the total donations.

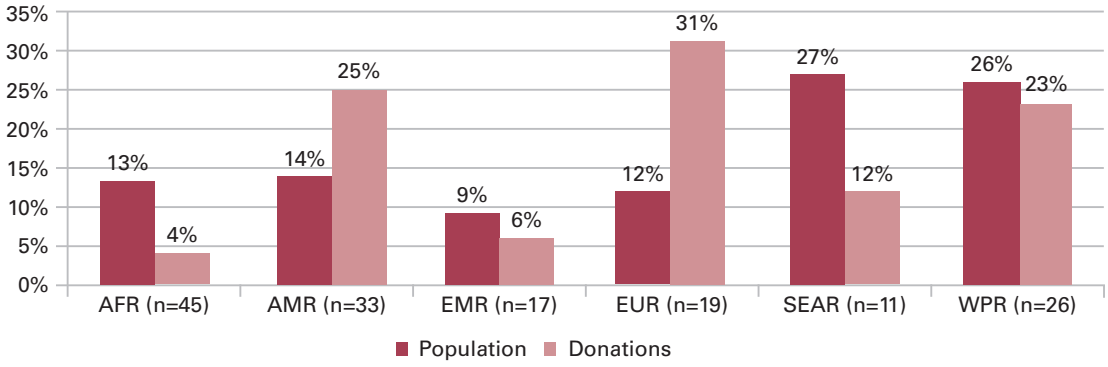
Figure 2.1: Global distribution of population and blood donations, 2011



Ten countries accounted for around 60% of global blood collections: (in descending order) United States of America, China, India, Germany, Japan, Brazil, Italy, France, Indonesia and the Russian Federation.

Analysed by region, it can be seen that 45 countries in the WHO African Region collected a total of about four million blood donations; these accounted for only about 4% of global donations, although these countries contain around 13% of the global population (Figure 2.2). The 11 countries in the South-East Asia Region reported the collection of 12% of global blood donations, although these countries represent 27% of the global population. In the European Region, reported donations represent 31% of the global total, although the region is inhabited by only 12% of the global population.

Figure 2.2: Regional distribution of population and blood donations, by WHO Region, 2011



AFR: African Region
AMR: Region of the Americas
EMR: Eastern Mediterranean Region
EUR: European Region
SEAR: South-East Asia Region
WPR: Western Pacific Region

There are currently no global standards for the estimation of national requirements for blood and blood products. The need for blood and blood products is dynamic and is dependent on many factors related to health service coverage, the level of development

of the health-care system and hospital blood usage. Nevertheless, the whole blood donation rate per 1000 population can be considered as a general indicator for the availability of blood for transfusion in a country and as an indicator of comparability in countries at similar levels of economic and social development. The lowest donation rates are found in low- and middle-income countries. In 2011, the donation rate (median) was 39.2 donations/1000 population (range 7.1–62.4) in high-income countries, 12.6 (range 1.5–35.8) in middle-income countries, and 4.0 (range 0.6–7.6) in low-income countries.

Seventy-seven countries reported collecting no more than ten whole blood donations per 1000 population in 2011 (Figure 2.3). Of these, 39 countries are in the WHO African Region, seven in the Region of the Americas, eight in the Eastern Mediterranean Region, six in the European Region, seven in the South-East Asia Region and ten in the Western Pacific Region (Figure 2.4). All are low- or middle-income countries (except Equatorial Guinea and Saint Kitts and Nevis).

Figure 2.3: Whole blood donations per 1000 population, 2011

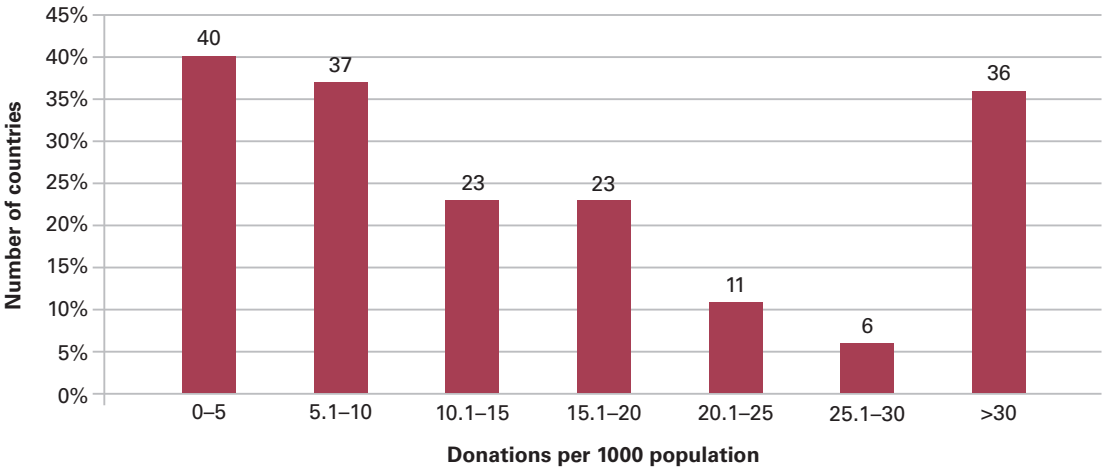
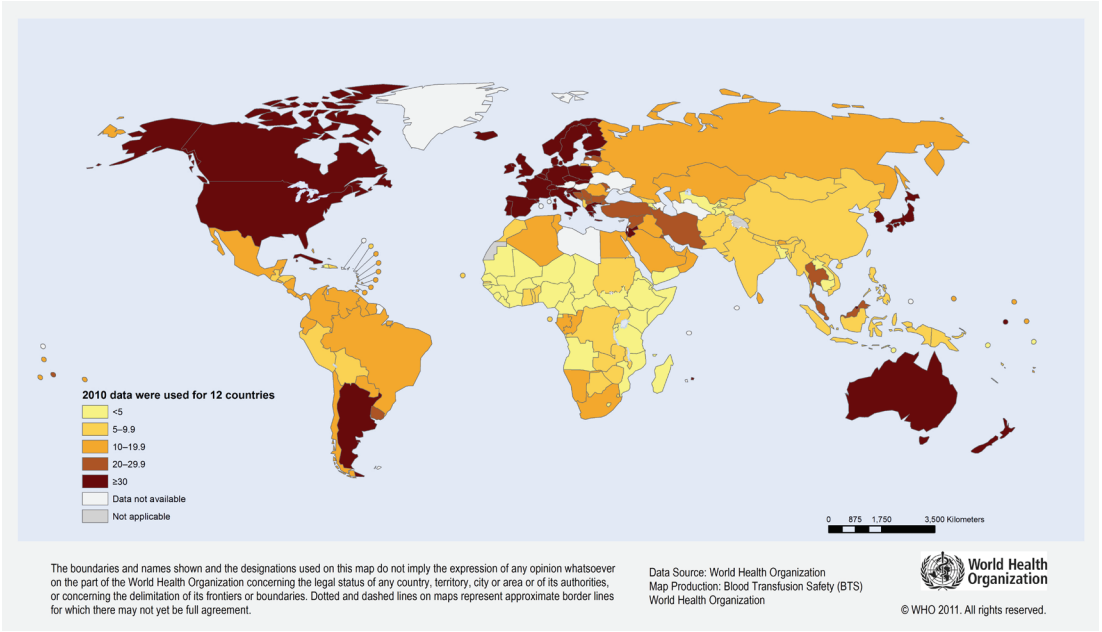


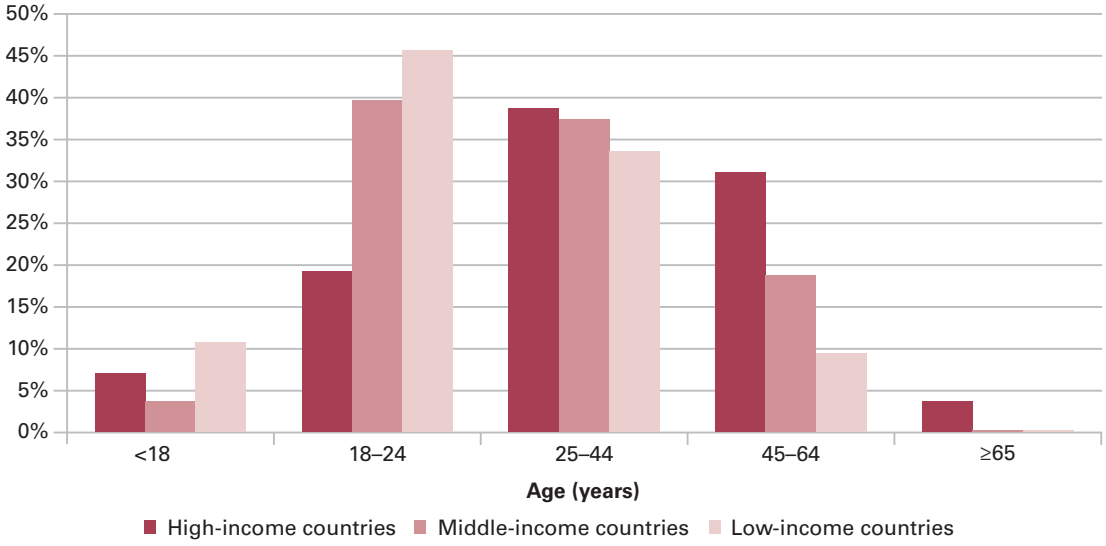
Figure 2.4: Whole blood donations per 1000 population, 2011



Demographic information about blood donors is important for formulating and monitoring donor recruitment strategies to meet blood requirements. Data from 104 countries on the gender profile of blood donors show that 30% of blood donations were given by female donors; of these, 18 countries reported less than 10% donations by women.

The age profile of blood donors shows that proportionally more young people donate blood in low- and middle-income countries than in high-income countries, perhaps reflecting the age structure of their populations; more than 40% of blood donations were given by donors aged 18–24 years in low- and middle-income countries, and only 19% in high-income countries (Figure 2.5).

Figure 2.5: Age profile of blood donors, 2011



Whole blood and apheresis donations

Seventy-six of the 177 responding countries reported collecting blood both as whole blood donations and through apheresis procedures. Of the total donations reported worldwide in 2011, 89% were donated as whole blood and 11% were donated by apheresis. In total, 11.4 million apheresis donations were reported globally. Data provided by some countries did not distinguish between apheresis donations of blood components for transfusion and plasma collected by apheresis for fractionation.

In high-income countries, 18% of all donations were collected through apheresis, as compared to 4% in middle-income countries and 0.2% in low-income countries (Table 2.1).

Table 2.1: Whole blood and apheresis donations, by income group of countries, 2011

Countries	Whole blood donations		Apheresis donations		Total
	Number	%	Number	%	
High-income (n=42)	43 721 559	82.3%	9 371 240	17.7%	53 092 799
Middle-income (n=99)	49 575 538	96.1%	2 011 572	3.9%	51 587 110
Low-income (n=36)	3 152 940	99.8%	7361	0.2%	3 160 301
Total (n=177)	96 450 037	89.4%	11 390 173	10.6%	107 840 210

Voluntary non-remunerated, family/replacement and paid donations

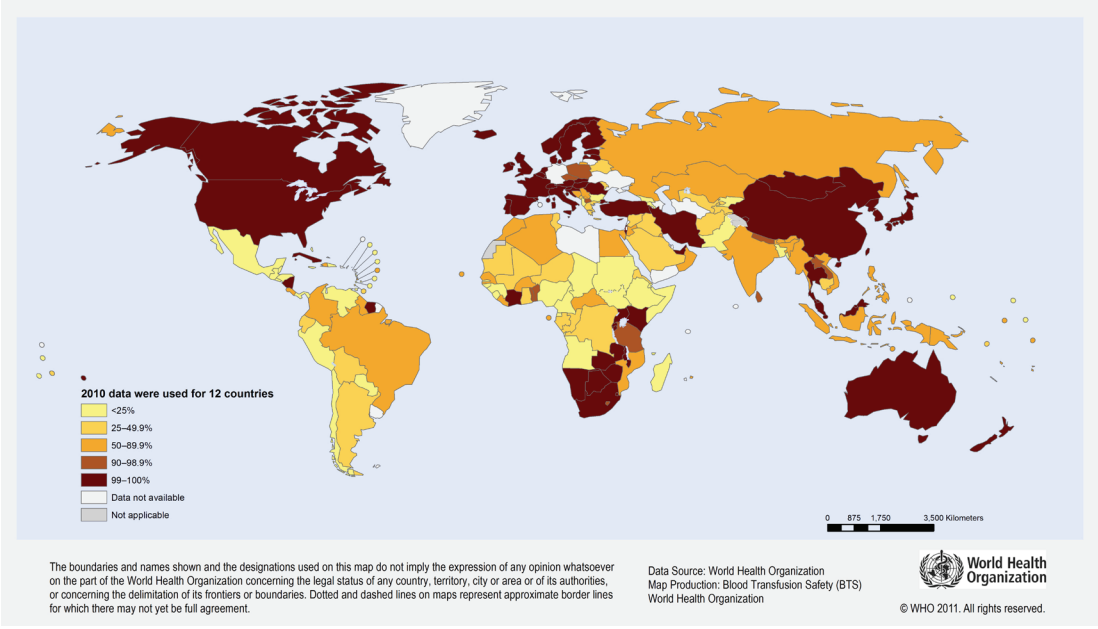
Information on types of blood donations was provided by 173 countries, accounting for 85.9 million whole blood donations and 8.6 million apheresis donations.

Of the total 85.9 million whole blood donations, 73.6 million (85.7%) were reported as voluntary non-remunerated donations, 11.7 million (13.7%) were from family or replacement donors and 335,000 (0.4%) were from paid blood donors. About 232 000 donations (0.3%) were reported as "other types/unknown".

Seventy-one countries collected more than 90% of their blood supply from voluntary non-remunerated blood donations (Figure 2.6 and Annex 2): 38 high-income countries, 22 middle-income countries and 11 low-income countries. Sixty countries reported collecting 100% (or more than 99%) of their blood supply from VNRD.

Seventy countries (6 high-income countries, 45 middle-income countries and 19 low-income countries) remained dependent on family/replacement and paid blood donors for more than 50% of their blood supplies in 2011. Twenty-three countries reported collecting a total of around 800 000 paid donations, of which 59% were apheresis donations.

Figure 2.6: Percentage of voluntary non-remunerated whole blood and apheresis donations by country, 2011



When analysed by the income group of countries, voluntary non-remunerated donations accounted for 98.0% of whole blood donations in high-income countries, 77.2% in middle-income countries and 59.0% in low-income countries (Table 2.2).

When analysed by WHO region, the proportion of voluntary non-remunerated whole blood donations varied from 59.2% in the Eastern Mediterranean Region to as high as 94.5% in the European Region and 98.5% in the Western Pacific Region. The proportion of VNRD in the African, Americas and South-East Asia regions was 71.2 %, 77.3% and 82.5% respectively (Table 2.3). Some regional percentages and the overall percentages

in particular income groups of countries were mostly determined by large countries with high numbers of collections.

Table 2.2: Types of whole blood donations, by income group of countries, 2011

Countries	Voluntary non-remunerated		Family/ replacement		Paid		Others/unknown		Total
	Number	%	Number	%	Number	%	Number	%	Number
High-income (n=41)	36 615 380	98.0%	693 329	1.9%	605	0.002%	38 516	0.1%	37 347 830
Middle-income (n=96)	35 356 101	77.2%	9 962 595	21.7%	305 139	0.7%	181 476	0.4%	45 805 311
Low-income (n=36)	1 618 873	59.0%	1 084 095	39.5%	29 209	1.1%	12 029	0.4%	2 744 206
Total (n=173)	73 590 354	85.7%	11 740 019	13.7%	334 953	0.4%	232 021	0.3%	85 897 347

Table 2.3: Proportions of voluntary non-remunerated whole blood donations by WHO Region and income group of countries, 2011

WHO Region	High-income	Middle-income	Low-income	All
AFR (n=45)	0.0% [a]	77.8%	62.8%	71.2%
AMR (n=32)	99.8%	41.8%	70.4% [b]	77.3%
EMR (n=18)	54.7%	60.0%	36.5%	59.2%
EUR (n=42)	97.2%	87.6%	33.1%	94.5%
SEAR (n=10)	–	84.8%	56.8%	82.5%
WPR (n=26)	99.9%	98.0%	34.0%	98.5%
All (n=173)	98.0%	77.2%	59.0%	85.7%

[a] Equatorial Guinea is the only high-income country in the African Region

[b] Haiti is the only low-income country in the Region of the Americas

An increase of 7.70 million blood donations from voluntary non-remunerated donors between 2004 and 2011 was reported by 156 countries that provided data for both years. The highest increases in VNRD were observed in the WHO South-East Asia (65%) and African (48%) Regions. The greatest increase in absolute numbers was reported in the Western Pacific Region (Table 2.4).

Table 2.4: Voluntary non-remunerated whole blood donations, by WHO Region, 2004 and 2011

WHO Region	2004	2011	Increase (number)	Increase (%)
AFR (n=39)	1 755 408	2 595 189	839 781	48%
AMR (n=32)	16 269 535	17 546 220	1 276 684	8%
EMR (n=13)	2 529 274	3 243 798	714 524	28%
EUR (n=39)	18 280 942	18 446 001	165 059	1%
SEAR (n=9)	2 047 407	3 385 304	1 337 897	65%
WPR (n=24)	17 250 313	20 615 219	3 364 906	20%
Total (n=156)	58 132 880	65 831 730	7 698 850	13%

Notable increases in the percentage of VNRD between 2004 and 2011 were reported (in alphabetical order) by Cape Verde (from 32.0% to 80.8%), Cook Islands (from 40.2% to 100%), Guyana (from 18.8% to 76.4%), Haiti (from 5.4% to 70.4%), Kenya (from 52.6% to 100%), Myanmar (from 25.0% to 73.6%), Nicaragua (from 41.6% to 100%), Niue (from 0 to 41.4%), Turkey (from 40.0 to 100%), United Arab Emirates (from 59.0% to 100%) and Viet Nam (from 25.3% to 88.8%).

GDBS data showed that most apheresis donations for clinical transfusion were given by voluntary non-remunerated donors. In the European region, 12.9% of apheresis donations were reported to be sourced from paid donors, although it is possible that the data may reflect the inclusion of some plasma donations for fractionation (Table 2.5).

Table 2.5: Number and percentage of apheresis donations, by types of donation and WHO Region, 2011

WHO Region	Voluntary non-remunerated		Family/ replacement		Paid		Others/ unknown	
	Number	%	Number	%	Number	%	Number	%
AFR (n=7)	25 194	99.9%	26	0.1%	–	–	–	–
AMR (n=7)	2 170 029	99.7%	4426	0.2%	–	–	1 505	0.07%
EMR (n=9)	11,745	40.4%	9,720	33.4%	7 629	26.2%	–	–
EUR (n=34)	2 925,133	86.5%	8820	0.3%	434 962	12.9%	12 300	0.36%
SEAR (n=4)	16 473	99.1%	143	0.9%	–	–	–	–
WPR (n=11)	3 070 499	98.8%	3349	0.1%	32 667	1.1%	–	–
Total (n=72)	8 219 073	94.1%	26 484	0.3%	475 258	5.4%	13 805	0.16%

Note: The data reported for the South-East Asia Region do not include India and Indonesia where large numbers of apheresis donations may have been collected but were not reported. The actual total global and regional numbers of apheresis donations are likely to be higher than the data summarized here.

Analysis by income group of countries indicates that, in middle-income countries, 0.8 % of apheresis donations were from family/replacement donors and 22.7% from paid donors. In low-income countries, the percentages were 3.0% and 92.2% respectively, although the total number of apheresis donations in this group of countries was very small (Table 2.6).

Table 2.6: Types of apheresis donations, by income group of countries, 2011

Countries	Voluntary non-remunerated		Family/ replacement		Paid		Others/ unknown	
	Number	%	Number	%	Number	%	Number	%
High-income (n=34)	6 687 581	99.4%	10 947	0.2%	14 731	0.2%	12 300	0.18%
Middle-income (n=33)	1 531 228	76.4%	15 368	0.8%	455 406	22.7%	1505	0.08%
Low-income (n=5)	264	4.8%	169	3.0%	5121	92.2%		
Total (n=72)	8 219 073	94.1%	26 484	0.3%	475 258	5.4%	13 805	0.16%

Blood component production

Based on data reported to the GDBS by 146 countries, 86% of whole blood donations collected globally were processed into components: 97% in high-income countries, 78% in middle-income countries and 40% in low-income countries. Table 2.7 shows that the majority (*34/36*) of high-income countries separate more than 90% of whole blood into components, as compared to only 17% (5/29) of low-income countries.

Table 2.7: Percentages of whole blood separated into components, by income group of countries, 2011

Countries	0–25%	25.1–50%	50.1–90%	90.1–99%	100%
High-income (n=37)	2	0	1	16	18
Middle-income (n=80)	12	14	11	30	13
Low-income (n=29)	12	6	6	3	2

Analysed by region, the lowest overall percentages of blood component preparation were in the WHO South-East Asia Region (43%) and the African Region (66%). The percentage was 75% in the Eastern Mediterranean region and >90% in the Americas, European and Western Pacific Regions (Table 2.8).

Table 2.8: Percentages of whole blood donations processed, by WHO Region and income group of countries, 2011

WHO Region	High-income	Middle-income	Low-income	All
AFR (n=37)	–	77%	51%	66%
AMR (n=21)	99.6%	95%	52%a	98%
EMR (n=13)	84%	74%	2%	75%
EUR (n=41)	96%	89%	99%	94%
SEAR (n=10)	–	45%	21%	43%
WPR (n=24)	99%	91%	15%	94%
Total (n=146)	97%	78%	40%	86%

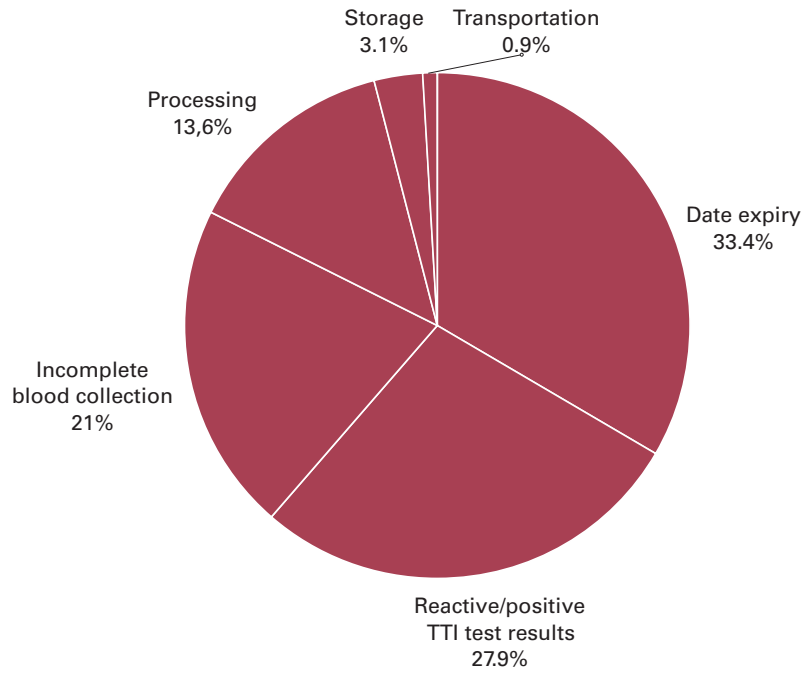
[a] Haiti is the only low-income country in the Region of the Americas.

Wastage of blood

The blood and blood products available to meet a country's needs (in effect, the blood used) is equal to the total volume of blood collected minus the units that are discarded. Accurate data on wastage, or the proportions of whole blood or blood components collected but not transfused or processed, are very difficult to obtain. The reasons for wastage are also difficult to obtain and verify, and may reflect many different factors including baseline rates of microbiological testing or outdating beyond recommended time-limits for storage. Data on rates of wastage of whole blood or blood components may be of value in identifying areas of a country's blood supply system for potential improvement in reaching self-sufficiency.

GDBS data for 2011 from 148 countries indicates that 3.5 million blood donations (whole blood/red blood cells) were discarded out of the 67.3 million whole blood donations reported. If this ratio (3.5 million blood donations discarded per 67.3 million donations) is applied to the 96.4 million donations reported globally, as many as five million whole blood donations may be discarded annually. The reasons for discard included date expiry (33.4%), reactive or confirmed positive test results for transfusion-transmissible infections (TTI) including HIV, hepatitis B, hepatitis C and syphilis (27.9%), incomplete whole blood collections (21.0%), processing problems (13.6%) and problems during storage (3.1%) and transportation (0.9%) (Figure 2.7).

Figure 2.7: Distribution of discards of blood donations, by reason for discard, 2011



The percentages of total blood donations (whole blood/red blood cells) discarded (Table 2.9 and Table 2.10) and those discarded due to reactive or confirmed positive results for transfusion-transmissible infections (Table 2.11 and Table 2.12) were generally higher in low- and middle-income countries, although there were wide variations in each income group of countries.

Table 2.9: Percentage of total donations (whole blood/red blood cells) discarded, 2011

Countries	Median	25% quartile	75% quartile
High-income (n=34)	5.2%	3.6%	8.4%
Middle-income (n=80)	8.1%	4.9%	13.6%
Low-income (n=34)	9.8%	5.6%	14.9%

Table 2.10: Percentage of total donations (whole blood/red blood cells) discarded, by WHO Region, 2011

Region	Median	25% quartile	75% quartile
AFR (n=41)	12.0%	7.0%	17.8%
AMR (n=31)	8.3%	6.3%	12.0%
EMR (n=13)	6.5%	5.9%	9.1%
EUR (n=35)	5.2%	3.5%	7.5%
SEAR (n=8)[a]	2.3%	1.4%	3.5%
WPR (n=20)	7.9%	3.0%	11.9%

[a] The low discard rate in SEAR may be due to partial reporting of discard data to WHO GDBS. In addition, some countries in the Region could provide data only on discards due to reactive/positive TTI test results.

Table 2.11: Percentage of donations discarded due to reactive or positive TTI test results

Countries	Median	25% quartile	75% quartile
High-income (n=26)	0.7%	0.2%	2.7%
Middle-income (n=63)	4.2%	2.1%	7.2%
Low-income (n=33)	6.6%	3.4%	11.5%

Table 2.12: Percentage of donations discarded due to reactive or positive TTI test results, by WHO region, 2011

WHO Region	Median	25% quartile	75% quartile
AFR (n=40)	9.1%	4.3%	13.2%
AMR (n=14)	4.4%	2.7%	6.2%
EMR (n=13)	4.8%	3.6%	6.7%
EUR (n=30)	0.8%	0.2%	4.8%
SEAR (n=8)[a]	1.2%	0.9%	1.6%
WPR (n=17)	3.4%	0.8%	7.3%

[a] The low discard rate in SEAR may be due to partial reporting of discard data to WHO GDBS.

Discards due to reactive or confirmed positive results for transfusion-transmissible infections in blood donations are considerably lower in high-income countries than in low- and middle-income countries. The prevalence of HIV in blood donations in high-

income countries is 0.003% (median), in comparison with 0.1% and 0.6% in middle- and low-income countries respectively. This difference reflects the variable prevalence of infection among members of the population who are eligible to donate blood, the type of donors (such as voluntary non-remunerated blood donors from populations at lower risk of infection) and the effectiveness of the systems for donor education and selection.

2.2 Provision of plasma-derived medicinal products

Volume of plasma for fractionation

Unlike blood for transfusion, the volume of plasma in litres sent for fractionation per 1000 population cannot be considered as a general indicator for the availability of plasma-derived medicinal products in a country: many countries do not collect any plasma for fractionation, but buy products on the global market. It can, however serve as a benchmark among countries at similar levels of economic and social development.

Data on the volume of plasma sent for fractionation in 2011 were obtained from 51 countries which reported the collection of a total of around 28.7 million litres of plasma for fractionation. A review of modern plasma fractionation in 2007 by Burnouf indicated that between 23 and 28 million litres of human plasma are fractionated annually in the world; this is consistent with the figure reported to the GDBS.

Most plasma for fractionation is collected in the Americas, European and Western Pacific Regions (Table 2.13) and 82.2% of the volume of plasma for fractionation is collected in high-income countries (Table 2.14).

Table 2.13: Volume of plasma for fractionation, by WHO region, 2011

WHO Region	Volume of plasma for fractionation (L)
AFR (n=1)	183 000
AMR (n=7)	14 913 690
EMR (n=2)	144 722
EUR (n=33)	7 179 338
SEAR (n=1)	11 200
WPR (n=7)	6 260 438
Total (n=51)	28 692 388

Table 2.14: Volume (L) of plasma for fractionation, by income group of countries, 2011

Countries	Volume of plasma for fractionation (L)	Proportion of volume of plasma for fractionation (%)
High-income (n=29)	23 572 576	82.2%
Middle-income (n=21)	5 111 534	17.7%
Low-income (n=1)	8 277	0.02%
Total (n=51)	28 692 388	100%

The volume of plasma for fractionation (and processing for PDMP) per 1000 population varied considerably between countries, ranging from 0.37 to 45 litres, with a median of

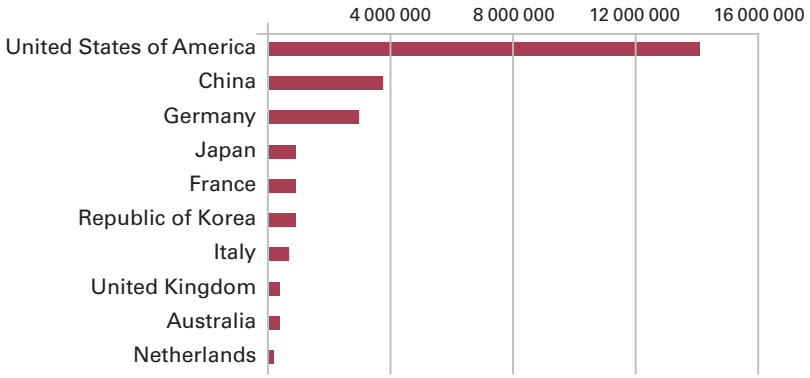
11.1 litres in high-income countries and 1.8 litres in low- and middle-income countries (Table 2.15).

Table 2.15: Volume (L) of plasma for fractionation per 1000 population, by income group of countries, 2011

Countries	Median	25% quartile	75% quartile
High-income (n=29)	11.1	6.2	15.2
Low- and middle-income (n=22)	1.8	1.1	3.6

Ten countries (United States of America, China, Germany, Japan, France, Republic of Korea, Italy, United Kingdom, Australia and The Netherlands) accounted for 90% of the total global volume of plasma sent for fractionation (Figure 2.8 and see Annex 3 for data sources).

Figure 2.8: Countries with the highest volume (litres) of plasma sent for fractionation, 2011



Method of collection

Analysis by collection method (recovered from whole blood or by apheresis) and region shows that only about a quarter of the total volume of plasma for fractionation was recovered from whole blood (Table 2.16). In Europe, 3.6 million litres of recovered plasma were fractionated, accounting for 52% of the plasma fractionated in the region. In the Americas and Western Pacific Regions, the majority of plasma for fractionation was source (apheresis) plasma. Recovered plasma accounted for 98%, 99.7% and 89% respectively of the total volume of plasma sent for fractionation in the African (South Africa), Eastern Mediterranean (Iran and Morocco) and South-East Asia (Thailand) Regions.

Table 2.16: Volume of plasma for fractionation, by collection method and WHO Region, 2011

WHO Region	Recovered plasma		Source (apheresis) plasma	
	Volume (L)	%	Volume (L)	%
AFR (n=1)	180 000	98%	3000	2%
AMR (n=5)	2 516 954	17%	12 022 247	83%
EMR (n=2)	144 293	99.7%	429	0.3%
EUR (n=29)	3 595 903	52%	3 223 521	48%
SEAR (n=1)	10 000	89%	1200	11%
WPR (n=7)	941 430	15%	5 319 009	85%
Total (n=45)	7 388 580	26%	20 569 405	74%

Note: Six additional countries reported collecting 734 403L of plasma for fractionation but did not indicate the collection method.

Analysis by collection method and by income group of countries shows that a significant proportion of plasma for fractionation was collected as source plasma in both high- and middle-income countries (Table 2.17).

Table 2.17: Volume of plasma for fractionation, by collection method and income group of countries, 2011

Countries	Recovered plasma		Source (apheresis) plasma	
	Volume (L)	%	Volume (L)	%
High-income (n=27)	6 618 444	28%	16 667 755	72%
Middle-income (n=17)	761 859	16%	3 901 650	84%
Low-income (n=1)	8277	100%	–	0%
Total (n=45)	7 388 580	26%	20 569 405	74%

Note: Six additional countries reported collecting 734 403L of plasma for fractionation but did not indicate the collection method.

Voluntary non-remunerated and paid (compensated) donors

Data on the types of donors who provide source plasma for fractionation is limited, although it is reported that large volumes of plasma are collected from compensated or paid donors in plasma collection centres operated by commercial plasma fractionators. Twenty countries reported that 100% of domestic source plasma for fractionation was given by voluntary non-remunerated donors in 2011 (Australia, Belgium, Canada, Croatia, Denmark, Finland, France, Italy, Iran, Luxembourg, The Netherlands, New Zealand, Norway, Republic of Korea, Serbia, Singapore, Slovenia, Sweden, Switzerland and Thailand). In these countries, the types of donors from whom plasma is recovered correspond to the types of blood donors giving whole blood donations.

Plasma fractionation and supply of plasma-derived medicinal products

Arrangements for plasma fractionation and the supply of PDMP differ. In some countries, PDMP are produced by a national or regional fractionator established by government or not-for-profit organization, such as a National Red Cross Society. Others have an agreement with a fractionator for the processing of domestic plasma through contract

or toll fractionation, while many countries purchase some or all of their PDMP from multinational private fractionators.

A total of 153 countries provided 2011 data to WHO on arrangements for plasma fractionation and the supply of PDMP; of these, 42 countries (21 high-income, 19 middle-income and 2 low-income) reported that all or part of the supply of PDMP was produced through domestic or/and contract fractionation of plasma collected in the country. These include one country in the African Region, seven in the Region of the Americas, two in the Eastern Mediterranean Region, 23 in the European Region, two in the South-East Asia Region and seven in the Western Pacific Region. Thirty-three of the 42 countries reported that plasma fractionation is carried out within the country; of these, nine reported that plasma is also sent for contract fractionation in another country. Nine of the 42 countries reported that domestic fractionation was not undertaken but that plasma was sent for contract fractionation in another country. A total of 111 countries reported that they rely entirely on imported products for their supplies of PDMP.

Information on fractionation arrangements and PMDP manufactured in 48 countries (including countries which provided data to the GDBS in 2008 or 2011) is given in Annex 4. Annex 5 provides information on the proportion of supplies of different PMDP manufactured through fractionation (e.g. domestic or/and contract fractionation) of the plasma collected in the country.

Twenty-three countries provided information on supplies of albumin, intravenous immunoglobulin (IVIG) and factor VIII (excluding recombinant products) and the proportion of products supplied through fractionation (e.g. domestic or/and contract fractionation) of plasma collected in the country. Australia, Morocco, the Netherlands, New Zealand, Slovenia and South Africa reported that 70% or more of three products (albumin, IVIG and factor VIII) were provided by fractionation of plasma collected in the country; France, Japan and Luxembourg reported 70% or more for at least two of these three products; and Iran, Italy and Singapore reported 70% or more for at least one of these three products (Annex 5).

Wastage of plasma, including unused recovered plasma

The collection of plasma for fractionation is the first step in the manufacture of plasma-derived medicinal products and impacts the quality and safety of the finished products. Accurate data on the amount of plasma available but not transfused or processed into PDMP are difficult to obtain and verify. In part, this reflects the need for information from multiple sources including blood transfusion services, hospitals, regulatory authorities and industry. In many high-income countries, a large proportion of the plasma available for fractionation is recovered from whole blood donations from voluntary, non-remunerated donors. However, large volumes of the plasma collected in developing countries are considered to be unsuitable for conversion into fractionated medicinal products as they do not meet the standards set by fractionators and regulators due to a lack of appropriate technology or inadequate quality systems, good manufacturing practices and regulatory controls. This plasma is therefore categorized as waste material and destroyed.

There are currently no reported data on the discard of recovered plasma. Based on available information through GDBS, it is estimated that globally there may be as much as 6.5 million litres (Annex 1) of recoverable plasma that is either not recovered

(transfused as whole blood) or is recovered but not used for fractionation, and discarded. As Burnouf suggests, for the purpose of this estimation, "recovered plasma wasted" could mean:

- Use of whole blood in the absence of component therapy: plasma is not produced (this would also depend on health-care needs in the country)
- Lack of appropriate freezing and storage capacity of plasma: plasma is discarded
- Plasma is produced but does not meet the requirements for fractionation: plasma is destroyed
- Clinical use of plasma where PDMP are indicated: plasma is not used in an optimal way.

An inadequate supply of plasma that meets internationally recognized standards for fractionation is considered to be one of the major factors limiting the global availability of plasma-derived medicinal products. Treatment using labile blood components is gradually being expanded in medical practice in developing countries and increased quantities of recovered plasma will become available for fractionation into PDMP to meet their needs. It is important for such countries to develop appropriate standards for donor recruitment, selection and care and to put in place appropriate blood component separation technology and fractionation capacity, quality systems and good manufacturing practices to improve the quality of plasma for fractionation and also explore the development of alternate mechanisms for contract fractionation of recovered plasma in this developmental and transitional period.

2.3 Clinical use of blood and blood products

Obtaining accurate data on the clinical use of blood and blood products is challenging due to the wide diversity and numbers of institutions and hospitals that perform transfusion, and the highly variable policies and procedures for traceability, documentation and recording of transfusions. Data on the clinical use of blood were reported by 139 countries to the GDBS (32 high-income countries, 71 middle-income countries and 36 low-income countries), identifying more than 51 000 hospitals performing blood transfusion serving a total population of around 3.1 billion. Transfusion rates varied markedly; a rate of 34.8 units of red cell components per 1000 population was reported by high-income countries whereas the transfusion rate was 9.4 units in middle-income countries and 2.9 units in low-income countries (Table 2.18 and Figure 2.19).

Table 2.18: Units of red cell components transfused per 1000 population, 2011

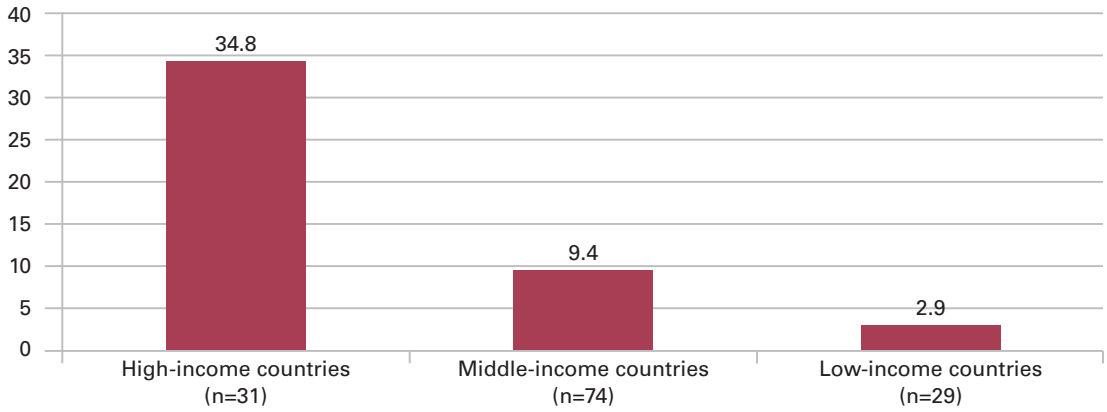
Countries	Median	25% quartile	75% quartile
High-income (n=33)	34.7	26.5	39.3
Middle-income (n=74)	9.4	5.5	13.7
Low-income (n=29)	2.9	1.8	4.0

Note: Three countries reporting partial data were not included in this analysis

Fundamental to any discussion about levels of need and demand is an understanding of the proportion of blood used for appropriate indications.The unnecessary or inappropriate use of blood is not only a demand on a scarce resource but also a waste of a product

and its associated costs. Research evidence is a major driver in defining the appropriate use of blood. A number of large clinical trials in transfusion have been undertaken using clinically relevant outcomes. These trials are challenging some established notions of the clinical benefits of transfusion. In the area of red cell transfusion, for example, a number of threshold studies have been published. These studies typically compared clinical outcomes in patients randomized to receiving either standard doses (more liberal transfusion strategy) or fewer doses (a more restrictive transfusion strategy). As a broad generalization, the combined weight of evidence from these trials of red cell transfusion does not support unrestricted use of red cell transfusions in many patient groups and often indicates a benefit for the use of fewer red cell transfusions – these results appear to argue against any intuitive desire to raise haemoglobin levels.

Figure 2.9: Units of red cell components transfused per 1000 population, 2011



Note: Three countries reporting partial data were not included in this analysis

Several measures may be used to assess how a country supports implementation of evidence-based practice. Attention is now increasingly being focused on improving clinicians' use of blood in accordance with evidence-based guidelines. National guidelines are a prerequisite for establishing systems for the appropriate clinical use of blood, such as clinical audit. In 2011, 109 countries reported having national guidelines in place. The presence of structures such as hospital transfusion committees can provide leadership within a hospital for optimizing the use of blood. However, hospital transfusion committees were reported present only in about half (54%) of the hospitals performing transfusions in low- and middle-income countries in comparison with 79% of hospitals in high-income countries.

Analysis of data reported to WHO GDBS indicates that 58% of hospitals in low- and middle-income countries conducted clinical audit, as compared to 91% of hospitals in high-income countries. Systems for reporting adverse transfusion events were present in 76% of hospitals in low- and middle-income countries and 93% of hospitals in high-income countries (Table 2.19). 34% (41/119) of low- and middle-income countries reported having a national haemovigilance system in place as compared to 86% (30/35) of high-income countries.

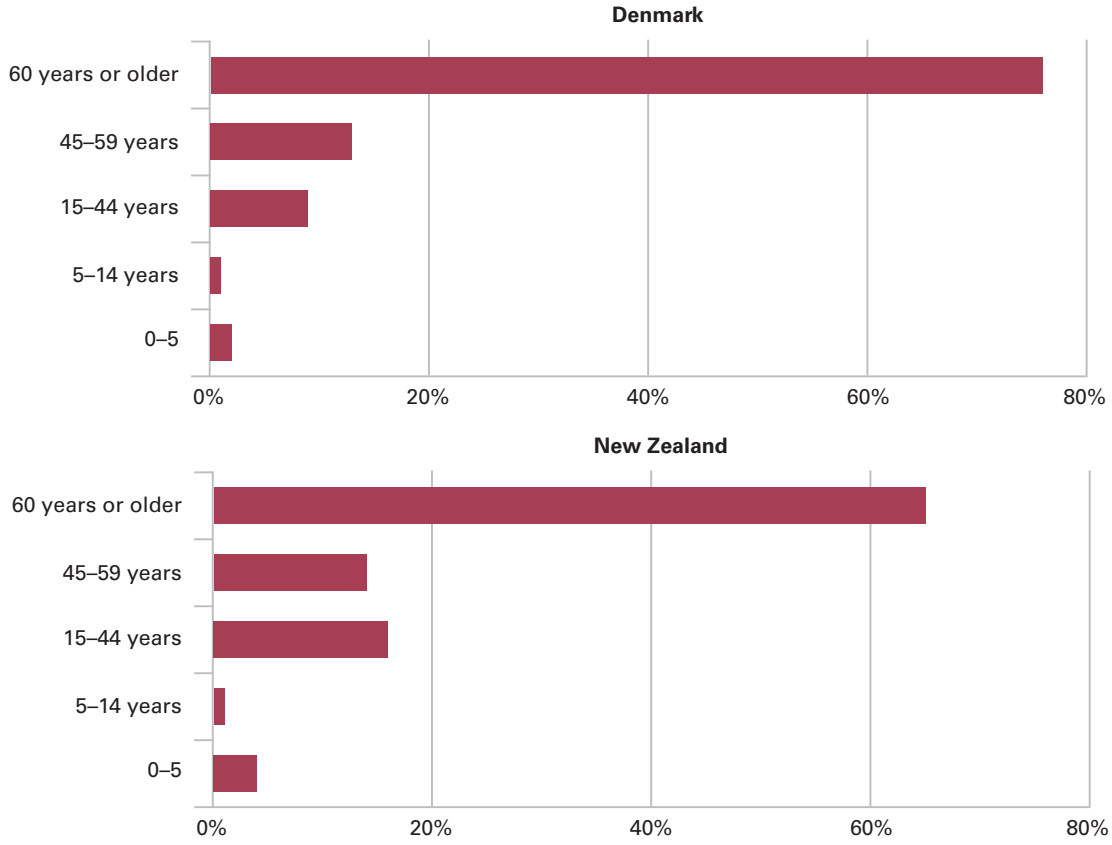
Table 2.19: Percentage of hospitals with systems for the appropriate clinical use of blood and blood products, 2011

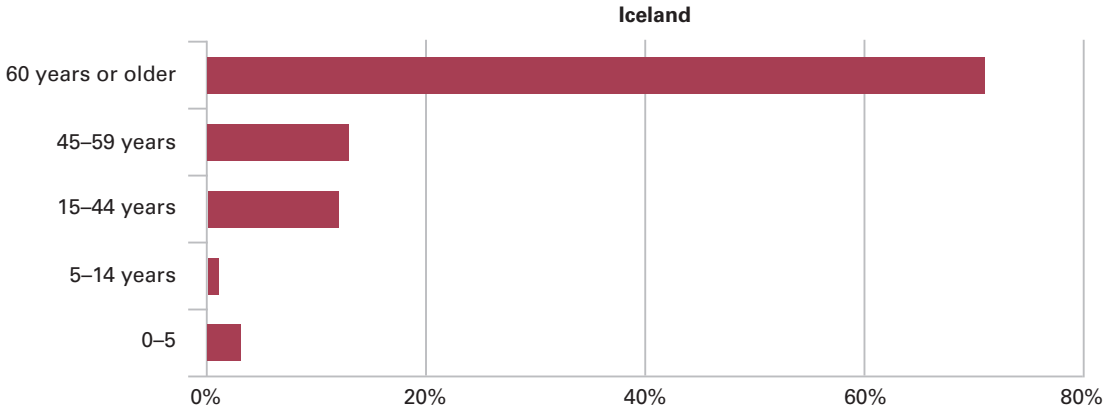
Hospitals performing transfusions	Hospital transfusion committee (n=21 124)	Clinical audit of transfusion practice (n=12 697)	Reporting adverse transfusion events (n=31 065)
High-income countries	79%	91%	93%
Low and middle-income countries	54%	58%	76%

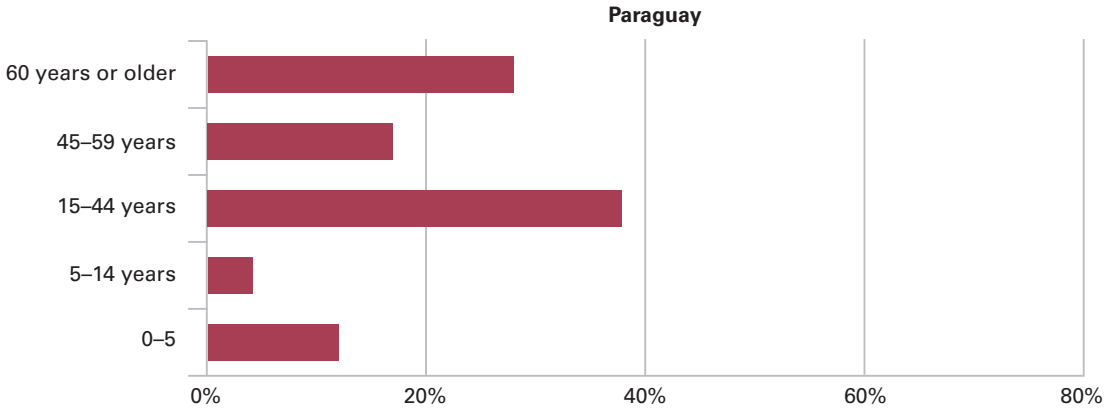
Blood utilization patterns in developed vs developing countries

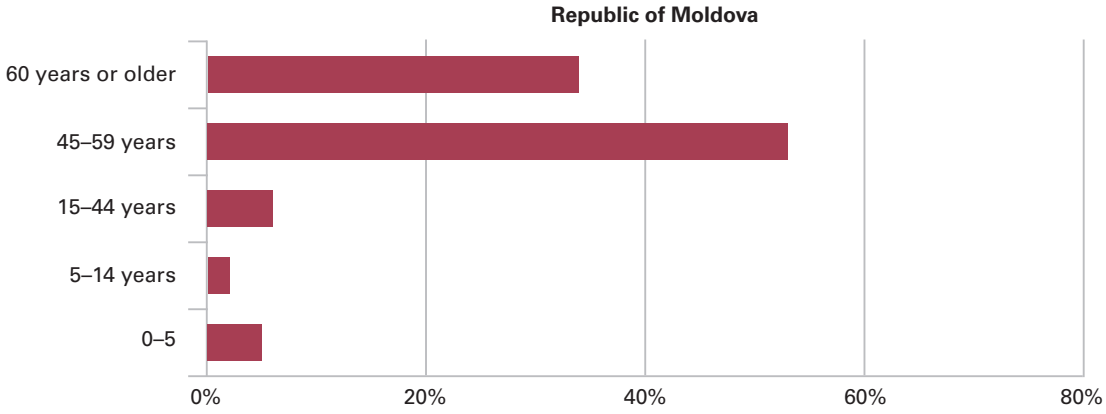
There is evidence of significant differences in patterns of blood use between high-, middle- and low- income countries in, for example, the age distribution of patients transfused. GDBS data indicate that in high-income countries the most frequently transfused patient group is over 60 years, which accounts for up to 76% of all transfusions. In low- and middle-income countries, up to 65% of all transfusions are for children under the age of five years, usually followed by females aged between 15 and 45 years. Figure 2.13 provides examples of the age distribution of patients transfused in high-income countries (Denmark, New Zealand and Iceland), middle-income countries (Paraguay, Republic of Moldova and Jordan) and low-income countries (Burundi and Benin). In high-income countries, transfusion is most commonly used for supportive care in cardiovascular and transplant surgery, massive trauma and therapy for solid and haematological malignancies. In low- and middle-income countries, it is more often used to treat pregnancy-related complications and severe childhood anaemia.

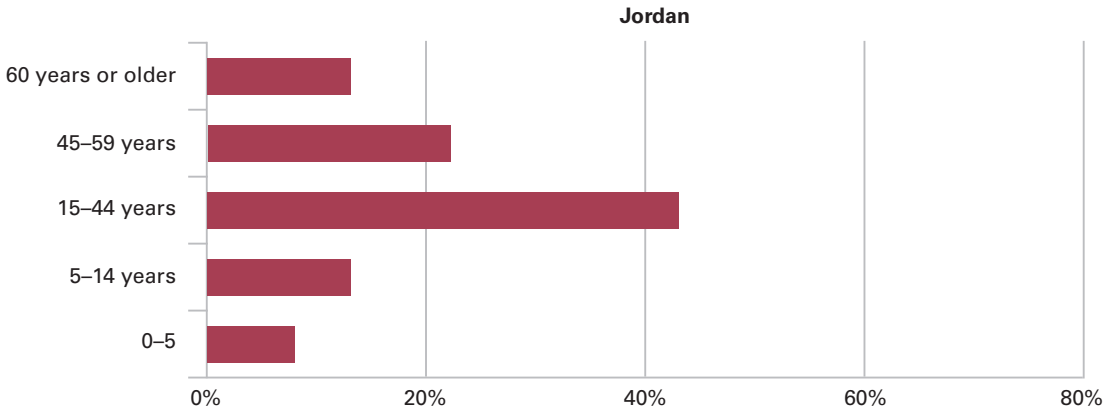
Figure 2.10: Age distribution of patients transfused in selected countries, 2001

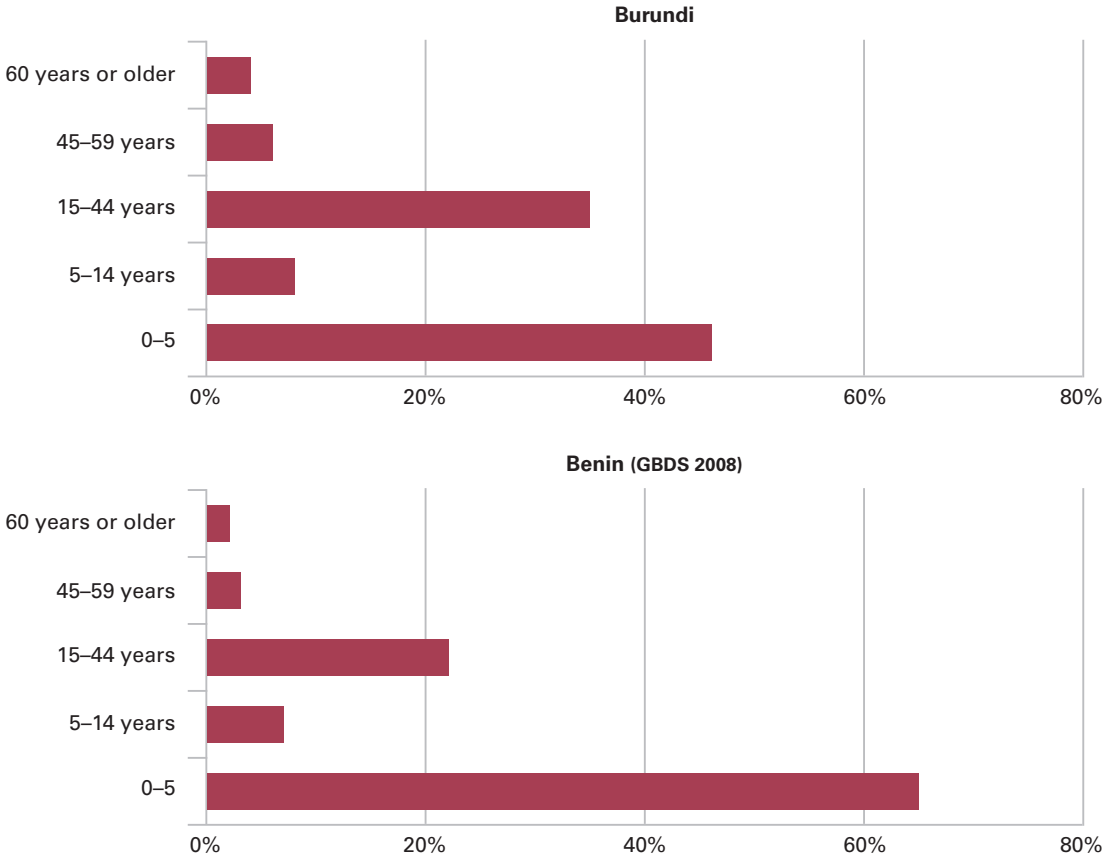



Iceland
60 years or older
45–59 years
15–44 years
5–14 years
0–5
0%
20%
40%
60%
80%


Paraguay
60 years or older
45–59 years
15–44 years
5–14 years
0–5
0%
20%
40%
60%
80%


Republic of Moldova
60 years or older
45–59 years
15–44 years
5–14 years
0–5
0%
20%
40%
60%
80%


Jordan
60 years or older
45–59 years
15–44 years
5–14 years
0–5
0%
20%
40%
60%
80%



Another measure of variation in clinical use is the proportion of blood that is transfused as whole blood rather than blood components, which can target specific deficiencies. By far the largest need for blood is the transfusion of red cells to treat profound anaemia; these patients do not require transfusions of platelets or plasma. GDBS data from 139 countries were analysed for the proportion of blood transfused as whole blood (Table 2.20), revealing great variations in the use of whole blood for transfusion among different income groups of countries. In high-income countries, whole blood is rarely used for transfusion while, in middle- and low-income countries, 3.4% and 83.1% of blood respectively was transfused as whole blood. As health systems develop and become able to offer a wider range of diagnostic and treatment options, component therapy becomes increasingly important for the clinical management of patients.

Table 2.20: Percentage of whole blood transfusion among all red cell components for transfusion, by income group of countries, 2011

Countries	Median	25% quartile	75% quartile
High-income (n=36)	0.0%	0.0%	0.1%
Middle-income (n=74)	3.4%	0.1%	34.1%
Low-income (n=29)	83.1%	39.5%	96.7%

The WHO Global Database on Blood Safety does not collect information on the use of PDMP. While data on their use are limited, there is adequate evidence that the use of such products has increased, especially in recent years, in part as a result of improved diagnostic capacities. In view of improving access to medical care in the developing world, particularly in emerging economies, the trend to increased use is likely to continue for the foreseeable future.

3 International initiatives for self-sufficiency in safe blood and blood products based on VNRD

Since the adoption of resolution WHA28.72 by the World Health Assembly in 1975, numerous global and regional resolutions, consultations, declarations, conventions and policies from a number of intergovernmental agencies, including the World Health Organization, the Council of Europe, the European Commission and other international organizations have recommended that countries should develop national blood systems based on voluntary non-remunerated donation with the objective of achieving self-sufficiency in safe blood and blood products. There are many successful examples from developing countries as well as the developed world where a strong foundation for sustainable blood systems has been laid, based on these policies.

This section provides brief accounts of the initiatives of key intergovernmental and international organizations working on the issue of self-sufficiency based on VNRD.

World Health Organization

The World Health Organization (WHO) is the directing and coordinating authority for health within the United Nations system. It is responsible for providing authoritative leadership on global health matters, sets norms and standards, articulates evidence-based policy options, monitors and assesses health trends and provides technical support to meet specific country needs. With the goal of self-sufficiency and universal access to safe blood and blood products, WHO has been at the forefront of the movement to improve blood safety as mandated by more than 25 successive World Health Assembly (WHA) resolutions, the earliest dating from 1975 and the most recent in May 2010, as well as regional resolutions and decisions that provide specific direction on strategies and activities within individual regions.

In 2000, Blood Safety was declared an organization-wide priority and was designated as the theme of World Health Day, 7 April 2000 with the slogan 'Safe blood starts with me'. This was co-sponsored by the International Federation of Red Cross and Red Crescent Societies and was celebrated by ministries of health, blood transfusion services, blood donor organizations, nongovernmental organizations, professional bodies and community organizations throughout the world.

WHO provides global leadership on matters critical to blood safety and availability and engages in collaboration and partnership where joint action is needed including establishing mechanisms such as, Global Blood Safety Network. WHO work closely with Collaborating Centers in Blood Transfusion Medicine and with NGOs in Official Relations and has also established the WHO Expert Advisory Panel on Blood Transfusion Medicine in fulfilling its core functions.

WHO fosters the harmonization of national and international efforts to ensure sufficient safe blood products through bilateral and multilateral collaboration and brings together

blood transfusion services, ministries of health and partner organizations through global collaborative and coordinating mechanisms, the Global Forum for Blood Safety. In 2005, the World Health Assembly adopted resolution WHA58.13 to establish World Blood Donor Day (WBDD) as an annual event and requested the Director-General to work with other organizations to promote the event. WHO, International Federation of Red Cross and Red Crescent Societies, International Society of Blood Transfusion and International Federation of Blood Donor Organizations as founding partners of World Blood Donor Day provide global leadership and coordination of global campaigns and events on 14 June each year to celebrate and promote WBDD, which unites the world in raising awareness of the need for safe blood and importance of voluntary non-remunerated blood donation.

WHO has convened several regional, interregional and global consultations, policy makers forums in collaboration with key international partners to share experiences and define strategies to address key issues and challenges including: 'Global consultation on 'Universal access to safe blood transfusion' 2007; Interregional workshop on 'Strategies and mechanisms for strengthening national blood programmes' 2007; Inter-regional consultation on Global consultation on '100% Voluntary non-remunerated donation of blood and blood components', 2009 and The Melbourne Declaration; Interregional consultation on 'Strengthening the role of nurses and midwives in ensuring safe clinical transfusion and patient safety' 2010; Inter-regional consultation on 'Leadership and management of blood supply systems' 2011; Inter-regional consultation on 'Blood donor selection and counselling' 2011; and Global consultation on 'Haemovigilance', 2012; Global Forum for Blood Safety and Global Blood Safety Network, 2011 and 2013; and 'High-level Policy Makers Forum on self-sufficiency in safe blood and blood products based on VNRD' 2103.

A realistic assessment of blood requirements is fundamental to effective planning for sufficient supply of blood and blood products within a national blood system. With involvement of technical experts in international consultations, WHO organized an Expert Consultation on 'Estimation of blood requirements' in 2010 (*10*) to review tools and methodologies for countries or regions to estimate blood requirements and assess unmet needs. A WHO Expert Consultation on "Achieving self-sufficiency in safe blood and blood products based on voluntary non-remunerated blood donation" was held in 2011 and a WHO expert consensus statement on achieving self-sufficiency in safe blood and blood products, based on VNRD (*7*) was published in 2012.

As one of its core functions, WHO articulates ethical and evidence-based policy options on access to safe blood and blood products and self-sufficiency in blood and blood products based on VNRD and provide guidance on integration of blood system in national health system and the strengthening of national blood system through development of national blood policy and strategic plans, government leadership and governance; legislative frameworks and regulatory mechanisms, human resource management and building capacity, effective organizational and management models and for sustainable financing system. WHO plays a leadership role in shaping the global agenda on blood safety and stimulates the generation, translation and dissemination of valuable knowledge.

In its key role in setting norms and standards, WHO develops recommendations, guidelines, best practices, tools and materials (training and learning) on various steps

of the blood transfusion process to ensure blood safety, and promotes and monitors their implementation. Key policy guidance and advocacy (aide-mémoire) documents, recommendations and guidelines have been produced and translated on topics of good policy process, developing a national blood system, voluntary non-remunerated blood donation, donor selection and counselling, TTI blood screening and blood grouping of all donated blood, quality systems in all processes from donation, testing, processing, storage and transportation, blood cold chain and clinical use of blood and good clinical transfusion practice. WHO strategies and guidance for prevention and management of HIV/AIDS, hepatitis, Malaria and Chagas disease, maternal and child health, health technologies and patient safety include 'blood safety and access to safe blood' as a key integral component. WHO builds capacity through provision of training, mentoring and skill building organized as national, sub-regional, twinning, regional and global level activities.

For translating policy into practice and using WHO norms, standards, and tools, WHO provides technical support, catalyses change, and builds sustainable institutional capacity through country-specific technical assistance projects in developing a national blood system for working towards equitable access to safe blood and blood products, their safe and rational use, and systems and mechanisms for traceability, adverse event reporting and haemovigilance. For monitoring the blood safety and availability situation and assessing global trends, information is collected, analysed and disseminated at national, regional and global levels through the WHO Global Database on Blood Safety.

Working towards self-sufficiency based on VNRD and promoting regional collaboration for access to safe blood and blood products are in line with a recent initiative by WHO on promoting local production capacity to improve access to different types of health products, especially in developing countries (*71,72*). The initiative also promotes the sharing and transfer of technologies, consistent with national law and international agreements, to support the strengthening of national capacity to increase access to essential health products.

Future direction of WHO in the area of blood safety and availability includes improving access to safe blood and blood products for universal health coverage through blood system strengthening and ethical and evidence-based policies; self-sufficiency based on VNRBD and global governance mechanisms; risk assessment and management for safety of donors, products and patients; public health emergencies of international concern; improving quality systems – donors, products and patients 'vein-to-vein'; clinical governance and systems for blood use and transfusion practices; evaluating innovative strategies and technologies; strengthening of collaboration and networks for joint action; and generating strategic information, monitoring, surveillance and vigilance.

European Directorate for the Quality of Medicines & HealthCare (EDQM) of the Council of Europe

The Council of Europe has a long history of setting standards in the field of blood transfusion and medicinal products derived from human blood and plasma. Among the guiding principles, self-sufficiency from voluntary and non-remunerated blood donation (VNRBD) is considered the cornerstone of a safe and sustainable supply of blood and blood components. This credo has been translated in a series of legal instruments

adopted by the Council of Europe, including Recommendation No. R (95) 14 on the "Protection of Health of Donors and Recipients in the Area of Blood Transfusion" (1995) (*73*) and the "European Convention on Human Rights and Biomedicine" (*74*) promoting VNRBD. The definition of VNRBD[5] given in Article 2 of the Appendix to Council of Europe Recommendation No. R (95) 14 is now the most widely used definition.

In Europe, the quality and safety of medicinal products derived from human blood or plasma must comply with the specifications of the European Pharmacopoeia (EDQM/ Council of Europe). In the case of labile blood components, the European Committee on Blood Transfusion (CD-P-TS) is responsible for setting harmonized standards for their preparation, use and quality assurance. The EDQM is in charge of the technical Secretariat of these activities.

The CD-P-TS is assisted by several working parties composed of experts who are highly knowledgeable in the many different areas of blood transfusion. The work of two of them is of direct relevance to self-sufficiency and VNRBD, namely the TS003 working party on "Blood Supply Management" and the TS081 working party on Voluntary and Non-Remunerated Blood Donation.

European Commission

The principles of voluntary unpaid donation and self-sufficiency are embedded within the European Union's legislation on blood safety. Article 20 of Directive 2002/98/EC of the European Parliament and of the Council (*75*) requires all European Union (EU) Member States to "take the necessary measures to encourage voluntary and unpaid blood donations with a view to ensuring that blood and blood components are in so far as possible provided from such donations." The legislation further clarifies that voluntary unpaid blood donation can contribute to safety and refers to the work of the Council of Europe in this field.

Every three years, the European Commission reviews the measures taken by EU Member States. The most recent report, dating from 2011, concluded that almost all EU Member States have legislation or guidance to ensure voluntary unpaid donation and self-sufficiency. Measures include small tokens and refreshments, given directly to donors as well as more public activities including campaigns to raise awareness of the need for blood donors. As a consequence, blood shortages in the EU are rare and rather limited.

In addition, the European Commission plays an active role in supporting EU Member States in organizational aspects of the supply of blood and blood components and funds dedicated projects with and for national authorities on blood safety. The DOMAINE project has identified and makes recommendations on good donor management

[5] Donation is considered voluntary and non-remunerated if the person gives blood, plasma or cellular components of his or her own free will and receives no payment for it, either in the form of cash or in kind which could be considered a substitute for money. This would include time off work other than that reasonably needed for the donation and travel. Small tokens, refreshments and reimbursements of direct travel costs are compatible with voluntary, non-remunerated donation.

practices and the EU Optimal Blood Use project provides guidance on optimal use of the limited supply of blood. The Commission also supports the work of the Council of Europe in this field. More projects are anticipated, including on the concept of patient blood management. All learning and projects are shared and discussed regularly with the national authorities competent for blood safety and quality in EU countries, for which the Commission organizes two meetings per year in Brussels.

International Federation of Red Cross and Red Crescent Societies

Blood safety is critical for safe blood transfusion and health systems. People in all countries have a right to expect that the blood and blood products supplied to them are gathered, produced and provided in a safe and sustainable way that supports their communities and their health systems.

The International Federation recognizes that "health security is a fundamental and indispensable prerequisite to global, national and individual development"[6] and supports the advancement of global health security by promoting voluntary non-remunerated blood donation and advocating for the safe provision of blood and blood products (*76*).

Voluntary non-remunerated donors are recognized to be the safest donors because they are motivated by altruism and the desire to help others and by a sense of moral duty or social responsibility. They are not placed under any pressure by hospital staff, family members or the community to donate blood and they entrust their blood donations to be used as needed rather than for specific patients. The only reward they receive is personal satisfaction and self-esteem.

While WHO recognizes that it is the responsibility of governments to ensure a safe and adequate supply of blood (*77*), National Red Cross and Red Crescent Societies in many countries, as auxiliaries to their governments, play an important role in promoting safe and sustainable blood programmes. National Society activities range from the provision of the national blood service, to the systematic recruitment of voluntary blood donors and the promotion of blood donation and advocacy for VNRD through, for example, annual participation in World Blood Donor Day.

Sustainable and quality blood services play a critical role in the health of any society and the existence of a quality blood service is critical in terms of disaster preparedness. While the availability of blood may be a major concern in the event of a disaster, its safety is also always of paramount importance in any emergency/disaster response. Blood is used for a multitude of life-saving purposes including assisting patients undergoing surgery, treating diseases including anaemia and malaria, caring for patients on chemotherapy, supporting women with complications during childbirth (postpartum haemorrhage) and patients on antiretroviral treatments. The unavailability of safe blood can lead to serious health consequences such as death from haemorrhage or the transmission of life-threatening infections, including HIV/AIDS, hepatitis B and C, syphilis and other infections. There should be preparedness plans to provide rapid response to emergency situations and for post-disaster reconstruction of blood transfusion services.

[6] Health Policy adopted at the 15th session of the General Assembly of the International Federation of Red Cross and Red Crescent Societies, Seoul, November 2005.

Voluntary non-remunerated donation is a key component in ensuring a safe and sustainable blood supply that meets the needs of all recipients. VNRD was enshrined as a fundamental principle of blood services when the 1975 World Health Assembly resolution WHA28.72 called on Member States to "promote the development of national blood services based upon voluntary non-remunerated donation of blood". This principle was reasserted by the Health Assembly in resolutions WHA58.13 in 2005 and WHA63.12 in 2010.

Patients must have equitable access to safe transfusion on the basis of their clinical needs, and the safety of the donor and patient must be considered paramount. The International Federation and its member Red Cross/Red Crescent National Societies promote equity, access, and the quality and safety of blood and blood components so that citizens can have confidence in the security and integrity of their blood system (*78*).

International Society of Blood Transfusion

The International Society of Blood Transfusion (ISBT) was established in 1935 and currently has over 1300 members from 101 countries. ISBT's mission is to "facilitate knowledge about transfusion medicine to serve the interests of donors and patients". It achieves this in a number of ways including the hosting of international and regional congresses, an active academy programme that supports educational events in various countries, maintenance of professional networks and through the publication of *Vox Sanguinis*, a scientific journal. The society places particular emphasis on supporting the development of blood transfusion services in medium and low Human Development Index countries.

ISBT has been a long-term supporter of voluntary non-remunerated blood donation. In 1980, in part in response to World Health Assembly resolution WHA28.72 (1975) on the utilization and supply of human blood and blood products, ISBT developed a *Code of Ethics for blood donation and transfusion (79)*. This sets out the ethical principles and rules to be observed in the field of transfusion medicine. The Code affirms the importance of voluntary non-remunerated blood donation and also identifies that blood is a public resource and that access should not be restricted. The Code has been endorsed by the World Health Organization, the International Federation of Red Cross and Red Crescent Societies and the International Federation of Blood Donor Organizations. The Code of Ethics can be accessed on the Society's website (www.isbtweb.org).

ISBT has a long history of collaboration with the World Health Organization with which it has an official relationship agreement. ISBT was one of the four founding partners of World Blood Donor Day, participates in the WHO Expert Committee on Biological Standardization and has also provided scientific and professional support to a number of recent WHO global consultations.

International Federation of Blood Donor Organizations

The IFBDO (International Federation of Blood Donor Organizations) is engaged in social and health-care voluntary work aimed to collaborate in the dissemination of worldwide advocacy on blood donation. This is an act of solidarity and a civic duty that saves the lives of millions of people every year. Today voluntary blood donor associations in 72 countries are members of the IFBDO.

Working with local authorities, the IFBDO promotes voluntary non-remunerated blood donation as a means for countries to reach self-sufficiency and achieve higher levels

of security in transfusion therapy in every single context. One of the major goals is to grant, through voluntary blood donation, a high level of protection to citizens and the protection of the right to health. Our main goal is to promote the "Blood Donation Culture", meant in its broadest sense. This objective can be achieved only with the development of interdisciplinary information, training, cultural and research initiatives that are the bases of our mission.

European Blood Alliance

In order to identify the gaps and challenges faced globally in moving towards self-sufficiency in safe blood and blood products based on voluntary non-remunerated donation, the European Blood Alliance (EBA) has played a leading role by chairing a working group of the European Committee on Blood Transfusion (CD-P-TS) on Blood Supply Management. In 2012, this group organized a survey on this subject including questions on self-sufficiency in whole blood (WB) and red blood cell concentrates (RBC) from voluntary non-remunerated donations in the countries of the European Directorate for the Quality of Medicines & HealthCare (*80*).

To the question on the assessment of self-sufficiency in whole blood/red blood cells, 23/27 countries (88.9 %) reported that they were 100% self-sufficient (or even over-sufficient); only 3/27 countries (11.1 %) reported that they were less than 100% self-sufficient. In five of the 26 European Union countries responding to the question, the percentage of WB/RBC based on VNRD was lower than 100%. In these countries, the percentage of non-VNRD based WB/RBC varied from 1% to 62%.

For plasma-derived medicinal products, EBA recognizes that Europe is not self-sufficient in plasma for fractionation based on VNRD, but encourages blood establishments in the European Union to reinforce the availability of recovered and source plasma based on VNRD (*81*).

Based on this situation, EBA has taken the following initiatives at international and national levels to support the development of a self-sufficient supply of blood components for transfusion and plasma-derived medicinal products based on VNRD in Europe.

EBA has reviewed and updated evidence to explain why voluntary non-remunerated donations should be preferred to paid donations. This review deals with blood safety for patients, continuity in the blood supply, donor safety and ethical/legal issues in relation to donation. It has integrated six proposals for action to further develop VNRD in Europe, which is currently rolled out as an EBA action plan. This review has been made accessible on the internet and has been widely publicized (*82*).

In Lithuania, where the proportion of non-VNRD is the highest in the European Union, the Ministry of Health has launched a programme to reach self-sufficiency from VNRD by 2016. EBA has been associated with this plan, in 2012 contributing to a workshop aimed at establishing a charter defining the roles and responsibilities of donor associations for communication to donors, in close collaboration with blood establishments. This workshop was marked by the signature by all stakeholders of a memorandum of understanding on collaboration in the promotion of VNRD and the adoption of ethical behaviour in relation to donors. In 2013, feedback from the Lithuanian Ministry of Health regarding the follow-up of this memorandum has been very positive.

For a long time, the definition of VNRD as currently used by the Council of Europe and the World Health Organization has been subject to a constant debate to distinguish VNRD and paid donations, particularly plasma donations. This has led EBA to develop awareness of ethical principles (*83*) concerning donors and to promote the terminology proposed by the Nuffield Council (*84*) in respect of donation of human bodily material, including blood and plasma. Clear definitions of recompense, reimbursement, compensation, remuneration, and an "Intervention Ladder" appear useful in the assessment of current practices and in the better determination of what should be ethically acceptable when encouraging donations to meet patients' needs for blood components and plasma-derived medicinal products.

4 Country examples of self-sufficiency in safe blood and blood products based on VNRD

The implementation of a policy for self-sufficiency in blood and blood products generally follows a stepwise progression in scope, from whole blood towards blood components for transfusion and further towards the provision of PDMP through the fractionation of plasma collected domestically, in alignment with the state of development of the national health system. Achieving self-sufficiency in the supply of blood and blood products from voluntary non-remunerated donations and ensuring the security of that supply are important national goals, and countries may set different timelines in the achievement of these goals, depending on their health system development (*7*).

Most low-income countries and even many middle-income countries in Africa and Asia are in the early stages of blood system development and are still working towards achieving self-sufficiency in blood components for transfusion. Countries with more developed blood systems, mainly high-income countries, having surplus plasma after meeting their clinical needs, have either established domestic fractionation facilities or contract fractionation arrangements with non-for-profit international organizations or for-profit multinational industry. In the Asia–Pacific region, for example, a small number of high-income countries have sufficient access to a broad portfolio of plasma products (coagulation factors, immunoglobulin, and albumin) through domestic fractionation (Australia, Japan and the Republic of Korea), contract fractionation (Hong Kong Special Administrative Region, Malaysia, New Zealand, Singapore and Taiwan, China) or importation. China is gradually establishing a modern plasma fractionation industry. Other countries in the region face shortages of PDMP and non-virally inactivated cryoprecipitate and, ultimately, to inappropriate treatment of patients(*61*).

The goal to achieve self-sufficiency is underpinned by evolving medical practice in these countries. Over time, the demand for plasma-derived medicinal products will continue to increase and with it the need to ensure a safe and secure supply of blood and blood products into the future. The per capita use of PDMP in the world's poorer economies is low by comparison with usage levels in middle-income and high-income markets and is confined to the small proportion of the population able to pay for health services. Many developing countries cannot afford the infrastructure for plasma collection or fractionation and rely instead on imported products (*67*). While notable efforts have been made by some countries to reach self-sufficiency in plasma-derived medicinal products based on voluntary non-remunerated donation, major challenges remain.

Global and national reviews of plasma fractionation arrangements have been undertaken by several countries attempting to plan the best way forward. These reviews examine the situation in different countries to help identify models and processes that could be applicable to their circumstances. The reviews also reveal key issues considered

by countries in trying to provide sufficient, safe blood and blood products for their populations (*67, 85–87*).

National blood systems in twelve countries, including arrangements for plasma fractionation, are described below to illustrate the range of approaches, common elements and challenges in moving towards or maintaining self-sufficiency. The descriptions are neither comprehensive in scope, depth or geographic distribution but are cited simply as examples of certain features of approaches taken.

Australia

Australia is the world's sixth-largest country by total area with a population of nearly 23 million. The primary objectives of the Australian blood sector are:

To provide an adequate, safe, secure and affordable supply of blood products, blood related products and blood related services in Australia, and

To promote safe, high quality management and use of blood products, blood related products and blood related services in Australia.

The Australian Red Cross Blood Service is a branch of the Australian Red Cross. It is the body primarily responsible for blood donation and related services in Australia. Before the Australian Red Cross Blood Service came into formal existence in 1996, the collection, processing and distribution of blood products throughout the country's health system was managed by individual State and Territory Red Cross Transfusion Services. At that time, over 30 agreements were in existence between the various stakeholders, including state and territory governments, the Australian Red Cross Blood Service and Commonwealth Serum Laboratories (CSL) Limited. Supply costs had tripled between 1991 and 1999 and Australia's blood supply system was fragmented with little leverage over escalating costs.

The National Blood Authority (NBA) is an Australian Government statutory agency, established under the National Blood Authority Act 2003 to improve and enhance the management of the Australian blood and plasma product sector at a national level. The NBA represents the interests of the Australian state and territory governments and sits within the Australian Government's Health and Ageing portfolio. It manages and coordinates arrangements for the supply of blood and blood products and services on behalf of the Australian Government and state and territory governments.

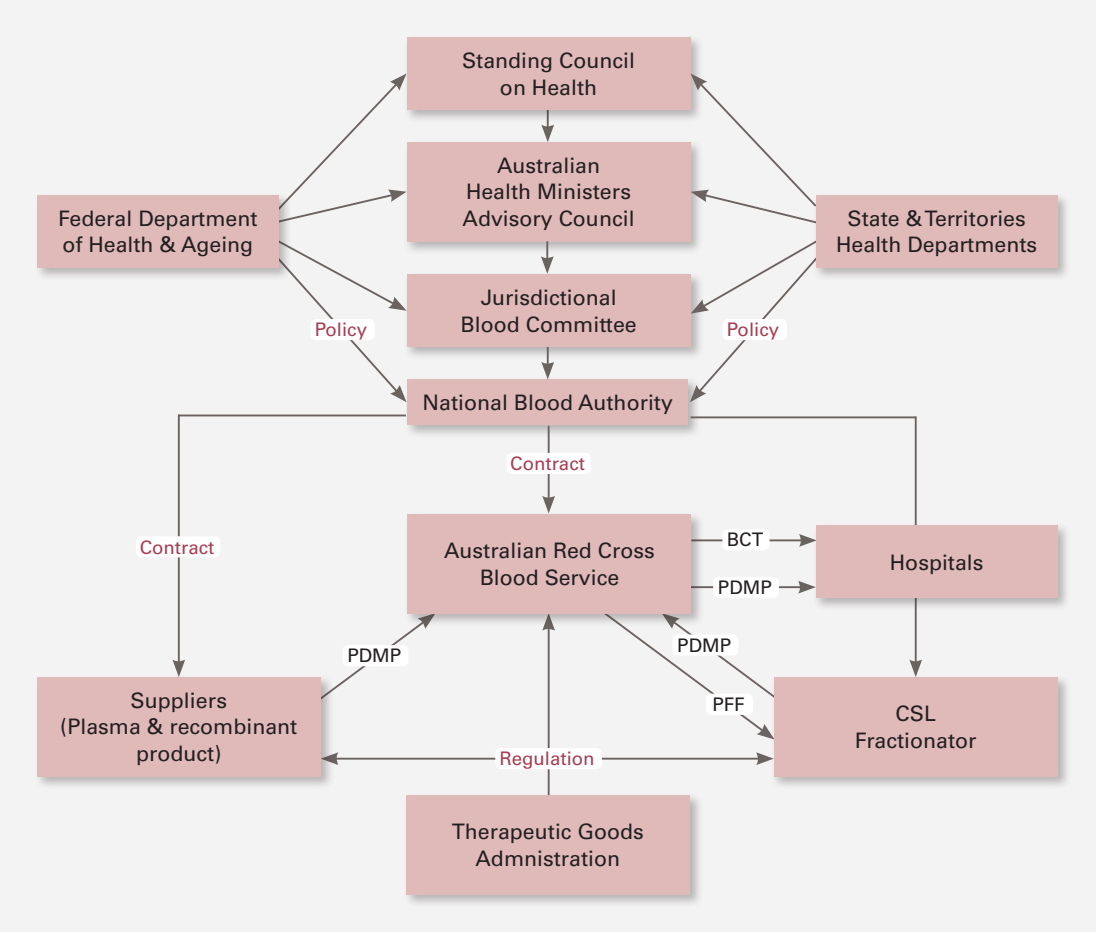
The Therapeutics Goods Administration regulates the safety, quality and efficacy of labile blood components and plasma-derived medicinal products.

The establishment of a national blood service has facilitated new levels of national and international cooperation, resulting in improved consistency, quality and safety across Australia. The unique features of the Australian system are the principle of voluntary non-remunerated donation to support the delivery of labile blood components and the striving for self-sufficiency in PDMP. The health system funds the blood service which has the responsibility of providing labile blood components and PDMP for clinical needs. The blood service collects approximately one million donations of whole blood a year. In 2012–2013, 525 tonnes of plasma were collected from VNRD and sent to CSL for fractionation. Patients do not have to pay for blood or blood products.

Self-sufficiency, although not clearly defined, is promoted in the National Blood Agreement (*88*). This specifies voluntary non-remunerated donations as the source for labile blood components and domestic fractionated PDMP, although it does not specify the source of blood for imported products. Australia is fully self-sufficient in labile blood components, albumin and factor VIII. In 2012–2013, Australia met 63% of its requirements for IVIG through self-sufficiency, with the remaining 37% being imported.

There are challenges and concerns about balancing the cost and capacity of the VNRD system versus imports to meet demands, which are predicted to continue to increase. Currently, imported non-VNRD plasma products are less expensive. The blood service does not control the distribution of recombinant coagulation factors in four of the six states.

Figure 4.1: Overview of the national blood system in Australia



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

The Australian Red Cross Blood Service is currently responsible for all collections of Australian blood and plasma, including both recovered and source plasma, all from voluntary non-remunerated donors. In Australia, the manufacture of most PDMP is

currently funded through a single supplier arrangement between the National Blood Authority, acting on behalf of all nine Australian jurisdictions, and CSL Limited. These products are sourced from the domestic blood supply and are manufactured in Australia (*67*). It is the current policy of the Ministry of Health and Ageing that plasma products are imported only when domestic supply cannot meet clinical need, or where supply chain risks must be addressed.

The history and development of CSL serves as an interesting example of the evolution of the fractionation industry. CSL started as a small government-run laboratory in 1916 to assist in meeting Australia's wartime needs for pharmaceutical vaccines and developed into the national fractionator for Australia. In 1991, it was corporatized and converted to a public company (CSL Ltd) while remaining wholly owned by the Commonwealth Government. In May 1994, the Commonwealth sold CSL by means of a 100% public floatation. With many acquisitions and mergers, it has now become a leading manufacturer in a US$7.5 billion plasma industry. By 2012, it consisted of a group of businesses including CSL Behring, a global provider of plasma-derived and recombinant products; CSL Plasma, one of the world's largest plasma collection networks that has more than 65 plasma collection centres in the United States of America and Germany, with 400 000 paid donors; and CSL Biotherapies, the chosen national plasma fractionator of Australia, Hong Kong, Malaysia, New Zealand and Singapore through contract fractionation of plasma from voluntary non-remunerated donors.

Information provided by the Australian Red Cross Blood Service, Australia.

Brazil

Brazil is a federal republic consisting of 26 states and the Federal District. It is the largest country in South America and the fifth largest country in the world, with a population of about 200 million. The first blood bank in Brazil was created in 1944 and there are now over 7000 haemotherapy services (blood banks) across the country.

In 1980, public policies began to address the abolition of the compensation of blood donors. In 1988, the Federal Constitution prohibited the sale of blood and blood products in the country, establishing blood donation as a strictly voluntary act. This led to the nationalization of the Brazilian blood supply and ended the trade in blood, allowing the consolidation of public haemotherapy services. Each state now has its own blood bank which forms part of a network of public blood banks (Hemorrede), complemented by private services. The National Policy on Blood, Blood Components and Haemoderivatives was established by federal law in 2001 and includes measures to ensure self-sufficiency in blood and blood products in Brazil and to harmonize public actions at all levels of government to achieve this goal. This policy is implemented within the Unified Health System (SUS) by SINASAN (the National System of Blood Components and Blood Derivates) (ICDRA session, 2002) (*89*).

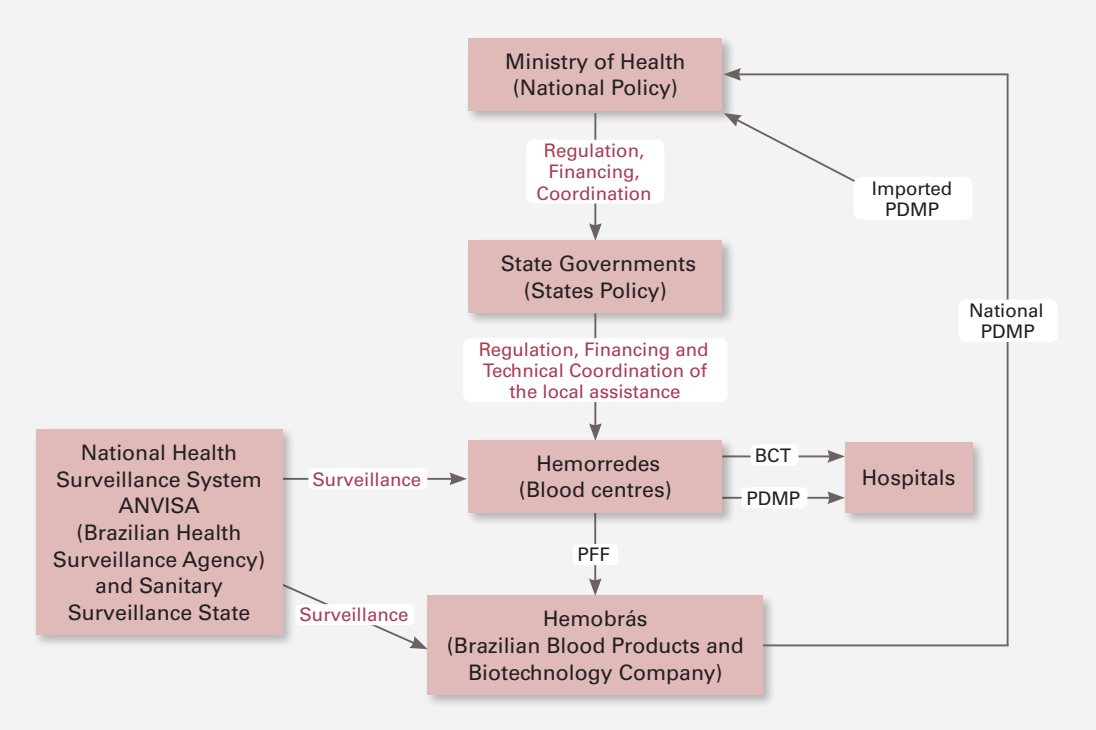
SINASAN is composed of networks of blood banks and the producers of plasma-derived medicinal products under the national leadership of the Ministry of Health, and with the support of ANVISA, the Brazilian Health Surveillance Agency. The governance structure of the national network of blood banks has been decentralized from national level to the states. There are 32 blood centers of greater complexity scattered across all states of Brazil; 65 medium complexity regional blood centres; 302 low complexity blood centres;

176 blood donation and transfusion services; 1733 transfusion agencies; and more than 7000 establishments performing blood transfusion.

In 2012, Brazil collected more than 6.3 million blood donations, corresponding to 19 donations per 1000 population. Of these, 60% were given by voluntary non-remunerated donors and 40% by replacement donors. No information is available about repeat donations. It is estimated that over 500 000 litres of plasma (70%) were recovered from these donations and about 150 000 litres were certified for the production of blood products.

The success of the strategy for voluntary non-remunerated donation and the safety of blood and blood products can be attributed to legislation, regulation by SINASAN, the commitment and technical cooperation of the networks of blood banks and transfusion services throughout the country and the regulation to ensure the quality of haemotherapy products.

Figure 4.2: Overview of the national blood system in Brazil– SINASAN



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

In 2001, to meet the growing demand for quality plasma-derived medicinal products, the Brazilian government launched a programme to use surplus plasma from blood component preparation for the production of coagulation factors, albumin and immunoglobulin. In 2004, the government created a public company, Hemobrás (Brazilian Blood Products and Biotechnology Company) under the Ministry of Health, for the production of plasma-derived medicinal products.

Currently, 50% of the needs for albumin, 40% for immunoglobulin and 15% for factor VIII are met through the fractionation of Brazilian plasma abroad. When in full operation, Hemobrás will be the largest plant of its kind in Latin America. It is designed to process approximately 500 000 liters of plasma per year. Future production of blood products is intended to meet national needs and increase self-sufficiency, reduce import costs which currently stand at over US$ 400million, and reduce the dependence on foreign laboratories. Hemobrás also produces recombinant drugs through biotechnology.

The main objectives of the Brazilian programme of blood and blood products includes maintaining compliance with ethical principles for the health and safety of blood donors, rationalizing the use of blood components and supplying the country with plasma-derived medicinal products produced from surplus domestic plasma. Completion of the construction of the Hemobrás plasma fractionation facility and the process of international technology transfer for the production of blood products will make it possible to achieve self-sufficiency.

Information provided by the Ministry of Health, Brazil.

France

France has a population of 65.5 million. The national transfusion service and national plasma fractionation arrangements are separated by law in France. Voluntary and benevolent blood donation has been regulated by French law from 1952 and, although modified in subsequent years, the principles of this law still govern transfusion practice in France today.

The national blood service, the Établissement Français du Sang (EFS), is a central government agency operating under the auspices of the Ministry of Health. It has held exclusive responsibility since 2000 for the collection of blood, plasma and platelet donations and guarantees the safety of the transfusion chain, from donors to patients. It operates throughout the territory (including French overseas departments) with 17 blood centres (14 across France and 3 in overseas departments), 152 permanent collection venues and 40 000 mobile collections per year. EFS supplies labile blood components directly to hospitals and collects plasma for fractionation by the domestic fractionator, the Laboratoire français du fractionnement et des biotechnologies (French Laboratory for Fractionation and Biotechnologies – LFB).

Linked to these primary roles, over which the EFS has a monopoly, is the performance of immunohaematological tests on recipients of labile blood products. This helps to secure very high safety levels for patients by ensuring immunological compatibility between labile blood products and recipients.

Additional activities, each of which is carried out within a specific legal framework, include:

- Preparation, screening, storage and distribution of human tissues and cells other than blood cells, as well as gene and cell therapy preparations
- Provision of care within the specific framework of its health centres, including phlebotomy, outpatient transfusion, plasma exchange, erythrocyte exchange, extracorporeal photochemotherapy, and collection of haematopoietic stem cells

- Production of blood components and blood products for non-therapeutic purposes, including teaching, research and production of reagents.

The national blood supply is based on 100% voluntary non-remunerated donation with 2.6 million whole blood donations in 2011. The total production of plasma was 926 673 litres (690 788 litres of recovered plasma and 235 885 litres of apheresis plasma). Self-sufficiency is regularly evaluated by EFS and reported to the Ministry of Health; it is monitored at national level by EFS headquarters and managed at regional levels with hospitals. Annual meetings are organized by the Ministry of Health with all suppliers and patients' associations.

EFS is primarily funded by the recovery of costs of the blood products from health-care institutions at a price, fixed by the Ministry of Health, that covers all costs involved in the transfusion process, including collection, screening, processing and distribution.

The blood sector in France is regulated by the Agence nationale de sécurité du médicament et des produits de santé (National Agency for the Safety of Medicines and Blood Products – ANSM). ANSM is an independent health watchdog which operates under the broad guidelines promulgated by the European Medicines Agency.

To ensure the provision of quality services, blood establishments must be approved by ANSM. This approval, which is granted for five years, is renewable and subject to strict administrative, technical, medical and sanitary conditions. ANSM inspects blood establishments at least biennially and leads the national haemovigilance network.

Blood donor organizations participate in promoting blood donation and organizing donation sessions, notably providing hospitality for donors. Their work also contributes to donor retention and conveying the values of blood donation: citizenship, solidarity, generosity and altruism. EFS contributes funding to these organizations to help them fulfill these roles. The Fédération Française pour le Don de Sang Bénévole (French Federation for Voluntary Blood Donation) is represented on the EFS Board of Directors. A representative of the Association Française des hémophiles (French Association of Haemophiliacs) also sits on the EFS Board of Directors. Other patient associations have formed partnerships with EFS to raise awareness of the importance of blood donation by highlighting the need for safe blood and blood products.

L'Agence de la Biomédicine (French Biomedicine Agency) oversees four key areas of human biology and medicine: organ, tissue and cell transplantation, assisted reproductive technology, prenatal and genetic diagnosis and human embryo and embryonic stem cell research. EFS is involved in the recruitment of voluntary bone marrow donors and carries out laboratory tests, in particular HLA-typing of candidate donors, prior to their inclusion on the French Bone Marrow Transplant Register.

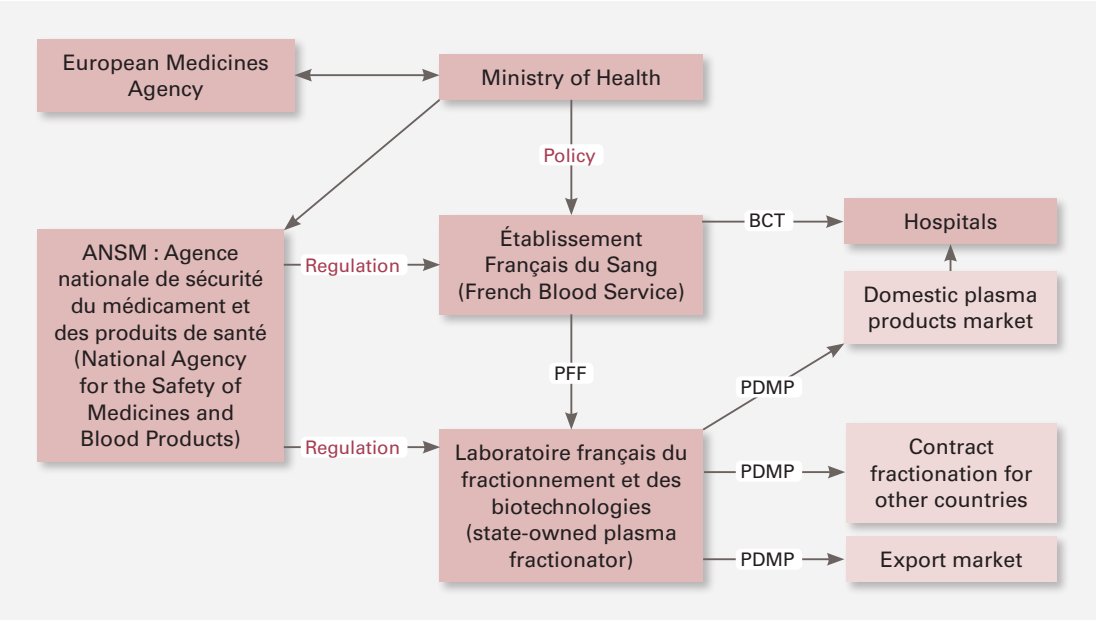
L'Institut de veille sanitaire (Institute for Public Health Surveillance) is responsible for the analysis of epidemiological data on blood donors from EFS.

The Laboratoire français du fractionnement et des biotechnologies (French Laboratory for Fractionation and Biotechnologies – LFB), which is a majority state-owned biopharmaceutical company, has exclusive rights to fractionate French plasma, and sells finished plasma products on the domestic market. There is no requirement, however, for French hospitals to purchase LFB products and they are free to acquire any

brands of plasma-derived medicinal products registered for sale in France. In addition to fractionating French plasma, the LFB undertakes contract fractionation for other not-for-profit entities in Belgium, Luxembourg, Brazil and Morocco and also sells finished plasma products on international markets, from which it derives 30% of its income. Currently, 75% of France´s requirements for albumin, 54% for IVIG and 14% for factor VIII are met through self-sufficiency based on voluntary non-remunerated donation.

Information provided by l'Établissement Français du Sang, France.

Figure 4.3: Overview of the national blood system in France



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

Iran (Islamic Republic of)

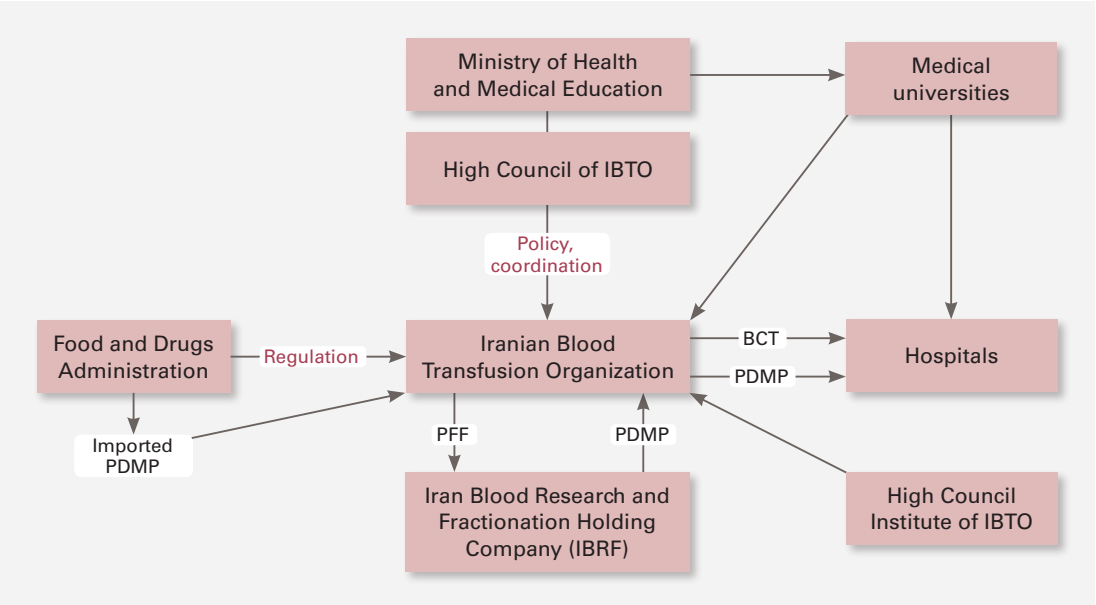
In Iran, which has a population of nearly 77 million, blood transfusion is an integral part of the national health system. Over the past three decades, the government of Iran has made substantial investments in primary and secondary health care and the country now has an advanced health system infrastructure. The Iran Blood Transfusion Organization (IBTO) was established in 1974 in accordance with a parliamentary law to centralize all blood transfusion activities, from donor recruitment to the production of blood components. IBTO is a public and non-profit national organization that relies on the Government of Iran for its budget and delivers all its basic services, including blood components, free of charge to both public and private hospitals. Self-sufficiency in blood and blood components has always been one of the main objectives of IBTO (*88*).

The High Council of IBTO, which is chaired by the Minister of Health and comprises professionals in blood transfusion medicine and science, is the main policy-making body. IBTO is audited regularly by the Ministry of Health, the Paul Ehrlich Institute and by some companies (Biotest and CSL) and) to increase the safety and quality of

blood products. IBTO headquarters regulates the main activities in blood centres. In 2013, there were a total of 212 blood donation centres: 121 blood collection centres, 33 blood collection and component preparation centres and 58 blood centres. These centers collect 80% of blood donations, with the remainder being collected by mobile teams in workplaces, educational institutions and cities not served by fixed sites (*90*). Upgrading the Infrastructure was the main strategy and priority action to achieve self-sufficiency in safe blood and blood products based on VNRD. IBTO has implemented good manufacturing practices for blood and blood components in order to protect the health of both donors and recipients.

In 2007, Iran achieved 100% voluntary non-remunerated blood donation (*91*). In 2012, over two million donations were collected, of which of which 75.2% were donated by regular and repeat donors and 24.8% by first-time donors. Females form 5.2% of the blood donor population. 97% of donated units were processed into blood components and only 3% were used as whole blood.

Figure 4.4: Overview of the national blood system in Iran



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

In 2005, IBTO entered into a contract with the Iran Blood Research and Fractionation Company (IBRC) for contract fractionation of surplus plasma (40,000 litres at that time). With increasing quality assurance and systems, 132 722 litres of plasma (recovered - 132,293 litres and apheresis - 429 litres) were sent for fractionation in Europe in 2011. While providing sufficient IVIG and factor IX to meet the country's needs, Iran is not yet self-sufficient in albumin or factor VIII. However, a cost analysis has shown the value of this arrangement, which has also resulted in a decrease in the cost of imported products. The process of obtaining approval for domestic plasma to be fractionated in Europe has also improved the quality and safety of blood components for transfusion.

Iran is relatively self-sufficient in labile blood components and 40% of its requirements for albumin, 100% for IVIG, 100% for factor IX and 15% for factor VIII are met through self-sufficiency based on VNRD.

Information provided by Iran Blood Transfusion Organization, Iran.

Italy

The founding principles of the Italian Blood System (IBS) are defined in Italian legislation (Law of 21 October 2005, n. 219) which recognizes voluntary non-remunerated blood donation as an essential activity for the National Health Service (NHS). It also recognizes national self-sufficiency in safe blood and blood products, including plasma-derived medicinal products from voluntary non-remunerated donors, as a primary need for the nation.

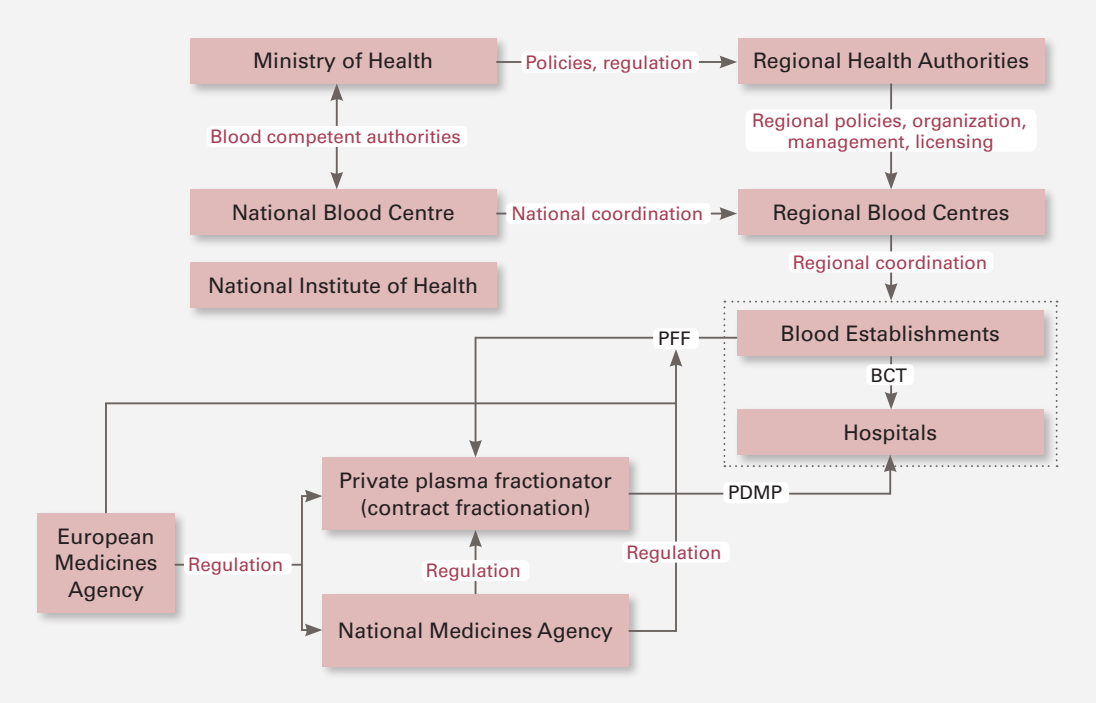
In Italy, health-care service delivery is delegated to 21 regional health authorities funded by the "national health-care fund" (~108 billion € in 2012), mainly derived from general fiscal revenues. The governance of the NHS is entirely public, but the contribution of accredited private health-care providers is acknowledged. The Ministry of Health is responsible for national coordination, legislation and control of the appropriate delivery of "basic" health-care services that must be guaranteed homogeneously and equitably nationwide by the regional health authorities.

Blood establishments are, by law, hospital-based and are increasingly being organized in wide transfusion medicine departments with consolidated processing and testing laboratories. These rationalizing interventions imply a progressive decrease in the high number of blood establishments (about 300) that currently exist, while maintaining governance of the vein-to-vein transfusion process exclusively by consultant physicians specialized in transfusion medicine. At the regional level, blood establishments are coordinated by the 21 Regional Blood Centres (RBCs); these, in turn, are coordinated at national level by the National Blood Centre, thus constituting the national blood network. The National Blood Centre acts as the national competent authority for blood on behalf of the Ministry of Health and also undertakes the role of coordination and technical–scientific control of all issues regulated by pertinent national and European legislation. A National Blood Technical Board has been established in the Ministry of Health, composed of the 21 directors of the Regional Blood Centres, four representatives of blood donor associations, four representatives of transfusion medicine scientific societies, two representatives of patient associations and the director of the National Blood Centre. The National Blood Technical Board is chaired by the Minister of Health and acts as a consultation body on all issues for which national blood legislation requires it to provide advice.

The Italian blood system collects 3.2 million voluntary non-remunerated donations per year (2.7 million whole blood donations and 0.5 million apheresis donations), which represents a donation rate of 53 donations/1000 population. 750 000 litres of plasma (75% recovered plasma, 25% apheresis plasma) collected from VNRD are sent for contract fractionation (2012 data).

More than 7.6 million labile blood components are produced annually and 3.2 million components (2.53 million red blood cells, 220 000 platelets, 450 000 fresh frozen plasma) are transfused to 660 000 patients (2012 data).

Figure 4.5: Overview of the national blood system in Italy



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

Every year since 2008, a national plan for self-sufficiency in blood and blood products from VNR donors has been formally issued. The need for labile blood components and plasma for fractionation is defined by systematic consultation between all the IBS actors and stakeholders, both in periodic meetings and by web-based IT. The definition of needs is based on a detailed examination of past usage by blood establishments and on their capacity to increase the collection of plasma for fractionation. Each year, forecasts for the next year are formulated and blood collection targets and plans are developed for the 21 regional blood collection programmes; in some regions this includes additional collections to support the three regions that are not self-sufficient, thus guaranteeing a balance between supply and demand at the national level. Driving products for self-sufficiency include red blood cells and plasma for fractionation while driving action includes the recruitment of new voluntary non-remunerated donors. Qualitative objectives are also defined annually, together with key performance indicators.

Eighteen out of the 21 regions are fully self-sufficient in labile blood components for transfusion. The overall level of self-sufficiency in plasma-derived medicinal products obtained from national plasma has increased very significantly since 2003. About 55% of Italy's demand for albumin (which is disproportionate in comparison with the average demand in Europe), 81% for IVIG and 53% for plasma-derived factor VIII are met through self-sufficiency based on VNRD. Important gaps among regions have existed over the last two decades and still exist, most south-central and southern regions and the greater islands being furthest from self-sufficiency. Most of the central and northern regions

have achieved, or are close to achieving, substantial self-sufficiency and are facing the challenging problem of having excesses of intermediate fractions (e.g. cryoprecipitate fraction) and/or finished products (factor VIII). Nationwide, there remains a strong need to correct the inappropriate clinical use of albumin and antithrombin. In instances where there is a surplus of products, programmes have been put in place either to donate part of the surplus to developing countries or to supply other countries or organizations on a cost-recovery basis. There exists unanimous consensus in the IBS that only appropriate PDMP needs (hence, not "demand") are to be considered as the main reference point in planning for plasma for fractionation and PDMP production.

In Italy, the commercialization of human plasma, as of any other blood component or part of the human body, is forbidden. Domestic plasma, as with other blood components, is the property of the regional health authorities and is recognized as a national strategic resource. It is sent for fractionation to the contracted pharmaceutical company which provides a full service, from the collection of frozen plasma at the blood establishments, through its processing, to the delivery of finished products to hospital pharmacies. Importantly, plasma, its fractions and the finished products, remain the property of the regions throughout the whole process. Fourteen out of 21 regions are associated in two consortiums for PDMP production, thus enabling optimal frequency in the distribution of finished products as well as favourable costs. The National Blood Centre, together with the Regional Blood Centres, promotes the exchange of products among regions whenever necessary and possible and provides indications to the Ministry of Health for the definition of exchange tariffs which, by law, must cover the costs sustained in the production of plasma and PDMPs.

Information provided by the National Blood Centre, Italy.

Japan

Japan has a total population of 128 million. In 2011, 5.3 million people donated blood and 1.2 million patients were transfused. Overall, the country has 100% self-sufficiency in all labile blood components and some plasma-derived medicinal products, except for albumin products of which 40% are imported.

This success in self-sufficiency has been attributed to learning from painful historical experiences in relation to blood donation and blood products which led to the growth of popular movements and the subsequent formulation of laws and policies and changes in the blood supply infrastructure. In the 1950s, syphilis-infected blood transfusions stimulated a popular movement for blood safety while, in the 1960s, paid donations not only led to the exploitation of poor donors but resulted in the transmission of hepatitis infection to some recipients. This subsequently led to the promotion of voluntary non-remunerated donation, a decision taken by Cabinet in 1964. By 1969, Japan had achieved 100% voluntary non-remunerated donation for labile blood components and by 1974, the country was self-sufficient. During the 1980s, the HIV-tainted blood scandal in which many patients with haemophilia became infected with HIV led to a movement for greater safety and self-sufficiency; this led to drastic changes to the existing blood policy.

Japan has a recognized system in place for the provision of a stable supply of blood products. The Ministry of Health, Labour and Welfare is responsible for policy-making and the legislative framework and oversees the overall management of the blood supply

system in the country, supervising blood collection by the Japanese Red Cross, the sole collector of blood in Japan. It also approves the manufacture of blood products by the Japanese Red Cross and provides guidance on blood usage. The Blood Advisory Council advises on the promotion of voluntary non-remunerated donation, blood safety and the appropriate use of blood.

In addition to having sole responsibility for blood collection, the Japanese Red Cross is by law the only manufacturer of labile blood components and is responsible for monitoring to ensure a stable supply and for conducting post-marketing surveillance. The Japanese Red Cross plans and sets targets for blood donation in conjunction with local governments. The information management system provides data on a daily basis on the status of the blood supply and demand as well as monthly reports on manufactured products.

Japanese blood transfusion services, through the Japanese Red Cross Society, are well-endowed with resources in terms of physical facilities and personnel. Overall, there are 169 fixed blood donation sites in the country, with 1833 motor vehicles used for specific activities (public relations, blood collection, and blood delivery). There are 1852 apheresis equipment and 5757 staff including physicians, pharmacists, laboratory technicians, nurses and administrative staff.

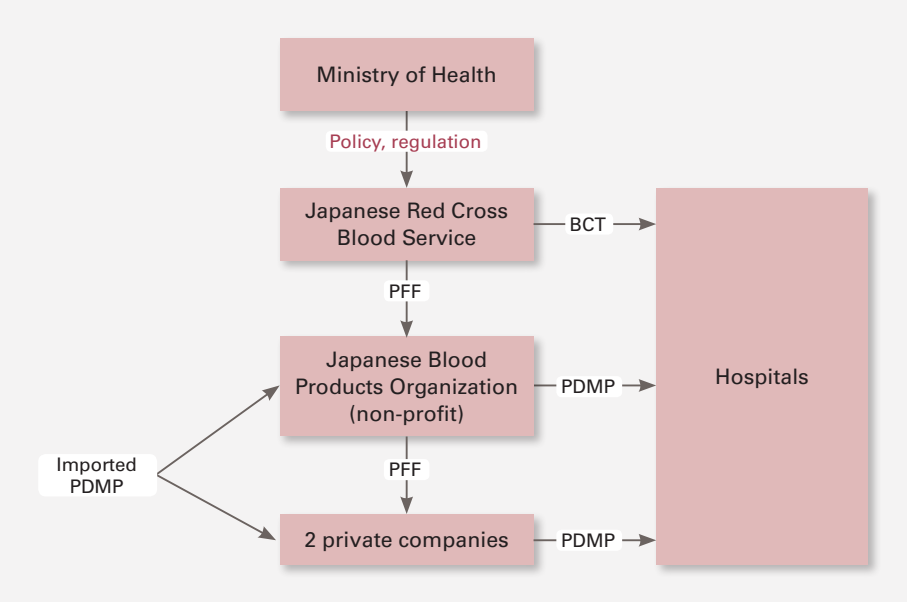
The Japanese Red Cross collects approximately 3 738 000 whole blood and 1 533 000 apheresis donations annually and 950 000 litres of plasma (recovered – 663,000 litres and apheresis – 287 000 litres) collected from VNRD were sent for fractionation in 2011. In 2011, the decision was made to integrate its plasma fractionation operations into one not-for profit enterprise which would construct a new large-scale facility with the goal of meeting the needs of the entire nation for plasma-derived medicinal products (*59*). Currently, 58% of Japan´s requirements for albumin, 95% for IVIG and 100% for factor VIII (19% recombinant products) are met through self-sufficiency based on VNRD.

To strengthen its independence from imports, the Japanese government enacted a law in 2003 that mandates the national government to instruct the prefectures on the volume of plasma needed for fractionation. The Blood Law and Pharmaceutical Affairs Law regulates blood sufficiency and blood safety respectively. The Blood Law stipulates 100% self-sufficiency as a general principle and requires blood collectors and manufacturers to be responsible for a stable supply and appropriate use and to submit data regularly. It prohibits paid donation and further stipulates that the Ministry of Health, Labour and Welfare should formulate a 5-year national action plan. The Pharmaceutical Affairs Law on the other hand regulates blood products in terms of safety and post-marketing surveillance.

The 2007 annual review of the Japanese blood programme by the Blood Products Research Organization (BPRO) underscored continuing progress toward national self-sufficiency in the supply of albumin and IVIG.

The system established to monitor imports and exports is a further strategy to ensure self-sufficiency. Manufacturers are obliged to submit monthly reports to the Ministry of Health, Labour and Welfare on the amount of plasma-derived medicinal products that are imported. In addition, exports are allowed in only exceptional circumstances, such as for humanitarian purposes in emergencies when requested by international organizations.

Figure 4.6: Overview of the national blood system in Japan



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

Guidelines for safety and traceability require the labelling of blood products to indicate the country of origin, collection method and country of manufacture.

The prevailing success notwithstanding, the country faces continuing challenges such as the looming shortage of donors due to demographic shifts emanating from declining birth rates. Currently there is a general decline in the number of donors among the under-30 year age-group. In order to counteract impending shortages, several measures have been put in place including the establishment of the National Committee for the Promotion of Voluntary Non-Remunerated Blood Donation. This acts as a Sub-Committee of the Blood Advisory Council and includes patient and student associations, the media, Lions Club, medical doctors and local government officials among its co-opted members. The second measure is the development of the National Action Plan for 2014 which sets numerical targets to increase donation rates among the younger generation, increase the number of repeat donors and to secure wider community support for blood donation. The third measure is the drive to increase awareness about the importance of blood donation among young people, including high-school students and young mothers.

The second major challenge is the low level of self-sufficiency in plasma-derived medicinal products, especially albumin and factor VIII (including recombinants) which is mainly due to the relatively high domestic manufacturing cost.

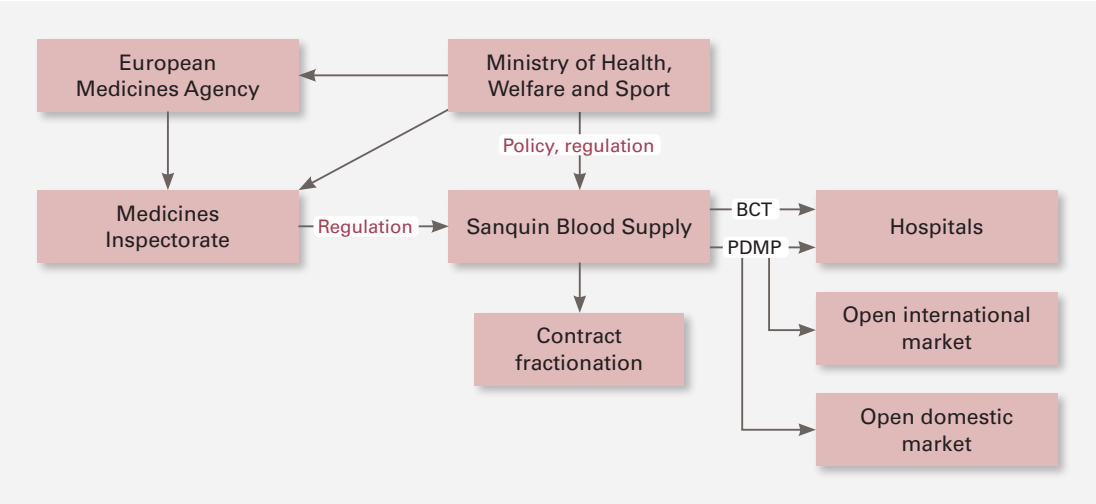
The way forward for promoting self-sufficiency in PDMP includes increasing public awareness of the blood law, promoting appropriate use of blood and blood products, research and development to encourage business integration of domestic manufacturers and for the government to reduce manufacturing costs.

Information provided by Blood and Blood Products Division, Pharmaceutical and Food Affairs Bureau, Ministry of Health, Labour and Welfare, Japan.

The Netherlands

The national blood system in the Netherlands comprises two principal stakeholders: the Ministry of Health, Welfare and Sport (MoHWS) and Sanquin Blood Supply, a not-for-profit foundation. The MoHWS formulates the country's national blood policy framework. The Sanquin Blood Supply Foundation ensures the safety and efficiency of the blood supply in the Netherlands, including whole blood collection, the supply of blood components for transfusion, and plasma collection and fractionation. Sanquin also develops and produces pharmaceutical products, conducts high-quality scientific research, and develops and performs a multitude of diagnostic services.

Figure 4.7: Overview of the national blood system in the Netherlands



BCT Blood components for transfusion
PDMP Plasma-derived medicinal products

Sanquin has a staff of nearly 3000, the majority of whom are employed in blood collection activities. There are four regional blood banks in the Netherlands and these centres operate a total of 116 collection sites, including mobile units. The Netherlands is self-sufficient in labile blood components which Sanquin supplies to 123 public hospitals, including eight teaching hospitals. It is more than 70% self-sufficient in all three products – albumin, IVIG and factor VIII (excluding recombinant products) – that are provided by the domestic plasma fractionation.

The Netherlands has a population of 17 million of whom 387 825 are active voluntary non-remunerated donors who give around 820 000 blood donations annually. Approximately 320 000 litres of plasma are collected each year (recovered – 155,000 litres and apheresis – 165,000 litres).

Under the Netherlands Blood Supply Act, all domestically sourced plasma is retained by Sanquin, primarily for use in the manufacture of plasma products for domestic consumption. If Sanquin has a surplus of plasma intermediaries or finished products

over the domestic demand, such excess may be sold to another not-for-profit entity or, if this is not possible, on the open international market. In the Netherlands, there is an open domestic market in respect of plasma-derived medicinal products. Hospitals are free to purchase preferred brands and have no obligation to acquire Sanquin products, although the majority of the hospitals do so.

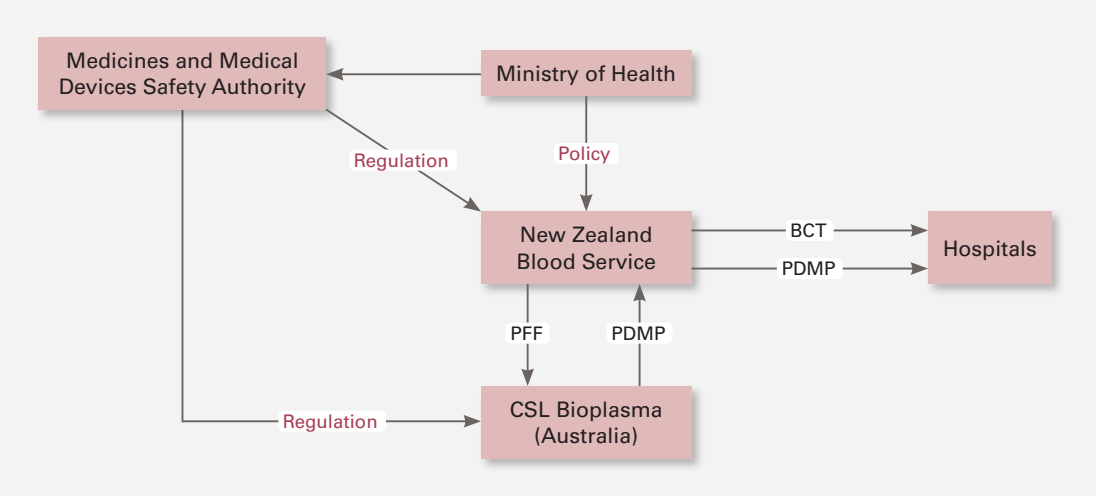
Information provided by Sanquin Blood Supply, the Netherlands.

New Zealand

New Zealand is a remote country with a dispersed population of 4.4 million. The national government is responsible for the provision of health care. Legislation is in place to define the responsibilities of the national blood service and also to prohibit payment for the donation of blood and tissues. Blood products and components are provided free of charge to patients.

The New Zealand Blood Service (NZBS) is government-owned and is the sole supplier of blood components and plasma-derived medicinal products to hospitals in New Zealand. It has a common electronic blood management system allowing the tracking and control of stock and the issue of blood products to patients nationally. NZBS forecasts the demand for labile blood components from hospital utilization data and, in consultation with clinicians and hospitals, estimates supply needs and adjusts collections to meet these needs. NZBS monitors the stock of all blood products on a real-time basis with standard reports issued daily and minimum and designated stock levels are set for every part of the supply system. Strong relationships are maintained with consumer groups, including haemophilia and immune deficiency associations.

Figure 4.8: Overview of the national blood system in New Zealand



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

The national blood supply is entirely based on voluntary non-remunerated donation, with approximately 150 000 whole blood donations and 23 600 plasmapheresis donations collected each year (2011 data). As in many high-income countries, IVIG is the product

driver for plasma collections. Plasmapheresis has been increased to the level required to meet the national need/demand for IVIG. NZBS produces plasma components for direct transfusion by apheresis. Plasma for fractionation is recovered from whole blood and additional plasmapheresis is undertaken to ensure sufficient plasma is produced to meet clinical needs. In 2011, approximately 51 000 kg of plasma were sent to Australia for contract fractionation. The manufacturing contract with the fractionator includes plasma specifications and incorporates an agreement to sell surplus plasma-derived factor VIII and albumin back to the fractionator. This ensures that the donor's gift is maximized. There is concern that the demand for this product will continue to increase and there are pressures from commercial companies to enter the market. However, NZBS can manage its own risks, maintain the security of supply and make optimal use of donations.

NZBS provides a "vein-to-vein" blood service, including the management and oversight of hospital-based blood banks. NZBS collects blood, produces labile blood components and provides these to hospitals, collects plasma, contracts for plasma to be fractionated offshore under a contract fractionation arrangement, and distributes plasma-derived medicinal products to hospitals. It is also directly responsible for hospital blood banks in the larger hospitals and provides a comprehensive transfusion medicine advisory service to all hospitals in the country on a 24-hour basis. NZBS operates under a "not-for-loss", or cost recovery, arrangement, which involves charging hospitals prices for delivered products and services that are sufficient to offset the operating costs of the Service. New Zealand is self-sufficient in blood components for transfusion and in plasma-derived medicinal products, with the exception of RhD immunoglobulin. NZBS is required to produce a rolling three-year strategic plan each year. This currently includes an on-going commitment to self-sufficiency in blood and blood products. New Zealand has examined alternative options but has determined that the most cost-efficient approach is to continue its existing contract fractionation arrangements with CSL Bioplasma, Australia.

Information provided by the New Zealand Blood Service, New Zealand.

Norway

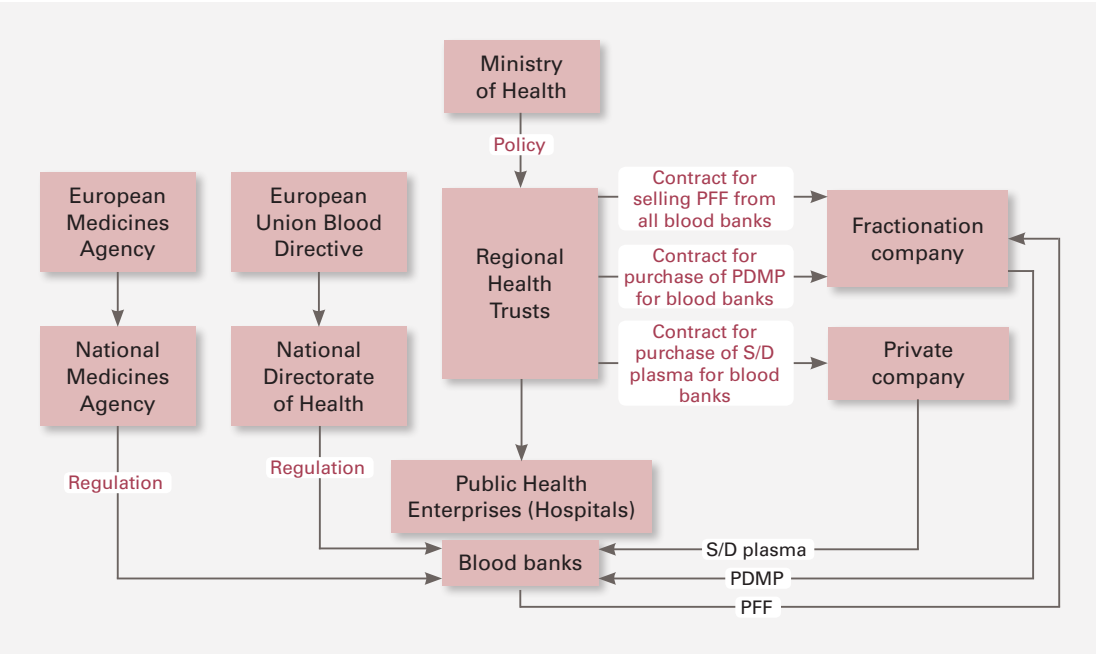
Norway is a country with five million inhabitants living in an area equal to about 80% of that of France. Norway's blood system is structured on a decentralized rather than a national model, reflecting 27 public health care enterprises, each comprising one or several public somatic hospitals (85 in all). Health care enterprises are organized into four regional public holding trusts that control the services of the public hospitals within their jurisdictions, and all health trusts operate their own blood banks. Public hospitals cover the vast majority of hospital activities in the country and their services are provided free of charge to all Norwegian citizens. A minority of elective, relatively simple procedures are performed by private health institutions. Transfusion is performed only in public somatic hospitals.

All blood banks are hospital-associated and the national blood supply is entirely based on voluntary non-remunerated donation with 213 000 whole blood donations in 2011. The total production of plasma is 55 210 kg (about 98% recovered plasma), all from voluntary non-remunerated donations.

Self-sufficiency in blood and blood products has been a national goal since 1980. A public investigation in 1986–1987 concluded that the volume of plasma produced domestically

was insufficient for a domestic fractionation plant to be established. Instead, the Health Directorate initiated a project for national self-sufficiency in plasma-derived medicinal products (albumin, factor VIII and factor IX) and, later, also IVIG and solvent/detergent-treated pooled human plasma based on the contract fractionation of Norwegian plasma. A pilot project for contract fractionation was initiated by the Red Cross and National Hospital Blood Centre in 1986. The pilot project provided valuable experience and was replaced in 1988 by the National Fractionation Project, coordinated by the National Institute of Public Health. All blood banks in Norway joined the national project. The project involved the collection of all plasma, tendering, arranging the contract with a fractionator, receiving all the fractionated products and distributing them to the blood banks in a closed, non-commercial, not-for-profit system. Throughout this process, plasma products were considered the property of the blood banks and could therefore be used by the hospitals without payment of customs duties, pharmacy profits and value added tax (VAT).

Figure 4.9: Overview of the national blood system in Norway



PFF Plasma for fractionation
PDMP Plasma-derived medicinal products
S/D plasma Solvent/detergent treated pooled human plasma

The project provided safe plasma-derived medicinal products for all Norwegian patients and was considered a success in terms of self-sufficiency in safe blood products (*92*). In 2007–2008, the consumption of IVIG reached a level that could not be sustained with domestic plasma. The shortfall was covered temporarily from the commercial plasma market (*93*) as a means of handling a supply crisis. However, in a permanent system, commercial products could not be distributed and used without paying customs duties, pharmacy profits and VAT. As a two-system supply was unacceptable from the point of view of free market competition, the Norwegian plasma supply system had to be restructured.

It should also be emphasized that the National Fractionation Project was formed in 1988 primarily to provide safe factor preparations for Norwegian haemophiliacs. In 2007–2008, more than 90% of factor VIII consumption was covered by recombinant factor VIII preparations. The very focus of the project had therefore changed; for this reason, the project had to be reorganized.

Since 2009, Norwegian plasma has been sold to a private "for-profit" fractionation company which also uses paid plasma donors and sells albumin, prothrombin complex and IVIG back to Norway. Baxter won the contract for 2009–2013, while Octapharma took over in July 2013. Furthermore, solvent/detergent-treated pooled human plasma from commercial plasma donors is bought from Octapharma to cover all national consumption of fresh frozen plasma. This system ensures that the consumption of albumin, plasma thromboplastin component, IVIG and solvent/detergent-treated pooled plasma is covered by products complying with European Union commercial and pharmaceutical standards. The main concern is that the new supply system conflicts with the altruistic foundation of the transfusion service, as the supply does not come from voluntary non-remunerated donors only.

A separate concern is that the consumption of labile components has increased by about 15% between 2000 and 2009–2010. The number of blood donors has not increased simultaneously, and there is a risk of a supply crisis for labile blood components (*93*).

A long-term effort is required to redress the balance between production and consumption and the suggested strategy is multipronged: re-establishment of a national agency for coordination of the activities of the blood banks and a combination of increasing the number of blood donors, reducing the use of erythrocyte concentrates, IVIG and fresh frozen plasma replacement products, fewer whole blood collections and more plasmapheresis. Firm emphasis should be placed on reshaping national self-sufficiency by voluntary non-remunerated donors only.

Information provided by the University of Oslo, Norway.

Republic of Korea

The Republic of Korea has a population of over 50 million. The responsibility for operating the national blood programme was delegated to the Korean Red Cross (KRC) in 1981. The blood service is the KRC's largest domestic programme and covers over 93.4% of the total blood supply. As the agency with nationwide responsibility for blood transfusion, its mission is to procure and supply safe blood to those who need it most as quickly as possible.

In 1981, KRC was delegated as the sole manager of blood services in the country, by presidential decree, and in 1994 was given further responsibilities by government for the collection and supply of blood fractionation components. Until then, there had been a few paid plasma collection centres, but this move completely eliminated paid donation and only voluntary non-remunerated donation was permitted. There is political commitment for voluntary blood donation in that donor campaign activities are graced by political leaders such as the Prime Minister. KRC has a well-organized administrative system for planning, ensuring the safety and quality of blood and blood products, and information management. It has 134 fixed blood donation centres, 96 mobile collection vehicles in 15 blood centres, three blood testing centres including molecular biology

laboratories, a blood transfusion research institute and a plasma fractionation centre under the management of KRC Blood Services Headquarters.

KRC Blood Services have a working relationship with government bodies, medical blood banks, and a private blood centre as components of the blood service in Korea. There is an integrated blood information management system (BIMS) which was implemented in 2003. It is connected to systems in government, hospital blood banks, and private blood centers through the blood information sharing system (BISS). BISS can transmit information between KRC and other bodies about blood ordering and enquiries about donor eligibility; it has also contributed to self-sufficiency and the safety of blood and blood products in the country since it enables the demand and supply to be estimated and appropriate measures taken.

In 2012, the Korean Blood Service (Korean Red Cross and other blood centres) collected over 2.7 million blood donations, of which 93.4% were collected by KRC, and supplied 6.12 million units of blood and blood products. The highest rate of blood donation was by people in their 20s (the minimum age for blood donation is 16) who comprised nearly 41% of donors. In general, about 5% of the Korean population donates blood every year; all donations are voluntary and non-remunerated. The progression towards 100% VNRD has been due to historical events, such as the 4.19 revolution, the commitment of the government and the KRC, and a highly effective blood donor programme. The first voluntary donations were given after the 4.19 revolution in 1960, based on the spirit of humanity and voluntary service for victims and in 1974, the Korean Red Cross stopped paid donations and switched to voluntary non-remunerated donation.

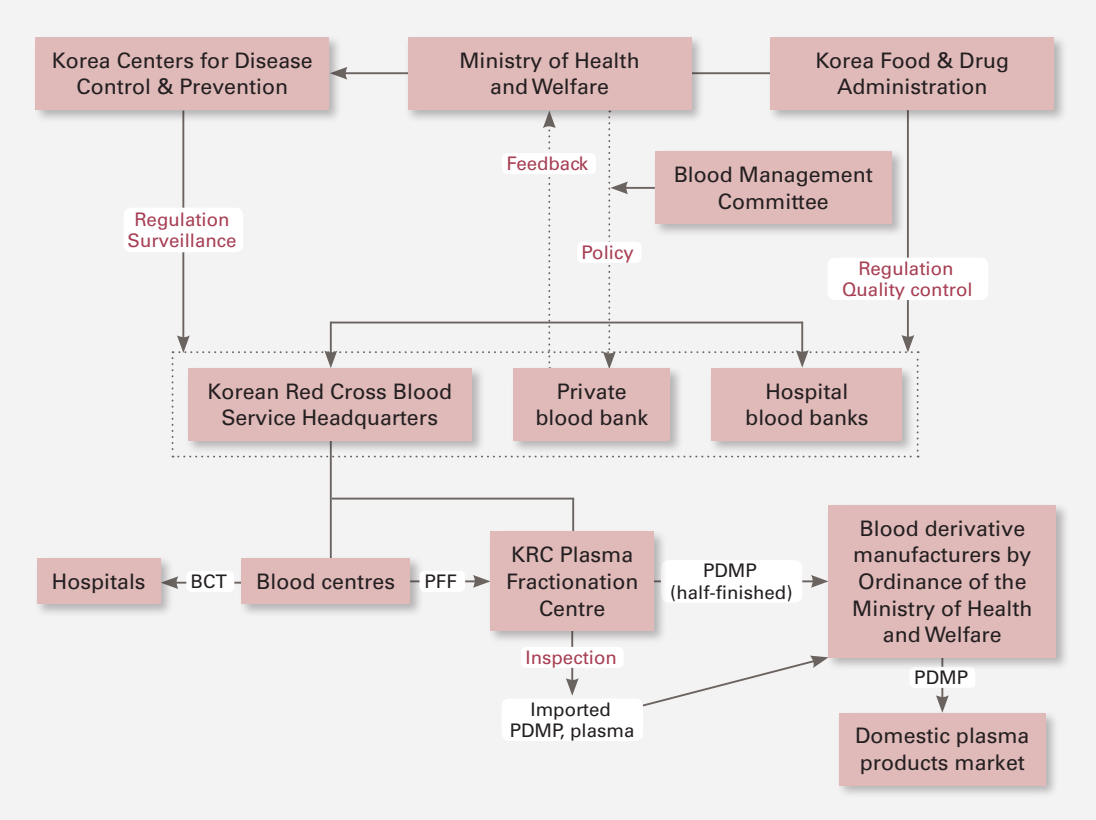
The high rate of voluntary blood donation can be attributed to vigorous scheduled campaigns by KRC which have included the world's largest human blood drop, an online blood donation hero photo contest, a blood donation hero campaign, sports events, corporate campaign and "Paint Korea Red" campaigns which have increased public awareness, the number of donations and donors self-esteem. Donors, as well as companies and organizations that recommend them, are given special recognition as heroes. To inculcate the spirit of blood donation from a young age, the sensitization campaign has been taken to kindergarten and primary school students. An effort to create a more convenient and friendly blood donation environment has also been a key factor in maintaining a high blood donation rate. From 2005, the government granted a subsidy of 55 million dollars to improve accessibility by donors and the number of blood donation centres increased from 95 in 2004 to 134 in 2013.

The plasma supply for pharmaceutical manufacturing consists of surplus plasma recovered from whole blood collections and source plasma from plasmapheresis in Korea. In 2011, 410 751 litres of plasma (recovered – 210,063 litres and apheresis – 200,688 litres) collected from VNRD were sent for fractionation. Shortages are typically covered by importation. The total plasma supply for fractionation in 2012 was 840 610 litres and the self-sufficiency rate was about 48.9% in terms of domestic demand. After introducing plasmapheresis in 1991, the number of plasma collections by KRC increased significantly. The widespread awareness of donors about the importance of plasma donation as well as the construction of additional blood donation centres has played a significant role in this remarkable growth (*94*).

The fundamental policy for supplying plasma derivatives was established by the government in 1978 following World Health Assembly resolution WHA28.72 (1975) which

urged countries to work towards self-sufficiency and avoid commercialism in the supply of human blood and blood products. Since then, the government has maintained a public arrangement for plasma fractionation by authorizing the delegation of the supply of plasma and plasma products to KRC through the revision of the Pharmaceutical Affairs Act in 1994.

Figure 4.10: Overview of the national blood system in the Republic of Korea



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

In accordance with this policy, permission to undertake fractionation and importation, the inspection of potentially importing blood collection centres, and regular audits of plasma importers, have been all granted was executed by KRC. KRC also pushed ahead with its plan to produce end-products and built a plasma fractionation centre in 1991, although the original plan was abandoned due to disputes about over-investment. Currently, KRC processes plasma for the manufacture of only a few intermediate products, including 20% albumin solution, immunoglobulin fraction and cryoprecipitate. These intermediaries are purchased and further manufactured to end-products by the fractionation companies. Due to the public management policy, the price of domestic plasma products has been maintained at a moderate level compared to other countries and the domestic fractionators have been able to improve their competitiveness.

As medical indications for IVIG steadily expand, the demand is expected to increase annually. Conversely, controversies about the efficacy of albumin are likely to cause

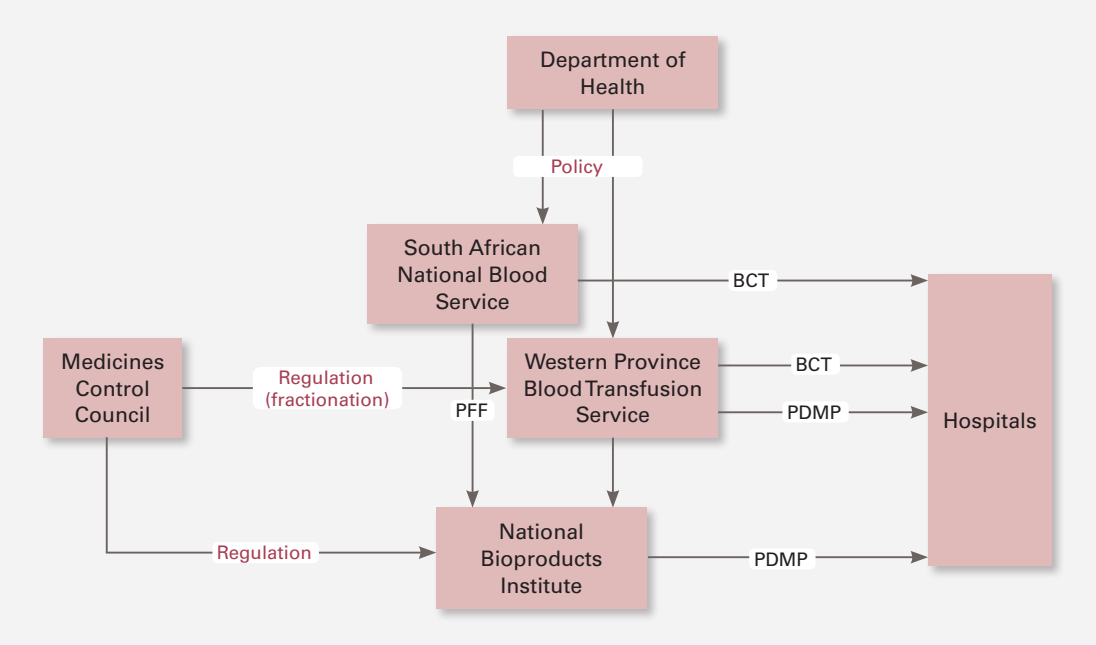
a gradual decrease in demand. The remarkable consumption of albumin is due to a traditional tendency towards prescription and, without regulation, over-consumption seems likely to continue for some time. The demand for coagulation factors is expected to diminish as recombinant products are gradually replacing plasma-derived products.

Information provided by the Korean Red Cross Blood Service, Republic of Korea.

South Africa

South Africa is a country with a population of more than 50 million. The HIV prevalence rate in the population aged 25–50 years is approximately 25%. Labile blood components and plasma-derived medicinal products are supplied by cooperation between two blood services and the domestic fractionator. The South African National Blood Service (SANBS) is a non-profit organization and operates throughout South Africa, with the exclusion of the Western Cape (population 4.5 million). SANBS is also regarded as a major role player in the provision of support to countries in the Southern African Development Community region. Its mission as "an organization of voluntary, non-remunerated blood donors, is to provide all patients with sufficient, safe, quality blood products and medical services related to blood transfusion, in an equitable, cost-effective manner". Its core business is to provide medical services in relation to blood transfusion, the processing of human blood and the supply of blood fractions and blood products. It collects around 830 000 whole blood units annually from approximately 450 000 voluntary non-remunerated donors (0. 9% of the eligible population).

Figure 4.11: Overview of the national blood system in South Africa



BCT Blood components for transfusion
PFF Plasma for fractionation
PDMP Plasma-derived medicinal products

The Western Cape is served by Western Province Blood Transfusion Service (WCBTS), which is a community-based regional health organization formed by an association

of voluntary blood donors that collects approximately 150000 units per year. Both organizations are "not for profit", non-government and self-supporting financially, based on a fee-for-service cost recovery model. Both blood services adhere to national standards, are based entirely on voluntary non-remunerated donation and are funded through the sale of products to hospitals and provincial government departments. Requirements for blood and blood products are estimated nationally and needs are forecasted by monitoring usage and communications with users.

Plasma is fractionated by the National Bioproducts Institute (NBI), a private, autonomous not-for-profit association and a non-governmental organization. Its mission is to improve health care through the provision of cost-effective, appropriate products and services that satisfy customer needs and international quality standards. It is the only plasma fractionator in South Africa capable of providing a comprehensive national fractionation service that includes the manufacture and distribution of a complete range of plasma-derived medicinal products. NBI's range of plasma-derived medicinal products comprises albumin solutions, coagulation factors, immunoglobulins and fresh dried plasma. Since its inception, NBI has worked on a self-sufficiency programme for plasma-derived medicinal products, in collaboration with the regional blood services in South Africa.

NBI's core business is to manufacture pharmaceutical products from human plasma, using a process of protein fractionation. The majority of this plasma (> 95%) is obtained from SANBS. The products are distributed throughout South Africa and, where surpluses exist, to the Southern African Development Community and other developing countries. NBI, together with SANBS and WPBTS, strives to achieve the Department of Health's goal of ensuring self-sufficiency in blood, blood products and plasma-derived medicinal products for all patients in South Africa. To this end, NBI endeavours to provide products and services from South African resources using plasma from healthy, voluntary, non-remunerated donors. By purchasing plasma from the blood services in South Africa, NBI is able to contribute financially to maintaining an excellent standard of blood transfusion for South African patients. The main challenge is that the demand for PDMP is exceeding the capacity of the fractionation plant and the quantity of recovered plasma available for fractionation.

Information provided by the South African National Blood Service, South Africa.

Sri Lanka

Sri Lanka has been able to achieve exceptionally good health indicators through a well-established preventive and curative health-care service delivered free of charge and other favourable social factors such as a high literacy rate. The National Blood Transfusion Service (NBTS) of Sri Lanka has been recognized as one of the model blood transfusion services among developing countries by the International Society of Blood Transfusion due to its achievements in supplying safe and quality blood and blood products to fully meet the requirements of public and private sector hospitals.

The total population of Sri Lanka is 21 million and self-sufficiency in blood and blood products steadily has improved over the years. NBTS has increased total blood collections from 190 000 in 2004 to over 350 000 in 2012, 99.4% being collected from voluntary non-remunerated blood donors. The annual rate of mobile blood collections has increased

from 53% in 2005 to 90% in 2012 and Sri Lanka has achieved an overall donation rate of 1.6 %. All units of donated blood are tested for five transfusion-transmissible infections, including HIV, and in 2011, Sri Lanka reported the lowest prevalence of HIV and other TTI in the region. Almost 100% of the collected blood is processed into components using modern technology. The service has a well-established haemovigilance system to cover donor, process and recipient adverse events.

The success of the National Blood Transfusion Service is the result of well-structured administrative and organizational systems being in place, supported by conducive national blood policies and regulations. Political commitment has also played a major role as the uninterrupted provision of quality health services, including safe blood and blood products, is one of the mandates of the government. Administratively, the NBTS is a fully government-owned organization which is nationally coordinated and managed under the preview of the Ministry of Health. The National Blood Centre is the headquarters of the service and there is a well-organized island-wide network of 88 hospital blood banks and one regional blood centre. Blood banks have been clustered into 16 clusters and a large blood bank within the cluster has been identified as the cluster centre.

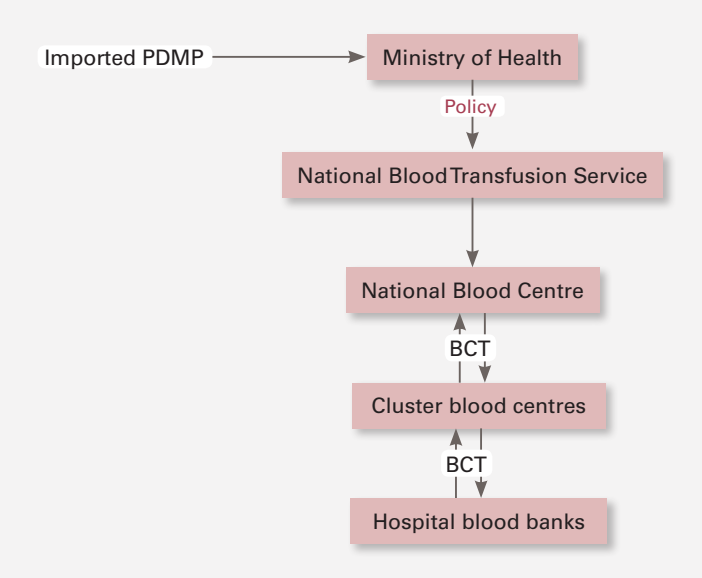
Sri Lanka has a national policy on self-sufficiency for blood and blood products stipulating that all blood should be collected from voluntary non-remunerated donors; a voluntary donor promotion programme, the "national blood force" reaches down to village level. Further, there are regulations on the importation or exportation of blood and blood products as well as estimations of the demand and supply of blood and blood products at national level.

Methods used to estimate national clinical requirements for blood and blood products and the sufficiency of supply include the collection and analysis of monthly statistics on requests and issues of blood and blood products at the National Blood Centre and other hospital-based blood banks, and daily monitoring of island-wide stock levels. Weekly review meetings are held to plan blood collections and component preparation and blood collection and production planning also takes place at monthly donor review meetings at regional and hospital level. Monthly review meetings are held with procurement agencies on stock levels and ordering, with special emphasis on consumables.

Self-sufficiency is also attributed to the emphasis placed by the government on public accountability for meeting patient needs. Paid donations are not permitted since the government is responsible for providing free health services for all the citizens of Sri Lanka. The mobile blood donation campaigns, which contribute to 85% of total collections, are organized by enthusiastic voluntary organizers.

Despite these successes in achieving self-sufficiency in blood components for transfusion, based on voluntary non-remunerated donation, there are still outstanding challenges. These include regional and seasonal variations in total whole blood collections, difficulties in providing uninterrupted supplies of platelets and cryoprecipitate to meet demands, unwillingness of clinical staff to accept alternative groups of platelets and red cells when rare groups are requested, the high cost of mobile blood collections and the difficulty in monitoring island-wide daily stock levels in order to redistribute blood stocks, when required. Furthermore, all fractionated products (factor VIII concentrate, albumin and IVIG) are imported and NBTS has no control over these.

Figure 4.12: Overview of the national blood system in Sri Lanka



BCT Blood components for transfusion
PDMP Plasma-derived medicinal products

Various measures to promote self-sufficiency have been considered to respond to these challenges. They include (i) increasing blood collections through wider public awareness and donor promotion, social marketing and the national blood force; (ii) improving blood component production through the establishment of platelet and cryoprecipitate apheresis centres and island-wide equipment maintenance centres; (iii) efficient blood stock management through a national computerized network of blood banks; (iv) export of excess plasma for contract fractionation; (v) improved clinical transfusion practice through the education of clinical staff on the appropriate use of blood and blood products; and (vi) the monitoring of imported plasma-derived medicinal products by the NBTS.

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Acknowledgements

The WHO Blood Transfusion Safety unit acknowledges the support of the Ministry of Health, Labour and Welfare, Government of Japan, in the development of this document *Towards Self-Sufficiency in Safe Blood and Blood Products based on Voluntary Non-Remunerated Donation: Global Status 2013*.

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Annexes

Annex 1

Data sources and presentation in Chapter 2

1 Blood safety data for the year 2011 from the following countries were used as a source for Chapter 2.

WHO African Region: (45/46)

Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon*, Cape Verde, Central African Republic*, Chad, Comoros, Congo, Cote d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea*, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe*, Senegal, Sierra Leone, South Africa, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, Zimbabwe

Data for the Seychelles were not included.

WHO Region of the Americas: (33/35)

Antigua and Barbuda, Argentina, Bahamas, Belize, Bolivia (Plurinational State of), Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, Uruguay, Venezuela (Bolivarian Republic of)

Data for Barbados and Grenada were not included.

WHO Eastern Mediterranean Region: (19/22)

Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Morocco, Oman*, Pakistan, Saudi Arabia, Somalia, South Sudan, Syrian Arab Republic, Sudan, Tunisia, United Arab Emirates, Yemen*

Data for Lebanon, Libya and Qatar were not included.

WHO European Region: (43/53)

Albania, Armenia, Belarus, Belgium, Bosnia and Herzegovina*, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Luxembourg, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino*, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, The Former Yugoslav Republic of Macedonia, Turkey, United Kingdom of Great Britain and Northern Ireland, Uzbekistan*

Data for Andorra, Austria, Azerbaijan, Cyprus, Hungary, Lithuania, Malta, Monaco, Turkmenistan and Ukraine were not included.

WHO South-East Asia Region: (11/11)

Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste*.

WHO Western Pacific Region: (26/27)

Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Papua New Guinea, Philippines, Republic of Korea, Samoa, Singapore, Solomon Islands, Tonga*, Tuvalu, Vanuatu, Viet Nam.

Data for Palau were not included.

*2010 data

2 Population data, income group classifications

Data reported for population were extracted from World population prospects: the 2010 Revision. Population Division, Department of Economic and Social Affairs, United Nations Secretariat, New York, 2011.

Income group classification is based on World Bank list of economies (July 2012). World Bank, Washington DC, 2012. http://siteresources.worldbank.org/DATASTATISTICS/Resources/CLASS.XLS)

The Cook Islands, Nauru and Niue have been classified into income groups using gross domestic product.

3 Data from 177 (91.2%) countries were available for the analysis (see table below).

The total population of responding countries is 6.84 billion, accounting for 98.6% of the global population.

WHO region	Total		High-income		Middle-income		Low-income	
	No.	No. responding countries (%)	No.	No. responding countries (%)	No.	No. responding countries (%)	No.	No. responding countries (%)
Africa	46	45(97.8)	1	1	19	18 (94.7)	26	26 (100)
Americas	35	33(94.3)	6	5 (83.3)	28	27 (96.4)	1	1 (100)
Eastern Mediterranean	22	19(86.4)	6	5 (83.3)	14	12 (85.7)	2	2 (100)
Europe	53	44 (83.0)	31	25 (80.6)	20	16 (80.0)	2	2 (100)
South-East Asia	11	11(100)	0	0	7	7 (100)	4	4 (100)
Western Pacific	27	26(96.3)	6	6 (100)	20	19 (95.0)	1	1 (100)
Global	194	177(91.2)	50	42(84.0)	108	99 (90.7)	36	36 (100)

Responding countries were often unable to answer all the questions in the questionnaire, leading to considerable variations in the number of responses obtained to different questions. The report therefore indicates the number of responses received for each question.

The exclusion of specific data from countries with large denominators (such as the total number of donations) could have a substantial influence on the regional or economic group sums or percentages that were calculated. Similarly, the inclusion of countries with large denominators (such as the total number of donations) could distort the regional average produced. This may apply to Tables 2.2, 2.3, 2.5 and 2.6.

Table 2.2: Types of whole blood donations, by income group of countries, 2011 Table 2.3: Proportions of voluntary non-remunerated whole blood donations, by WHO Region and income group of countries, 2011	a. Data from 173 countries were used for analysis. Data from Germany have not been included in this analysis. b. The aggregated data for middle-income group in WHO South-East Asia Region may be dominantly influenced by data of India. c. The aggregated data for the middle-income group in the Western Pacific Region may be dominantly influenced by data from China.
Table 2.5: Number and percentage of apheresis donations, by types of donations and WHO Region, 2011 Table 2.6: Types of apheresis donations, by income group of countries, 2011	a. Data from 72 countries were used for the analysis. Data from Germany and Pakistan have not been included for this analysis. b. Data from India and Indonesia were not available. Large number of apheresis donations may be collected in the two countries but were not reported. c. The aggregated data for middle-income group in the Western Pacific Region may be dominantly influenced by data from China.
Table 2.8: Percentages of whole blood donations processed, by WHO Region and income group of countries	a. The aggregated data for the middle-income group in the WHO South-East Asia Region may be dominantly influenced by data from India. b. The aggregated data for the middle-income group in the Western Pacific Region may be dominantly influenced by data from China.

4 Partial data

Fifty-two countries provided partial data with estimated percentages of the national number of donations covered by the report ranging from 30% to 99%. Seventeen countries reported more than 90% of national collections. Five countries reported data less than 50%. In generating the global overview, the percentages were used to calculate adjusted numbers. The percentages were also used to calculate the donations per 1000 population.

In some cases, in order to provide aggregate data, it has been necessary to assume that this partial information is representative of the whole country. It is recognized that this may present a more favourable picture than in reality, particularly for low- and middle-income countries where, when partial data is provided, the data often relate to major cities; these tend to have better facilities, equipment and management, and have wider coverage, leaving other areas with a poorer situation unreported. Caution should be taken not to generalize these data.

5 Countries achieving 100% voluntary non-remunerated blood donations

The majority of the countries on the list provided data for GDBS 2011. Countries that did not respond to GDBS 2011 data collection, but have consistently reported 100% or

close to 100% (>99%) voluntary non-remunerated blood donations in the past, were also included in the list.

6 Updated indicators

Due to slight differences in the availability of country data and the adjustment of data submitted by a small number of countries as the result of validation, some indicators in this report may differ from those provided in WHO Fact sheet N°279: Blood Safety and Availability, which was published in June 2013.

7 Estimating the global wastage of recovered/recoverable plasma

Currently no data are reported through GDBS on the volume of recovered plasma that is discarded. The method developed by Thierry Burnouf (2011) was used to estimate the recovered plasma wasted globally.

For the purpose of this estimation, "recovered plasma wasted" means:

- Use of whole blood in the absence of component therapy: plasma is not produced (this would also depend on health-care needs in the country)
- Lack of appropriate freezing and storage capacity of plasma: plasma is discarded
- Plasma is produced but does not meet the requirements for fractionation: plasma is destroyed
- Clinical use of plasma where PDMP are indicated: plasma is not used in an optimal way.

WHO GDBS 2011 data were used as the basis for this estimation.

Number of whole blood donations in the world annually: 96 million

Number of whole blood donations available for component separation in the world annually: approximately 94 million

Volume of whole blood donations collected:

- 90% of 480ml/donations: ± 40.6 million L/year
- 10% of 225 ml/donations: ± 2.1 million L/year
- Total: ± 42.7million L whole blood

Volume of recovered plasma potentially available each year:

± 42.7million million L x 48% (hematocrit value) = ± 20.5 million L/year

Recovered plasma used for transfusion

- The median ratio of units of fresh frozen plasma (FFP) /plasma: units of red cell components (red blood cell + whole blood) transfused is around 0.28 for both high-income and middle-income countries.
- Recovered plasma used for transfusion: 94 million*0.28 = +/- 26.3 millions of donations per year
- 250 mil plasma/donations

Recovered plasma used for transfusion: +/-6.6 million L/year

Recovered plasma for fractionation: 7.4 million L per year

Estimates of recovered plasma wasted:

	Yearly volume (million L)
Volume of recovered plasma potentially available	20.5
Recovered plasma used for transfusion	6.6
Recovered plasma for fractionation	7.4
Plasma wasted	20.5 -6.6 -7.4 = 6.5

Reference: *Burnouf T. Volumes of recovered plasma wasted in the world and plasma fractionation options to improve access to plasma derivatives: an overview.* Presented during the WHO meeting "Improving access to safe blood products in low- and middle-income countries: a framework to improve public health", June 2012, Geneva.

Annex 2:

Countries reporting the collection of more than 90% blood donations from voluntary non-remunerated donors, 2011

No.	Country	100% VNRD*
1	Australia	*
2	Austria	*
3	Bahrain	
4	Belgium	*
5	Benin	
6	Botswana	*
7	Brunei Darussalam	*
8	Burundi	*
9	Canada	*
10	China	*
11	Cook Islands	*
12	Cote d'Ivoire	*
13	Croatia	*
14	Cuba	*
15	Cyprus	*
16	Czech Republic	
17	Democratic People's Republic of Korea	*
18	Denmark	*
19	Estonia	*
20	Finland	*
21	France	*
22	Hungary	*
23	Iceland	*
24	Iran (Islamic Republic of)	*
25	Ireland	*
26	Israel	*
27	Italy	*
28	Japan	*
29	Kenya	*

30	Lao People's Democratic Republic	
31	Latvia	*
32	Lesotho	
33	Luxembourg	*
34	Malawi	*
35	Malaysia	*
36	Malta	*
37	Monaco	*
38	Mongolia	*
39	Namibia	*
40	Nepal	
41	Netherlands	*
42	New Zealand	*
43	Nicaragua	*
44	Norway	*
45	Poland	
46	Portugal	*
47	Republic of Korea	*
48	Romania	*
49	Rwanda	*
50	San Marino	*
51	Singapore	*
52	Slovakia	*
53	Slovenia	*
54	South Africa	*
55	Spain	*
56	Sri Lanka	
57	Suriname	*
58	Swaziland	*
59	Sweden	*
60	Switzerland	*
61	Thailand	*
62	The former Yugoslav Republic of Macedonia	
63	Togo	
64	Turkey	*
65	Uganda	*
66	United Arab Emirates	*
67	United Kingdom of Great Britain and Northern Ireland	*
68	United Republic of Tanzania	

69	United States of America	*
70	Zambia	*
71	Zimbabwe	*

* Countries reporting the collection of 100% or close to 100% (>99%) of blood donations from voluntary non-remunerated blood donors.

Annex 3

Volume (litres) of plasma sent for fractionation, 2011

(based on WHO Global Database on Blood Safety 2011 data, unless stated otherwise)

No.	Country	Recovered plasma	Apheresis plasma	Total	Litres of plasma processed per 1000 population	Data source
1	Argentina	68 150	0	68 150	1.7	a
2	Armenia		14 600	14 600	4.7	
3	Australia	79 175	366 316	445 491	19.7	
4	Austria	50 000	500	50 500	6.0	GDBS, 2008
5	Belarus	19 218	19 217	38 435	4.0	
6	Belgium	61 794		61 794	5.7	GDBS, 2008
7	Brazil	85 745	0	85 745	0.4	
8	Bulgaria	13 758		13 758	1.8	
9	Canada	243 059	22 247	265 306	7.7	
10	Chile	20 000	0	20 000	1.2	b
11	China	0	3 858 000	3 858 000	2.8	
12	Croatia	11 803		11 803	2.7	
13	Czech Republic	53 300	194 000	247 300	23.5	GDBS, 2008 c
14	Denmark	64 800	0	64 800	11.6	
15	Estonia	4758	0	4758	3.5	GDBS, 2008 d
16	Finland	78 790	2000	80 790	15.0	
17	France	690 788	235 885	926 673	14.7	
18	Germany	1 176 334	1 819 590	2 995 924	36.5	e
19	Greece			15 402	1.5	EDQM/CoE, 2008 f
20	Hungary	68 360	0	68 360	6.9	GDBS, 2008
21	Iran (Islamic Republic of)	132 293	429	132 722	1.8	
22	Israel	47 070	0	47 070	6.2	g
23	Italy	558 920	189 062	747 982	12.3	
24	Japan	610 000	340 000	950 000	7.5	

25	Kazakhstan	34 007		34 007	2.1	
26	Kyrgyzstan	8277		8277	1.5	
27	Latvia			823	0.4	EDQM/CoE, 2008
28	Lithuania			72 715	22.0	EDQM/CoE, 2008
29	Luxembourg	4845	1686	6531	12.7	h
30	Malaysia	28 312	3247	31 559	1.1	
31	Morocco	12 000	0	12 000	0.4	
32	Netherlands	135 000	210 000	345 000	20.7	
33	New Zealand	35 040	16 020	51 060	11.6	
34	Norway	54 213		54 213	11.0	GDBS, 2008 i
35	Poland	73 580	17 751	91 331	2.4	
36	Republic of Korea	172 545	730 016	902 561	18.7	GDBS, 2008
37	Republic of Moldova	3663	319	3982	1.1	
38	Russian Federation	123 023		123 023	0.9	
39	Serbia	12 000	650	12 650	1.3	
40	Singapore	16 358	5410	21 768	4.2	
41	Slovenia	16 669	360	17 029	8.4	
42	South Africa	180 000	3000	183 000	3.6	j
43	Spain			270 975	5.8	EDQM/CoE, 2004 k
44	Sweden	103 998	43 935	147 933	15.7	GDBS, 2008 l
45	Switzerland	84 641	1569	86 210	11.2	
46	Thailand	10 000	1200	11 200	5.4	m
47	United Kingdom of Great Britain and Northern Ireland	22 604	471 409	494 013	7.9	GDBS, 2008 n
48	United States of America	2 100 000	12 000 000	14 100 000	45.0	o
49	Uruguay			10 000	3.0	p
50	Uzbekistan	19 690	988	20 678	0.7	GDBS, 2008
51	Venezuela (Bolivarian Republic of)			364 489	12.4	q

EDQM European Directorate for the Quality of Medicine & Healthcare

COE Council of Europe

a The Blood Products Plant at the University of Córdoba has initiated a voluntary plasmapheresis donation programme but data on the number of donors and volume of plasma obtained were not reported.

b Only a small proportion of PMDP used in the country are produced through contract fractionation.

c The volumes reported for 2008 to the GDBS were collected by centres operating outside blood transfusion services. In 2011, it was reported to the GDBS that all products are imported.

d In 2011, it was reported that all PMDP are imported from abroad.

e Henseler O, Paul-Ehrlich-Institut. http://www.pei.de/EN/home/node.html (accessed: 22 March 2013).

f *The Collection, Testing and Use of Blood and Blood Components in Europe. 2008 Report*. Strasbourg, European Directorate for the Quality of Medicine & Healthcare/Council of Europe. http://www.edqm.eu/site/The_Collection_Testing_and_Use_of_Blood_and_Blood_3pdf-en-30141-2.html (accessed: 20 February 2013).

g Surplus recovered plasma is sold by MDA National Blood Services to the local fractionator. Products (IVIG) are sold by the fractionator directly to users.

h Plasma is sent to a foreign fractionator for contract fractionation. Hospitals are free to select the suppliers of PDMP.

i The volume reported to GDBS 2008 is included in the table. In 2011, it was reported that "all plasma is sold to Baxter. All FFP transfused is Octaplas bought from Octapharma. All other plasma products are bought from Baxter."

j This information was provided by the South African National Blood Service and was obtained from the National Bioproducts Institute, South Africa. Of the total 180 000 litres of plasma used for fractionation, Western Province Blood Transfusion Service used 30 000 litres at its own small fractionation facility.

k *The Collection, Testing and Use of Blood and Blood Components in Europe. 2008 Report*. Strasbourg, European Directorate for the Quality of Medicine & Healthcare/Council of Europe. http://www.edqm.eu/site/The_Collection_Testing_and_Use_of_Blood_and_Blood_3pdf-en-30141-2.html (accessed: 20 February 2013). Based on partial data (data from Catalonia) reported to GDBS 2011: recovered plasma 54 360 litres; apheresis plasma 4576 litres. Total plasma 58 936 litres.

l The following comments were provided to GDBS 2011: there is a commercial fractionation industry in Sweden, so plasma is imported and products exported. Some plasma is sold to another commercial fractionator so plasma is also exported. However, such work is not carried out by the blood centres.

m 10 000 litres of plasma were used for domestic fractionation. 50 000 litres were sold abroad for fractionation.

n All plasma is imported from countries clear of indigenous cases of variant Creutzfeldt-Jakob disease, including the United States of America and some European countries.

o Estimated data reported in the literature. See Flood et al (2006) and Lamb (2009) for more information. Based on data reported to GDBS 2011, 1 193 218 litres recovered plasma were shipped from American Red Cross Blood Services for fractionation.

p Massa C. "Plasma fractionation programme in Argentina: local and regional activities". Presentation in WHO meeting, "Improving access to safe blood products in low- and middle-income countries". Geneva, 14–15 June 2012.

q GDBS, 2011. The number is estimated, based on reported comments and the volume of plasma produced and transfused.

Annex 4

Fractionation arrangements and PMDPs manufactured

(based on WHO Global Database on Blood Safety 2011 data, unless stated otherwise)

No.	Country	Fractionation arrangements	Products manufactured through domestic or contract fractionation				Data source
			Albumin	IVIG	Factor VIII	Factor IX	
1	Argentina	a	Yes	Yes	Yes	Yes	
2	Armenia	a	No	No	No	No	
3	Australia	b	Yes	Yes	Yes	Yes	
4	Austria	b					GDBS, 2008
5	Belarus	a					GDBS, 2008
6	Belgium	a					GDBS, 2008
7	Brazil	a, c	Yes	Yes	Yes	Yes	
8	Bulgaria	a, d	Yes	Yes	No	No	
9	Canada	c	Yes	Yes	No	No	
10	Chile	c	Yes	Yes	Yes		
11	China	a, b	Yes	Yes	Yes	Yes	
12	Croatia	b, d	Yes	Yes	No	No	
13	Czech Republic	c					GDBS, 2008
14	Democratic People's Republic of Korea	a	Yes				
15	Denmark	c					GDBS, 2008
16	Estonia	c					GDBS, 2008
17	Finland	c, d	Yes	Yes	Yes	Yes	
18	France	a	Yes	Yes	Yes	Yes	
19	Greece	a, c	Yes				
20	Hungary	a					GDBS, 2008
21	India	c					GDBS, 2008
22	Iran (Islamic Republic of)	a, b, c	Yes	Yes	Yes	Yes	
23	Israel	b, d	No	Yes	No	No	GDBS, 2008
24	Italy	b	Yes	Yes	Yes	Yes	
25	Japan	a, b, d					

26	Kazakhstan	a, d	Yes	No	No	No	
27	Kyrgyzstan	a	Yes	Yes			
28	Luxembourg	d	Yes	Yes	No	No	
29	Malaysia	c	Yes	Yes	Yes	Yes	
30	Morocco	a, c	Yes	Yes	Yes	Yes	
31	Netherlands	a	Yes	Yes	Yes	Yes	
32	New Zealand	c	Yes	Yes	Yes	Yes	
33	Norway	d					GDBS, 2008
34	Poland	b, c, d	Yes	Yes	Yes	Yes	
35	Republic of Korea	a, b, c	Yes	Yes	Yes	Yes	
36	Republic of Moldova	a	Yes	No	No	No	
37	Russian Federation	a, d	Yes	Yes	Yes	Yes	
38	Serbia	a	Yes				
39	Singapore	c	Yes	Yes	Yes	No	
40	Slovenia	a, c	Yes	Yes	Yes	Yes	
41	South Africa	a, d	Yes	Yes	Yes	Yes	
42	Spain	b	Yes	Yes	Yes	Yes	
43	Sweden	b					GDBS, 2008
44	Switzerland	b, c, d	Yes	Yes	Yes	Yes	
45	Thailand	a, d	Yes	No	No	No	
46	United Kingdom	a					GDBS, 2008
47	United States of America	b, c, d					GDBS, 2008
48	Uzbekistan	a					GDBS, 2008
49	Venezuela (Bolivarian Republic of)	a	Yes	Yes	Yes		

a Domestic plasma fractionation carried out through the public/not-for-profit sector.

b Domestic plasma fractionation carried out through the for-profit sector.

c Plasma sent for contract fractionation in another country.

d Plasma sold to manufacturers of plasma-derived medicinal products and products purchased from manufacturers or other suppliers.

Annex 5

Percentage of supplies of PMDP manufactured from domestic or/and contract fractionation of the plasma collected in the country

(based on WHO Global Database on Blood Safety 2011 data, unless stated otherwise)

No.	Country	Albumin	IVIG	Factor VIII (excluding recombinant products)	Remarks
1	Argentina				a
2	Australia	100	78	100	
3	Brazil	50	40	3	
4	Bulgaria			0	
5	Canada	79	30	n.a.	b
6	Chile	10	10		
7	Finland				c
8	France	75.3	54	77	
9	Iran (Islamic Republic of)	35	100	9	
10	Israel	0	45	0	d
11	Italy	55	81	53	
12	Japan	58.1	95	100	
13	Kyrgyzstan	16			
14	Luxembourg	80	80	0	e
15	Morocco	100	100	100	
16	Netherlands	80	70	85	
17	New Zealand	100	100	100	
18	Republic of Moldova	100			
19	Serbia	12	0	0	f
20	Singapore	71.8	18.9	9.3	
21	Slovenia	70	90	100	
22	South Africa	100	95	100	
23	Spain	100	48	100	g
24	Sweden				h
25	Thailand	5			i

a The National Blood Programme has no such information. However, it is estimated that about 70% of the requirements of albumin, 50% immunoglobulin and less than 30% of Factor VIII are met through domestic production.

b Data provided by Canadian Blood Service (CBS). Based on report by Héma-Québec, the percentages are 85% for Albumin and 12 for IVIG. All factor VIII supplied are recombinant.

c Finland is a member of the European Union, which is open for competition. All major plasma fractionation companies are active in Finland. Hospitals or group purchasing organizations of hospitals usually purchase products with the best price. Plasma products made out of domestic plasma are not preferred. If calculated based on the amount of plasma required to produce the amount of products needed in Finland, the country is self-sufficient in factor VIII, factor IX, albumin and prothrombin complex concentrate. In 2011, Finland was 50% self-sufficient in IVIG and S.C. immunoglobulin.

d Surplus recovered plasma is sold by MDA National Blood Services to the local fractionator. Products (IVIG) are sold by the fractionator directly to users.

e Plasma is sent to a foreign fractionator for contract fractionation. Hospitals are free to select the suppliers of PDMP.

f Intravenous immunoglobulin and factor VIII and factor XI are 100% imported.

g Based on partial data (data from Catalonia) reported to GDBS 2011.

h The following comments were provided to GDBS 2011: there is a commercial fractionation industry in Sweden, so plasma is imported and products exported. Some plasma is sold to another commercial fractionator so plasma is also exported. However, such work is not carried out by the blood centres.

i 10,000 litres of plasma are used for domestic fractionation. 50,000 litres were sold abroad for fractionation.