PPB/PER/BBP/GUD/001 **Rev. No. 1**

MINISTRY OF HEALTH

PHARMACY AND POISONS BOARD

Guidelines for licensing of blood establishments for the manufacturing of Human blood, components and haematopoietic progenitor stem cells in Kenya

September 2016

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1 INTRODUCTION

Blood and blood components are applied in life-threatening situations of severely ill patients. Coupled to this is the heightened public awareness of the Quality and Safety issues of blood, blood components and blood products and haematopoietic progenitor cells(HPC). It is therefore recommended that high standards of quality, safety and efficacy for blood and blood products are sustained through the application of the principle of Good Manufacturing Practice (GMP) during the collection, testing, processing, storage, dispatch, quality control, and quality assurance of the products.

The implementation of the principles of GMP by Blood Facilities, as well as the inspection of Blood Facility by the Regulatory Authority is imperative to ensure the quality, safety and efficacy of blood and blood products manufactured/collected in these Facilities.

These guidelines are intended to be used in conjunction with other established GMP guidelines to provide guidance on the requirements to license Blood Facilities (including apheresis facilities) and licence Blood components and blood products. It will provide guidance for the collection, testing, processing, storage and distribution as well as the manufacturing and the quality control of blood, blood components and blood products.

1.1 PURPOSE

The purpose of this document is to provide guidance to owner and operators of Blood Facilities on the relevant regulatory requirements needed to maintain the compliance status of their operational activities. The document shall provide useful regulatory insight into the collection, preparation, storage, release, distribution, quality control and quality assurance of whole Blood, Blood component, Blood products and haematopoietic progenitor stem cells. Applicants are encouraged to familiarize themselves with the information contained in this document prior to applying for a license to operate as a Blood establishment.

1.2 Scope

These Guidelines are hereby made to provide guidance to applicants and the public on the regulatory requirements for licensing a Blood establishment in Kenya.

PART I

REQUIREMENTS FOR THE COLLECTION, STORAGE, PROCESSING AND DISTRIBUTION OF WHOLE BLOOD, BLOOD COMPONENTS BY BLOOD TRANSFUSION FACILITIES

Definitions: For the purpose of this document the following terminologies shall apply

(a) '**apheresis**' means for the process by which blood drawn from a donor, after separating plasma or platelets or leucocytes, is re transfused – simultaneously into the said donor;

(b) 'autologous blood' means the blood drawn from the patient for re-transfusion unto self later on;

(f) '**blood**' means and includes whole human blood, drawn from a donor and mixed with an anti-coagulant and it includes blood and blood components; and shall include haematopoietic progenitor cells that are harvested from cord blood or thru any other prescribed means too.

(c)

(d) "**blood components**" means a preparation, obtained, derived or separated from a unit of blood drawn from a donor

(e) '**blood establishment'** means a place or organization or unit or institution or other arrangements made by such organization, unit or institution for carrying out all or any of the operations for collection, apheresis, storage, processing and distribution of blood drawn from donors and/or for preparation, storage and distribution of blood components;

(f) "**Blood transfusion Unit**" A facility located within a hospital that receives and stores already screened blood and blood components, conducts pre-transfusion tests (compatibility testing) on patients' blood samples; issues blood or blood components for clinical transfusion; and monitors blood utilization (haemovigilance)

(g) '**blood product'** means a drug or medicinal substance manufactured or obtained from pooled plasma or blood by fractionation, drawn from donors,

(h) **'donor'** means a person who voluntarily donates blood after he has been declared fit after a medical examination, for donating blood, on fulfilling the criteria given hereinafter, without accepting in return any consideration in cash or kind from any source but does not include a

professional or a paid donor.

(i) Licensing Authority. Organization mandated by law to carry out regulatory activity.

(j) Inspection Team-

(k) Inspection report

(h) 'leucapheresis' means the process by which the blood drawn from a donor, after leucocyte concentrates have been separated, is re-transfused simultaneously into the said donor;

(i) 'plasmapheresis' means the process by which the blood drawn from a donor, after plasma has been separated, is re-transfused during the same sitting into the said donor;

(j) 'plateletpheresis' means the process by which the blood drawn from a donor, after

platelet concentrates have been separated, is re-transfused simultaneously into the said donor.

(k) 'professional donor' means a person who donates blood for a valuable consideration, in cash or kind, from any source, on behalf of the recipient – patient and includes a paid donor or a commercial donor;

(l) 'replacement donor' means a donor who is a family friend or a relative of the patient –recipient.
(J)"Technical Committee"-Members comprising of PPB,KNBTS,KMLTTB,KPDM,KNC,etc.

Part A

1.3 Guidelines for establishment of a blood establishment.

The applicant shall meet the minimum requirements as per the Kenya National Blood Transfusion Service; "Guidelines for Establishing Blood Facilities in the Republic of Kenya -2015" Refer to Annex __ (provide a hyper link)

Part B

1.4 Licensing of Blood Establishment and /or Manufacturing of blood products.

Application for registration and/or renewal of licence for the operation of Blood Transfusion Facility for processing of Human Blood and manufacture of Blood components shall be made to the Licensing Authority appointed by the government of Kenya as the case may be and shall be accompanied by licence fees of as per the type of blood establishment class and an inspection fees of Kshs for every inspection thereof or for the purpose of renewal of licence.

Provided that if the applicant applies for renewal of licence after the expiry but within six months of such expiry the fee payable for the renewal of the licence shall be Kshs XXXX and inspection fees of Kshs XXXX.

Any renewal application received after the expiry of the previous licence the application shall be considered as a fresh application. Any application made before the expiry of the said licence as the case may be, the applicant shall continue to operate the same till the orders on his application are communicated to him.

A fee of Kshs XXX shall be paid for a duplicate copy of licence issued if the original is defaced, damaged or lost and the copy shall bear the word "DUPLICATE COPY".

Part B

1.5 Application Process

On receipt of the application for registration or renewal of such licence, the Licensing Authority shall, -

(i) verify the statements made in the application form.

(ii) Cause the manufacturing and testing establishment to be inspected in accordance with the regulatory authority requirements and

(iii) In case the application is for renewal of licence, call for information of past performance of the licensee.

If the regulator in collaboration with KNBTS is satisfied that the applicant has fulfilled the minimum requirements laid down in "The Establishment of Blood Facilities in Kenya (2015)", a report shall be prepared and forwarded

along with the application form (in triplicate) for registration of the establishment.

If, on receipt of application and the inspection report, the Licensing Authority is satisfied that the applicant has fulfilled the minimum requirement laid down, the Licencing Authority shall grant or renew the licence.

Licence Rejection

Provided that the Licensing Authority in receipt of the inspection report and is of the opinion that the applicant has not fulfilled the minimum requirements, he shall, for reason to be recorded in writing, refuse to grant or renew the licence, as the case may be.

1.2 Duration of Licence

An original licence or a renewed licence, unless sooner suspended or cancelled, shall be valid for a period of two years from the date it is granted or renewed for local and three years for in foreign establishments

Inspection

Before a licence is granted or renewed, the Licensing Authority as the case may be, shall make arrangement for inspection of the establishment in which Blood facility is proposed to be operated and shall be inspected by two or more inspectors with an expertise in the field concerned.

The Inspectors shall examine all sections of the premise(s), appliances, equipment and the process of manufacture intended to be employed or being employed.

The Inspectors shall forward a detailed descriptive report giving their findings on each aspect of the inspection along with their recommendations to the Licensing Authority.

Re application after rejection

If within a period of six months from the rejection of an application for a licence, the applicant informs the licensing Authority that the conditions laid down have been met and deposits an inspection fee of Kshs xxx to the Licensing Authority, an inspection team shall be set up and an inspection conducted. If the conditions are satisfactory for registration, the applicant shall be granted or renewal of licence shall be issued.

Appeal

Any establishment which is aggrieved by the order passed by the Licensing Authority, as the case may be, may within thirty days from the date of receipt of such order, shall have the opportunity to appeal to the

management board of the Licensing Authority. The Board of management will then review the appeal and make recommendations as it deems fit.

If the applicant exceeds the stipulated six months period, then the application will be treated as a new application and all conditions of a new applicant shall apply

Additional Information
The licencing authority may from time to time ask for additional information either before licencing or during the period the licence in in force as the need may arise

Cancelation and or Suspension of Licence
The Licensing Authority may for such licences granted or renewed by him, in writing, cancel or suspend the licences. The licences may be cancelled or suspended for such period as he deems fit, either wholly or in respect of some of the items to which it relates. The order may include stopping collection, storage, processing, manufacture and distribution of the blood and blood products and there upon ordering the destruction of any stocks thereof in the presence of an Inspector.

Appeal after Suspension/ Cancelation
A licensee whose licence has been suspended or cancelled, within three months of the date of the order shall be granted an opportunity to appeal to the board of management of the licencing authority after evidence of appeal fee has been established.

Inspection Scope
Further to the issuance of a licence to a licensee, the licensee:

(i) The licensee shall allow the inspectors, with or without prior notice, access to any premise where blood transfusion activities are carried out.

(ii) The licensee shall allow Inspectors to inspect all registers and records maintained and to take samples of the manufactured products and shall supply to Inspector such information as he may require for the purpose of ascertaining whether the provisions of the Act and Rules thereunder have been observed.

(iii) The licensee shall from time to time report to the Licensing Authority any changes in the expert staff responsible for the operation of the facility and any material alterations in the premises or plant used for that purpose which have been made since the date of last inspection.

(iv) The licensee shall on request furnish the Licensing Authority as directed any batch unit of blood products from time to time. Samples of such quantity as may be considered adequate by such Authority for any examination and, if so required, also furnish full protocols of the test which have been applied.

(v) The licensee shall on being informed by the Licensing Authority that any part of a batch/unit of the substance has been found not to be conforming with the standards of strength, quality or purity and on being directed to withdraw from sales and in the particular circumstances of the case recall all issues already made from that batch/unit.

Additional Information

(vi) No blood or blood components manufactured under the licence shall be issued unless the precautions necessary for preserving its properties have been observed throughout the period after manufacture. Further no batch/unit manufactured under this licence shall be supplied/ distributed to any person without prescription of Registered Medical Practitioner.

(vii) The licensee shall destroy the stocks of batch/unit which does not comply with standard tests in such a way that it would not spread any disease/infection by way of proper disinfection method.

(viii) All bio-medical waste shall be treated, disposed off or destroyed as per the provisions of the Kenya National Health Care Waste Management Plan 2008-2012

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(ix) The licensee shall neither collect blood from any professional donor or paid donor nor shall he prepare blood components and/or manufacture blood products from the blood drawn from such a donor.

1.6 Types of Blood Facility Licenses

CLASS A

Shall perform the following: Recruitment, donor education, donor selection, counselling, phlebotomy, blood storage, blood transportation, donor notification, QMS

CLASS B

Shall perform all in class A plus, blood grouping both forward and reverse preparation of basic components like Packed Red Cells, paediatric packs,

FFP's, QMS

CLASS C
Shall perform all in class A&B plus, Transfusion Transmissible Infections screening, Platelets, Cryoprecipitate, QMS

CLASS D
Shall perform all in classes A, B&C plus, Apheresis, reference laboratory, specialized transfusion practices, PCR, QMS

CLASS Manufacturing Facilities. Shall solely perform manufacturing of blood products(PDMPs).

License Exemption

- Any blood collected by a medical practitioner in the course of medical treatment and for the purposes of diagnosis or of testing for a medical condition; or

- Any blood manufactured by a medical practitioner for use in an emergency to save life or limb/function for a particular patientunderthe practitioner's care.
- Blood imported solely for the purpose of export that remains subject to the control of the Kenya Customs and that is not subject to manufacture in Kenya
- It is proposed that provisions will be included to enable the urgent use of Blood for a life-threatening or seriously debilitating condition – these will mirror the provisions proposed in relation to medicines.
- stockpiled as quickly as possible in order to create a preparedness to deal with a potential threat to public health that may be caused by a possible future emergency;and
- made available urgently in order to deal with an actual threat to public health caused by an emergency that has occurred.
- Hospital blood Transfusion unit not undertaking Recruitment, donor education, donor selection, counselling, phlebotomy, blood storage, blood transportation, donor notification,

Part C

1.7 Licensing of Blood Manufacturing Facilities and Products

1.8 Licencing of Manufacturing of blood components and Plasma Derivatives

Licences required for Blood Products

All products that are defined as Blood must obtain a product license (unless exempted). This is consistent with the approach to be adopted for other therapeutic products whereby product licensing will replace entry on the Kenya Regulatory Authority (For more informationabout the product licensing by Regulatory Authority,please refer to the guidelines on Regulatory Authority website).

The requirements for product licensing will vary depending on the risk posed by the product.

1.9 Licensing based on risk of blood

Class 1: Blood and Blood Components, that include packed red cells, fresh frozen plasma, paediatric packs, cryoprecipitate, platelets etc. and

Class 2 Plasma derived Products including but not limited to, albumin, globulins, irradiated red cells, washed red cells etc

1.0 Requirements for Class 1and Class 2 Blood product license applications

In order to obtain a Class 1 or Class 2 product licence, the applicant will be required to submit an application demonstrating that the product conforms to the established standards for safety, quality and efficacy, and that the applicant has in place quality systems for the manufacture of Blood unless exempted.

A product licence would only be issued if Regulatory Authority is satisfied that the product meets the required level of safety, quality and efficacy.

The main difference between Class 1 and Class 2 is that additional preclinical and clinical data/evidence will be required to support the safety and efficacy of Class2 product applications.

1.1 License holder must ensure compliance with conditions

To maintain a product license, the holder must ensure that the Blood that is the subject of the license complies at all times with the information submitted in the product license application, and any certifications made therein, and with the approved product information and labeling. As a consequence of this, any changes to any of the information upon which the product license was based must be the subject of an additional application(either for a variation or a new license) and be authorized by Regulatory Authority.

Generally, a product license will remain valid provided the fees are paid and the product license is not suspended or revoked.

The following parts of this document provide more detail about each of the aspects of the proposed regulation of Blood and blood products.

PART E

3.1 CLASSIFICATION OF BLOOD

Classification based on risk
Blood intended for supply in Kenya will be classified according to the degree of risk inherent in the use of the product.

The product classifications will be determined using the following factors
- the level of manipulation of the Blood;
- the intended effect of the product
- the storage of the product; and
- the risk of cross infection

Majority of products currently regulated as blood and blood components will be Class 1

Class 1 Blood will include:
(a) whole Blood or its components derived through its minimal primary separation; and
(b) processed, stored, maintained or preserved for future use; and
(c) Manufactured using reagents approved by Regulatory Authority for the purpose; and
(e) Manufactured such that the biological, pharmacological and therapeutic properties are not significantly altered.

Class 2 for manipulated Blood.

Class2 Blood will be that:
(a) is not a Class 1 Blood; and
(b) is processed, stored, maintained or preserved for future use; and
(c)is manufactured from Class 1 Blood such that the biological,

pharmacological and therapeutic properties are significantly enhanced or altered.

Blood kits

Blood kits will be regulated in accordance with the highest classification of any Blood component of the kit.Other therapeutic products included in the kit, if not assessed and approved prior to the Blood kit application, will be assessed through the provisions for ancillaries.

3.2 STANDARDS

Regulatory Authority may determine Standards for Biologicals (including Blood) and that these will be set out in Orders.
All Biologicals must conform to all relevant Standards except with the written consent of Regulatory Authority.For example, Blood must conform to:

•a core set of standards relating to good manufacturing practice – all classes of Blood will be expected to comply with these Standards;

•additional subject specific Standards, for example, for plasma.Such subject specific standards may be based partly or wholly on existing industry standards or international standards;

•Standards relating to quality management systems for the manufacture of Blood.

PART G

3.3 TYPES OF PRODUCT LICENCES

Blood may only be imported,exported or supplied with a Product Licence

Blood and blood product may only be:

•imported into Kenya; or
•exported to a third country from Kenya; or

•supplied in Kenya by, or with the written approval of, the holder of a product licence issued by Regulatory Authority, unless specifically exempted.

Other types of Product Licence

In addition to the two broad categories of product licence (for Class 1Blood and ..Class 2 Blood), Regulatory Authority may issue (in relation to either Class 1 or Class 2 Blood):

•an export only product licence - An applicant intending only to export a product from Kenya to a third country may obtain a special type of product licence, an 'export only product licence', in respect of the product;

•in-country product licence - an in country product licence will be issued to a local manufacturer who intends to supply products within the country.
In all cases, a product licence for Blood and blood product will only be granted on the basis of an application submitted to Regulatory Authority which demonstrates that the potential risks are outweighed by the therapeutic benefit of the Blood and blood product.
As part of its assessment of the application, Regulatory Authority will also need to approve product information documents, labelling and in some cases certifications by the applicant before a product licence can be granted.

3.4 Ancillary products

The safety and quality of a medical device or a medicine ancillary to the Blood must be verified in accordance with the requirements for medical device guidelines and the ancillary action of the device must be verified having regard to the intended purpose of the Blood before a product license can be issued.

Annex

3.5 APPLICATION FORM FOR GOOD MANUFACTURING PRACTICE INSPECTION FOR PHARMACEUTICAL MANUFACTURING FACILITIES

APPLICATION FORM FOR GOOD MANUFACTURING PRACTICE INSPECTION FOR BLOOD ESTABLISHMENTS AND TRANSFUSING FACILITIES

1. PARTICULARS OF APPLICANT/LICENSE HOLDER

Name_____

Physical Address_____

Country_____Telephone_____

Fax_____E-mail_____

2. PARTICULARS OF SITE TO BE INSPECTED

Name of site_____

Physical Address - (including GPS coordinates if different from 1. above)
_____
Country_____Tel_____
County/State _____
Fax_____E-mail:_____
Note: Separate application to be filled in for each individual site

3. CONTACT PERSON ON SITE

Name of contact person_____

Tel:_____Fax:_____

E-mail:_____

4. AUTHORISED REPRESENTATIVE/AGENT IN KENYA

Name of Local Technical
Representative_____

Tel;_____

5. TYPE OF BLOOD COMPONENTS /PRODUCTS

Type of human blood products and components (Tick where applicable)
(a) Whole Blood
(b) Adult packed Red Cells
(c) Paediatric Packed Red Cells
(d) Platelet Concentrate
(e) Platelet Rich Plasma
(f) Plasma
(g) Fresh Frozen Plasma
(h) Cryoprecipitate (anti- hemophilic factor)
(i) Others (list) _____

6. INSPECTION TYPE (Please tick where applicable)

First Inspection Re – inspection after failure

Routine Re- inspection date…… Previous inspection

Other (please specify) ……

7. LINES TO BE INSPECTED

DOSAGE FORM	**Tick where applicable**	***CATEGORY**	****ACTIVITIES**
Small Volume Parenteral			
Large Volume Parenteral			
Others (specify)			

**Activity means any of the following:

- Formulation (dispensing, mixing, blending)
- Processing (compression, emulsification etc)
- Packing

- Quality Control
- Appropriate Storage (raw material, finished products)

8. REGISTRATION OF PRODUCTS

Have you registered any products in Kenya?
or

Have you submitted dossier for registration? YES NO
If YES, list the products applicable. (Attach a separate sheet if needed)
……

I hereby certify that the above information is correct and apply for Good Manufacturing Practice inspection of the above-named site(s).

Signature of applicant…… Date……

Print Name……

Notes:
1. Please submit a copy of the Site Master File (not more than 25 pages) together with
this application.

Annex 3: Guide to developing a Site Master File
Annex 1: Guidelines for GMP Inspection of pharmaceutical manufacturing plants

2. This application must be submitted together with the appropriate fee (see annex 2) to:
The Registrar
Pharmacy and Poisons Board
P.O Box 27663- 00506
Nairobi, Kenya

ANNEX 4:

PV 1
(rev.2.0)

MINISTRY OF HEALTH
PHARMACY AND POISONS BOARD
P.O. Box 27663-00506 NAIROBI
Tel: (020)-3562107 Ext 114, 0720 608811, 0733 884411 Fax: (020) 2713431/2713409
Email: pv@pharmacyboardkenya.org

Initial Report
Follow-up Report

SUSPECTED ADVERSE BLOOD AND BLOOD PRODUCTS REACTION REPORTING FORM

REPORT TITLE:
……

NAME OF INSTITUTION: ……INSTITUTION CODE: ……

ADDRESS: ……CONTACT: ……

COUNTY: ……

****

PATIENT NAME/ INITIALS…… IP.OP. NO……D.O.B/AGE……

PATIENT ADDRESS……WARD/CLINIC……GENDER šMALE š FEMALE

ANY KNOWN ALLERGY
WEIGHT……kg
NO
HEIGHT ……cm
Yes (Specify)……

PREGNANCY STATUS
NOT APPLICABLE
Not Pregnant
1st Trimester š 2nd Trimester š 3rd Trimester

DIAGNOSIS (what was the patient being treated for?)……
REASON FOR TRANSFUSION……
CURRENT MEDICATIONS……

PREVIOUS TRANSFUSION: š YES š NO
COMMENT:……
PREVIOUS REACTION: š YES š NO COMMENT:……

DATE AND TIME OF ONSET OF REACTION……
BRIEF DESCRIPTION OF THE TRANSFUSION REACTION……

VITAL SIGNS: BEFORE: BP……. DURING: BP……. AFTER: BP…….

T…….	T…….	T…….
P…….	P…….	P…….
R…….	R…….	R…….

CLINICAL SIGNS: šGENERAL: Fever, Chills/Rigors, Flushing, Nausea/ vomiting
š DERMATOLOGICAL: Urticaria, Other skin rash
š CARDIAC/ RESPIRATORY: Chest pain, Dyspnoea, Hypotension, Tarchycardia
š HEMATOLOGICAL: Unexplained bleeding

Others……

LIST OF ALL DRUGS /BLOOD	**BRAND NAME/ TYPE**	**DOSE /NO. OF**	**ROUTE AND FREQU**	**DAT E STAR**	**DAT E STOP**	**INDICA TION**	Tick suspec ted

AND BLOOD PRODUCTS USED IN THE LAST 3 MONTHS PRIOR TO REACTION. IF PREGNANT, INDICATE DRUGS USED DURING THE 1st TRIMESTER	OF BLOOD PRODUCT	UNITS	ENCY	TED	PED		Medicine

(Refer to scale overleaf)

SEVERITY OF THE REACTION ACTION TAKEN OUTCOME

CAUSALITY OF REACTION

(Refer to scale overleaf)

Mild Blood/ product withdrawn Recovering

Certain

Moderate Initiate investigation Recovered

Probable/ Likely

Severe Requires another transfusion Possible

Fatal š

Unlikely

Unknown Conditional/ Unclassified

Unassessable/Unclassifiable

ANY OTHER COMMENTS.....

.....

LABORATORY INVESTIGATION:
šN/A
OUTCOME……
.
:……
……
:……
……

HB……g/dL

ASSESSMENT:

TYPE OF REACTION: š SEPTIC š ACUTE HEMOLYTIC š ALLERGIC š FEBRILE

NONHEMOLYTIC

š TRALI š DELAYED š HEMOLYTIC š ANAPHYLACTIC š POST-TRANSFUSION PURPURA

š MILD FEBRILE REACTION š OTHERS (SPECIFY)……

DIAGNOSIS……
…

……

……

NAME OF PERSON REPORTING
……DATE……
EMAIL ADDRESS…… ……PHONE NUMBER……
DESIGNATION
……SIGNATURE……