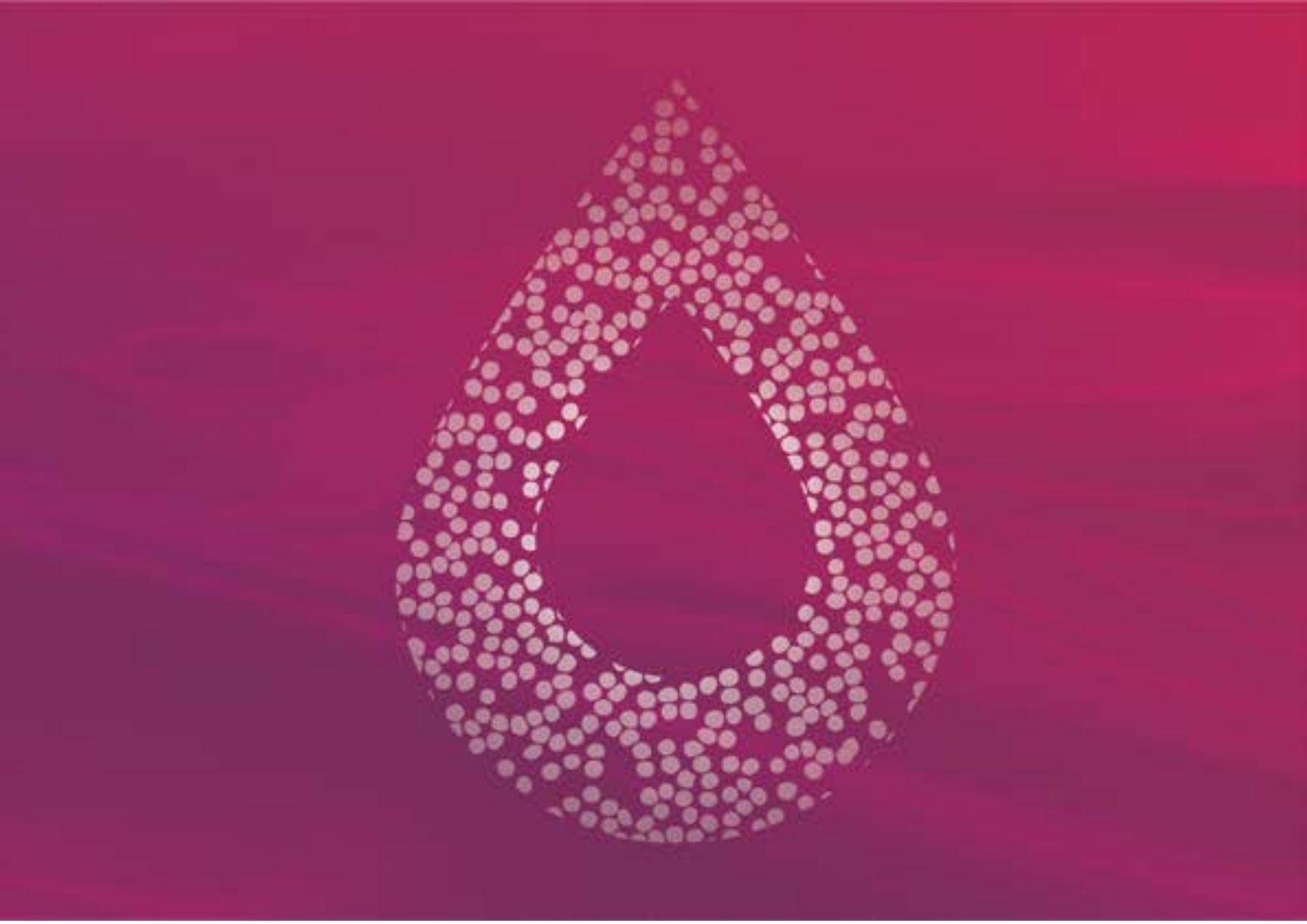

GUIDANCE ON CENTRALIZATION OF BLOOD DONATION TESTING AND PROCESSING

World Health Organization

GUIDANCE ON CENTRALIZATION OF BLOOD DONATION TESTING AND PROCESSING

World Health Organization

Guidance on centralization of blood donation testing and processing

ISBN 978-92-4-002082-5 (electronic version)
ISBN 978-92-4-002083-2 (print version)

Suggested citation. Guidance on centralization of blood donation testing and processing. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

Design and layout by L'IV Com Sàrl

CONTENTS

PREFACE

The purpose of a national blood system is to ensure timely access to quality, safe and sufficient supplies of blood and blood components for all the patients needing transfusion. However, many low- and middle-income countries are still unable to provide sufficient supplies of whole blood and blood components for patients at all times or in all geographical locations. Vulnerable groups in these countries, such as women with peripartum haemorrhage and children with anaemia from malaria, are often the worst affected by insufficient or unsafe blood supplies. A major barrier to the achievement of universal access to safe blood transfusion in these countries is their ineffective and inefficient blood supply systems. These systems are often fragmented, composed of many small-scale blood establishments, operated by multiple players and have varying levels of performance owing to resource and infrastructure limitations.

Experience in many countries has demonstrated that a nationally coordinated and effectively regulated network of blood establishments, in which key functions are centralized, has many advantages. Centralization optimizes use of resources, reduces overall costs, promotes compliance with quality and safety standards, improves patient access to the most suitable blood components for transfusion, and enhances resilience in emergency situations that affect blood supply or safety. The World Health Organization's *Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023* recommends countries to consolidate blood donation testing and processing in appropriate facilities. Such facilities should have effectively implemented quality systems to overcome the shortcomings that often exist in decentralized blood systems that are highly fragmented and to achieve the strategic objective of building functioning and efficiently managed blood services.

Guidance on centralization of blood donation testing and processing provides a strategic framework to assist Member States in deciding whether to centralize blood donation testing and processing and how to choose the most suitable centralization model for the unique characteristics of the blood system of each country. The guidance document explains the key steps in planning a blood establishment to centralize activities. It also offers practical guidance on implementing quality, risk management and information management systems, and on managing the infrastructure, human and financial resources necessary for a blood establishment that will perform centralized blood donation testing and processing.

Centralization of blood donation processing can play an important role in increasing the availability of quality plasma for fractionation. This guidance is complementary to the *Guidance on increasing supplies of plasma-derived medicinal products in low- and middle-income countries through fractionation of domestic plasma.* The guidance document provides a strategic framework to assist Member States in increasing their volume of quality plasma suitable for fractionation to help address unmet needs for plasma derived medicinal products.

ACKNOWLEDGEMENTS

The development and publication of the guidance was coordinated by Yuyun Maryuningsih (Team Lead, Blood and other Products of Human Origin, Health Products Policy and Standards Department, WHO Headquarters, Switzerland). The contribution of the following individuals and technical groups is gratefully acknowledged.

The working group members who contributed to drafting the chapters:

Vee Armstrong*, Quality and Regulatory Consultant, Australia
Judith Chapman, International Society of Blood Transfusion
Ubonwon Charoonruangrit, former director of National Blood Centre of the Thai Red Cross Society, Thailand
Jay Epstein*, Working Party for Global Blood Safety, International Society of Blood Transfusion, United States of America
Alan Kitchen*, WHO Expert Advisory Panel for Transfusion Medicine
Yuyun Maryuningsih, WHO Headquarters, Switzerland
Washington Samukange, Paul-Ehrlich-Institut, Germany
Diana Teo*, WHO Expert Committee on Biological Standardization
Hirokazu Tsuno, Japanese Red Cross Kanto-Koshinetsu Block Blood Center, Japan
Marion Vermeulen, South African National Blood Service, South Africa
Junping Yu, WHO Headquarters, Switzerland

* Core editing group members.

The individuals and organizations who reviewed and commented on the draft guidance document:

Yetmgeta Eyayou Abdella, WHO Regional Office for the Eastern Mediterranean, Egypt
Paul Ashford, International Council for Commonality in Blood Banking Automation (ICCBBA)
Juan Almeyda, Ministry of Health, Peru
Thida Aung, Ministry of Health, Myanmar
Mauricio Beltran Duran, WHO Regional Office for the Americas, USA
Blood Transfusion Service, Ministry of Health, Kuwait
Central Medical Laboratory, Ministry of Health, Belize
Nabajyoti Choudhury, Health City Hospital, Assam, India
Jean-Claude Faber, LuxConsulTrans, Luxembourg
Saliou Diop, National Blood Transfusion Centre, Senegal
Peter Flanagan, New Zealand Blood Service, New Zealand
Jose Fuentes, Ministry of Health, Peru
Mahrukh Getshen, Jigme Dorji Wangchuck National Referral Hospital, Bhutan
Yasser Ghaleb, National Blood Center, Sanaa, Yemen
Iranian Blood Transfusion Organization, Islamic Republic of Iran
Alireza Khadem Broojerdi, WHO Headquarters, Switzerland
Justina Kordai Ansah, National Blood Service, Ghana
Andre Loua, WHO Regional Office for Africa, Republic of Congo
Dora Mbanya, Centre Hospitalier et Universitaire Yaoundé, Cameroon
Neelam Marwaha (Department of Transfusion Medicine, PGIMER, India)
Arelis Medina, National Blood Programme, Dominican Republic
Ministry of Health, Argentina
Ministry of Health, Costa Rica

National Blood Centre, Poland
National Blood Programme, Paraguay
Sangeeta Pathak, Max Super Speciality Hospital, India
May Raouf, Dubai Blood Center, United Arab Emirates
Ni Ken Ritchie, Jakarta Blood Transfusion Service, Indonesia
Galo Franco Saltos, Ministry of Health, Ecuador
Jinho Shin, WHO Regional Office for the Western Pacific, Philippines
Aparna Singh Shah, WHO Regional Office for South-East Asia, India
Jean Baptiste Tapko, former regional adviser for blood safety, WHO Regional Office for Africa, Republic of Congo
Claude Tayou Tagny, Centre Hospitalier et Universitaire Yaoundé, Cameroon
Teguh Triyono, Chairman for Indonesian National Blood Services Committee, Indonesia
Alisha Tucker, Blood Bank, Ministry of Health and Wellness, Jamaica
Elizabeth Vinelli, Honduras Red Cross Blood Program, Honduras
Tomislav Vuk, Croatian Institute of Transfusion Medicine, Croatia
Evgeny Zheleznyakov, WHO Regional Office for Europe, Denmark
Hasan Abbas Zaheer, Pakistan Red Crescent Society, Pakistan
Shimian Zou, National Heart, Lung, and Blood Institute, National Institutes of Health, USA

LIST OF ABBREVIATIONS AND ACRONYMS

anti-HCV	antibody to hepatitis C virus
anti-HIV	antibody to human immunodeficiency virus
BE	blood establishment
EQAS	external quality assessment scheme(s)
FFP	fresh frozen plasma
GBT	Global Benchmarking Tool
GDBS	Global Database on Blood Safety
GLP	good laboratory practice
GMP	good manufacturing practice
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
ISO	International Organization for Standardization
IT	information technology
IQA	internal quality assurance
LMIC	low- and middle-income countries
MOU	Memorandum of Understanding
NAT	nucleic acid testing
NEQAS	national EQAS
NGO	nongovernmental organization
NRA	national regulatory authority
PCM	phase change material
PDMP	plasma-derived medicinal product
QMS	quality management system
TTIs	transfusion-transmissible infections
USA	United States of America
VNRD	voluntary non-remunerated blood donation
WHA	World Health Assembly
WHO	World Health Organization

GLOSSARY

Apheresis	The process by which one or more blood components are selectively obtained from a donor by withdrawing whole blood, separating it by centrifugation and/or filtration into its components, and returning those not required to the donor
Blood cold chain	System for storing and transporting blood and blood products, within the correct temperature range and conditions, from the point of collection from blood donors to the point of transfusion to the patient
Blood components	A constituent of blood (erythrocytes, leukocytes, platelets, cryoprecipitate, plasma) that can be prepared by various separation methods and under such conditions can be used either directly for therapeutic purposes or for further processing and manufacturing
Blood donation processing	Any activity involved in the production of blood components from blood donations, including preparation, manipulation, preservation for storage, packaging and final product release
Blood donation testing	The laboratory testing or screening of blood and blood components for infectious agents and blood group serology
Blood establishment	Any structure, facility or body that is responsible for any aspect of the collection, testing, processing, storage, release and/or distribution of human blood or blood components when intended for transfusion or further industrial manufacturing. It encompasses the terms "blood bank", and "blood centre"
Blood product	Any therapeutic substance derived from human blood, including blood for transfusion (i.e. whole blood and blood components), plasma for fractionation (either separated from whole blood or prepared by apheresis), and plasma-derived medicinal products
Blood service	The organization responsible for the collection, screening, processing, storage and supply of blood and blood components for therapeutic use. It encompasses the term "blood transfusion service."
Blood supply system	Is the responsibility of the (National) Blood Service and consists of blood establishments that collect, test, process and distribute whole blood and blood components intended for transfusions, as well as plasma intended for further manufacturing into plasma-derived medicinal products. Includes hospital blood banks
Blood transfusion system	Consists of care centres (hospitals, surgical centres and outpatient facilities, and sometimes ambulances) that utilize blood and blood components for the treatment of patients
Centralization	A process by which the distributed activities of an organization become concentrated in a smaller number of geographical locations
Effectiveness	The extent to which a specific intervention, procedure, regimen or service, when deployed in the field in routine circumstances, does what it is intended to do for a specified population

Efficacy	The extent to which a specific intervention, procedure, regimen or service, produces the intended result under ideal conditions
Efficiency	The capacity to produce the maximum output for a given input
External quality assessment schemes	External assessment of a laboratory's overall performance in testing exercise material of known, but undisclosed content and comparison with the performance of other laboratories that have tested the same material
Global Benchmarking Tool	Primary means by which WHO objectively evaluates regulatory systems, as mandated by World Health Assembly Resolution 67.20 on Regulatory System Strengthening for medical products
Good laboratory practice	A quality system concerned with the organizational process and the conditions under which nonclinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported
Good manufacturing practice	All elements in the established practice that will collectively lead to final products or services that consistently meet appropriate specifications and compliance with defined regulations. The part of quality assurance that ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use, and as required by the marketing authorization or product specification. GMP is concerned with both production and quality control
Haemovigilance	Set of surveillance procedures covering the entire transfusion chain from the collection of the donation and processing of blood and its components to their provision and transfusion to patients and their follow-up. Includes the monitoring, reporting, investigation and analysis of adverse events and adverse reactions related to the donation, processing and transfusion of blood, and taking action to prevent their occurrence or recurrence
Lookback	An investigation into the fate of components of previous donations, and the status of recipients of those donations, donated by a donor now identified as currently, or previously, infected with a transmissible infectious agent
National regulatory authority	Legally established bodies that promulgate medicines regulations and enforce them. The NRA is the entity or entities in charge of assuring the quality, safety and efficacy of medicinal products as well as ensuring the relevance and accuracy of product information
National blood system (or programme)	National system that incorporates the blood regulatory system, the blood supply system and the blood transfusion system
Nongovernmental organization	A state-independent organization with which the United Nations has a relationship; an organization founded on private initiative in order to fulfil aims of public interest
Nucleic acid testing	A testing methodology, which uses amplification technology targeting specific genomic sequences, to detect the presence of microbial nucleic acid in a sample. May also be referred to as "molecular screening". Many nucleic acid tests designed for donor/donation testing combine detection of HBV, HCV and HIV in a single test

Pathogen reduction technologies	The process of treating the blood component soon after collection (through chemical or biological mechanisms) to reduce the infectivity of any pathogens present, while still maintaining good-quality blood components for transfusion
Plasma-derived medicinal product	Any therapeutic product derived from human plasma and produced by an industrial-scale manufacturing process that pools multiple units. Also called plasma derivatives or plasma-derived products
Quality management system	A management system that directs and controls an organization with respect to quality, and that ensures that steps, processes, procedures and policies related to quality activities are being followed
Safety	The minimization of any health risks to blood donors through the donation process and any health risks to recipients from blood products
Sufficiency	A secured supply of blood and blood components sufficient to meet the needs of the country's health care system
Traceability	Ability to trace each individual unit of blood, blood component or derivative from the donor to its final destination (patient, manufacturer of medicinal products, disposal) and vice versa
Transfusion-transmissible infection	An infection that can result from the transmission of an infectious agent into an individual through donated blood or blood components

EXECUTIVE SUMMARY

This guidance document provides decision-makers, particularly in low- and middle-income countries, with a framework to guide them if they are considering moving to centralization of blood donation testing and processing in designated blood establishments (BEs) as a strategy to improve the overall function and efficiency of the national blood system. Practical advice on the creation of such BEs is provided. Guidance in this area contributes to meeting a strategic objective of the World Health Organization (WHO) *Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023* to promote functioning and efficiently managed blood services.

Multiple barriers to the safety and availability of blood components for transfusion were identified in the 2015 Global Database on Blood Safety, many of which derive from weak oversight, insufficient financing and fragmentation of the national blood system. The present guidance emphasizes the fundamental role within the health system of a national blood policy with a legal foundation and government responsibility to assure: a) coordination and stable funding of the blood system; and b) uniform compliance with internationally recognized standards for blood product quality and safety. Moreover, centralization of key functions of the blood service within a limited number of blood establishments, particularly testing and processing of blood donations, can overcome shortcomings that often exist in decentralized blood systems that are highly fragmented. Experience in many countries has demonstrated that a nationally coordinated and effectively regulated network of blood establishments in which key functions are centralized has many advantages. For example, such a system optimizes use of resources, reduces overall costs, promotes compliance with quality and safety standards, improves patient access to the most suitable blood components for transfusion, and enhances resilience in emergency situations affecting blood supply and safety.

This document provides a roadmap for consideration of whether to centralize blood donation testing and processing and the steps needed to implement these functions in selected blood establishments. It progresses from a general discussion of the potential benefits and risks of such centralization to a review of the conditions that should be met by a centralized blood establishment in a given national setting. Recognizing that the characteristics of the blood system are unique to each country, the document then identifies the principal questions that should frame the decision to move forward and the necessary elements of the development plan. Critical functions and infrastructures that should be in place in a blood establishment that performs centralized donation testing and processing are summarized and mechanisms for monitoring and evaluating the outcomes of centralization are described.

CHAPTER 1

INTRODUCTION

1.1 Purpose and scope of the guidance

This document provides guidance on setting up centralized blood establishments (BEs) for the testing and processing of blood donations and associated activities including the distribution of blood and components. It covers the activities necessary to: assure product quality and efficacy; minimize the risks of incorrect blood groups being assigned and of transmission of infectious agents through transfusion; ensure sufficiency in blood components; and optimize resource use. This includes increased utilization of recovered plasma for fractionation to provide plasma-derived medicinal products (PDMPs).

This guidance addresses the testing and processing of blood donations intended for use in transfusion but does not cover any activities associated with stem cell and tissue donations, nor does it cover any recipient-related pretransfusion activities such as compatibility testing. The focus is on best practices in centralized testing and processing as a key strategy in the consolidation of blood system operations. Implementation of centralized testing and processing may require the reorganization of other operations in the BEs, for example blood collection and donor management. Where relevant, this guidance document comments on the potential impact of centralization on these other activities.

The document is also intended to draw the attention of decision-makers and key stakeholders to the expected benefits of centralization, namely to promote stabilization and technological advancement of the blood system that will enhance patient access to safe and quality-assured blood products. Actions taken to centralize functions of the blood service may also serve as opportunities to raise public awareness of the blood supply as a national resource and to garner public support for a national blood system built on community-based voluntary non-remunerated donation.

1.2 Target audience

The guidance document is intended for:

- blood services, national (including provincial) blood regulatory authorities, government departments and nongovernmental organizations (NGOs) involved in the oversight of national blood systems and programmes;

- policy-makers in various government departments that are considering reforming or improving fragmented health care systems, specifically through the consolidation or centralization of BEs focusing on testing and processing activities; and

- international blood experts, international professional societies, consultants, health system experts, academic institutions and regulatory bodies, which are interested in supporting, following up and monitoring the transformation activities.

1.3 Background

An important goal of a national blood system is to ensure timely access to safe and sufficient supplies of blood and blood components for transfusion. The World Health Assembly (WHA) has endorsed multiple resolutions directed towards achieving this goal. Most recently, WHA resolution 63.12 on the *Availability, safety and quality of blood products (1)* urges Member States "to promote the full implementation of well organized, nationally coordinated and sustainable blood programmes with appropriate regulatory systems". This is to be achieved through government commitment and support of a national blood programme with quality management systems, by means of a legal framework, the national blood policy and adequate resources. The World Health Organization (WHO) recommends that all activities related to blood collection, testing, processing, storage and distribution should be coordinated at the national level through effective organization and integrated blood supply networks *(1)*. The national system will either facilitate or hamper the attainment of this objective, depending on whether a regional centralized or a decentralized fragmented structure is in place. Experience in many countries has shown that consolidation of the key operations, namely, blood testing and processing, and centralization or the establishment of a network of regional BEs, reduces the overall costs of providing a safe and sufficient blood supply. Moreover, the safety of the blood supply is generally better where activities are centralized because there is more control and ensuring a quality focus is easier. Internationally, the trend has been towards consolidation or centralization of activities as blood systems develop, which makes it possible to improve the efficiency and resource utilization of the system and the safety of its products *(2, 3)*.

The *Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023* (Action framework) *(4)* guides Member States to achieve a safe and sufficient supply of blood products through implementation of strategies to overcome the challenges identified in the Global Database on Blood Safety 2015 survey (GDBS 2015). Responses from 173 Member States to the GDBS 2015 identified the following challenges, many of which can be addressed through centralization of functions within the blood service.

1.3.1 Lack or inadequacy of a national blood policy and legislation to establish a nationally organized and managed blood programme

Of the 173 countries that responded, 123 (71%) reported the existence of a national blood policy, and 134 (77%) had a government unit responsible for overseeing blood products. However, national bodies to support effective implementation of the national blood policy and strategic plan, such as a national committee or its equivalent, are often not empowered or functional in low- and middle-income countries (LMIC).

Only 104 of the 173 responding countries (60%) reported having specific legislation related to the safety, effectiveness and quality of blood transfusion.

1.3.2 Inadequate funding and support for the national blood programme

Blood programmes in some countries are operated by organizations that are not able to assure the quality of blood, cost efficiency or good governance. The government may be unable to assure an adequate budget and financing of blood programmes is often given low priority. Such countries report a lack of adequate, sustainable and specific funding to maintain their blood programmes. Limited financing of blood services impedes efforts to improve blood safety, particularly in LMIC.

Governments should ensure that adequate, sustainable financing for the national blood programme is integrated within the financial structure of the national health care system. This can be achieved through mechanisms such as specific national and local budget allocation, cost recovery and health insurance, or a combination of these.

1.3.3 Multiple blood services and operators within the blood system, functioning at differing levels of performance owing to resource and infrastructure limitations

Fragmented blood systems, with blood services that are often operated by many players, pose a significant challenge in a number of countries. This situation often leads to problems with coordination and to a lack of collaboration among different stakeholders. It may also lead to unnecessary competition for blood donors, which will increase the cost and effort needed to recruit donors and negatively affect the principle of voluntary non-remunerated donation. In some countries, blood services continue to fall under the umbrella of laboratory services, which are often not nationally coordinated.

Based on the GDBS 2015 data, the median number of annual donations processed per laboratory performing blood testing was 9300 with an interquartile range (IQR) of 1500–30 000. When analysed per WHO region, major differences were observed between them, reflecting different organizational models and varying efficiencies.

An ineffective and inefficient blood supply system composed of many small-scale blood banks is a common barrier to implementation of testing for transfusion-transmissible infections (TTIs) using more sensitive assays. Data from the GDBS 2015 indicated that 25 out of 141 (18%) countries that responded to the question use rapid tests to screen all or part of their blood supply for infectious agents. Although some of these rapid tests have high sensitivity, they are often handled manually, which leads to a greater potential for error. This, together with the widespread use of poor-quality and significantly less sensitive rapid tests in many LMIC, contributes to raising the risk of transmission of bloodborne infections.

Many countries lack a centralized system for evaluation and validation of test kits and reagents. There are no minimum performance requirements to guide the selection and procurement of the test kits and reagents and procurement decisions are too often determined solely by price. Additionally, fragmentation in procurement of consumables often results in higher costs than can be obtained through centralized "bulk" purchasing.

Interruptions to the regular supply of test kits, reagents and consumables were reported by 21% of countries. This is usually due to insufficient budgetary allocation or to ineffective and inefficient procurement system and supply chain management, which may be managed by different hospitals or laboratories, or centrally at national level. This may result in the procurement of poor-quality goods tendered at the lowest price, and in the same test kits and reagents being procured for all laboratory services without any consideration for the specific needs of blood services. Multiple supply contracts, for example, for the same test kits, reagents and consumables, or contracts that are of insufficient

duration, are contributing factors. In addition, trade restrictions, customs and border clearance delays, and transport logistics may limit the range of reagents and consumables available to the blood service.

1.3.4 Non-standard and non-uniform practices resulting from lack of strong national coordination

Selection of low-risk donors and methods of laboratory testing of donations for confirmation of blood group and evidence of TTIs are fundamental strategies to ensure blood safety. When rigorous standards for donor recruitment and selection and for donation testing and processing are either not applied or fail, transfusion of blood products poses a serious risk of transmission of infectious agents and incompatibility. Unfortunately, current systems for blood donation testing and processing are inadequate in many LMIC and there is a pressing need to introduce, strengthen and effectively implement policies, strategies and quality assurance regulations for blood products.

Donor selection guidelines may be lacking in detail, and predonation assessment of donors is often inadequate. Globally, instances occur of donated blood not undergoing adequate ABO and RhD blood grouping or testing for TTIs as recommended by WHO. At the operational level, the effectiveness of blood testing is often constrained by the fragmentation and lack of coordination of blood services, inadequate infrastructure, shortages of trained staff and poor quality management systems (QMS). Inconsistent application of QMS provides little assurance of testing and product quality. As a result, in many countries, recipients of blood and blood products remain at an unacceptably high risk of acquiring bloodborne infections or being exposed to life-threatening grouping mismatches that could easily be prevented.

1.3.5 Weak QMS and operational inefficiencies leading to wastage

The absence of strong QMS in BEs is a major impediment to ensuring safe and efficacious blood supplies. The quality and effectiveness of blood components depends on careful collection, ABO and RhD blood grouping and TTI testing, processing, product quality control testing, labelling, storage and distribution. Constraints include lack of an effective culture of quality and of national standards, inadequate data and documentation, limited training opportunities and poor quality assessment. Collection of blood from unsafe and unsuitable donors, use of poor-quality infectious disease testing assays, inadequate storage and transportation conditions, and poor stock management lead to the loss of at least five million blood units every year, further limiting the availability of blood products.

Treatment using labile blood components is gradually being expanded in medical practice in LMIC, resulting in increased quantities of recovered plasma being available for fractionation into PDMPs. However, in many of these countries, a large proportion of the processed plasma is categorized as waste material and destroyed. This wastage occurs because appropriate technology, regulatory controls, a QMS and good manufacturing practice (GMP) are not in place. The plasma is therefore rendered unsuitable for conversion into fractionated medicinal products by contract fractionation programmes operating in accordance with internationally recognized regulatory requirements. It is important for such countries to develop appropriate standards for donor recruitment, donor selection, infectious disease testing and blood component separation technology in an environment that applies QMS and GMP to assure plasma of a quality suitable for fractionation.

The possibility for self-fractionation of domestically sourced plasma that meets internationally recognized quality standards can also be explored, although for many smaller countries it may not be cost-effective or practical to develop a national fractionation facility. The facilitation of collaboration between LMIC through appropriate regulatory standards

and transfer of technology is a vital part of a global approach to improving access to PDMPs through fractionation of domestic plasma. In many cases, approaches such as selling plasma/plasma fractions, exchanging plasma/plasma fractions for finished products, or contracting fractionation with an external fractionator and manufacturer of PDMPs may be considered as the most appropriate ways of utilizing plasma collected from donors, either via whole blood donation or plasmapheresis.

1.3.6 Inability to meet health care system demand for whole blood and blood components

Globally, 66 out of the 173 countries (38%) that responded to the GDBS 2015 reported an annual blood donation rate below that generally considered as the minimum necessary to meet a nation's basic requirements for blood. This is thought to be 1% of the population per year although the requirements are higher in countries with advanced health care systems. High-income countries with well-structured health systems and blood programmes based on donations from voluntary non-remunerated blood donors are usually able to meet the demand for blood products. In contrast, in LMIC, chronic blood shortages are common. These countries often do not have structured blood donor programmes and as a result cannot attract or retain sufficient numbers of donors to meet the need for blood in emergencies or for planned surgery and regular transfusion. Of the 117.4 million blood donations collected globally, 42% are collected in high-income countries, which comprise only 16% of the world's population.

An important barrier to adequate blood supplies is the heavy reliance on family or replacement donations to meet patient needs instead of community-based donations to maintain a sufficient inventory of blood components. Worldwide, 58 (34%) of the 173 countries that responded to the GDBS 2015 depend on family or replacement donations and paid donations to cover more than 50% of their population's need for blood. Lack of government commitment to a nationally coordinated blood service that optimizes resources and avoids destructive competition between individual service providers, contributes to dependence on family or replacement donations. The Action framework advocates the active transitioning from family or replacement donations to 100% voluntary non-remunerated blood donations and elimination of paid donations.

Ensuring an adequate supply of essential PDMPs is also critical to meeting a population's health needs. Availability of PDMPs is insufficient in numerous LMIC, and shortages still occur in high-income countries. Except for the United States of America, most plasma collected in high-income countries is fractionated to meet those countries' own needs, and the potential for generating surplus products sufficient to meet the needs of other countries is therefore small. Moreover, import of such products would be prohibitively expensive. LMIC, where feasible, should therefore provide sustainable supplies of PDMPs using plasma collected by their establishments from their own populations, even if fractionation is carried out in high-income countries. Currently, however, the donations collected in a number of LMIC are either not processed, and transfused as whole blood, or the processed plasma is discarded, leading to loss of plasma that could potentially be used for PDMP manufacture.

Countries that lack a nationally coordinated blood system are often unable to meet their national requirements for whole blood and blood components at all times or in all geographical locations *(5)*. In many countries, the development of blood services has been largely restricted to major cities and universal access is still not guaranteed for those most in need of safe blood.

1.3.7 Inability to establish national standards and implement effective compliance monitoring systems

Of the 173 countries that responded to the GDBS 2015, 149 (86%) reported the establishment of standards for preparation of blood components, 118 (68%) the existence of national external quality assessment schemes for TTI testing, and 104 (60%) the existence of national external assessments of blood group serology and compatibility testing. Roughly half (94 of 173) of the respondent countries reported systems of licensing for blood establishments, and half (93 of 173) reported systems for the regular inspection of BEs by a national regulatory authority (NRA) or other entity. Thirty-two per cent (56 of 173) reported that national blood transfusion services were accredited.

Many countries lack effective mechanisms for quality oversight and monitoring, or programmes to enforce the implementation of standards and sustain the functionality of the QMS.

Safe blood supplies are most severely compromised in a fragmented blood system with ineffective monitoring and regulatory oversight.

1.3.8 Lack of emergency preparedness

Newly emerging and re-emerging infectious agents have the potential to threaten blood safety (for example, West Nile Virus and Zika virus) through transmission via transfusion. They may also compromise blood supply quality and sufficiency (for example, during respiratory virus outbreaks) by constraining blood donation and collection and disrupting operations. The recent experience of many blood services worldwide during the pandemic of SARS-CoV-2 has shown the importance of establishing a nationally coordinated blood system so that effective vigilance against the potential threat from emerging infections can be upheld, measures to collect and distribute blood products can be maintained and a national contingency plan be made and, when necessary, put into effect *(6, 7)*.

In addition to regular horizon scanning for emerging infections, it is essential for BEs to be prepared for natural disasters (for example, fires, floods or earthquakes) and disasters caused by human activity (for example, armed conflicts and data security breaches). National coordination is essential for blood inventory management during disasters *(8)*. Whereas a national plan should be in place to ensure the supply of blood and components in emergency situations, coordinated with the national emergency response plan, the specific circumstances may require planning and actions at the provincial or regional level rather than the national level. Each blood centre should have a contingency plan in place to manage losses of, or threats to, facilities and infrastructure.

CHAPTER 2

POTENTIAL BENEFITS AND RISKS IN CENTRALIZATION OF BLOOD DONATION TESTING AND PROCESSING

2.1 Potential benefits

The potential benefits can be realized by appropriate integration of key functions such as testing and processing into a centralized facility. Consolidation of activities carried out by multiple disparate and independently operating BEs confers certain advantages in volume, scale and convergence of procedures, which support improvements in efficacy, efficiency and cost-effectiveness. The anticipated benefits include the following:

2.1.1 Enable efficiencies of scale

Consolidating key testing and processing activities leads to efficiencies of scale from the larger numbers of samples and blood components tested and processed. A wide range of activities or approaches that are constrained or inappropriate because of high costs, technical limitations or human resources requirements in BEs processing small volumes can be more cost-effectively carried out. Such efficiencies of scale enable different approaches to be taken, which may be both cost-effective and improve overall quality, including: use of standardized automated equipment leading to greatly improved component safety and quality; exploitation of scientific and technological advances such as nucleic acid testing (NAT) and pathogen inactivation; donor red cell irregular antibody testing; implementation of dedicated information management systems; quality control testing of blood components; equipment and reagent validation, and participation in external quality assessment schemes (EQAS).

2.1.2 Achieve economies of scale

Economies of scale can be achieved through standardization of automation and consumables to a single platform or supplier and adopting central contract or procurement functions. Improved leveraging power from volume advantage enables the centralized BE to negotiate more favourable terms, for example for local stockpiling of critical materials, reagents and equipment parts for contingencies, as well as potential equipment lease options.

2.1.3 Improve quality, safety and efficacy of blood components

Integration of processes, equipment and materials, together with large volume processing in a centralized BE, can result in a greater consistency of blood components, as well as an overall improvement in quality, safety and efficacy, leading in turn to better patient outcomes.

2.1.4 Introduce specialized blood components and enable further processing

Larger volume processing enables the BE to make available specialized blood components, for example, maintaining a bank of phenotyped red cell components including rare types. It also enables further processing of blood components such as irradiated red cells and platelets, and pathogen-reduced units and small pool products such as cryoprecipitate. In addition to providing patients with more optimal blood components (for example, red blood cell components instead of whole blood, or single-donor apheresis platelets instead of pooled platelets), this ensures that donated blood is used more efficiently and safely.

Additionally, the centralized BE may consider the eventual introduction of pathogen reduction technologies. The existence of centralized hubs makes the introduction of such technologies easier and more cost-effective than in dispersed small BEs.

2.1.5 Improve span of control

Span of control over the activities of the blood system is increased by centralization, enabling more effective planning and coordination and more efficient allocation of limited resources. The establishment of competent authorities to assess and monitor compliance with standards is facilitated. New programmes can be more efficiently and effectively implemented while evidence-based policy-making and integration with other components of the health care system can be streamlined. Emergency preparedness for the blood supply is also strengthened – with fewer elements to manage during an emergency, it is easier to scale up operations more quickly when required.

2.1.6 Optimize operational efficiency

Integrating testing and processing activities streamlines these functions within the blood system and reduces unproductive duplication of activities and ineffective deployment of personnel and resources. Unnecessary waste from inefficient use of donated blood and outdated blood products as a result of multiple small, individually managed, blood inventories is reduced. With a more streamlined supply chain, materials and supplies inventories can be better managed and are able to hold buffer stocks for emergencies. Equipment maintenance programmes are more cost-effective, resulting in improved performance efficiency and durability of equipment.

2.1.7 Improve quality standards and practices

Streamlining testing and processing activities based on different platforms and systems into one platform or system results in improved quality through standardization and increased consistency of practices and products. Greater uniformity is achieved in quality management, including more consistent documentation and processes. Better access to quality controls and reference standards, as well as the ability to introduce improved data analysis methods based on larger population sizes, enables quality trends to be monitored more accurately. Adverse trends and events can then be identified and corrected in a timelier manner.

Expanded operations and activities will support installing a dedicated quality team that can promote better quality practices and quality improvement, as well as providing training on topics relevant to quality. This facilitates regular audits and assessments, improves management of adverse events and strengthens haemovigilance. It will also support the implementation of more stringent international quality standards, including GMP and good laboratory practice (GLP).

2.1.8 Strengthen support infrastructure

Critical support functions, such as human resources, budget management, facilities management, procurement, supplies inventory and logistics, can be strengthened in a larger facility. Employing competent and dedicated personnel who focus on running these functions will contribute to improving the overall productivity and effectiveness of the organization. These personnel include trained facility management team members with the knowledge and expertise to set up and maintain GMP in all areas of processing, and laboratories capable of applying GLP. The higher volume of activities, transactions, materials and products also enables the BE to harness automation and information technology systems to further improve operational efficiencies.

2.1.9 Attract and retain a skilled, motivated and focused workforce

Expanding the scope of activities creates the potential to increase the range of roles available and potential for development, while enabling employees to concentrate their activities on blood adequacy, quality and safety. This provides opportunities for the centralized BE to establish good career pathways and training programmes for its staff, with better prospects for development and advancement. The ability to provide jobs with standardized and competitive remuneration, coupled with improved career prospects and opportunities will enable the BE to attract and retain sufficient skilled, motivated and competent staff. There is potential to develop specialized expertise in niche areas of transfusion science as well as in research and development, and it will be easier to identify and foster leadership competency and good medical and technical expertise. Additionally, the centralized BE would be ideally placed to offer scientific and clinical training to external laboratory and clinical staff involved in transfusion activities in the hospitals and institutions that it serves.

2.1.10 Improve access to and availability of blood products

Improving the quality and efficiency of testing and component processing, as well as the introduction of value-added components, increases the number, safety and efficacy of blood products provided. Centralized management of blood product inventories together with arrangements for appropriate distribution of blood products will reduce wastage and product outdate. At the same time, improvements in quality that enable compliance with international standards and GMP requirements will allow surplus plasma, which would otherwise be discarded, to be fractionated into PDMPs. This will improve the availability and quality of blood products for all the patients served by the BE network. There will also be additional cost savings from the reduced need to purchase commercially manufactured PDMPs.

2.1.11 Improve blood system network and coordination

Integrating testing and processing functions carried out by multiple independent BEs of varying size, complexity and performance levels into centralized hubs helps to improve coordination of the blood system within the country. The centralized BEs, as hubs for testing and processing activities, can be developed into centres of excellence providing specialized services and training/reference services to other BEs. This supports strengthening of the networks within the national blood system, promoting improved coordination and development of national capability and facilitating

national-level strategic and policy planning and implementation. Regulations and standards can be more effectively enforced and limited resources, such as trained staff, more effectively deployed. It also improves the capacity of the national blood system to respond to disasters or major disease outbreaks.

2.1.12 Improve public confidence

Centralization may facilitate the establishment and maintenance of robust and fully functional linkages with hospital blood bank laboratories and clinical users, thereby enhancing the quality and safety of the entire blood transfusion chain. Improvements in the safety, efficacy and availability of blood products contribute to better patient outcomes and increased safety. These in turn inspire public confidence in the blood system. Cost savings from greater operational efficiencies will also decrease the economic burden.

Centralization should therefore result in a cost-effective and operationally efficient BE, with sufficient well-trained staff and a robust QMS, using standardized systems and processes that ensure a consistent and improved level of blood product quality and safety. Further establishment of local networks between centralized BEs and other components of the blood system, as well as networks between centralized BEs, will support well-coordinated and effective national and regional blood systems that are able to supply safe and sufficient blood products for the health care systems and ensure equitable access to safe blood products for the populations served.

2.2 Potential challenges and risks

Notwithstanding the many benefits that can be achieved from the centralization of activities, there are also potential pitfalls that might result in failure to achieve the desired benefits. Careful attention must be paid to these risks when planning the centralization of blood testing and processing and appropriate precautionary actions taken to mitigate them. Failed efforts can result from a lack of understanding of the local context (for example, limitations due to geography, local dependence on resources of neighbouring countries for equipment and bio-medical engineering expertise, and the need for external funding to sustain operations).

2.2.1 Lack of stakeholder support

The support of key stakeholders is crucial to achieving a successful outcome. These stakeholders would include the government (central and local), organizations in charge of blood services, blood donors, the public, hospitals, and clinical groups and suppliers, among others. The plan to centralize activities may be obstructed or hampered if there is strong resistance from one or more of these groups. Resistance may come from the BEs that will be involved in centralization or from other BEs. Opposition is often fueled by concerns about reduced income, perceived loss of prestige and work, or uncertainty regarding blood stock availability.

2.2.2 Staff resistance

Resistance may also come from current staff of a BE that is being transformed into a centralized facility. They may be concerned that they will have to take on increased workloads and/or a new and unfamiliar type of work if they are transferred to other functions. Staff may also be worried that their jobs will be downgraded leading to a reduced income and/or less job satisfaction. The integration of activities previously performed by multiple BEs means that redundancies and job losses will be another source of anxiety. The leadership of the BEs may resist changes if they perceive that they

will result in a loss of professional prestige. Workplace culture issues may also surface if workforces from different BEs are integrated into the centralized BE.

2.2.3 Loss of system resilience from disruption of centralized operations

Consolidation of critical testing and processing activities in a centralized BE poses the risk of serious disruption to the blood supply if the operations of the BE are interrupted. This can result from failure of equipment and reagents, supply chain disruptions or facility failure. Insufficient funding can compromise or impede development and improvements in blood safety. Transport failures can affect the quality and integrity of samples and blood products. Natural disasters can hinder operations within the BE and/or disrupt transport and communication links with other BEs and hospitals.

2.2.4 Poor quality and safety practices

There is a risk that poor quality and safety practices from the preexisting BEs may be transferred to the centralized BE and exacerbated. Alternatively, old practices may be retained and not scaled up or updated to cope with the larger volume and complexity of operations. This situation is compounded if existing staff are assumed to have the skills and knowledge needed to cope with new job expectations and changed processes, and there is a failure to strengthen training programmes or ensure staff competence.

2.2.5 Transportation and logistics difficulties

Centralization may place greater demand on supply chains because of increased journey times and/or a need for multi-segment journeys (i.e. van to train to van). Longer supply chains are more vulnerable to weather, congestion and other external factors. Difficulties may also arise where there is poor accessibility due to geographical barriers and/or unreliable transport systems. In large countries or countries with limited transport options, longer distances and times for shipment of blood donations, laboratory samples and processed blood components may increase risks from temperature excursions and other adverse events during transport.

2.2.6 Timely access to whole blood and blood components is affected

Access to whole blood and blood components may be delayed after the testing and processing functions have been relocated to the centralized BE. Other than difficulties with transportation mentioned in 2.2.5, this can also result from miscommunication or lack of coordination between the centralized BE and the hospital or distribution centre. Centralized BEs may also be less willing to customize particular blood components for hospitals with which they have had no previous relationship.

2.2.7 Weakened communication and coordination with other parts of the transfusion chain

When testing and processing functions are taken over from another BE, the coordination and communication between blood collection centres and hospitals that used to interact with that BE may be weakened. In a stand-alone BE conducting only testing and processing activities, too narrow a focus on these activities may result in poor awareness of other critical functions of the blood safety value chain such as donor recruitment, blood collection and clinical transfusion. This may lead to miscommunication or suboptimal coordination during patient emergencies. It may also lead to less influence on the quality and safety of donated blood or on the appropriate clinical use of blood products

and on patient blood management. Prioritizing only testing and processing activities for centralization may also result in the BE investing less in initiatives that are important to the integrity and quality of the whole transfusion chain.

2.2.8 Organizational inefficiencies

There is a potential for introducing too much complexity and bureaucracy within the organization leading to slower decision-making and responses to problems, unnecessary increases in staff numbers and inefficient use of resources.

2.2.9 Insufficient funding

In the short term, budget shortfalls may arise during the process of centralization owing to insufficient planning beforehand and to cost overruns during the project. For example, inadequate planning of building and equipment requirements may result in higher than expected costs if more equipment and infrastructure work is required.

In the longer term, budget shortfalls may result from failure to establish a sustainable funding model for the operations of the centralized BE. The BE could also become cost-ineffective, particularly if detailed cost–benefit and risk assessments were not carried out in advance, or the projected cost savings are not realized.

CHAPTER 3

KEY CONSIDERATIONS IN CENTRALIZATION OF BLOOD DONATION TESTING AND PROCESSING

Although they are based on common organizational models, there is variation in the structure, composition and function of blood systems and programmes, which are generally unique to the environment within each country. Wide diversity is also seen between individual BEs, which vary in size, range of activities, infrastructure and resourcing. It is therefore not possible or even desirable to assess the suitability of, or measure the effectiveness of, a centralized BE on the basis of single absolute characteristics such as size of the facility or volume of blood tested or processed. Rather, such decisions need to be made following an evaluation of the overall situation based on key considerations such as those outlined in this chapter.

3.1 Understanding the need for centralization

Often the considered and carefully planned centralization of blood donation testing and processing will provide significant benefits as outlined in Section 2.1. To understand whether a centralized BE is necessary or would be advantageous, it may be helpful to consider a number of simple questions about the current provision of blood and components:

- Are there any specific guidelines or requirements in the national blood policy, or is anything set out in the national blood programme that would either support, or reason against, centralization?
- Are the blood services in the country managed by single or multiple organizations?
- Are all BE activities standardized?
- How are BE activities regulated?
- Which region or area of the country is under consideration?
- How many BEs are there in this region or area?

- Are these establishments able to supply the blood and components required at the time needed?
- What activities are carried out by these establishments – do they all collect, test and process?
- Are these activities carried out routinely or only when required?
- Are quality and safety of all blood components in the region standardized and regulated?
- How are each of the establishments currently funded?
- Have any incidents or problems with any of these establishments been reported? If so, what were they, what were the outcomes and how were they resolved?
- Are there any existing plans for centralization, or has the suggestion been made in the past, but not acted upon and why?
- Can centralization of activities improve the organization of the blood service network to increase patient access to products and reduce costs?
- What are the current costs involved in collecting, processing and testing in multiple locations? Would centralization result in cost savings and other efficiencies?
- Will transportation and communication infrastructures in the country permit timely, affordable and quality-assured movement of blood donations, donor blood samples for testing and blood components for transfusion?

If reasonably reliable answers to the above questions can be obtained it should be possible to determine the potential need for and benefits of centralization.

3.2 Structure of the national blood system

The way in which the blood system is organized in the country will affect the process of centralization. Possible scenarios for centralization based on the most common blood system models are outlined below

(i) One national blood service with a consolidated structure and organization

Some countries have a single national blood service within which a small number of centralized BEs carry out processing and testing only, or in some cases, processing only. This model is suitable where the national blood service operates as a monopoly in the country or region, and one or more regional BEs operate as centralized BEs performing processing and testing functions for the other "customer" BEs, which are responsible for blood collection and blood product distribution. This model operates in Australia, Japan and across the United Kingdom's blood services. Independent regulatory oversight of the blood service is especially important in this setting in order to protect against potential risks that a privately run and monopolistic blood service could stop operating or cease to control the costs of blood, putting the blood supply at risk.

(ii) Many separate organizations and structures, each with one or more centralized BEs for processing and testing

This model is seen countries such as Germany, South Africa, Thailand and the USA. Various organizations are involved in the blood system and some centralized BEs provide processing and testing for different organizations. In this model, the centralized BE may belong to one organization and provide testing and processing services to its own organization or to others through contractual agreements. Although this approach may not provide a single national body, as long as there is national coordination and oversight, and a national blood programme with the appropriate national standards supported by independent audit, this model can provide effective centralization.

(iii) A stand-alone organization managing a BE that only provides testing and/or processing services for other BEs

This model may be appropriate for countries where various organizations are involved in the blood system, but it is not feasible or possible for a centralized BE to be established by the existing organizations as described in (ii). In this situation, a stand-alone organization may be the most appropriate solution. Such BEs exist in Namibia and the USA.

Centralization will often be more difficult where many organizations are involved in the blood supply. In such a situation, there must be clear understanding and agreement from the start, among all parties involved, on key parameters and expectations. These include expected volume of blood to be processed and tested and proximity to and accessibility of the blood collection and distribution centres.

In countries where a variety of organizations (such as private, governmental, military and hospital-based) operate without effective regulatory oversight, blood services may be driven by political expediency or by market forces and competition, with less consideration for minimum standards or operational efficiency. It is therefore important for governments to:

- define clear national policies and standards that apply to all those involved in the provision of blood and components;
- implement effective regulatory oversight;
- take effective action to improve the quality of blood products and the provision of blood services; and
- address inefficiencies and lack of coordination of a fragmented system.

3.3 Which functions should be centralized?

Centralization of testing and processing activities can be implemented at one stroke or gradually (step-by-step) in the country. Ideally, centralization and integration of testing and processing functions is part of, or an initial phase in, an overall restructuring of the blood system to improve blood product accessibility and quality. In some situations, it may be feasible to first partially centralize processing and fully centralize testing or vice versa. The benefits of centralization of testing and processing have been described previously (see Chapter 2). Other functions that will benefit from integration efforts include the management of blood donor and blood collection activities, and of storage, inventory and distribution procedures. Appropriate management systems can be implemented depending on the extent of integration.

3.3.1 Integration of the whole process from blood donation to blood product distribution

Integration of the whole process is the ideal model, as it combines the advantages of the models described in sections 3.3.1 and 3.3.2, but without the limitations. The necessary amount and type of blood can be collected at the most convenient blood centres, the inventory can be managed appropriately according to the demand in each region, and the distribution of the necessary volume of blood products can be achieved, based on the needs of the different hospitals.

3.3.2 Integration of blood collection and donor management activities

Integrating blood collection and donor management with the testing and processing functions in the centralized BE can help to improve the quality and efficiency of blood collection. The type of blood donation (for example, whole blood or apheresis) and the type and volume of components processed can be optimized according to the location of the blood centre and the clinical demand for different blood products. Blood that is collected in centres closer to the centralized BE can be more efficiently transported and processed into products with more stringent time limits for preparation and storage, such as fresh frozen plasma, cryoprecipitate and source plasma intended for coagulation factor concentrates. For a variety of reasons, including volume of demand and shorter shelf life, platelet concentrates may be produced more efficiently in a centralized BE. Apheresis collection centres can be differentiated from whole blood collection centres according to the characteristics of the blood donors in the region and capability and location of the collection centre. Donors can also be managed according to the needs of the BE and the clinical demand. Integrating blood collection and donor management activities in the centralized BE is a useful step that can be taken during the transition from hospital-based replacement donations to community-based donations, as the centralized BE can manage blood collection and donor management.

3.3.3 Integration of storage, inventory management and distribution

Integrating these functions with the testing and processing functions in the centralized BE can improve the overall management of blood components in the region or country. Central coordination of these functions has proven invaluable during disasters. The processed blood components are not returned to the different blood collection establishments but are stored in the centralized BE and distributed according to the needs of the hospitals. One potential drawback of this system is that the BEs and/or blood services that collected the blood may expect priority access to the blood components. However, this would not be a problem in the case of a single, centrally managed national blood service.

3.3.4 Integration of other functions

3.3.4.1 Training/reference centre

A centralized BE can play a role as a training/reference centre for other BEs in the region, as a national centre of excellence, or as a model for other countries planning consolidation. Where centralization is to be implemented gradually, one national centre of excellence can be established. Then other BEs can be set up step-by-step, learning from the experience acquired. Staff in the newer centralized BEs can undergo training beforehand at the initially established national centre. Other countries considering the establishment of centralized BEs can also learn from the experience at the "model" centre and staff can be trained there before taking up their new positions.

3.3.4.2 Blood group reference laboratory activities

Most countries have access to a reference laboratory for red cell typing, testing of rare blood types, and human leukocyte antigen (HLA) and platelet testing, which provides support to hospitals and other blood centres. The reference laboratory function can be centralized together with the blood grouping and antibody screening, and the centralized BE will provide support not only to hospitals, but to other centralized BEs without a reference laboratory. One advantage of locating the reference laboratory function at the centralized BE is better accessibility to blood components that can be used for the preparation of in-house panel red cells for irregular antibody identification and monoclonal antibody production. The reference laboratory can play a major role in communication with hospitals performing transfusion in the region.

3.3.4.3 TTI reference laboratory activities

A reference laboratory for TTI testing is also available in many countries. It provides confirmation of reactive donor results as well as preparing quality assurance screening panels and internal reference controls, such as weak reactive samples. The reference laboratory should also either be responsible for, or participate in, the evaluation and selection of new test kits for donation testing. Reference laboratory functions can be centralized together with donation testing, and panels and controls can be provided to centralized BEs that undertake testing but do not have a reference function.

3.4 Legislative considerations

Ministries of health have the ultimate responsibility for ensuring an adequate supply of good-quality, safe and effective blood and blood products for their population as part of their oversight of public health. This is best achieved through the establishment of a nationally organized and sustainably funded blood system under independent and well-informed regulatory oversight. The centralization of BE activities should be included at the highest level of national policy, development planning and strategic initiatives, with adequate resourcing supported by the government. *(11)*

A national blood policy enacted in law serves to define the responsibilities of the ministries of health, empower the national blood regulatory authority, and determine the structure of the blood service. Under the national blood policy, a strategic model for organization of the blood system and its integration within the public health system is defined and implemented. This model should determine the number and geographical location of blood collection and processing centres and the logistics of product storage and distribution to hospitals, with the goal of optimizing blood product availability and efficient use of resources.

Roles and responsibilities should be defined for governmental and nongovernmental components of the system, including the operators that collect and process blood donations, their laboratory testing facilities and transfusion services. A mechanism should be established for programme coordination and monitoring, including haemovigilance and a legal framework established for blood regulation. A body should also be established under the ministry of health for policy- and decision-making related to blood safety and availability, with a provision for obtaining advisory inputs from stakeholders. Mechanisms of financing should be defined to ensure stability at all levels.

A stable blood system depends on sustainable national commitment to provide resources for human capital, physical infrastructure and operating budgets. In most settings, a mixture of cost recovery and external subsidy by governmental and other parties will be needed to sustain the blood service and the blood regulator. Development, execution and transparent reporting of costing are necessary to demonstrate to funders that spending is appropriately managed and to help strengthen the case for funding support.

The centralized BE must have a clear statement on its vision, mission, goals, strategic objectives and action plans in accordance with the national blood policy. The fundamental mission should include ensuring donor safety, availability of blood components for clinical use and plasma for manufacturing into PDMPs, and efficient management including minimizing waste. Evaluation of outputs should be performed consistently and in accordance with agreed indicators, by self-assessment and by the regulatory authorities.

3.5 Good governance

The concept of centralization is aimed at achieving economies of scale and harmonization of practice standards to ensure quality, safety, efficacy and sufficiency of blood and blood products for patients. Therefore, centralized BEs should operate in strict accordance with good governance principles and should recognize the responsibility of being a role model. In addition, centralized BEs need to be efficiently organized and managed according to modern scientific principles including risk management, evidence-based decision-making and use of advanced digital tools and technologies. In ensuring good governance and oversight over the new system of centralization of testing and processing activities, the following considerations are relevant:

- How will it function in the context of the national blood programme and the overall health system in terms of the:
  - role of the health authority in decision-making on blood safety policies;
  - relationship with local and national government and health authorities;
  - integration of the BEs within the public health system (for example, monitoring of blood supplies, response to emergencies, haemovigilance);
  - role of the local community in decision-making on programme implementation;
  - role in national emergency response and contingency plans;
  - efficient use of health system resources?

- Who will be responsible for the oversight of such a system (in terms of performance and governance)?

It is important to ensure that there is a single authority with overall oversight of national blood supply safety and availability. Ideally the government should have the ultimate oversight and responsibility for ensuring the robustness and resilience of blood supply.

The liabilities for blood product safety, quality and availability are important issues that must be agreed upon well in advance between BEs and blood collection centres and hospitals (depending on which model is adopted). Clarity regarding roles, responsibilities and expectations must be established with blood collection centres and hospitals, either through contractual agreements or memoranda of understanding (MOUs). How this fits in with the national blood supply expectations and need must also be clarified.

3.6 Blood regulation

The quality, safety and efficacy of blood and blood products depends on strict adherence to internationally recognized national standards ("blood standards") that apply to all steps in their production and use. Recognizing the importance of adoption of and compliance with blood standards, World Health Assembly Resolution 63.12 (2010) *(1)* drew attention to the need for "appropriate regulatory systems" as an essential element of a "nationally coordinated and sustainable

blood system". Blood regulation consists of the establishment in law of a NRA, often under oversight of the ministry of health, as an "independent, competent authority" with legal authorization to set and enforce standards for blood collection, testing, processing and further manufacturing. In countries where there is no NRA, pending the establishment of a national blood regulatory system, the government must ensure that the relevant codes and standards are selected or established, ideally by experts in the field from the blood service and clinical users. Clear roles and responsibilities must be established between the NRA and BEs and must reflect independent decision-making by the NRA.

It can be argued that a self-regulating blood service has the capacity to assure the quality and safety of blood and blood components without governmental regulation. In the absence of regulation, external accreditation bodies can play a role in helping BEs to meet internationally recognized standards. However, independent governmental blood regulation overcomes various pitfalls of self-regulation that include vulnerability to conflicts of interest and inability to enforce compliance by all the BEs. Additionally, independent regulation adds a level of assurance that promotes public confidence in the blood system. Based on historical experience, governmental blood regulation is dominant in World Bank defined high-income countries, common in upper-middle-income countries, and present or under development in many lower-middle-income countries and low-income countries.

The need for blood regulation arises from the inherent dangers of blood and blood products, and the complexities of preparation of whole blood and blood components for transfusion and the manufacture of PDMPs. By setting and enforcing blood standards, blood regulation optimizes blood quality, safety and availability within a national blood system. It functions to protect the health and safety of blood and plasma donors, assure blood and blood product safety for patients, help the country to address its blood needs, promote efficient management of the blood system, and enable use of plasma to make plasma-derived medicines. Additionally, blood regulation enables monitoring of the status of the blood system, including collection of data on blood product availability and any adverse outcomes in both donors and recipients ("haemovigilance"). It also facilitates regional and international cooperation on providing blood therapies (for example, non-domestic fractionation of domestic plasma to supply PDMPs) and permits timely and effective responses to emerging blood safety threats and opportunities afforded by new technology. Blood regulation can further promote adequacy of the blood supply, and equitable access to transfusion therapies including essential plasma-derived medicines. *(12, 13)*

Blood standards are specifications for the collection, testing and preparation of blood and blood components, which are aimed to assure their quality, safety and efficacy for therapeutic use. They encompass donor assessment and deferral to determine suitability for donation; the collection, testing, processing, labelling, storage, transportation and appropriate use of blood and blood components; and mechanisms for identification and reporting of adverse events and adverse reactions to blood donation and transfusion (haemovigilance). Full traceability from donations to end-products to points of care and back again enables actions to be taken when:

- quality and safety issues are determined to be relevant to the donors and their previous donations;
- patients experience adverse events attributable to the products; and
- when deviations in manufacturing necessitate product recalls.

Assuring the quality of blood component preparation also enables generation of plasma suitable for manufacture of PDMPs.

BEs that collect, test and process blood donations should be authorized by their NRAs and should be regularly inspected for evidence of compliance with requirements and standards including applicable GMP. Authorization of BEs consists of a procedure to receive and evaluate documentation from the applicant describing the premises, equipment, operating procedures, employee training and qualification and management systems that will be in place for blood collection and processing. This may include review of data from quality control testing of products. A legal provision should exist that allows the NRA to grant authorizations of either unlimited or limited duration. For authorizations of unlimited duration, measures should be in place to ensure continued adherence of the product or process to quality, safety and efficacy standards (for example, through a vigilance system or a routine compliance monitoring system). If the authorization is of limited duration, approvals should be renewed after a predefined time interval. The NRA may elect to prepare its own report, rely on evaluation reports prepared by other national authorities or use a combination of these approaches. GMP inspections or certifications should be part of the authorization requirements. The same standards should apply to authorization of domestically produced and imported blood and blood products.

Blood regulation should also extend to oversight of the substances and medical devices used in the preparation of blood and blood components through certifications, manufacturing authorizations and inspections according to the applicable regulatory classification of the substance or device. These substances and devices include (but are not limited to):

- anticoagulant solutions
- additive solutions for red blood cells and platelets
- devices used in donor health assessments (blood pressure and pulse monitors, thermometers, haemoglobin analysers)
- test kits for detection of transfusion-transmissible infections in donors
- blood grouping, typing and compatibility test reagents
- systems for microbial detection
- apheresis equipment
- automated and manual blood processors
- blood bag collection systems
- centrifuges
- automated red cell washers
- gamma and X-ray irradiators
- sterile connection devices
- automated and manual plasma extractors

- plasma freezers
- PR technologies
- computerized data management systems.

Authorizations and GMP inspections should also verify that BEs use only approved substances and medical devices for the preparation of blood and blood components.

Trust in the performance of regulatory tasks by the NRA may be fostered by independent assessment of regulatory functions related to blood and their execution in the country concerned. *(14)* Recently WHO has included blood product regulation in its Global Benchmarking Tool + Blood (GBT + blood), which is designed for continuous assessment of regulatory functions within an NRA. As the assessment outcome, the level of blood regulation by a specific NRA will be determined and the performance rated as a maturity level, with observed deficiencies defined as a basis for continuous improvement. Where blood regulation by an NRA is determined to be functioning at a fully functional level (maturity level 3) or advanced level (maturity level 4), other NRAs in the region may consider the assessment outcome as sufficient to allow them to rely on the decisions of that NRA. For example, a less mature or less well-resourced NRA might accept the determination of a more mature NRA in the same region that a specific donor testing platform and test kit for HIV, blood collection container, blood grouping reagent or other blood related substance or device should be authorized for marketing.

3.7 Organizational considerations

Centralization of testing and processing generally requires significant organizational changes including the establishment of new governance and managerial structures. At a high level, government and policy-makers must recognize the national blood programme and its goal of achieving safe sufficient and quality-assured blood products. Consensus among the relevant stakeholders is needed as to the centralized BEs that will be selected. Stakeholders include national authorities (such as the national health authority), blood services (including those run by NGOs such as Red Cross and Red Crescent organizations), end-users (such as small BEs, hospitals, institutes and donor and patient organizations), and relevant professional and scientific bodies. The roles and responsibilities of the centralized BE should be recognized and formalized in a contract or MOU.

In considering the different models and scenarios, the following questions are relevant:

- Extent of the consolidation: Will a network of BEs be established or, at the other extreme, will the blood supply system be integrated into one or a few centralized services?
- Are the activities to be carried out in the same location?

Different approaches will have different financial and managerial implications. Following centralization of testing and processing, the centralized BE may or may not retain the blood collection activities. Conversely, BEs that transfer their testing and processing activities to a centralized BE may become collection-only BEs, or collection, storage and distribution BEs. The "hub and spoke" model can be adopted in these instances, and it is important that due consideration be given to coordinating the management of the "spoke" centres.

Management of the blood product inventory is an important aspect of the centralized BE's operations. Depending on which of the scenarios described in Section 3.2 is adopted, different organizational arrangements would need to be considered:

(i) National blood service with consolidated structure and organization, with regional BEs for processing and testing: in this model, the inventory management is performed by the national blood service and the blood inventory is managed at the national or regional level. Where feasible, this may include blood inventories in hospital blood banks where blood is transfused.

(ii) Many separate organizations and structures, each with one or more centralized BEs for processing and testing: in this model, the centralized BE may return the processed blood components to the blood collection BE. Where blood donation, donor management and blood distribution activities are also centralized, the inventory can be more efficiently managed.

(iii) Stand-alone organization managing a BE for processing and testing and serving other BEs: in this model, similar to (ii), the inventory management can be more efficient if blood donation, donor management and blood distribution activities are also consolidated.

Most importantly, centralization of testing and processing will add significantly to the organizational and managerial complexities of the BE. Suitable management mechanisms and administrative systems for the new model need to be established or existing ones strengthened to ensure effective functioning at all points in the network. It is also crucial that any BE selected is able to demonstrate effective management and good governance, including quality assurance, risk- and evidence-based decision-making, transparency, and effective performance and quality monitoring.

Leaders and managers of all the facilities should demonstrate a common commitment to quality and safety by setting expectations for those who work at the BE and encouraging a positive quality and safety culture to flourish. The new models will require teams that are able to collaborate to get the job done. There is a need for effective cooperation and communication with the rest of the network – with other BEs and other components of the blood chain (blood collection centres, hospitals and the transport logistics chain). For example, the inventory management team needs to work closely with donor recruiters, component processing staff and end-users to identify distribution needs.

The management system for the premises and facilities, human resources and specialized equipment needs to be established to ensure the sustainable and cost-effective operation of the centralized testing and processing. To support these activities, a sound procurement policy and procedures should be in place and they should be implemented in a cost-effective manner.

3.8 Quality systems

Ensuring the implementation of a uniform QMS and achieving an improvement in the quality of blood components is a major reason for implementing the strategies of centralized testing and processing. At a national level, there must be clear agreement between the BEs and the authorities responsible for regulating blood product safety and quality regarding the national standards applicable to blood products and how they are tested and processed. International standards may need to be applied when a certification is needed for a particular purpose such as collection of plasma for fractionation to produce PDMPs. A set of standards must be in place relating to donation, processing and distribution in all the facilities in the network.

The national blood system should include an organized haemovigilance programme, i.e. surveillance procedures for monitoring, reporting, investigation and analysis of adverse events and adverse reactions related to the donation, processing and transfusion of blood and blood products, and the responsibility and authority to take actions to prevent the occurrence or recurrence of adverse events and reactions. BEs involved in collection, testing and processing of whole blood and blood components for transfusion play an essential role in the haemovigilance system. To be effective, haemovigilance requires bidirectional traceability of information relevant to donors, products and patient outcomes throughout the entire transfusion chain from blood donation to product administration. Therefore, traceability of information is a quality function of the BE. Bidirectional traceability of information needs to be assured through integration of data management between the blood collection establishments, the centralized BE and hospitals.

The centralized BE should implement a GMP-compliant or equivalent QMS in all its operations and comply with national standards and guidelines. International Organization for Standardization (ISO) standards can be used for compatible specific operations but are not equivalent to GMP. ISO laboratory standards are specifically written for diagnostic laboratories, and at the time of preparation of this document there were no blood service specific ISO standards. In addition to regular quality control of blood components as essential medicines, quality assurance of blood components may be considered and developed. When most of the equipment and reagent procurement processes are performed by the centralized BE, evaluation of in vitro diagnostic devices and equipment specifications is crucial and must be transparent.

Participation in relevant EQAS, identification of appropriate quality indicators and routine monitoring reports will allow the progress of quality improvement to be regularly evaluated. Special tools such as joint internal audit or supervision may be used to ensure the implementation of quality standards across BEs. The centralized BE must have a system in place for external accreditation and be externally audited by an authorized organization. Customer BEs should also undergo external accreditation and auditing. There is a potential role for the centralized BE in national quality programme activities. This could include participation in training, evaluation and validation activities for other BEs. The BE could also undertake the running of a national EQAS (NEQAS) if it has the capacity to do so.

Where possible, the proposed BE that will undertake centralized testing and processing functions should already meet national and GMP standards or have commenced implementation and be close to achieving compliance. An audit of the BE to determine the level of current practice compared to national and GMP standards is useful to inform decision-making on centralization.

3.9 Operational considerations

When considering centralization, it is important to determine the optimal number and size of centralized BEs that will be needed in the country or region. If the BE is either too small or too large, it may not be able to operate efficiently. *(16)* Consolidating or enlarging smaller centres would offer the greatest advantage. The number of centres must be sufficient to ensure accessibility and yet not be so great that the ability to maintain consistency and meet quality standards is compromised. Furthermore, an appropriate emergency preparedness strategy is needed to take into account the risk of a centralized BE being affected by natural disasters or other contingencies, which can result in a blood shortage in the region or country.

3.9.1 Factors to consider when determining the number and location of centralized BEs

The following factors should be considered when determining the number and location of the centralized BEs.

3.9.1.1 Geographical features of the country

In countries where cities or regions are separated by geographical features such as forests, rivers and mountains or in countries comprising many islands, a higher number of centralized BEs may be required to maintain accessibility.

3.9.1.2 Number of blood collection and blood distribution centres and hospitals in the region that will be served by the centralized BE

Donated blood must be transported to the centralized BE, and, after testing and processing, the blood components must be transported to the BEs that distribute them to the hospitals. Efficient management of blood distribution is critical in systems that involve different locations for blood collection and storage. Blood may also need to be moved from one hospital to another to meet demand, for example, when a rare blood type is needed. Areas with a greater number and variety of hospitals and health care facilities may have more blood collection and distribution centres, and this will affect the number and size of the centralized BEs. The distance, accessibility and type of hospitals is also important when identifying the most appropriate locations for the centralized BEs. The decision on location of each centralized BE will also need to take into account the likely mode of transportation of blood and blood components, as described in Section 3.9.1.3. Redundancy should also be a consideration when deciding on the number and location of centralized BEs.

3.9.1.3 Transportation and management of the cold chain

Various modes of transport, including road, rail, air and waterways, among others, can be used, provided the cold chain is maintained. Ideally, centralized BEs should be located close to or with good access to highway exits, train stations, airports or ports, depending on the mode of transportation to be used. The mode of transportation will differ from country to country and from region to region, depending on the geographical features, and the transport systems available:

- If there is a good road network, transportation by cars or trucks is a good option, and can be outsourced if reliable transport providers are available.
- In countries with a well-developed railway network, transportation by train is a good option, provided suitable transportation containers are available.
- Other options include transportation by air (including drone delivery) in countries that are geographically segmented (including those with many islands), or by boats and ships in countries with easy access to waterways, provided suitable transportation containers are available. Small civilian unmanned aerial vehicles, or drones, have recently become a viable option for the transportation of blood products and could be especially useful in remote or rural areas that are difficult to access. *(17, 18)*
- In all situations where a transport route involves several segments (for example, van to station, loading onto a train, changing train at an intermediate station, collection by van from final station) it is essential to have clearly defined responsibilities, handover protocols and contingency plans to minimize the risk of delay.

Because products such as fresh frozen plasma and plasma intended for fractionation into coagulation factors require the shortest possible time intervals between collection and processing, and between processing and storage, it is essential that the transportation time should be as short as possible and that the cold chain is stringently maintained. In countries where the national blood service has a consolidated structure and organization, there is an option to limit the blood centres collecting blood intended for preparation of fresh frozen plasma, cryoprecipitate or plasma for further fractionation into coagulation factor concentrates to those sited closer to the centralized BE. Platelet concentrates, which have a shorter shelf life, also need special consideration. Temperature-controlled transportation containers and vehicles should be used to maintain the quality of blood and blood components. Ideally, containers should not require electric charge, and coolers based on phase change materials are preferable.

3.9.1.4 Integration with other functions

Where blood collection, storage, inventory management and distribution functions are also consolidated and/or integrated with the centralized BE, accessibility for blood donors and hospitals should be taken into consideration.

If more than one centralized BE is needed, a decision on whether the centralized BEs are to be established simultaneously or in phases is necessary. This decision will depend on various factors including the capacity of the project team(s), availability of funding and other necessary resources, and any potential disruptions to blood supply that may occur during the transition period.

3.9.2 Determining the size of the centralized BE

The size of the centralized BE and the planning of the facility should take into account several important factors as listed below.

3.9.2.1 Volume of blood and samples to be processed and tested per day

Larger economies of scale and better operational cost-effectiveness are achieved the greater the volumes of blood and blood samples to be processed and tested. Theoretically, in countries with multiple small blood service organizations that are independently operated, centralization of processing and testing activities would be likely to confer greater advantages and benefits compared to existing operations. These benefits would accrue if the numbers are sufficient to enable automation systems to be implemented. Automation increases efficiency and effectiveness and reduces costs, as well as contributing to the rationalization of human resources. In addition, implementation of internationally recognized standards, including GMP, requires definition of roles and responsibilities, which cannot be achieved in a small BE with a small number of staff.

3.9.2.2 Facility considerations

Ideally the feasibility of using an existing facility should be considered, as building and establishing new facilities, as well as hiring staff, is likely to be more costly. Where new facilities are required for the centralization, the costs of building may significantly increase the overall cost of centralization.

3.9.2.3 Equipment

How much equipment is required depends on the throughput of the available equipment, and the feasibility of automating the process. The testing and processing working space must be sufficiently large to accommodate the equipment, and to allow for future expansion in response to changing needs. Automation can reduce the number of staff required to carry out the operations, but often requires bigger spaces.

3.9.2.4 Future-proofing the facility

While the size of the centralized BE depends on the number of blood donations and associated samples to be tested and processed, it should allow for future expansion.

3.9.2.5 Public infrastructure

It is important to consider public infrastructure, such as transportation systems, as described in Section 3.9.1.3, when planning the centralized BE. This will also influence the number of centralized BEs required. The centralized BE must be geographically well located in terms of accessibility from the blood collection and distribution centres. The organization of logistics will depend on the transport systems and delivery options that are in place and must ensure that the cold chain can be maintained at all times. Contingency planning for all eventualities including natural disasters is also essential. The role of the centralized BEs during emergencies and how they will function within the emergency health system must also be carefully considered.

CHAPTER 4

STEPS IN PLANNING THE SETTING UP OF A BLOOD ESTABLISHMENT TO CENTRALIZE ACTIVITIES

4.1 Assessing the current status

To develop a full centralization model and plan, the current situation must be fully understood. Up-to-date data must be obtained and analysed, and there must be a clear understanding of why centralization is required and the expected outcomes. Ideally there should be a national blood programme in place as a prerequisite for centralization of BEs. This programme may identify the need for centralization at some stage in the development of the blood service based on key considerations including the presence of a nationally coordinated blood service. Potential risks should be considered during the planning phase and throughout the project's implementation. Identified risks should be analysed, communicated and addressed adequately.

The assessment should include the answers to the following questions:

4.1.1 What is the existing situation and why is this no longer acceptable, or why would centralization be advantageous?

A full situation analysis must be performed. This should identify the geographical characteristics and infrastructure of the region; the organization(s) that manage blood services; the sites for centralization; the number of donations collected by each site and the collection patterns (regular or periodic); the type of donors at each site; the blood usage and usage patterns at each site including rate of product outdating; the blood testing practices at each site; any specific needs at any site; and any current or potential problems affecting or associated with any of the sites.

4.1.2 What centralization options are available?

All the possible centralization options need to be identified and their advantages and disadvantages determined. Which sites should be centralized; which activities need to be centralized (for example, it may be that only testing and processing need to be centralized and collection activities can remain disseminated); where should the centralized site be located (existing or new site)? Depending on the activities planned at the centralized site it may be possible to use an existing site that requires few physical changes.

4.1.3 How would centralization meet the needs of the national blood programme (if one exists)?

Is there a national blood programme? If not, the centralization programme is an opportunity to develop one. If there is one, does it require centralization at some level and does the planned centralization fit with its requirements? Does the programme raise any objections to centralization? If the planned centralization does not meet the requirements of the national blood programme, should the centralization plan be changed to meet these requirements and, if so, how? It is possible that centralization may not be supported by the national blood programme for reasons that are not directly related to the provision of blood and components, for example community reasons or political commitments to maintain certain services.

4.1.4 Is there support from the government and/or NGOs (if relevant)?

- Government endorsement for centralization would be expected. Financial support may be required.
- If active support is not given, i.e. no resources are made available, at the very least a documented agreement by the government (for example, ministry of health) would almost certainly be necessary for centralization to be implemented.
- If the blood programme is the responsibility of an NGO, it is important to find out whether the NGO fully supports the centralization.
- In settings of shared governmental and nongovernmental responsibility for the blood service, a formal public–private partnership model should be established to clarify the respective roles and responsibilities of the partners.

4.2 Blood establishment development plan

Once the drivers for centralization have been fully understood, and the overall high-level centralization plan specifying the number of BEs and their location, has been agreed, a full development plan should be drawn up. This plan should cover all of the individual elements needed to centralize activities, including the setting up of the required working groups to cover all these elements. The plan must include timelines and the expected outcomes at each of the time points. This plan is then used to drive and monitor all the development activities.

4.2.1 Management team

A top-level management team should be appointed under a dynamic, committed and qualified leader. This team should not be too large but should include relevant senior staff from the centralized BE, one senior individual from each of the BEs to be centralized, at least one appropriately qualified representative from the local or national health authority, and a representative of the body responsible for the national blood programme (ministry of health or NGO). If the national blood programme is run by an NGO, but depends on government support, representatives from both government and the NGO should be included. A hospital association representative and high-level professional clinical representative may also be required, for example, from the national haematology society or the national transfusion society, if one exists.

4.2.2 Identification of all of the individual activities being centralized

All of the individual BE activities being centralized must be identified and separate workstreams put in place for each. The workstreams may be general, for example laboratory or processing, or more specific, for example quality control of blood components, immunohaematology or infectious disease testing, depending on the activities being centralized and the resources available. An important aspect of the planning stage is to ensure that, at this point in the process, clear and final decisions have been made about the activities to be centralized.

In addition, the management team, either on their own or with assistance from additional advisers, should identify the required centralization outcomes for each of the individual activities.

4.2.3 Working groups

Working groups should be set up covering all of the activities and workstreams identified. Ideally all these individual activities and workstreams would have their own team of suitably qualified staff and run concurrently. Each team should comprise individuals who have the required knowledge and expertise in that particular field.

However, if resources (including individuals undertaking the work) are limited, personnel with relevant knowledge and expertise in more than one field or work area may need to be in more than one working group. Mobilization of staff between the centralized BE and customer BEs can also be considered.

The working groups should be given clear instructions on their purpose and expected outcome(s), together with the time frame for completion of their tasks. They should then develop their own strategies, plans and timelines for their centralization work.

The working groups should regularly update the management team on their progress, any obstacles or problems encountered and whether they expect to finish the work on schedule.

4.2.4 Timelines and monitoring

The overall timescale for the project, from the start to the completion of all centralization activities and the centralized BE coming online, must be determined. This is largely dependent upon the size of the project, but also on the resources available and the timescales for their availability. Determining the timescale for the overall project may need to take into account external factors or requirements, for example a deadline set by the body responsible for managing the national blood programme, or the need to use the funding during a specific financial period.

Timelines should then be drawn up for each workstream of the centralization project. Sufficient leeway should be built in to allow for unexpected issues arising. Regular monitoring of all the individual workstreams as well as of the overall project is essential. This ensures that any time slippage is identified as early as possible so that actions can be taken to help return the project to schedule.

Critical points in the project and timelines should be identified and be subject to more frequent monitoring and reporting to enable immediate intervention if problems arise.

4.3 Organizational structure

The organizational structure of the centralized BE needs to be determined. The individual sections and work areas required should be identified, together with the numbers of staff required, and the knowledge, education and skills required for each role. The planned structure must be suitable for the range of activities to be performed by the BE.

An organization chart should be drawn up to show the overall organizational structure and the roles and responsibilities. The overall structure and organization chart should be in line with the requirements of the national blood programme but should also meet the needs of the consolidated service.

As well as providing clarity for the staff of the BE and for hospitals using the blood and components supplied, the organization chart is important in ensuring the understanding of high-level government and/or the NGO and in maintaining support for the BE and the national programme.

4.4 Infrastructure

Advance planning of the infrastructure of the centralized BE is important. Once the intended activities of the centralized BE have been discussed and agreed, and once an organizational structure has been developed and approved, planning for the recruitment of staff and the provision of the required equipment, consumables, disposables, furniture and general supplies can be initiated. This will involve a range of individuals representing the different sections within the BE.

The design of the centralized BE must establish the appropriate infrastructure and systems to support its facilities and equipment. This will include the water supply, electricity, communications services, sanitation, refrigerators and cold rooms for storage of blood and components, blood testing and blood testing reagents, platelet incubators, freezers for frozen reagents and components, transportation of blood and blood samples, waste disposal and safety systems for information technology, among others, in accordance with the relevant standards and GMP. Infrastructure such as human resources, procurement, finance, support services (for example, cleaning and maintenance) all need to be developed and specified. In some cases, for example if the centralized BE is developed at an existing BE, these may already exist but must be assessed for suitability.

Recruitment or mobilization of staff may need to be staggered if different sections and activities within the centralized BE come into operation at different times. As part of the recruitment process, jobs for appropriately qualified staff from the original disseminated sites should be considered before external recruitment begins.

4.4.1 Facility

As part of the initial planning for centralization, a decision on whether to establish the centralized BE in an existing building or in a new, purpose-built building is required.

A number of factors need to be taken into consideration when making this decision:

- What is the extent of the centralization and how much space is needed?

  Centralization of specific activities may not require any significant building alterations or work. In such cases the whole centralization project may be simpler, quicker and cheaper.

- Is one (or more) of the existing BEs suitable for conversion to a larger centralized BE?

  Is the size of the building sufficient for the additional activities and is there capacity for the required expansion? Is the building in a suitable location for transport links and to enable a sufficient number of appropriately trained staff to be recruited? Is the existing structure of the building GMP-compliant, or can it be made suitable? Is the amount of work required to convert the site so great that a new building would be cheaper and provide a generally better outcome?

- If a new building is preferred, is there suitable land available in a location with good transport links and can a sufficient number of appropriately trained staff be recruited? Is there sufficient funding to build and maintain the site?

Regardless of whether an existing or a new building is used, the centralized BE's premises should follow international standards such as the WHO Design guidelines for blood centres and comply with WHO guidelines on good manufacturing practice for blood establishments (GMP for BE). The plans should also include features needed to support staff well-being.

4.4.2 Human resources

When centralization is planned, human resource issues are often a leading cause of anxiety, and staff resistance has been identified as a key risk (see Section 2.2.2). Many operational staff will be worried about losing their jobs and many management staff may be concerned about demotion. These concerns must be addressed to provide staff with sufficient time to make alternative job arrangements or to relocate. Voluntary cutback packages can be offered or where possible a process of natural attrition can be implemented.

Additionally, ensuring that sufficient qualified, competent and trained staff are available and continue to be recruitable, both at the time of centralization and over the longer term, is essential.

4.4.3 Operational policies and procedures

Operational policies and procedures should already be in existence as part of the requirements of the national blood programme. However, if there is no national programme, or if the existing policies and procedures are not appropriate, they need to be developed as part of the centralization process and could eventually be integrated into a national blood programme.

Policies and procedures should include testing algorithms, standards and specifications for blood components, and regulatory and quality requirements and standards. Even if they already exist, the centralization project is an opportunity to review and update all algorithms, standards and specifications.

In addition, evaluation and validation plans for all equipment, reagents, assays and other items to be purchased and introduced through the centralization process need to be developed.

4.4.4 Major equipment

Centralization of activities will automatically increase the number of donations requiring testing and processing at each centralized site. The equipment in place must be suitable for handling the large numbers of samples and donations and appropriate for the intended use.

The expected number of donations to be processed needs to be known. A review of all planned activities of the centralized BE will identify what items of equipment are required. This information can be used to decide on the most appropriate equipment and the amount of equipment needed to be able to handle the expected number of donations. Not only should there be sufficient equipment to perform the required activities for the planned number of donations, but also to ensure that either extra capacity or back-up equipment is available to provide sufficient capacity when equipment is unavailable, due to breakdown, failure or planned maintenance. Automation should be introduced whenever possible to reduce the errors that are associated with manual procedures.

Different approaches to the acquisition of equipment may be chosen depending on budget, financial rules and the procurement system, but the equipment must have been installed, set up by the supplier and properly validated by the BE prior to use. Evaluation and validation plans are required for all the major items of equipment. Verified international device certifications should be obtained in settings where plasma will be shipped to another country for fractionation. Smaller items also require validation, but evaluation may not be necessary.

In addition to the equipment itself, any support services required to enable the equipment to function properly must also be identified and put in place. Power supply, water supply, temperature and humidity requirements must all be ascertained and put into place before the equipment is procured.

Finally, the facilities to provide the required preventive maintenance and meet the servicing requirements of the equipment must be in place. Although some equipment may have a significant element of user-level maintenance, formal manufacturer-approved maintenance and servicing must be available when required, and within an appropriate time frame. Contracts for equipment should include operator training and provision of the recommended maintenance and servicing, as well as an uninterrupted supply of any consumables and/or disposables that are required.

4.4.5 Information system

A computerized information system (blood management system) should be included in the plans for centralization. Planning should take into account the interfaces required to other systems and equipment. This is particularly important if the centralization only covers part of the blood service activity, as links to the other parts of the system (for example, donor management) are critical. Management of legacy information and the transition from an existing system to a new information system can be complex and needs careful planning and validation.

4.4.6 Network logistics

An organized logistics plan should be established for delivery of supplies to the participating BEs; for safe and GMP-compliant transport of collected blood donations and laboratory samples to the centralized testing and processing facility; and for quality-controlled transport of blood components either back to the collection centres or directly to hospitals.

4.5 Finance and funding

The centralized BE should carry out appropriate budget planning and budget sourcing. The budget may be integrated in the health system as a government fundamental funding or cost-recovery practice.

Finance and funding activities need to take into account a number of separate elements:

- the current total spending on the collection, testing, processing, storage and provision of blood and components across all of the individual BEs to be centralized;
- the total cost of centralization;
- the ongoing costs of the centralized service – a full budget is needed;
- the overall source(s) of funding for the centralized service;
- sustainability of funding.

The first step is to determine the current total spending on providing blood and components across all of the BEs to be centralized. In some cases, funding may come from different sources, different government departments or through different routes, so that the total costs may not be obvious. Once the current spending is known, that can form the basis for determining the potential budget for the centralized service.

A full budget needs to be drawn up to cover the costs of the centralization. It is important to bear in mind that while the centralization activities are being carried out, the existing activities have to continue. As part of the overall planning for centralization, agreement in principle for the funding and its source(s) must already have been obtained. The budget should be able to provide accurate figures for the overall expected spending on all of the centralization activities.

Once centralization has taken place, the centralized BE needs to have the appropriate budget to enable it to provide the services required of it in the long term. An ongoing operational budget for the BE must be established and the source(s) of funding need to be identified and agreed.

4.6 Partnerships and agreements

In order to foster engagement, agreement and effective collaborations, the centralized BE should enter into joint agreements such as MOUs or contracts with the national blood programme authority, national government, local government, regional and local health services, and other relevant organizations such as donor organizations, NGOs and staff organizations. There should be an MOU between the BEs that are currently undertaking testing and processing activities ("customer" BEs) and the BEs that will take over those activities as a centralized BE. Customer BEs that are signatories to the MOU should be in agreement that blood components will be provided only by the specified centralized BE.

In addition to ensuring regular customer service and satisfaction, if blood distribution is conducted by the centralized BE, it should provide written service contracts to hospitals, other clinical users, researchers, fractionators and other

customer BEs. If blood distribution is still conducted by the customer BEs, the written service contract should be provided by each customer BE to hospitals in their area. The contract should be regularly reviewed, at least annually.

4.7 Communication

A critical part of the centralization process is clear, accurate and regular communication between all those involved in and affected by the centralization.

The purpose of communication is to inform, and then seek views, opinions and feedback. Although high-level plans may be in place, communication with all those involved or affected directly or indirectly is essential and they should be identified at the beginning of the centralization project.

These groups and individuals may include:

- staff in the customer BEs that are being centralized
- labour organizations and unions (if any)
- patient representative groups (if any)
- community groups
- donor associations
- local and regional health care system officials
- staff who will be working in the centralized BE
- national blood programme representatives (government and/or NGO)
- ministry of health
- relevant national professional bodies.

These groups and individuals can then be divided according to the level and nature of communication needed. Communication with some groups may consist simply of updates about the status of the project. For other groups and individuals, communication is about engaging with them to ensure their active involvement in the project, encouraging them to provide ongoing feedback and to help to shape the planning. Uniform national-level public communication is important to encourage suitable blood donation.

Communication to the wider international community may be considered, especially if assistance is required from international organizations such as WHO, the International Federation of Red Cross and Red Crescent Societies or other international societies.

Communication should continue for some time after the successful development and go-live of the centralized BE. Feedback demonstrating the success of the project, which both supports the local community and provides evidence to the government, may help when seeking their support for future projects.

4.8 Emergency preparedness

The centralized BE should develop emergency preparedness and emergency action plans and have procedures and resources ready to deal with accidents, disasters, political unrest, blockades and epidemics. In addition to alternative laboratory methods, kits and equipment, emergency preparedness should include alternative logistics support, redundancy (duplication of critical components of functions) and IT systems back-up. A back-up facility and network plan are needed to address the possibility that a centralized BE might become entirely unable to function in an extreme situation. In circumstances where it is not possible to ensure a back-up facility, it may be necessary to establish contingency arrangements with other organizations within or outside the country.

CHAPTER 5

PRACTICAL CONSIDERATIONS FOR A BLOOD ESTABLISHMENT THAT WILL PERFORM CENTRALIZED BLOOD TESTING AND PROCESSING

A BE should meet the key criteria set out in Chapter 3 before it can be selected to perform centralized testing and processing. In addition, the following systems should be put in place.

5.1 QMS and GMP

The BE should either have a QMS in place or be in the process of implementing a QMS that meets the WHO requirements of GMP or other equivalent international standards. While the key elements of any code of GMP are outlined in this chapter, they do not replace the need for full compliance with a selected code.

A quality manual should define the system and, as a minimum, should cover the following processes:

- control of documentation and records;
- reporting and investigation of problems, adverse reactions in donors and recipients, errors, out-of-specification components and customer complaints (this process should include component recall and lookback);
- planning and control of changes that need to be made (change control);
- internal audits (self-inspections);
- continuous improvement.

The quality manual should also describe the governance, business strategy and financial arrangements of the BE.

GMP is based on managing risks to the quality and safety of blood and blood components that occur during manufacture, and implementation of GMP together with the QMS should therefore be considered a priority.

5.2 Risk management and safety

Implementation of GMP is focused on managing the risks to quality and safety of blood components; however, it is also important for the BE to identify risks to the project and organization as a whole. Examples include inadequate funding for operations, critical supplier failure or loss of operational capacity due to a disaster. The creation and maintenance of organizational and quality Risk Registers is a key part of risk management. *(22)* Each risk should be listed on the register together with its consequences and assigned a "risk score" based on severity and likelihood. A corrective action plan, or Risk Treatment Plan, aimed both at reducing or removing the risk, and at mitigating the consequences if the risk arises, should be developed for each risk. Priority should be given to those risks with the highest risk scores.

The Risk Register and status of actions should be regularly reviewed by management. If necessary, the risk score should be amended.

Maintenance of staff safety is a key responsibility of the BE. While GMP-compliant premises will provide safe workflows and environments, staff should receive training in infection control and handling of potentially biohazardous waste and should have access to sufficient personal protective equipment.

5.3 Organization, roles and responsibilities

The BE should be organized in such a way that there is sufficient capacity and capability, and clear accountability for the organization and the quality and safety of its operations (see also Section 4.3).

5.3.1 Key roles

The following are key roles that should be established, and each incumbent should have the relevant qualifications and experience:

- Director – the director is responsible for all activities at the BE and ultimately for the quality and safety of the blood components provided to users.

- Processing/testing (operational) manager – the incumbent in this or these role(s) is responsible for the processing and testing activities. Under GMP, this responsibility covers the whole manufacturing chain including donation, donation testing, processing, inventory and distribution. The role may be a joint role held by a single manager, or two different roles held by two managers, provided the responsibilities are clearly defined.

- Quality manager – the quality manager is responsible for oversight of the QMS. The incumbent must be independent from the processing/testing manager, with neither reporting to the other. The quality manager should report directly to the director.

- Physician – a physician should be in overall charge of donor safety, including notification and counselling of donors with reactive results on testing. While donor assessment and follow-up activities may be performed by other staff who are not physicians, they should be competent health care professionals with appropriate training. These staff may report to the operational managers, but the physician should be present or contactable to provide advice and, if necessary, medical assistance in the event of severe donor reactions.

- Finance manager – this staff member is responsible for financial tracking and reporting. Alerts should be raised if budgetary targets are exceeded. The logistics department (stores) often reports to the finance manager.

- In addition to these roles, staff should be appointed to manage or supervise the quality control laboratory and the IT department.

- Depending on the size and activities of the BE there may be other specific roles identified (e.g. inventory manager), which need to be filled prior to centralization.

It is recommended that a coordinator is nominated to liaise with the collecting BEs in the event of problems that need to be addressed or changes that need to be made.

5.3.2 Organization chart

The BE should draw up an organization chart that shows its hierarchical structure. The key functional activities and their inter-relationships should be shown, together with clear reporting lines (see also Section 4.3).

5.3.3 Job descriptions

Each role at the BE should be defined in a job description that sets out the responsibilities of that role, including quality-related responsibilities and the required qualifications and experience. The job description can be used in the planning and delivery of training. Each staff member should review and sign their job description.

5.4 Infrastructure

The infrastructure of the BE should be established according to good business practice, GMP and quality risk management principles. Most importantly, it should be based on ethical practice, for example, appropriate and ergonomic workspace, access to personal protective equipment where necessary and fair wages. It should support the business and quality objectives of the BE and have the capability and capacity to meet the increased demands of centralized testing and processing without compromising quality and safety.

5.4.1 Premises

Premises should be designed to minimize risk to quality, safety and efficacy of blood components, and safety of staff (see also Section 4.4). It is possible to begin centralization of some processes using the existing infrastructure of BEs with adequate capacity, design and potential for growth, avoiding the need to build a new centre. Whether utilizing an existing facility or developing a new one, the following requirements must be met.

- The size must be adequate for the volume of work anticipated and to ensure the safety of staff.

- The design should allow one-way workflows to be established, to reduce errors and contamination.

- The construction materials used need to allow effective cleaning. Walls and floors should be non-absorbent, and any holes, cracks and joins should be sealed. Work benches and other furniture should be made from material

that is easy to clean, for example laminate or stainless steel. No curtains, window blinds, carpets or unsealed wood should be used in areas where donations and samples are handled, tested, processed or stored.

- Physical separation of work areas should be ensured in accordance with GMP, for example, processing, testing and labelling work areas should be separated. A dedicated area to receive, check and sort donations and samples sent from other BEs is needed. In-process, for example, untested, components, should be held in quarantine and not stored together with components released for use. Incoming materials and reagents from suppliers should be stored in a dedicated logistics area.

- An uninterrupted power supply should be available for critical equipment, especially component storage facilities.

- Environmental control systems (for example, temperature controls and alarms) should be installed in all donation, component and sample handling, testing, processing and storage areas. Any temperature and/or humidity restrictions stipulated in the operating specifications for equipment used in these areas should be adhered to. Temperatures, and if required, humidity levels, in these areas should be regularly monitored to ensure that they remain within the acceptable ranges.

- A security system should be in place to ensure that only authorized staff can access the handling, testing, processing and storage areas. External contractors, such as equipment maintenance engineers, should not enter these work areas unless approved and accompanied by a staff member.

5.4.2 Cleaning and maintenance

Contamination of blood and blood components is one of the biggest risks to blood safety. Premises should therefore undergo regular cleaning and maintenance to minimize contamination. These activities may be carried out by staff employed by the BE or by external contractors. All cleaning and maintenance staff or contractors should undergo GMP training before they commence work. Records of training, as well as of all cleaning, maintenance and inspection activities should be maintained.

- Cleaning procedures and solutions should be validated by the technical staff in accordance with the QMS and authorized by the quality manager. Floors, walls, windows and work surfaces should be cleaned regularly by trained staff who understand the importance of using only approved cleaning products and following the correct procedures. Work instructions should clearly specify any limitations on cleaning, for example, some equipment should only be cleaned by technical staff.

- Biohazardous waste should be disposed of in clearly marked bins with lids, and regularly removed from the work areas to a secure collection point. External contractors employed to remove this waste for incineration should be certified to handle biohazardous materials and should submit regular written reports to the BE on the disposal of waste.

- The premises should be regularly inspected by maintenance or other designated technical staff for any damage, deterioration or evidence of pest activity. If found, remedial action should be taken as soon as possible.

- Equipment such as air-conditioning units and emergency generators should be cleaned and maintained regularly. Generators should be periodically tested.

5.4.3 Critical materials

Critical materials are materials that, if faulty, can affect the quality, safety or supply of blood components. Examples include blood bags, sample tubes and testing reagents. The BE should therefore have a material management system in place to ensure that critical materials are purchased from reliable suppliers and are qualified before use to confirm performance.

- The BE selected to undertake centralized testing and processing needs to reach an agreement with the BEs that will be sending samples and donations to it, on the type of blood bags and sample tubes that will be used. The type of sample tube, size, anticoagulant and volume, needs to be compatible with the serological testing reagents, testing assays and laboratory automation devices being used. Standardization of the type or brand of blood bag will maximize both efficiency and component quality and offer potential cost savings. However, the BE may approve more than one supplier for each critical material as part of planning for business continuity. A specification should be developed for each type of critical material by the user of the material in accordance with the QMS requirements. This document should set out the expected quality and performance requirements for the material and should either form part of the contract with the supplier, or if there is no contract in place, be attached to the purchase order. It is also recommended that the specification includes documentation requirements for each delivery of materials, for example a Certificate of Analysis from the manufacturer for each batch or lot number.

- Suppliers of critical materials should be formally approved by the BE based on their delivery, customer service and response times for problems. Their performance should be reviewed regularly, for example, annually.

- The critical materials received should be held in quarantine until they have been qualified and approved for use. The extent of qualification activities should be based on the risk level of the materials and may range from a simple inspection of goods and the accompanying Certificate of Analysis, to sampling and testing and comparison of results to those of previous deliveries. Once the materials have been qualified, they should be formally released for use and moved into a "released" storage area. All deliveries of critical materials should be qualified, even if the lot number is already in use at the BE.

- Materials should be handled and stored according to manufacturers' instructions; therefore, it is important to be aware of specified temperature limits and, if any, humidity requirements.

- The performance of critical materials should be monitored regularly to ensure they consistently meet specifications.

- Defective or nonconforming materials should be immediately removed from use and separated from conforming materials that remain in use. Ideally this should involve clear labelling of the defective materials, and their storage in a dedicated, secure "reject" area. All faults or performance issues should be reported to the supplier.

- As appropriate, contractual mechanisms should be in place to ensure that defective or nonconforming materials are either replaced as a matter of urgency or the BE is recompensed for them.

- Records should be kept of each step from receipt to performance monitoring, including environmental monitoring of storage areas.

5.4.4 Critical equipment

Critical equipment is equipment that can affect quality and safety if it fails. Examples include refrigerated blood centrifuges, laboratory equipment for donation testing, equipment for temperature-controlled storage of reagents and kits, and storage of components. The BE should have an equipment management system in place to ensure that equipment is qualified and validated before it is approved for use. Once installed it should be monitored during use and regularly cleaned and serviced.

Standardization of equipment both within the BE, and with other BEs performing centralized testing and processing, is recommended. This helps to ensure consistent quality and safety, cost savings and additional capacity to undertake increased testing and processing in the event of equipment failures or a disaster at one site.

- Equipment specifications should be developed by the user of the equipment in accordance with the QMS, prior to purchase of new equipment. These documents should set out physical and performance requirements against which the equipment can be qualified and validated before it is approved for use.

- On receipt, equipment should be labelled to show it is undergoing qualification and validation and is not to be used in routine work. The supplier or manufacturer will usually assist with the qualification and validation of complex equipment such as an automated testing platform. However, the BE holds overall responsibility for ensuring the equipment is adequately qualified and validated and approving it for use.

- The equipment should be operated in an environment that meets the specifications of the manufacturer; therefore, it is important to understand what the acceptable ranges are. If the equipment has to be operated within specific temperature and humidity limits, these should be monitored daily.

- The equipment should be used, cleaned, maintained, calibrated and serviced according to the manufacturers' instructions.

- Equipment performance should be monitored regularly. Performance monitoring is usually carried out daily, but some checks are made at longer intervals, for example, alarm checks and calibration checks.

- If equipment performance drifts or fails, the equipment should be removed from service until the fault has been remedied. The faulty equipment should be clearly labelled to prevent its use before being repaired.

- Records should be kept of each step from equipment receipt to performance monitoring. Records should include cleaning, environmental monitoring of laboratory areas, and corrective actions taken to address problems.

5.4.5 The blood cold chain

The processes and equipment involved in the transport and storage of blood and components, from collection to distribution, constitute the "blood cold chain". Similar considerations apply to assure the identity, quality and integrity of laboratory samples obtained at the time of donation.

The quality and safety of blood components can be compromised if they are not maintained at appropriate temperatures between collection and distribution either for transfusion or manufacture into PDMPs. It is therefore essential that the

cold chain is capable of maintaining those temperatures for the required time periods. Temperature specifications for whole blood and components are set out in the applicable blood standard and/or regulation. Calibration and validation of all temperature-controlled equipment is required, together with continuous temperature monitoring.

5.4.5.1 Transport

BEs should be strategically located with ready access to rapid, easy and secure means of transport, including under adverse weather conditions. The use of road, rail and air transport of products and laboratory blood samples should be approved and monitored by the participating BEs.

Transport containers used to hold and transport blood and blood components at different stages throughout the cold chain, or to hold and transport laboratory blood samples to the centralized BE, should be robust, made of materials that allow thorough cleaning, and be able to be secured with a lock or tamper evident tape.

The methods of packing blood or components into transport containers will differ depending on a number of factors including the required temperature range to be maintained, the number and type of components to be packed, and the duration of the transport.

- Each packing configuration should be validated to provide evidence that the temperature requirements can be met throughout the transportation period. Frozen coolant packs must be buffered from the blood packs, for example with cardboard dividers, to prevent any haemolysis.
- To minimize the number of validations needed, it is strongly recommended that the BEs agree on standardization of the containers used, the type of coolant bricks, and the packing configurations.
- If available, a temperature monitor or datalogger should be included in the packed container to confirm the temperature during transport.
- Containers and coolant packs should be cleaned between each use to minimize contamination.
- Records should be kept of temperatures reached during transport and of products discarded because of problems with the cold chain.
- Records should be kept of all cleaning activities.

Each shipment should be accompanied by documentation listing the donation numbers, and for whole blood transported for processing, collection details of each donation as listed in Section 5.7.5. On receipt, each donation should be checked and verified against the documentation.

Blood samples for testing should also be transported in separate containers under conditions validated to meet the specifications of the manufacturer of the testing systems. In a situation where samples cannot be transported separately and need to be transported with the whole blood donations, the sample racks must be wrapped in plastic to prevent contamination of the blood packs, and the variation of the packing configuration must be validated. Documentation accompanying the shipment should list the identification numbers of all blood samples, and each sample should be verified against the list on receipt.

The mode of transport will depend on geographical considerations and may include aeroplanes, drones, boats, trains, trucks, taxis, cars and motorcycles. The modes and the carriers should be assessed on the basis of their ability to handle temperature-sensitive shipments, provide security for the containers, and meet the delivery time constraints for the required routes. The assessment may involve an audit of the carrier, followed by validation of the transport routes. Detailed requirements for handling, security, time frames and contingency planning should be set out in a contract. The carrier's performance should be monitored regularly.

The participating BEs must have a clear understanding of the importance of correct transport in maintaining the integrity of blood donations, blood components and blood samples. The validated packing configurations and modes of transport should be set out in documented instructions with a written agreement that participating BEs will adhere to them.

5.4.5.2 Storage facilities

The BE should have adequate storage facilities to enable the whole blood and components to be correctly stored at the required temperatures, with sufficient capacity to allow:

- appropriate segregation of untested components from released components; and
- separation of components that have come from different BEs, if required.

The BE should also have adequate storage facilities to enable donor samples to be stored separately from blood components, both on receipt and after testing is complete. The facilities should operate at the appropriate temperature required to maintain sample integrity for the expected duration of storage. For samples that have completed testing, the minimum storage time required will be stated in the applicable blood standard and/or regulation. This period can vary significantly from several days following testing, to a frozen sample archive retained for 12 months or longer.

The equipment should meet the international refrigeration standards for design, function and monitoring. On receipt, equipment should be qualified and validated before use. The BE should also have schedules and records for regular:

- calibration and validation;
- maintenance and servicing;
- cleaning, in particular the surfaces that come into direct contact with the components; and
- monitoring of temperatures and alarm functions.

5.4.5.3 Handling and processing environment

Extreme fluctuations in the core temperature of components can compromise their quality and safety. It is therefore important to ensure that components are handled and processed in controlled environments and for controlled time periods to minimize these fluctuations. For example, whole blood donations held at room temperature prior to processing into platelets should be processed within 24 hours of collection. Red cell concentrates should be removed from storage at 2 to 6°C in small numbers for labelling and release and then returned to storage as soon as possible to ensure that the core temperatures are maintained.

5.4.6 Inventory management

Inventory management includes ensuring that the cold chain is maintained, that the components are stored under the correct environmental conditions and are separated from components that have not completed the process of testing and release labelling. The components should be sorted into blood groups and those with the shortest expiry dates should be at the front.

Demand planning should ensure that there are sufficient stocks of the different blood groups and types of components to meet clinical needs, while minimizing loss through expiry. This involves tracking of orders against processing outputs at least daily, providing forecasts and calling in donors of a particular blood group where required to respond to a potential shortage. Wastage due to expiry of blood components should also be closely monitored. An effective blood management computer system is invaluable for good inventory management. The inventory at the BE may be separate or shared.

If the agreement with the collecting BE requires components from that BE to be returned to it, the donations received must be kept separate at all times from donations collected at other BEs. This requires additional work and an extra transport step, namely return to the collecting BE and subsequent transport to end-users.

A shared inventory is recommended as an option that will help to reduce wastage through expiry. Routine stocks and filled orders are sent directly to end-users, minimizing the transport steps. Good relationships with the end-users are important in demand planning activities.

5.4.7 Process control programme

Testing at the BE should be performed on fully automated platforms. Minimum testing should include:

- blood group serology:
  - confirmation of ABO and RhD blood groups

- testing for transmissible infectious agents:
  - serological screening for syphilis related antibodies, hepatitis B surface antigen, anti-HIV and anti-hepatitis C virus.

It is strongly recommended that, where feasible, the following are considered:

- nucleic acid testing to further reduce the risk of transfusion-transmissible infections; and

- screening for and characterization of clinically significant irregular red cell antibodies to prevent haemolytic reactions.

All test assays should be the most recent version and should have been evaluated for their sensitivity and specificity and approved for use by the BE. In countries where substances and medical devices used in the preparation of blood and blood components are regulated, all reagents, substances and test assays must also be approved by the NRA before they can be used by the BE. Regular monitoring of all processes, including testing systems, should be a critical part of the BE's activities. This will provide assurance that components and test results meet quality standards and enable problems to be quickly identified so that a full investigation can be conducted, and corrective actions taken.

Testing algorithms to manage initial reactive results for infectious disease testing should be documented. These should describe the outcome for the blood components as well as the donor, including determinations based on repeat and confirmatory testing. Counselling of donors with confirmed positive results of infectious disease testing should be provided.

The most important monitoring activities are component quality control and testing quality assurance.

5.4.7.1 Component quality control

Quality control testing of components is critical to ensure that their required quality is maintained.

- The BE should establish a sampling plan to ensure that a number of samples of each type of component manufactured is selected for testing. The number should be representative but is often set at 1%. If the total number of a component made is very small, a minimum of four samples is usually required.
- The selected components should be tested against specifications set out in international standards. Examples of tests include volume, haemoglobin, haemolysis, pH, cellular counts and factor VIII assays. Testing for microbial contamination should also be included.
- Unless consumed during testing, the selected components should be quarantined until all testing is complete and only released for use if the results meet the specifications. Any out-of-specification results should be investigated, and corrective action taken.
- Component quality control should be performed regularly and at intervals that ensure timely action can be taken if the process starts to drift or fail.

5.4.7.2 Blood testing quality assurance

- Test reagent lots should be prequalified prior to use as described in Section 5.4.3.
- Testing runs should incorporate control samples and results should not be approved unless the results of testing the control samples meet the applicable specifications.
- Manufacturers of blood testing assays include controls in the assay kits. However, where possible, the BE should also use an internally prepared or commercially sourced weak positive control to monitor the assay cut-off zone. This control does not replace the assay controls provided but augments them.
- The BE should also participate in EQAS. These programmes provide independent assessment of testing performance and comparisons with peer laboratories. It is critical that EQAS panels are treated as routine samples and not singled out for special attention. If EQAS panels are not available, the BEs can develop an internal quality assessment (IQA) panel and circulate it to other BEs.

5.5 Personnel and training

Staff are key to the successful manufacture of safe, good-quality blood components. Establishing a BE may require the introduction of shift working or possibly round-the-clock operations to manage the agreed workloads and turnaround times. Not only should there be sufficient staff to maintain operations, but these staff should follow the

correct procedures and understand why they need to do so. This involves selecting suitable people and establishing a good training framework for new and current staff.

Recruitment policies should ensure that newly employed staff have the appropriate qualifications for their role as defined in the job description. Staff should undergo a training programme before they commence unsupervised work.

The BE's training programme for new staff should include the following:

- training against the job description and the documented procedures used in the role;
- GMP and infection control principles, with emphasis on the consequences of not following procedures correctly;
- a competency assessment at the end of the training programme, which could involve practical work under observation and a written test;
- records of training and competency.

Staff should not be permitted to work without supervision or to sign records until they have demonstrated competency and been approved to start doing so.

The training programme should also include ongoing training and refresher courses for current staff.

In some BEs, staff who have been employed for many years may have no training records to demonstrate competency. In such cases, the use of a "recognition of prior learning" tool may be helpful to provide documented evidence of competency. For example, an appropriately trained senior manager may certify the staff as competent based on experience, observation and other relevant factors.

5.6 Funding

The success of centralization depends on the receipt of adequate funding for the BE to perform its activities effectively. The source of funding will differ according to the country, the organization of the blood supply and support from the government. The most effective model would involve national funding of the BE, but the BE's activities could also be supported on a cost-recovery basis whereby the collecting BE pays for the provision of a processing and testing service.

There should be full accountability for the use of the funds received, and the management should regularly review expenditures against the budget.

5.7 Information management systems

Significant risks to blood quality and safety arise from human error and lack of traceability. These risks, and the risk of inconsistency, can be mitigated by reducing manual operations and human decision-making as far as possible, through use of digital tools and information management systems.

The BE should therefore have an electronic blood management system (BMS) in place that not only captures critical information, but automates as many critical steps, algorithms and decision points as possible. Where possible, laboratory screening equipment should be interfaced directly with the BMS.

The BMS must be validated before use, and any changes managed through change control and validated before being uploaded into the system. Access to the system, and high-risk actions such as the ability to change critical data, should be restricted to authorized staff, for example through the use of unique passwords. The performance of the BMS should be monitored and all information should be backed up at regular intervals, with incremental back-up performed daily where feasible. Checks should be performed periodically to ensure that the backed up data can be retrieved. Operating systems should be regularly updated and appropriate malware protection including antivirus software installed to ensure data privacy and system integrity.

A contingency plan should be in place to manage any unplanned BMS outages. The effectiveness of the plan should be checked periodically through simulation exercises.

Records should be kept of all changes, performance monitoring, checks and backups.

5.7.1 Component release

Formal release of components ready for use is a critical activity. Checking is needed to ensure that the components have met the release specifications, and usually involves application of a "release label" to each component to physically differentiate these components from those that have not yet been released. Release specifications include checking that:

- Donor assessment, including a review of the donor's donation history (for return donors) and any deferrals or restrictions, has been correctly performed and the donor is eligible to donate.
- The components have met all weight and timing requirements during processing.
- ABO and RhD grouping have been performed and confirmed against any historical group (the ABO and RhD group of first-time donors can be confirmed by repeat testing using different antisera).
- Testing for clinically significant irregular red cell antibodies (if required by the NRA) has been performed and the results are negative.
- Testing for infectious agents has been performed and results are non-reactive.

There is a high risk of error if these checks are carried out manually. Therefore, wherever possible, this critical step should be performed by the BMS.

5.7.2 Equipment interfacing

Interfacing TTI testing and grouping platforms to the BMS can reduce the potential for errors during checking of results and manual transcription of data. The raw data, specifically the control data, should still be checked by the staff operator before upload, but ideally the BMS should incorporate a testing algorithm to drive the interpretation of results based on the uploaded data. The physical and software interface between the BMS and testing platforms should be validated.

5.7.3 Barcodes and barcode scanners

All blood donations, laboratory samples and blood components should be labelled with unique identification codes that permit bidirectional traceability. Since the centralized BE will process the blood donations collected at multiple blood centres, there is a need to assign a specific code for each centre that sends its blood units to the centralized BE. Additionally, to improve traceability, the inclusion of a specific code that will identify the period (for example, the year) of collection is recommended.

The use of barcoded identifiers and barcode scanners allows positive identification of samples and donations, thereby further reducing the risk of manual transcription errors. However, the quality of barcode printing can be variable and should therefore be regularly monitored. The barcode scanners should also be checked regularly for accuracy.

Where manual transcription into records, or manual entry of critical data into the BMS cannot be avoided, the entries should be checked either by a second operator or by double-blind entry.

5.7.4 Donor identifiers

Each donor should be identified by a unique number that is assigned at the donor's first visit, and subsequently used whenever the donor presents to donate. In addition to the donor's number, each donation should be assigned a unique number that is printed out in a set of barcoded labels used to identify that donation, test blood samples and any component made from that donation. The number should not be reused within the minimum time period specified in local requirements. This period should be sufficient to prevent duplicate labelling of in-date products and to enable lookback activities for a defined time period. It is essential that the BE performing the centralized processing and testing, and the BE collecting the donations, reach an agreement on the type of barcode and the sequences of numbers to be used as identifiers to ensure uniqueness if ISBT128 is not used. They also need to agree on the way in which labelling of the donation's primary and secondary packs is performed. Such an agreement must ensure that the barcoded labels are compatible with the BMS and any scanners used by the central BE or its equipment, and that duplication of donation numbers between the BEs is avoided.

5.7.5 Critical information that should accompany donations and samples to the BE

Donations and samples transported to the BE for processing and testing should be accompanied by records containing, as a minimum, the following information, which is necessary for processing:

- name of BE
- donation number
- date and time of collection
- duration of donation (time taken for donation to be completed)
- biological sex of the donor.

If the components are to be released and stored at the BE in a centralized inventory, the donor details and questionnaires should also be sent to the BE for checking as part of component release.

The information can be provided as manual records, or on a computer storage medium that is uploaded into the BE's BMS. Ideally, the BMSs of the BEs should be compatible and linked, particularly if there is to be a centralized inventory.

5.7.6 Traceability

Traceability of the process of manufacture of components from collection to dispatch is a critical element of GMP. This requires keeping records of the donors and staff involved, in addition to details of the equipment, materials and processes used during the manufacture of every component. While these details can be recorded manually, the most efficient and effective way of managing this information is to record it electronically.

Good traceability, manual or electronic, not only provides evidence that all steps have been followed correctly, but also enables problems with quality to be investigated.

Traceability supports product recall and/or recipient follow-up in the event of adverse incidents. It is essential that rapid tracking from a donation back to the original donor, and from there to all other donations, products and test results from that donor, can be achieved. Traceability systems need to be designed and managed in a manner that supports this aim and should be regularly audited.

5.7.7 Tracking of shipments

Software should be installed for monitoring the dispatch and receipt of blood products and laboratory samples including information on mode and conditions, and times of shipment and arrival.

5.8 Establishing relationships with stakeholders

The BE should ensure that relationships are established with key stakeholders such as health care institutions, clinical end-users, national reference laboratories and agencies and other BEs. These relationships will help to build stakeholder confidence in the BE and in the changes involved in centralizing processing and testing.

A good relationship with each collection BE is essential for ensuring that appropriate safe processes are used for the collection and transport of donations and samples, and for the resolution of any problems.

Blood transfusion committees that meet regularly and include representatives from hospitals as well as clinicians are an effective way of maintaining relationships with clinical end-users. Transfusion practice trends, adverse reactions identified through haemovigilance, and changes to a BE's activities or components, which may affect clinicians, can be discussed. This provides the BE and the stakeholders with assurance that clinical needs can be met.

Regular communication with national reference laboratories or agencies can provide the opportunity for the BE to discuss its needs for EQAS panels and to obtain help with testing problems. Reference laboratories can also provide independent confirmation of testing results for samples that screen reactive for infectious diseases, which in turn can be helpful for donor counselling.

In countries where the blood supply is not regulated, an NRA should be established under law and fully implemented. It is important to maintain effective communication between the NRA and the blood service, recognizing that the NRA is a critical stakeholder. Regulation often proves the most successful where there is a strong relationship between the NRA and the BEs that facilitates collaboration on drafting regulatory documents or standards, and discussion of regulatory changes and their impacts.

5.9 Regulatory aspects

The regulatory requirements for the blood supply in a country are set by the government-appointed NRA and all BEs must meet those requirements. The NRA, often in consultation with other national stakeholders, will either develop a country-specific code of GMP and a national blood standard, or adopt and adapt guidance from WHO or other internationally recognized standards.

Blood and blood products are included on the WHO Model List of Essential Medicines; however, there are differences between the manufacture of biological products, such as blood components, and the manufacture of pharmaceutical products. NRA inspectors of BEs should therefore not only be specialized in GMP auditing but should also be knowledgeable about the blood manufacturing process. Ensuring that inspectors are appropriately prepared is an important consideration at the start of implementation of regulation.

Each BE will be required to demonstrate compliance with the nominated code of GMP and the blood standard during inspections conducted by the NRA. If compliance is successfully demonstrated, the NRA will authorize the BE to engage in activities for preparation of blood components. Ongoing compliance will continue to be assessed by the NRA during regular inspections. The NRA will be responsible for scheduling and carrying out these inspections.

If regulation is already in place, and the BEs are certified or licensed, there may be a requirement for the changes involved in centralizing processing and testing to be approved by the NRA. In some cases, this approval may need to be obtained before the changes are introduced. Close liaison between the BEs and the regulator is therefore highly recommended. Good communication between the NRA and the national blood service is also important for monitoring blood availability, donor and recipient safety, and efficiency of the blood system, and to enable a coordinated response in emergencies.

5.10 Quality aspects

The quality manager has oversight of the QMS and should take responsibility for ensuring that regular meetings are held to review the BE's performance against quality and safety indicators, as well as reviewing the effectiveness of the QMS. *(1)*

The product quality review meeting can be combined with management review into a Management and Product Quality Review meeting. Participants should include the director, the quality manager, senior management and a representative from the collection BE. The BE performance and quality and safety indicators should be agreed by senior management.

The product quality aspects that should be reviewed are listed in GMP. Examples include:

- out-of-specification components and their investigations
- material defects and supplier performance
- customer complaints and recalls
- nonconformances and deviations
- adverse events in donors and recipients.

BE-specific product quality indicators should also be established and reviewed, for example:

- results from EQAS or IQA panels
- failed runs from infectious disease testing
- outcomes of internal inspections and audits
- outcomes of regulatory inspections or inspections by other accreditation agencies.

The Management and Product Quality Review meetings should be formally documented, and the minutes and actions circulated to attendees.

CHAPTER 6

MONITORING AND EVALUATION

6.1 Responsibilities for monitoring and evaluation

It is important to demonstrate the success of centralization of donation testing and processing. For this purpose, all aspects of the BE's performance should be monitored and evaluated regularly. This includes not only the service provided to customers and any impacts on availability of blood components, but also the effectiveness of the BE's QMS and the quality and safety of its components.

6.1.1 Service provision

The efficiency and effectiveness of the service provided to customers should be monitored and evaluated by the national blood service or the organization with oversight of the BE, and the national health authority. Key indicators should include availability and patient access to blood products and the efficiency of the centralized BE. The BE should also review and assess service provision as part of the Management and Product Quality Review as discussed in Section 5.10.

6.1.2 QMS and GMP

The quality manager should be responsible for establishing and maintaining a schedule of internal audits to monitor the effectiveness of the QMS and compliance with GMP. Staff selected to be internal auditors should be trained in auditing and independent of the function they are requested to audit. The frequency of audits should be based on the potential risk of the function and the outcomes of the previous audit, but it is recommended that the interval between audits of the manufacturing chain is no longer than 12 months.

Where the BE is regulated, the effectiveness of the QMS and compliance with GMP is also assessed regularly by the NRA. The outcomes of both internal and external audits should be reviewed at the Management and Product Quality Review.

6.1.3 Product quality and BE performance

The quality and safety of all components made should be reviewed regularly at the Management and Product Quality Review as discussed in Section 5.10.

6.2 Monitoring and evaluation

6.2.1 Key outcomes and performance indicators (KPIs)

In addition to the quality indicators listed in Section 5.10, the management and financial performance of the BE and the effectiveness of centralization should be monitored regularly. The outcomes and performance indicators should be established in collaboration with the national blood service or the organization with oversight of the BE, together with the national health authority and the collecting BE. Examples of recommended indicators are given below.

6.2.1.1 Fulfilment of customer orders

A key objective of centralization is to provide a better service to customers through improved management of the inventory and the supply of components with more consistent quality and efficacy. Impacts on the blood supply should be measured by a review of the numbers of customer orders that have been fully met and provided on time. Regular customer feedback should be elicited and reviewed.

6.2.1.2 Turnaround time

The quality and type of components that can be made from donations is affected by the time between collection and the commencement of processing. It is therefore important to review the time taken for donations to be processed and tested. This is particularly important where components are returned to the collecting BE.

6.2.1.3 Transport failures

Transport failures can result in the temperatures inside the transport container exceeding the acceptable range, or in delays in receipt of the shipment at the BE. Such failures can affect the type of component that can be made from the whole blood or cause the whole donation to be discarded. Inadequate packing of components such as frozen plasma, and rough handling by transporters can also result in losses due to component damage.

6.2.1.4 Loss of donations

The loss of donations or components should be monitored. These losses should be investigated to ensure there are no recurrences of preventable losses. Examples of losses include:

- expiry of inventory
- process failures such as overweight/underweight collections, incomplete records, labelling errors, incorrectly packed transport containers, missing or invalid blood samples
- equipment or material failures such as blood pack faults and out-of-calibration centrifuges, among others
- quality control failures such as lipaemic donations and excess haemolysis
- high numbers of donors carrying bloodborne infectious agents

- laboratory testing issues such as poor specificity of TTI test assays
- ABO and RhD blood-grouping issues, such as group mismatches.

6.2.2 Investigations and corrective actions

The data derived from monitoring should be analysed to identify trends. Every instance of an adverse trend, a delay or failure should be investigated, and corrective actions taken to prevent further occurrences.

If process, equipment or material failures or out-of-specification results, which affect the quality or safety of components that have been distributed to customers are identified, those components may need to be recalled as part of the corrective action. The decision to recall or not to recall should be risk-based and documented.

6.2.3 Risk Registers

The Risk Registers and Risk Treatment Plans should be reviewed regularly. Where Treatment Plans have been unsuccessful, or are incomplete, the reasons should be investigated and, if necessary, the treatment should be modified. Where Treatment Plans have been successful, it may be possible to amend the risk score (see Section 5.2).

6.2.4 Epidemiological monitoring

Epidemiological indicators are also an essential part of monitoring and evaluation and contribute to decision-making on blood safety, for example, the timely development of new or amended donor selection criteria. Epidemiological monitoring should include:

- infectious disease prevalence, incidence and residual risk
- rates of, and reasons for, donor deferrals
- percentage of first-time, lapsed and repeat donations
- haemovigilance
- horizon scanning for emerging and re-emerging infections.

6.3 Frequency of evaluation

The frequency of evaluation will vary according to the type of indicator. Most should be reviewed monthly, for example, component quality control results, KPIs and epidemiology monitoring. Some indicators, such as the outcomes of internal audits, can be reviewed every 3 to 6 months, while Risk Registers should be reviewed every 6 to 12 months. Supplier performance is often only evaluated annually. However, any significant or critical deviations should be reported and investigated at the time they occur.

REFERENCES

1. World Health Assembly resolution 63.12 (https://apps.who.int/iris/bitstream/handle/10665/3086/A63_R12-en.pdf?sequence=1&isAllowed=y, accessed 12 July 2020).
2. Yu W. The management for blood safety in China. ISBT Sci Ser. 2008;3:68–70.
3. Aubuchon JP, Linauts S, Vaughan M, Wagner J, Delaney M, Nester T. Evolution in a centralized transfusion service. Transfusion. 2011;51:2750–57.
4. WHO Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/action-framework-to-advance-uas-bloodprods-978-92-4-000038-4).
5. Ayob Y. Managing fractionated product in developing countries. ISBT Sci Ser. 2009; 4:329–31.
6. Franchini M, Farrugia A, Velati C, Zanetti A, Romanò L, Grazzini G et al. The impact of the SARS-CoV-2 outbreak on the safety and availability of blood transfusions in Italy. Vox Sang. 2020;10.1111 (https://onlinelibrary.wiley.com/doi/full/10.1111/vox.12928, accessed 12 July 2020).
7. Sasongko PL, van den Hurk K, Thijssen-Timmer DC. Blood supply milestones in the Netherlands in the first weeks of COVID-19. ISBT Sci Ser. 2020 (https://onlinelibrary.wiley.com/doi/full/10.1111/voxs.12562, accessed 12 July 2020).
8. Nollet KE, Ohto H, Yasuda H, Hasegawa A. The great east Japan earthquake of March 11, 2011, from the vantage point of blood banking and transfusion medicine. Transfus Med Rev. 2013;27:29–35.
9. Aubuchon JP, Linauts S, Vaughan M, Wagner J, Delaney M, Nester T. Evolution in a centralized transfusion service. Transfusion. 2011; 51: 2750–57.
10. Nollet KE, Ohto H, Yasuda H, Hasegawa A. The great east Japan earthquake of March 11, 2011, from the vantage point of blood banking and transfusion medicine. Transfus Med Rev. 2013;27:29–35.
11. Wang Y, Wu Y, Chen Y, Li C, Lu L, AuBuchon JP et al. The journey toward safer and optimized blood service in China: national strategy and progress. Transfusion. 2016;56:3112–20.
12. WHO Guidelines on management of blood and blood components as essential medicines. In: WHO Expert Committee on Biological Standardization: sixty-seventh report. Geneva: World Health Organization; 2017: Annex 3 (WHO Technical Report Series, No. 1004; https://www.who.int/bloodproducts/brn/ManBloodEM_GL_WHO_TRS_1004_web_Annex_3.pdf?ua=1, accessed 12 July 2020).
13. Epstein J. Best practices in regulation of blood and blood products. Biologicals. 2012;40:200–204.
14. Assessment criteria for national blood regulatory systems. In: WHO Expert Committee on Biological Standardization: sixty-second report. Geneva: World Health Organization; 2013: Annex 7 (WHO Technical Report Series, No. 979; https://www.who.int/bloodproducts/NationalBloodRegSystems.pdf?ua=1, accessed 12 July 2020).
15. WHO Global Benchmarking Tool + Blood (GBT + blood) for evaluation of national regulatory systems of blood products including whole blood, blood components and plasma-derived products. Geneva: World Health Organization; 2019 (https://www.who.int/medicines/regulation/benchmarking_tool_plus_blood/en/, accessed 20 August 2020).
16. Pereira A. Economies of scale in blood banking: a study based on data envelopment analysis. Vox Sang. 2006;90:308–15.

17. Amukele T, Ness PM, Tobian AAR, Boyd J, Street J. Drone transportation of blood products. Transfusion. 2017;57:582–88.

18. Ling G, Draghic N. Aerial drones for blood delivery. Transfusion. 2019;59:1608–11.

19. Design guidelines for blood centres. Manila: WHO Regional Office for the Western Pacific; 2010 (https://apps.who.int/iris/handle/10665/207576, accessed 19 July 2020).

20. WHO guidelines on good manufacturing practices for blood establishments. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fifth report. Geneva: World Health Organization; 2011: Annex 4 (WHO Technical Report Series, No 961; https://www.who.int/bloodproducts/publications/GMP_Bloodestablishments.pdf?ua=1, accessed 19 July 2020).

21. Guidelines on good manufacturing practices for blood establishments. In: WHO Expert Committee on Biological Standardization: sixty-ninth report. Geneva: World Health Organization; 2011: Annex 4 (WHO Technical Report Series, No. 961; https://www.who.int/bloodproducts/publications/GMP_Bloodestablishments.pdf?ua=1, accessed 20 October 2020).

22. ISO 31000 Risk management – guidelines. Geneva: International Organization for Standardization; 2009.

CONTACT

World Health Organization
Department of Health Products Policy and Standards
20 avenue Appia
CH-1211 Geneva 27
bloodproducts@who.int
https://www.who.int/bloodproducts

9789240020825