



Zambia Medicines Regulatory Authority

Guidelines on Licensing of Blood Establishments

Contact details:

Head Office, Plot No 2350/M, Off Kenneth Kaunda International Airport Road
P.O. Box 31890, Lusaka, ZAMBIA
Tel: +260 211 220429,
E-mail: pharmacy@zamra.co.zm;
Website: www.zamra.co.zm

	Name	Designation	Signature	Date
Prepared by	Mr. Matthews Mwale	Director- Licensing, Surveillance and Enforcement		29/09/26
Reviewer	Mr. Makomani Siyanga	Director-General		29/09/2026
Approver	Hon.Prof. Roma Chilengi, MP	Minister of Health		06.10.26





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FOREWORD

The Medicines and Allied Substances Act No. 3 of 2013 requires that blood and blood components manufactured in Zambia meet acceptable standards of quality, safety and efficacy and at the same time, be assessed to have been collected, tested, processed and stored in facilities that comply with current Good Manufacturing Practices (GMP)/Good Practices Guidelines.

This document is intended to provide guidance to applicants for the preparation of submissions in accordance with the blood establishment licensing in Zambia.

The Authority licenses establishments involved in the collection, testing, processing, storage, release, and distribution of blood and blood components in Zambia and monitors their quality and safety profiles for Serious Adverse Blood Related Events.



ACKNOWLEDGEMENTS

I wish to take this opportunity to express my heartfelt gratitude to everyone who contributed to the drafting of these guidelines.

Special thanks are extended to the German Ministry of health through the Global Health Protection Programme (GHPP) and the Paul-Ehrlich-Institut-BloodTrain project for their invaluable logistical and technical support throughout the entire process leading to the development of these guidelines. BloodTrain is a project under the GHPP umbrella and seeks to increase the quality, safety, and efficacy of blood and blood products through regulatory systems strengthening in Africa.

I further extend my thanks to the technical working group, comprising members from the Paul Ehrlich Institut (PEI), the Zambia National Blood Transfusion Service (ZNBTS), and the Zambia Medicines Regulatory Authority (ZAMRA), who worked tirelessly to develop and finalise these guidelines.

Additional thanks go to our esteemed stakeholders: the Ministry of Health (MoH), the Zambia National Transfusion Blood Service (ZNBTS), the Churches Health Association of Zambia (CHAZ), the Nursing and Midwifery Council of Zambia (NMCZ), Zambia Union of Nurses and Midwives Organisation (ZUMWO), the University of Zambia (UNZA) School of Health Sciences, the Private Practitioners Association (PPA), the University Teaching Hospitals (UTH) - Adult, the Health Professions Council of Zambia (HPCZ), the Presidential Delivery Unit (PDU), and the Sickle Cell Association. Their discussions and commendable inputs significantly improved this document.

The development of these guidelines marks a significant milestone in the regulation of blood and blood components in Zambia, and will ensure that all blood and blood components made available to the Zambian people are safe, effective, and of acceptable quality.

Makomani Siyanga (Mr)

Director-General

Zambia Medicines Regulatory Authority



1. DEFINITION OF TERMS

In these guidelines, unless the context otherwise states:

adverse event	means any undesirable or unintended occurrence associated with transfusion or donation. It includes all adverse reactions, incidents, near misses, errors, deviations from standard operating procedures and accidents
adverse reaction	means any unintended response in a donor or a patient associated with the collection or transfusion of blood or blood components
allogeneic donation	means blood and blood components collected from an individual and intended for transfusion to another individual, for use in medical devices or as starting material or raw material for manufacturing into medicinal components;
apheresis	means a method of obtaining one or more blood components by machine processing of whole blood in which the residual components of the blood are returned to the donor during or at the end of the process
applicant	means any legal or natural person, established within or outside Zambia, seeking to obtain or having obtained the License to render blood transfusion service in terms of the blood regulations or a marketing authorisation holder of the blood product;
authorisation	means a procedure for approval of blood and blood components, or to the processes for preparation of these components after they have undergone an evaluation to determine the quality, safety, and efficacy of the components.
authority	means the Zambia Medicines Regulatory Authority or its acronym 'ZAMRA' established under section three of the Act;
autologous donation	means blood and blood components collected from an individual and intended solely for subsequent autologous transfusion or other human application to that same individual;
autologous transfusion	means a transfusion in which the donor and the recipient are the same person and in which pre-deposited blood or blood components are used;
blood	means whole human blood collected from a donor and processed either for transfusion or for further manufacturing, excluding blood specimens intended for pathology testing;
blood component	means a constituent of blood (erythrocytes, leukocytes, platelets, cryoprecipitate and plasma) that can be prepared by various separation methods and under such conditions that it can be used either directly for therapeutic purposes or for further processing/manufacturing;



blood drive or mobile site	A temporary or movable facility used for the collection of blood and blood components which is located outside of, but under the control of the blood establishment.
blood establishment	means any structure, facility or body that is responsible for any aspect of the collection, testing, processing, storage, release or distribution of human blood or blood components when intended for transfusion or industrial manufacturing. This does not include hospital blood banks;
blood product	means any therapeutic substances derived from human blood, including whole blood, blood components and plasma-derived medicinal products.
closed system	A system in which the blood pack assembly is manufactured under clean conditions, sealed to the external environment and sterilized by an approved method. Apart from the act of blood collection (when a needle is exposed and enters the donor's arm) the integrity of this assembly must not be breached in any way.
deferral	means suspension of the eligibility of an individual to donate blood or blood components, such suspension being either permanent or temporary;
distribution	means the act of delivery of blood and blood components to other blood establishments, hospital blood banks, importers, wholesalers and manufacturers of blood components, other than the issuing of blood or blood components for transfusion;
donor	means a person in defined good health conditions who voluntarily donates blood or blood components, including plasma for fractionation;
good manufacturing practice	means 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.
haemovigilance	means a set of surveillance procedures covering the entire transfusion chain, from the donation and processing of blood and its components, to their provision and transfusion to patients and their follow-up. It includes the monitoring, reporting, investigation and analysis of adverse events related to the donation, processing and transfusion of blood, and taking actions to prevent their occurrence or recurrence
health facility	means any site, fixed or mobile, providing services for the prevention, diagnosis and treatment of disease or illness and includes a diagnostic centre, a hospice and a hospital (Health Professions Act No. 24 of 2009);
hospital blood bank	means a unit within a hospital which stores, issues, and may perform compatibility tests on blood and blood components exclusively for



	use within hospital facilities, and includes hospital-based transfusion services;
inspection	means formal and objective control to identify problems in accordance with standards adopted to assess compliance with these guidelines;
licensing	means authorisation by the Authority for the manufacturing, importation, exportation or distribution of blood and blood components;
manufacture	means all operational processes or steps — including purchase or selection of materials and products, production, quality control, release, storage and distribution of products and the related controls — used to produce a blood product. This includes also the donation process.
site	in relation to a blood establishment, means any premises at which the blood establishment carries out any prescribed activities, but shall not include any premises not owned or managed by the blood establishment at which blood is collected, or any mobile blood collection unit;
medical doctor	means a person registered as a medical doctor under the Health Professions Act No. 24 of 2009;
mobile site	means a unit or site used for the collection of blood and/or blood components, operating temporarily or at movable locations off-site from a permanent collection site, under the responsibility of a blood establishment.
national blood transfusion service	or its acronym NBTS means a designated department, which is under the Ministry for the time being responsible for health, to establish policy and standards, oversee and coordinate all blood supply safety activities including, recruitment of blood donors, collection, storage, and production of blood and blood components, test for transfusion transmissible infections, transport and distribute blood, as well as guide appropriate use of blood and blood components through designated blood centres.
open system	A system which has been opened to the environment but every effort has been made to prevent microbial contamination by operating in a clean environment, using sterilized materials and aseptic handling techniques.
plasma	means the liquid portion of the blood in which the cells are suspended which are separated from the cellular portion of a whole blood for therapeutic use as fresh frozen plasma or further processed to cryoprecipitate and cryoprecipitate-depleted plasma for transfusion;
plasma for fractionation	means the liquid part of human blood remaining after separation of the cellular elements from blood collected in a container containing



		an anticoagulant, or separated by continuous filtration and/or centrifugation of anticoagulated blood in an apheresis procedure, intended for further manufacturing;
plasma, fresh-frozen		means the supernatant plasma separated from a whole blood donation or plasma collected by apheresis, frozen and stored;
plasma-derived medicinal product		means any therapeutic product derived from human plasma and produced by an industrial-scale manufacturing process that pools multiple units;
processing		means the standard technical procedures used to prepare blood and blood components for transfusion and includes methods of identification of blood and blood components and tests for suitability for the intended purpose and the performance of tests for transfusion transmissible diseases;
production		means all operations involved in the preparation of blood components, from collection through processing to completion as a finished product (blood component).
quality management system		means 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.
recipient		means a person to whom blood or blood component is administered to
responsible person		Means a pharmacist, veterinary surgeon, veterinary para professional or pharmacy technologist.
serious adverse event		means any untoward occurrence associated with the collection, testing, processing, storage and distribution of blood or blood components— (a) that might lead to death or life-threatening, disabling or incapacitating conditions for patients or (b) which results in, or prolongs, hospitalisation or morbidity;
serious adverse reaction		means an unintended response in a donor or a patient associated with the collection or transfusion of blood or blood components— (a) that is fatal, life-threatening, disabling or incapacitating or (b) which results in, or prolongs, hospitalisation or morbidity;
technical master file		means a compilation of scientific data provided by a Blood Establishment which includes a description of the steps of manufacture and detailed technical and scientific data or information that must satisfy the Authority that the blood or blood components,



transfusion
transmissible
infection
good practice

manufactured using the steps of manufacture described will meet set requirements.

means an infection that can be transmitted by the transfusion of blood or blood product;

means all elements in established practice that collectively lead to final blood or blood components that consistently meet pre-defined specifications and compliance with defined regulations.



In pursuance of Section 68 of the Medicines and Allied Substances Act No. 3 of 2013, these guidelines are hereby made to provide guidance to applicants on the regulatory requirements for licensing a blood establishment in Zambia.



2. INTRODUCTION

The Zambia Medicines Regulatory Authority (ZAMRA) is a statutory body established under the Medicines and Allied Substances Act No. 3 of 2013. Among other things, ZAMRA is mandated to regulate blood establishments. These guidelines are therefore, meant to provide guidance to operators of new and existing blood establishments in Zambia.

The purpose of these guidelines is to guide blood establishments in the preparation of an application for licensing and approval of processes for the manufacture of blood and blood components. It describes the scope and information expected in an application for licensing of establishments to demonstrate the safety, quality and efficacy of blood and blood components.

In addition to these guidelines, blood establishments shall be expected to comply with current WHO guidelines on GMP/GPG. In order to receive a licence, an applicant must demonstrate compliance with the principles of Good Manufacturing Practice (GMP)/Good Practice Guidelines. A GMP/GPG inspection will be carried out as part of the licensing process.

3. GENERAL PROVISIONS

Pre-application meetings

- 3.1. Prior to applying for licensing, an establishment may request a meeting with ZAMRA as an opportunity to define the purpose of the application and to discuss various application requirements. Such a meeting may also be requested by either ZAMRA or the establishment to discuss the application at any point during the application process.
- 3.2. A written request for a pre-application meeting should be directed to the Director-General and received by ZAMRA not less than one month prior to the proposed meeting date and should contain at least the following information;
 - i. the purpose of the meeting;
 - ii. a brief description of the issues to be discussed at the meeting;
 - iii. two or more proposed dates and times for the meeting; and
 - iv. a note indicating if participation by other areas of ZAMRA might facilitate the discussion



4. APPLICATION PROCESS

- 4.1. An application for a new licence, licence renewal or amendment of a blood establishment involved in donor screening, collection, testing, processing, labelling, storage, release and distribution or one or more of the under-listed activities shall be made in writing via the online portal.
- 4.2. A manufacturer of blood, blood components or plasma for fractionation is required to submit an application containing all necessary documents to the Authority. The information should be sufficient to enable the Authority assess and determine that the processes will result in good quality, safe and efficacious blood and blood components for transfusion including plasma for fractionation.
- 4.3. An application for licensing of a blood establishments shall be made via the online portal or in the manner as may be prescribed by the Authority.

Applicants must ensure that all relevant information is accurately entered in the applicable fields on the online application portal.

5. CONTENTS OF AN APPLICATION

- 5.1. To ensure a comprehensive and efficient review process, applicants must provide all necessary documents and information as part of their application. The following items are required to accompany the application, and all documentation should adhere to the specified format and language requirements. An application should be accompanied by the following supporting documents;
 - i. A duly signed covering letter addressed to the Director-General;
 - ii. Technical Master File (TMF) as per annex I;
 - iii. Proof of payment as per prescribed fees;
 - iv. Quality Manual if available;
 - v. Full Registration for the Responsible Person
 - vi. Annual Practicing Certificate for the Responsible Person
 - vii. An application checklist as per annex II (Application checklist for a Pharmaceutical Licence)

All documentation submitted shall be in English and must be legible. Applicants must ensure that all required documents are correctly uploaded to the relevant sections of the online application portal.



6. EVALUATION OF AN APPLICATION

6.1. The Authority in considering an application;

- i. Shall satisfy itself that the blood establishment is fit for the purpose it is seeking a license to conduct; donor screening, collection, testing, processing, labelling, storage, release and distribution of blood and blood components.
- ii. May consult with other agencies and experts with knowledge of transfusion medicine and blood and blood components.
- iii. Shall conduct a regulatory inspection of the blood establishment

6.2. Where the Authority is satisfied that all requirements for licensing of the blood establishment have been met, it shall issue to the applicant, a Licence.

6.3. The licence shall be valid for a period of 2 (two) years.

7. SCREENING OF AN APPLICATION

7.1. The Authority shall conduct screening of all application-related materials for completeness. The screening process is separate from the review/evaluation process.

Application screening and request for additional information

- 7.1.2. If there are significant omissions or inadequacies that prevent a review of the application, the Authority may issue a notice of rejection or a request for additional information via the online portal.
- 7.1.3. Where a request for additional information is issued, timelines for submission of the additional information shall be stipulated. Further processing of the application shall cease until the applicant provides sufficient responses to any queries raised.
- 7.1.4. The response to the solicited information must be provided by the date indicated; however, the blood establishment may request an extension to this date in writing, providing sound justification for the failure to provide the solicited information within the stipulated timelines.



- 7.1.5. If the establishment fails to provide all requested information by the stipulated date without any proper written justification to the Authority, a Notice of Rejection to issue, renew or amend a licence may be issued.
- 7.1.6. Following receipt of a Notice of Rejection, the establishment may re-file the entire application.
- i. This application will be processed as a new application and assigned a new reference number
 - ii. Information and material filed in the original application that remains unchanged, should be clearly identified in the cover letter.

8. REVIEW/EVALUATION OF AN APPLICATION

Review/evaluation of an application and request for additional information

- 8.1. If the application is acceptable for review, the application becomes part of the review workload, after which the Authority evaluates the information and supporting evidence. Applicants can follow the progress of the application via their tracking number.
- 8.2. During the review of an application, the Authority may request for additional information via the online portal.
- 8.3. An establishment must provide the Authority with the additional information by the date specified in the request; however, the establishment may request an extension.

9. INSPECTIONS

Pre-licensing Inspection

- 9.1. The Authority shall carry out an on-site inspection to complement the review of an application. The scheduling of the inspection will be done in consultation with the establishment.
- 9.2. The issuance of a licence would be based on the outcome of the inspection. An on-site inspection may be used to
- i. review evidence, documentation or data;
 - ii. Verify the quality management system;
 - iii. observe processes;



- iv. view a demonstration of new equipment.

10. APPLICATION OUTCOMES

- 10.1. An application for a licence may result in issuance of a licence or a rejection.

Licence issuance

- 10.1.1 When the Authority completes the review of the information and evidence in the establishment's application and finds it acceptable, it shall issue a licence that allows the establishment to proceed with implementation of its activities as stipulated under the licence and summarises at minimum the following information:

- i. name of the licensed establishment;
- ii. blood components that the establishment may process;
- iii. processing activities that the establishment is authorised to perform;
- iv. physical address of each building and the processing activities to be conducted at each location; and
- v. any terms and conditions of the licence

Rejections

- 10.2. Where the applicant does not meet the requirements, the Authority may reject the application for a licence.

- 10.2.1. The Authority may issue a Notice of Rejection to issue or renew a licence or an amendment to an existing licence in any of the following circumstances:

- i. if the establishment provided inadequate evidence to support the proposed processes;
- ii. if there were inaccuracies in the application;
- iii. if false or misleading statements were made; or
- iv. if the processes reviewed were found to pose an unacceptable risk to human safety or to the safety of blood.



10.2.2. The Notice of Rejection outlines the reasons for the rejection and provides the establishment with the opportunity to be heard in writing if not satisfied by the Authority's decision, to the Director General. If still unsatisfied by the Authority's decision, the establishment may appeal to the Minister in line with the Act. The establishment may choose to re-apply.

Re-application

10.2.3. When an application is re-submitted

- i. the re-submitted application will be processed as a new application and assigned a new tracking number;
- ii. the information and material filed in the original application, and that remains unchanged, should be clearly identified in the cover letter.

11. RENEWALS

11.1. A licensed blood establishment should submit an application for renewal of their Licence at least 90 days before the expiry of the licence through the online portal. The application should be accompanied by proof of payment, supporting documents and a copy of an updated Technical Master File (TMF).

11.2. An inspection may be conducted before renewal of the blood establishment licence.

12. AMENDMENTS

12.1. Situations may arise where a blood establishment may require to amend certain details, e.g., labelling, manufacturing address, etc. These may either be of minor or major nature. The applications shall be made via the online portal or as may be prescribed by the Authority.

12.2. The Authority considers that changes fall into two categories which are listed below:

Major Changes: A substantial change in a blood establishment's activities is any change:

- i. To the manufacturing processes or conditions which have a significant potential to impact on the quality and safety of the product. These may include changes to infectious disease product release testing and changes to manufacturing conditions such as the introduction of new technologies or changes to manufacturing parameters.



- ii. to the sites from which the blood establishment operates or to the prescribed activities to be carried out at each site,
 - iii. to approved processes which would result in a failure to comply with the requirements of set standards, or
 - iv. to the quality system which is likely to have a substantial impact on the conduct of, or might compromise the safety of, any of the prescribed activities which the blood establishment has been authorised to undertake.
- 12.3. A blood establishment shall not make any substantial change in the prescribed activities which it undertakes without the prior written approval of the Authority. Such changes need regulatory approval from the Authority prior to implementation. Requests for such changes should be submitted in writing to the Authority, be accompanied by the prescribed fee and should include a justification for the change and supporting documentation, such as protocol(s) and validation report(s).
- 12.4. A GMP/GPG inspection may be required prior to the introduction of changes to critical steps of manufacture.

Minor changes: a non-substantial change in a blood establishment's activities is any change : —

- i. that could have minimal or no adverse effects on the blood establishment's overall activities, including approved processes and quality system and does not compromise the safety of any of the prescribed activities which the blood establishment has been authorised to undertake.
 - ii. not likely to have a detectable impact on the quality or safety of the product. For example, 'like- for-like' equipment replacement (e.g. replacement of one centrifuge with another centrifuge) would be unlikely to affect the manufacturing process if the change control mechanism is implemented satisfactorily.
- 12.5. A non-substantial notification does not require prior acceptance, but must be notified to the Authority.
- 12.6. The blood establishment shall notify all non-substantial changes to the Authority. Notification by a blood establishment of a non-substantial change in its activities must be made in writing to the Authority within a period of two weeks from their occurrence. A non-substantial change in a blood establishment's activities is any change:



- 12.7. On the instance where an application is submitted as a notification by the blood establishment, but on evaluation, the Authority reclassifies it to a substantial change, it may no longer be deemed as a notification and the blood establishment shall be notified within a period of two weeks from receipt of the notification by the Authority.

Incorporation of Changes in the Technical Master File (TMF)

- 12.8. After a TMF has been determined to be satisfactory by ZAMRA; it represents the agreed manufacturing conditions for that component or components. As such, the manufacturing conditions and the TMF cannot be changed without notification to, or approval by the Authority. The Authority recognises that changes to the manufacturing conditions will occur from time to time.
- 12.9. Changes, both major, and minor, on approval, should be incorporated into the TMF. To assist the Authority in approving changes, each submitting blood establishment is requested to include in the TMF:
- i. a summary of changes between the previous version and the updated version, and
 - ii. Supporting documentation justifying the proposed change. This Documentation should include a description of the changes, a description of how the effect of these changes on product quality will be assessed, and describe how the changes will be implemented, documented and validated. The documentation should describe, but not be limited to, the procedures to be used when introducing changes to a starting material, product component, processing equipment, method of production or testing.
- 12.10. As changes will often be made to a TMF, annual submissions of the TMF specifying the changes are required.

13. TIMELINES

- 13.1. The Authority shall, within ninety days of the receipt of an application, issue a licence to the applicant if the applicant meets the licensing requirements. This timeline is suspended during periods where additional information is required from the applicant.

14. FEES

- 14.1. A prescribed fee is payable at the time of making an application as per the fee schedule.



ANNEXURES

Annexure I: Content of Technical Master File (TMF)

A TMF shall contain but not limited to:

1. General Information

1.1. Contact information

- Name and official address of the blood establishment
- Names and street addresses of the site, buildings and production units located on the site
- Contact information of the BE including 24 hrs telephone number of the contact personnel in the case of product defects or recalls.

1.2. Activity summary

- Brief description of manufacture, import, export, distribution and other activities authorised or requiring authorisation by ZAMRA.
- Any other activities carried out on the site
- Description of non-blood related activities on-site, if any

1.3. Previous years' activities

- Number of donors in the previous calendar year
- Number of donations in the previous calendar year
- Number of produced blood components in the previous calendar year
- Details of hospitals and blood banks supplied or intended to be supplied

2. Personnel

- Names of key personnel including: Responsible person, Head of Quality Control and/or Quality manager, Production manager, Medical Director and other relevant key personnel.
- Total number of staff indicating their departments and responsibilities

3. Quality Management System



- A brief description of the quality management system applied at the blood establishment and reference to standards used.
- Responsibilities related to the maintaining of the QMS including senior management.
- Current organisation chart showing hierarchical structure of the establishment with clear delineation of the areas of responsibility and lines of authority.
- Information of activities for which the site is accredited and certified including dates and contents of accreditations, names of accrediting bodies.

4. Premises

The establishment must provide the following:

- Short description of the site (size, location and adjacent environment)
- Description of the processing and storage facilities indicating the number of rooms, their dimensions and environmental classification, where relevant. Simple floor plan of collection, production, laboratory and storage areas.
- Description of environmental monitoring system (e.g. temperature)

5. Equipment

- The establishment must provide a list of all critical equipment including the functions of each.
- The application must contain adequate evidence of successful validation of the equipment performed at the establishment, including installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ), as applicable.
- Description of preventive maintenance programs and recording system
- The establishment should include in their application evidence that all medical devices have been registered by ZAMRA, where applicable.
- Description of critical computerised systems and arrangements for their validation

6. Materials and reagents

- A list of all materials and medical devices used in the collection and manufacturing process, including respective ZAMRA registration numbers, where applicable



- If a material is neither registered nor listed by ZAMRA, the manufacturer's name, a Certificate of Analysis for the material and the rationale for the choice of material should be provided
- If the material is a medicinal component it should be registered by ZAMRA failure of which a justification for its use should be provided.

7. Manufacturing

- The blood establishment should provide a description of the manufacturing process.
- The manufacturing process encompasses the whole transfusion chain, from donor selection until storage and issuance. Every step, critical equipment and setting that might affect the quality and safety of the final product needs to be documented and approved.
- The processes to manufacture various blood components differ and thus it is necessary to have separate flow charts. Blank draft flow charts are attached in the annex. Flow charts for any not provided processes need to be developed or amended accordingly.

7.1.A description of the process validation should include, but not be limited to:

- Demonstration that the process and product meet specifications and the factors which will determine an acceptable or unacceptable result. In-process controls and tests performed on the product with acceptance criteria and the rationale for specifying these limits. Process validation of all critical processing steps (e.g. pathogen reduction), which may affect product quality, and an indication if there have been prolonged storage steps.
- Tests that assure the identity, purity, and safety of the product, including but not be limited to: cell viability, cell number, microbial assessment, dose of specific cell types, product volume, and functional potency (if applicable).
- Details of procedures taken to prevent (cross) contamination (e.g. details of the segregation of operations and product particularly if the manufacturing area is used for the processing of different products).
- Details of procedures implemented to avoid possible contamination throughout the entire process: collection, transport, quarantine, testing, manufacturing, storage, release, labelling and transfusion / transplant.

7.2.Laboratory testing



- Test methods used for transfusion-transmitted infections and blood group serology testing in accordance with the requirements.
- The provision of scientific principles with details of testing procedures and algorithms.
- A list of testing kits and reagents should be included in an appendix along with their ZAMRA registration number (where applicable). Tests and test kits used by the testing laboratory should be verified for the purpose for which they will be used.
- The internal procedure for out of specification test results.
- Any additional tests that may be necessary under certain circumstances to increase safety for susceptible recipients (e.g. tests for CMV) if applicable.
- The use and requirements for nucleic acid amplification technology (NAT) testing).

7.3. Labelling

- The BE should include details of labelling procedures for products.
- For each allogeneic blood component that the establishment proposes to process, the establishment must provide ZAMRA with the proposed final blood container label. In the case of allogeneic blood for transfusion, the establishment must provide the draft text of the circular of information. Labels for autologous blood and labels added to units of blood following transformation (transformation labels) do not need to be provided to ZAMRA for review.
- A description of the procedures for the containment and labelling of products from donors confirmed to be positive for infectious agents (if applicable) and arrangements for the quarantine storage of non-conformant product.

7.4. Storage, stability, shelf-life and transportation

- Storage conditions should be provided for all relevant products detailed in the TMF. Where applicable, details of validation tests performed to establish product viability post storage should be provided together with the generated data.
- Storage conditions and management of non-conforming and contaminated (viral/microbiological), products should be detailed.



- Description of validated protocols used to ensure the recommended storage temperature is maintained during transportation and over the proposed storage period. The anticipated extremes of ambient temperature of transport should be detailed.
- Demonstration of product stability and end of storage specifications should be provided.
- Procedures for disposal of unused product and the handling of expired products should be detailed.

8. Release procedure for finished products

- Description of product release procedure.
- The methods and specifications selected to determine acceptability of product for release should be substantiated.
- Procedures for handling returned product and, if applicable, acceptance criteria should be detailed.

9. Quality Control Testing

- Description of quality control testing procedures on blood and blood components produced by the blood establishment.

10. Documentation

- Description of the documentation system including but not limited to arrangements for the preparation, revision and distribution of necessary documentation for collection of blood and manufacture of blood components.

11. Management of suppliers and contractors

- Brief description of the qualification system for contractors and suppliers of critical materials and services.
- List of activities carried out by third parties (e.g. testing, cleaning, storage, transport) indicating which steps and name and address of the organisation that acts as the third party.

12. Haemovigilance system

- Description of the adverse events/adverse reaction investigation and reporting system and management of look-back procedures.

13. Complaints and product recall



- Description of the arrangements for the handling of complaints and product recalls.

14. Quality risk management

- Brief description of QRM methodologies used by the establishment as well as its scope.

15. Self-inspections



Annexure II: Application Checklist for Pharmaceutical Licence (Blood Establishment)



Zambia Medicines Regulatory Authority

Application Checklist for Pharmaceutical Licence (Blood Establishment)

	YES	NO	NA
1. Pre-Application Preparation			
1.1. Gather all required documentation in English and ensure legibility	☒	☐	☐
1.2. Ensure all information is accurate and up-to-date.	☐	☐	☐
2. Application Submission			
2.1. Complete the online application form on the ZAMRA portal.	☐	☐	☐
2.2. Accurately fill in all required fields on the online portal.	☐	☐	☐
3. Required Documents			
3.1. Duly signed Cover Letter addressed to the Director-General	☐	☐	☐
3.2. Current Technical Master File (TMF):	☐	☐	☐
3.3. TMF in the prescribed format.	☐	☐	☐
3.4. Proof of payment for the prescribed fees.	☐	☐	☐
3.5. Quality Manual (if available).	☐	☐	☐
3.6. Full registration documents for the Responsible Person.	☐	☐	☐
3.7. Annual Practicing Certificate for the Responsible Person.	☐	☐	☐
3.8. Duly signed Cover Letter addressed to the Director-General	☐	☐	☐
4. Additional Requirements			
4.1. Verify that all uploaded documents are correctly placed in the relevant sections of the online portal.	☐	☐	☐
4.2. Review all entries and attachments for completeness and accuracy before submission.	☐	☐	☐

Post-Submission

- ✓ Monitor the application status via the tracking number provided by ZAMRA.
- ✓ Respond promptly to any requests for additional information from ZAMRA.
- ✓ Prepare for any required inspections as part of the application review process.



Publication bibliography

CPMP/BWP: Guideline on Requirements for Plasma Master File (PMF) certification. Available online at https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-requirements-plasma-master-file-pmf-certification_en.pdf, checked on 6/30/2023.

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Health Canada Guidance Document: Guidance Document: Blood Regulations. Available online at <https://transfusionontario.org/wp-content/uploads/2020/06/blood-guid-sang-ligne-eng.pdf>, checked on 6/30/2023.

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- 1 Ghana FDA Guidelines for Licensing Blood Facilities and Blood Products Listing FDA/SMC/BPU/GL-BFL/2015/06, version 01
- 2 WHO guidelines on good manufacturing practices for blood establishments. WHO Technical Report Series 961 (2011). (ISBN: 978 92 4 120961 8). [Online]. Available: https://www.who.int/bloodproducts/publications/GMP_Bloodestablishments.pdf
- 3 Guide to the preparation, use and quality assurance of blood components, European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS) 20th Edition
- 4 NABH, India, Standards on Blood banks/Blood centres and Transfusion Services, 1st edition 2007

