# FOOD AND DRUGS AUTHORITY

# REGULATORY FRAMEWORK FOR BLOOD, BLOOD COMPONENTS AND BLOOD PRODUCTS

**Document No.: FDA/BPD/POL-01**

**Effective Date: 4th January, 2021**

**Version No.: 02**

## BACKGROUND

The legislative basis for regulating blood and blood-derived medicinal products rest with the Food and Drugs Authority (FDA). Whole blood, blood components and blood products are regulated as biological products in accordance with the Public Health Act 2012 Act 851.

**OBJECTIVE**: To facilitate the evaluation and registration of Plasma Derived Medicinal Products (PDMP), and the audit, licensure and listing of Blood and Blood Components (BBC) towards operational compliance with Good Preparation Practice (GPP) and Good Manufacturing Practice (GMP).

**SCOPE**: The framework shall be applicable to the registration of Plasma Derived Medicinal Products (PDMPs) and the listing of Blood and Blood Components.

**Note:** The FDA shall leverage the regulatory framework to facilitate regulatory decisions towards licensing a Blood Facility and listing whole Blood and Blood components.

## THE REGULATORY FRAMEWORK

Guiding Principles

The implementation of the framework for the regulation of Plasma Derived Medicinal Products (PDMP) and whole Blood and Blood components as essential medicines shall sort to:

- sustain nationally regulated self-sufficient blood systems;
- protect donors against exploitation and prohibit financial gain;
- protect the safety of both donors and recipients
- base whole blood, blood components and PDMPs standards and controls on a quality management system derived from GPP and GMP in order to assure the quality, safety and availability of these products;
- ensure that all medical devices/diagnostics, reagents and other blood screening /testing reagents are used in Blood facilities are evaluated and regulated by the FDA

- ensure that all ABRs/SABREs are documented and investigated on-site and reported to the FDA within published timelines
- ensure that the regulations for whole blood and blood components, as well as PDMPs are complementary, and incorporate the essential elements and core functions specified in the FDA guidelines, Policies and statements from the National Blood Service Ghana and other recognized promoted Best practice (e.g., WHO, EMA, USFDA, TGA, Health Canada, etc.,)

**PROCESS/PROCEDURE**

The regulatory framework for blood involves the listing of Blood and Blood components, the licensing of the blood facilities where whole blood and blood components and blood products are prepared and periodic operational compliance audit of the blood facility.

Owners and/or operators of Blood facilities shall be required to license their facility with FDA, unless they are exempted as defined by the FDA. A list of blood component prepared, or processed for distribution shall be declared by the blood facility, and subsequently listed by the FDA.

A facility is considered a Blood Facility, and needs to hold a Blood Facility license to operate if that facility:

- conducts donor assessment and selection
- collects whole blood and blood components
- prepares blood components
- conducts specific serological and nucleic-acid-based tests for various infectious disease pathogens, such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis to reduce Transfusion-Transmitted Infections (TTI's)
- label whole blood and blood components
- store whole blood, blood components and blood product
- release and distribute blood, blood component and blood products
- conduct compatibility testing on blood and blood components exclusively for use in hospital facilities, including hospital-based transfusion activities

- carry out secondary processing of blood components such as;
    - Irradiation/Cell wash/Pack splitting
- collect blood and/or blood components for pre-deposit autologous transfusion
- import blood from abroad

The classes of blood facilities and their permitted scope of operation are presented in the table below:

| CLASS | BLOOD FACILITY | PERMITTED ACTIVITIES / PROCESSES |
|---|---|---|
| **Ia** | Hospital Blood Bank | Storage, Compatibility Testing and Issue for Transfusion |
| **Ib** | Hospital Blood Bank & Collection Area | Donor Management and Collection of Whole Blood (performed by ABC), Storage, Compatibility Testing and Issue for Transfusion |
| **II** | Collection Site | Donor Management, Collection of Whole Blood |
| **IIIa** | Area Sub-Centre /sub Zonal Blood Centre | Donor Management, Collection of Whole Blood, Donation Testing and Confirmatory Testing (performed by ABC/ZBC), Processing, Storage, Release/Issue to Hospital Blood Bank |
| **IIIb** | Area Sub-Centre / sub Zonal Blood Centre | Donor Management, Collection of Whole Blood, Donation Testing (performed in-house), Confirmatory Testing (performed by ABC/ZBC), Processing, Storage, Release/Issue to Hospital Blood Bank |
| **IV** | Area Blood Centre / Zonal Blood Centre | Donor Management, Collection of Whole Blood, Apheresis, Donation and Confirmatory Testing (performed in-house), Processing, Storage, Release/Issue, Distribution for further Manufacture |
| **V** | Plasma Fractionation Centre | Receipt of Blood Component for further Manufacture |

- ***ABC –Area Blood Centre***
- ***ZBC: Zonal Blood Centre***
- ***Donation testing includes; TTI testing, ABO blood typing, RhD typing and confirmation of RhD negative. Donation testing involves initial testing using enzyme immunoassays which include ELISA, repeat testing of initial reactive and confirming repeat reactive.***
- ***Confirmatory testing applies to TTI and RhD typing.***

If you are not sure which one you are, please contact the FDA by emailing: fda@fdaghana.gov.gh; Telephone: (+233 –302)233200, 235100 or Fax: (+233-302)229794, 225502.

A facility that receives Blood and Blood Components (BBC) from another facility for direct transfusion, *i.e.* without conducting compatibility testing or engaging in transit storage at the site of transfusion is not classified as a Blood facility. Such a facility will not be assessed for compliance with Good Preparation Practices (GPP) and/or Good Distribution Practices (GDP) as long as a service level agreement or a similar arrangement exist that demonstrates that the facility receive BBC's from specified and accredited facilities that are licensed to operate as Blood Facilities.

**BLOOD FACILITY (BF)**

To operate as a blood facility you must;

- have a blood facility license;
- be audited by the FDA at least once every year
- have a system for reporting any Serious Adverse Blood Reactions or Events (SABRE)to FDA; Specifically, Safety Monitoring Department –Haemovigilance
- have a system to ensure that all consumables, including medical device/diagnostics have been evaluated and registered with the FDA
- have a system to report diagnostic/medical device failures to the FDA
- have a system to submit an annual compliance report
- pay a facility licensing and component listing fee at the time of first licensure, and a license renewal fee every three years

**BLOOD FACILITY AUDIT AND COMPLIANCE**

The blood facility will be audited by the FDA when you first apply for Blood facility license and at least once every year to maintain the facility license. Following each audit, the applicant (operator/owner) will be sent an official communication with the observations documented at the time of the audit. The observations will be presented with corresponding recommendations to facilitate implementation of corrective actions.

Once fully implemented, the Blood facility will be adjudged as compliant with Good Preparation Practices, Good Manufacturing Practice (GMP), Good Storage Practices (GSP) and Good Distribution Practice (GDP). Such a facility shall be recommended for licensure, and to maintain the facility license, the blood facility shall be audited twice every year (announce and unannounced) for compliance with best practices.

The facility will be required to complete a Blood Facility compliance report before an announced audit or unless it is triggered by an audit.

The officer responsible for completing the compliance report shall ensure that all sections in the reporting form are completed and the content of the completed form are true and accurate. The blood facility shall submit Blood facility compliance report to the FDA audit team before an announced audit. It is the responsibility of the Quality Assurance (QA) officer or an officer with a higher rank to prepare and sign the report.

## PREPARING TO AUDIT A BLOOD FACILITY

Once a Blood Facility has been highlighted for an audit, a letter from the FDA will be dispatched to the facility stating the proposed date for the audit. An auditor will follow up with a telephone call to confirm the readiness of the Blood Facility for the scheduled audit. When arranging a date for an audit there will normally be a minimum of four weeks' notice. In most cases, the team will comprise of a lead auditor and two other auditors. The audit process will usually be completed in two (2) days. It is strongly recommended that the following persons are present at the opening and closing/exit meetings:

- Chief Executive Officer (CEO)
- Medical Superintendent
- Matron
- Director of Nursing
- Head (Manager) of Blood Facility
- Consultant Haematologist

- Administrator (Hospital)
- Quality Manager
- Other senior members of staff in management position

## AUDITING A BLOOD FACILITY

During an audit, the team will:

- interview relevant personnel
- review documents
- conduct site visits
- review processes/procedure

Site visits may include any facility involved in producing, preparing, storing and distributing Whole Blood, Blood Components and Blood Products, and the shall include, but not limited to the following areas:

- donor selection/screening area
- blood collection area
- preparation and/or manufacturing areas
- testing/screening
- stock and stock management
- storage equipment/device and areas
- temperature monitoring
- environmental temperature monitoring
- returns areas and management
- bio-waste management
- general premises and maintenance
- documentation and records
- Quality Management System / Operating Procedures
- Blood and Blood component release protocol or arrangement
- Medical devices/diagnostic and other consumables/reagents.

The audit team may ask for additional documentation and samples for verification and testing during the audit. They may also change the focus of the audit if they suspect serious non-compliance and/or non-conformance.

At the closing meeting the lead auditor will provide feedback and discuss any identified deficiencies or findings with the auditee (Head of Blood Facility shall be in attendance) you and agree on the findings and timelines for corrective actions.

## GRADING OF AUDIT FINDINGS

Deficiencies found during audit are graded at three (3) levels as presented below:

- **Critical non-conformance**: any non- conformance in a process or a written procedure which directly affects the safety of the donor or patient.
- **Major non- conformance**: a serious non- conformance in a process or a written procedure but does not in its own affect the safety of the donor or patient.
- **Minor non- conformance**: a non- conformance in a system or process or there is insufficient information to classify it as a major or critical.
- **Observation**: an inadequacy in a system or process that is not a failure to comply with standard.

## APPLYING FOR A BLOOD FACILITY LICENSE

The Blood facility shall complete a Blood Facility Licensure and product listing application forms (FDA/BPU/A-LBF/2015/01 - Application form for Licensing Blood Facilities in Ghana) and (FDA/BPU/A- LBBP/2015/01 -Application form for listing Blood and Blood Products in Ghana), and pay an application fee to the FDA. The application forms and supporting guidance documents shall be downloaded from the FDA's website, www.fdaghana.gov.gh. The completed form shall be sent (one hard copy and one soft copy) to the FDA, and addressed to the Chief Executive Officer (CEO) (see section 2 of the form for guidance). Alternatively, the completed form shall be sent to the FDA- addressed to the CEO- via fda@fdaghana.gov.gh.

The submission shall trigger an audit of the Blood facility. Upon successful audit of the facility and demonstration of compliance, the facility will be issued a license and the products prepared in the facility listed. A blood facility shall receive its licensure within 160 days of receipt.

To maintain your licensure, you will be inspected at least once every year to ensure that the facility remain in compliance with the requirements of the legislation.

## RESTRICTION OF OPERATIONAL SCOPE OR SUSPENSION OF LICENSE

Following an audit, if the auditor finds critical deficiencies or the agreed Corrective and Preventive Action (CAPA) plan from previous audit deficiencies have not been resolved, the lead auditor shall recommend that a new license with a restricted scope of operation is issued to replace the current or existing license. Further, the FDA may refuse, or suspend a license. In extreme cases, the FDA may withdraw a license or increase audit visits to address a regulatory issue without compromising access to safe Blood, Blood Component and Blood Product

## BLOOD FACILITY VARIATION

Blood facilities shall not make any substantial change to the prescribed activities for which it has been licensed to perform without prior written approval by the FDA. Should the license holder decide to change/alter any activity contained in their licensure, the blood facility shall submit an application to the FDA to vary the licensure.

All applications shall be submitted to the FDA for consideration prior to implementation by the blood facility. Variations to blood facility licenses shall be classified as either **Administrative** – requiring a limited amount of assessment by the FDA or **Technical** – requiring significant assessment by the FDA with possible scheduling of a site audit.

**Note**: If the operation of the Blood facility goes through any major change which will alter the approved activities, sites or personnel, the Blood facility shall apply for a variation to the licensure before making the change. See variation forms for Blood Facility licensure at www.fdaghana.gov.gh.

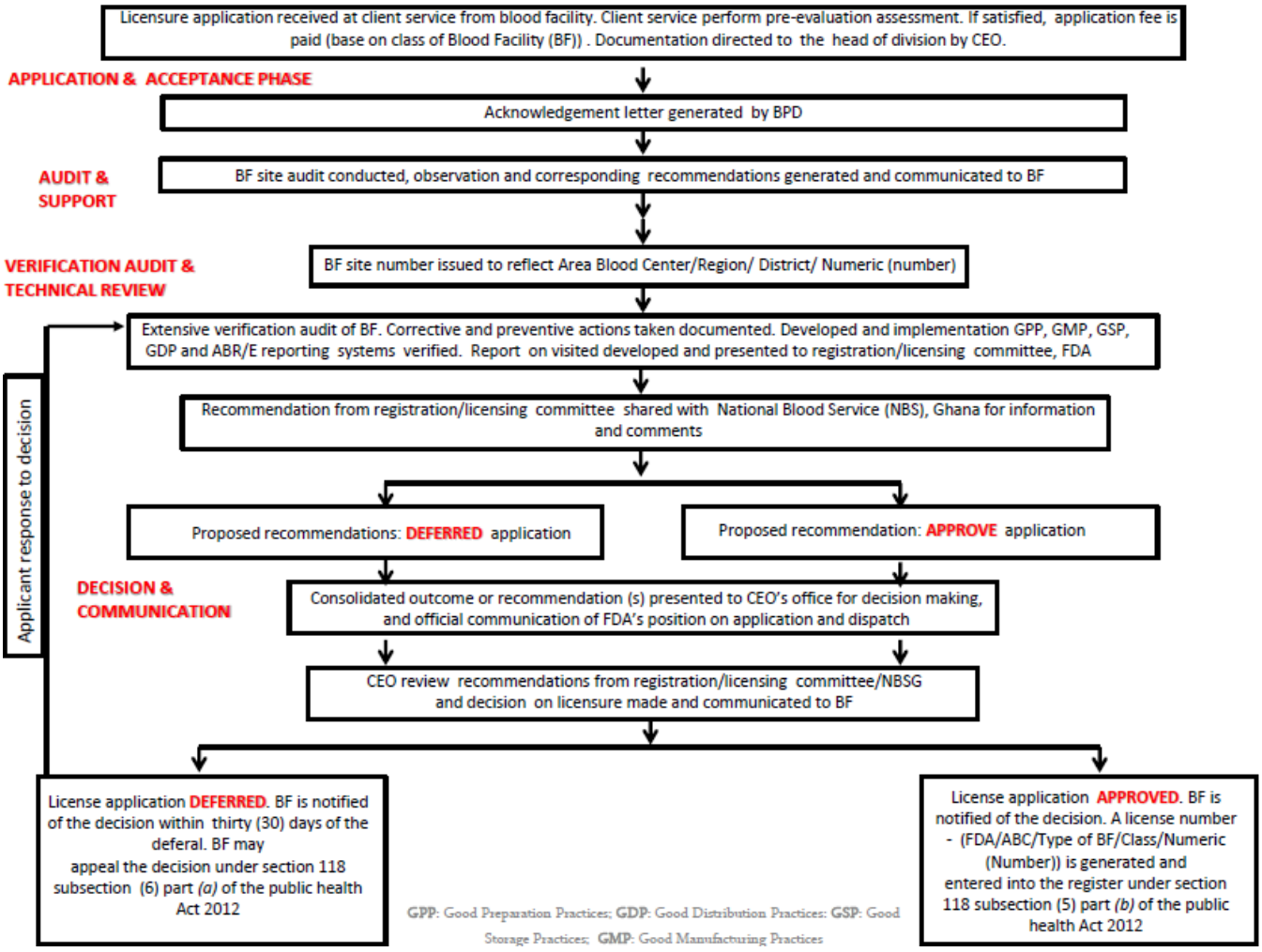
## REPORT A SERIOUS ADVERSE EVENT OR REACTION RELATED TO BLOOD TRANSFUSION AND REPORTING A DIAGNOSTIC FAILURE

A licensed Blood facility shall report all Serious Adverse Event and Reactions (SABRE) related to blood to FDA using the documented procedures for reporting SABRE.

Similarly, all diagnostic failures, including false positives and false negatives shall be reported to the FDA through the standard procedure for reporting.

If you have questions about SABRE or diagnostic failures, please send an email to: drug.safety@fdaghana.gov.gh.

# THE REGULATORY PATHWAY FOR BLOOD AND BLOOD COMPONENT PRODUCT LISTING



## PLASMA DERIVED MEDICINAL PRODUCTS (PDMPS) AND MANUFACTURERS

Marketing authorization holders located outside of Ghana that import or offer for import blood products into Ghana are required to register as importers of Biological Products and subsequently register their product with the FDA pursuant to section 118 of the Public Health Act 2012 Act 851. Applicants shall provide the name of the local agent for Ghana, and the name of each local distributor, and any other entity or person who imports or offers for import these blood products.

A guidance document that provides the regulatory requirements for the registration of human plasma – derived medicinal products have been published on the FDA's website - Guideline for the Registration of Human Plasma-Derived Medicinal Products (PDMPs). The guideline is applicable to all plasma-derived medicinal products either manufactured in-country or imported into Ghana, and containing an active or inactive ingredient that is derived from human blood either sourced from a local Blood facility or abroad. Due to the associated risk of transmitting infectious agents, the safety of these products is assured through the requirements as described in the published guidelines.

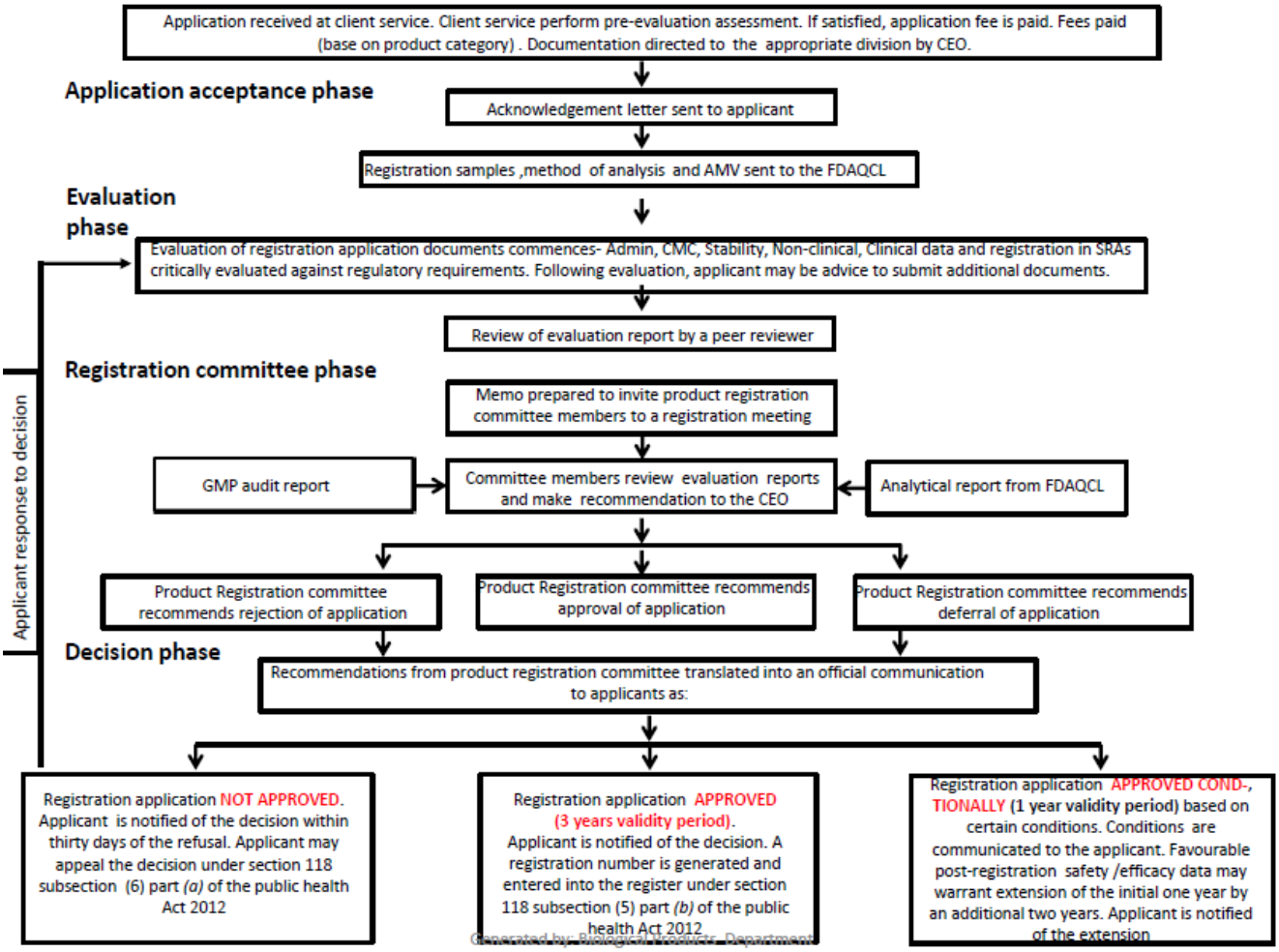
Applications for human plasma-derived medicinal products will be evaluated based on the products' Quality, Safety and Efficacy submissions. The published guideline outlines the requirements for the Plasma Master File (PMF) and the specific quality documentation required to support registration of these products.

Documents pertaining to the collection and control of source materials should be provided as a standalone PMF. Two sets of the application, including the product dossier and the PMF shall be submitted in softcopy in a CD/DVD (do not submit in hardcopy) together with the appropriate product registration fee for the registration of the human plasma-derived medicinal product. The classify factor VIII concentrate, factor IX complex concentrate (coagulation factors II, VII, IX and X) and human normal immunoglobulin as PDMPs. Anti-D, anti-rabies, anti-tetanus and anti-snake are treated. Note that reference to the relevant PMF/s may be made in the sections in the dossier provided below:

a) CTD section 3.2.S.2.3, if the PMF relates to a drug substance; or

b) CTD section 3.2.R.1 (ICH CTD) or 3.2.Q.1 (ACTD), if the PMF relates to an excipient.

# THE REGULATORY PATHWAY FOR REGISTERING BLOOD PRODUCTS



**Approved by:**

**……**

**Delese A. A. Darko (Mrs.)**
**Chief Executive Officer**
**Food and Drugs Authority (FDA)**

**Date: _____/_____/_____**