



Zambia Medicines Regulatory Authority

GUIDELINES ON HAEMOVIGILANCE IN ZAMBIA

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**i. Abbreviations**

AABB	Association for the Advancement of Blood & Biotherapies
AE	Adverse Event
AR	Adverse Reaction
BE	Blood Establishment
FBC	Full Blood Count
FFP	Fresh Frozen Plasma
HBB	Hospital Blood Banks
HFP	Haemovigilance Focal Person
HTC	Hospital Transfusion Committees
HV	Haemovigilance
IBCT	Incorrect Blood Component Transfused
INH	International Haemovigilance Network
ISBT	International Society for Blood Transfusion
NHO	National Haemovigilance Office
PBC	Provincial Blood Center
PDMPs	Plasma Derived Medicinal Products
RBCs	Red Blood Cells
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
TTI	Transfusion Transmissible Infections
WB	Whole Blood
WBC	White Blood Cells
WHO	World Health Organisation
ZAMRA	Zambia Medicines Regulatory Authority
ZNBS	Zambia National Blood Transfusion Services
ZNBS HQ	Zambia National Blood Transfusion Service Headquarters



ii. Definitions

The following definitions apply for the haemovigilance system in Zambia and are in their majority based on WHO's definitions (1,2) concerning blood and blood products and definitions from the EU Blood Guide (9)

(AE) Reporting	Sending information on adverse events to the haemovigilance system for further investigation, analysis and feedback.
Adverse Event (AE)	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 (AR)	Any unintended response in donor or patient associated with the collection or transfusion of blood or blood components.
Blood Collection	The procedure whereby a single donation of blood is collected in an anticoagulant and/or stabilizing solution, under conditions designed to minimize microbial contamination, cellular damage and/or coagulation activation of the resulting blood donation.
Blood Component	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 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.



Blood Products	Any therapeutic substances derived from human blood, including whole blood, blood components and plasma-derived medicinal products (PDMPs). However, in this Guideline, the term “Blood Products” excludes PDMPs.
Blood Related Adverse Event	A blood related adverse event is an incident and/or reaction in which harm resulted, or potentially could have resulted, from the transfusion/administration of a blood product.
Corrective Action	Action taken to eliminate the cause of a detected nonconformity or other undesirable situation.
Donor	A person in defined good health conditions who voluntarily donates blood or blood components, including plasma for fractionation.
Epidemiological Surveillance	The continuous gathering, analysing, and interpreting data about diseases, and disseminating conclusions of the analyses to relevant organisations and audiences.
Haemovigilance	Haemovigilance is 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.
Haemovigilance Feedback Report	Report of aggregated analysed data from the haemovigilance system.
Imputability	The likelihood that a serious adverse reaction in a recipient can be attributed to the blood or blood component transfused or that a



serious adverse reaction in a donor can be attributed to the donation process

Incident

Any untoward occurrence associated with an activity or process, such as the collection, testing, processing, storage and distribution of blood and blood components, or in the transfusion or administration.

**Incorrect Blood
Component
Transfused (IBCT)**

All events related to IBCT must be included in haemovigilance reporting, even if the event did not result in injury or damage.

Manufacture

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.

Near Miss

An error or deviation from standard procedures or policies which, if undetected, could result in the determination of a wrong blood group or issue, collection or administration of an incorrect, inappropriate or unsuitable component, but which was recognized before the transfusion took place.

Notification

Mandatory information on a notifiable event to the regulatory authority.

Preventive Action

Action taken to eliminate the cause of a potential nonconformity or other potential undesirable situation.

**Quality Management
System**

A management system that directs and controls an organisation with respect to quality and that ensures that steps, processes, procedures and policies related to quality activities are being followed



Serious Adverse Event	Serious adverse events are those that might have led to death or life-threatening, disabling or incapacitating conditions for recipients or donors, or which might have resulted in prolonged hospitalization or morbidity.
Serious Adverse Reaction	Unintended response in donor or in recipient associated with the collection or transfusion of blood or blood components that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs hospitalisation or morbidity.
Traceability	The ability to reliably follow the information trail from donor to recipient and vice versa in a timely manner. Traceability is essential to ensure the ability to recall at-risk products, to identify recipients of non-conforming products that may require additional follow-up, and to fully investigate adverse events.
Trace-Back	The process of investigating a report of a suspected transfusion-associated adverse reaction in a recipient to identify a potentially implicated donor.
Transfusing Facility	Healthcare facilities where blood and blood components are transfused to patients
Transfusion Reaction	A transfusion reaction refers to an undesirable response to a transfusion, which may or may not be a result of a clinical incident depending on the nature of the event.



1. Introduction

Haemovigilance (HV) is a set of surveillance and corrective or preventive procedures in response to adverse events and adverse reactions, both in donor and recipient and the epidemiological follow up of donors. A haemovigilance system ensures efficient, detailed and timely reporting of incidents in the transfusion chain to allow review, analysis and reaction of responsible stakeholders to improve the safety of blood and its components. The system further covers the manufacturing process from donation to issue of a blood product unit. This requires well-organized reporting structures and defined roles and responsibilities to enable the efficient involvement of all stakeholders. Haemovigilance is therefore an integral part of quality management systems for continual improvement of product quality and safety of processes (3).

The Zambia Medicines Regulatory Authority (ZAMRA) is a statutory regulatory body established by the Medicines and Allied Substances Act, No.3 of 2013. Its functions include regulation of Medicines and Allied Substances in Zambia. Safety monitoring of medicines is an integral part of regulation. All haemovigilance activities pertaining to safety monitoring must comply with the MASA and regulations made thereunder.

The Zambia National Blood Transfusion Service (ZNBTS) is a Statutory Board under the Ministry of Health (MoH) established under Statutory Instrument (SI) 147 of 1997 with the mandate to supply blood to all patients in Zambia, the blood supply and blood transfusion system is centrally coordinated. ZNBTS has 10 Provincial Blood Centers that are responsible for: donor recruitment and blood collection; laboratory testing and processing of blood; promotion of appropriate clinical use; and technical support to hospitals/health facilities.

Blood products are essential medicines whose use can be life-saving. Thus, the availability, safety and efficacy of blood products is a pivotal component in national health systems. However, the processes within the transfusion chain bear risks – to transfusion recipients, blood donors and even health care personnel involved in handling and manufacture of blood components.

Haemovigilance is a shared responsibility of all stakeholders involved in the entire transfusion chain and the national regulatory authorities. It involves operational linkages between clinical departments, hospital blood banks, blood establishments and national authorities. Reporting and analysis of adverse events and reactions associated with transfusion requires close co-operation between the clinical department where transfusion takes place, the hospital blood



bank that issue the transfused blood component and the blood establishment that collect and distribute the blood unit (if different from the hospital blood bank) (1,2).

In Zambia haemovigilance covers adverse events and adverse reactions related to the entire blood manufacturing process and clinical transfusion. The goal of the haemovigilance system is surveillance of all processes involved of the blood transfusion chain, collecting and analysing data and use the achieved knowledge for regulatory feedback to increase the overall safety of the process of transfusion.

This guideline is issued by the Authority pursuant to section 68 of the Medicines and Allied Substances Act (No. 3) of 2013. The Act provides for safety monitoring of medicines (including blood and blood products) and allied substances.

The guideline provides general principles relating to the process for reporting Adverse Reactions and Adverse Events in the Blood Transfusion Chain and applicable to all haemovigilance activities.

All persons intending to report adverse Reactions and adverse events in the Blood Transfusion Chain are encouraged to use this guideline as appropriate to their spheres of competence, activity and responsibility.

The Authority may amend any part of this guideline from time to time.



2. Scope of the guideline

This guideline is intended to be used by those involved in any part of the blood transfusion chain in Zambia such as clinical departments, hospital blood banks, blood establishments and the national medicines regulatory authority. It covers all haemovigilance activities and processes that occur throughout the transfusion chain for blood and blood components for human use. Adverse reactions from Plasma-Derived Medicinal Products (PDMPs) are outside the scope of this guideline.

The activities and processes in the transfusion chain are as outlined in the table 1 below:

Table 1.

DONORS	RECIPIENT	PRODUCT	PROCESSES
<u>Blood Donation:</u> – Adverse Donor Reactions – Look-back – Trace-back	<u>Transfusion:</u> – Adverse Reactions (all severities) – Other adverse events/Incidents (e.g. IBCT) – Near misses	<u>Blood Products:</u> – RBC – Platelets – FFP – Whole Blood – Cryoprecipitate – WBC	<u>Incidents</u> – Donor selection – Collection – Handling – Processing – Testing – Storage – Distribution – Transport



3. Haemovigilance Governance Structure

The haemovigilance system is organized and implemented under the responsibility of ZAMRA and ZNBTS in a network (Figure 1) integrating different levels: national (National Haemovigilance Office – ZNBTS HQ), Blood Establishments (Provincial Blood Center) and Transfusing facilities.

Haemovigilance is undertaken at the transfusing facilities and blood establishment levels, supported by a decentralized national data collection and reporting process via the National Haemovigilance Office.

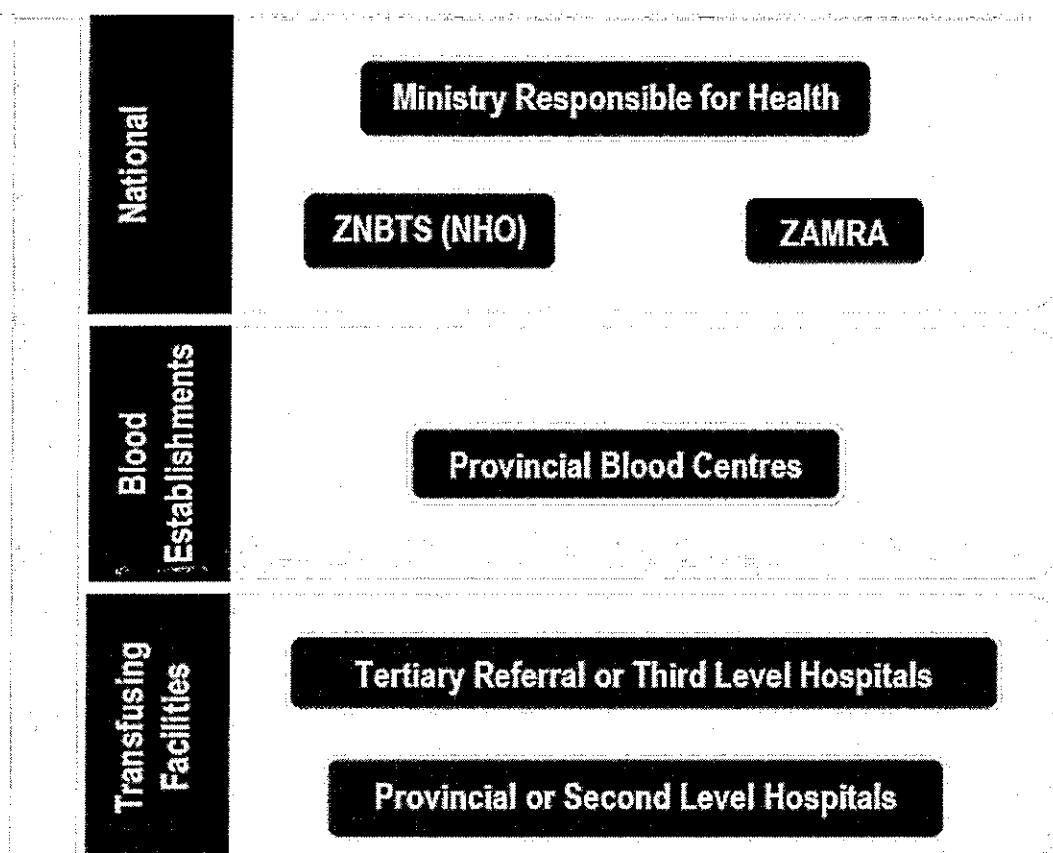


Figure 1. Haemovigilance Governance Structure (source: National Haemovigilance Framework for Zambia).



4. Roles and Responsibilities

Information flow, both reporting and feedback, is the essential basis for an efficient and well-functioning haemovigilance system. To achieve the unhindered intertwining of all involved parties, the roles and responsibilities within the haemovigilance system must be clearly defined and officially assigned.

4.1 Transfusing facilities

Transfusing facilities are healthcare facilities where blood and blood components are transfused to patients. Transfusing facilities have different internal stakeholders with varying roles and responsibilities in the haemovigilance system. These include transfusing wards, hospital blood banks, haemovigilance focal persons and hospital transfusion committees.

Adverse events, incidents and near misses in clinical areas and Hospital Blood Banks (HBBs) must be identified, managed and reported within the institution. Prevention is key; hence hospital policies and procedures should be developed and monitored bearing that in mind, this includes staff training and competency assessment. Various clinical governance review and reporting structures exist, including oversight by the hospital transfusion or blood management committee.

Transfusion must be conducted in accordance with the Clinical Guidelines on Appropriate Use of Blood and Blood Products for Zambia. Transfusing clinicians have the responsibility to monitor their patients and identify any signs of adverse reactions. All suspected transfusion reactions must be managed immediately according to the Clinical guidelines to minimise and prevent further harm to the patient. Each transfusing facility should appoint a haemovigilance focal person to coordinate haemovigilance activities.

4.1.1 Responsibilities of attending bedside healthcare staff (Nurses) within Transfusing Facilities:

Bedside healthcare staff attending to patients should:

- i. Positively identify the transfusion recipient (patient).
- ii. Monitor patients during and after transfusion for signs of Adverse Reactions (ARs).
- iii. Identify Adverse Events (AEs) and ARs.



- iv. In case of suspected AR, manage patient immediately in accordance with clinical guidelines for transfusion.
- v. Notify the attending Physician of suspected AE/AR immediately.
- vi. Continue managing patient as per applicable guidelines and instructions from the attending Physician until stabilised.
- vii. Perform bedside investigation of the suspected reaction according to facility procedures.
- viii. Maintain records of the complications in the patient's medical record, including the report from the investigations thereof.

4.1.2 Responsibilities of the transfusing ward attending physician:

- i. Request blood and blood products using the prescribed standard blood request forms.
- ii. Prescribe blood products in accordance with national guidelines for clinical use of blood.
- iii. Monitor patients for possible ARs.
- iv. In the event of suspected AR, manage patient immediately to minimise harm.
- v. Document details of the suspected transfusion reaction on Transfusion reaction report form – initial report (**form 1a**) and send together with required samples to the Hospital Blood Bank (or any blood bank which performed pre-transfusion testing and/or issued the units).
- vi. Take necessary laboratory samples and send to appropriate laboratory for investigation as well as requesting other diagnostic tests such as chest x-rays as applicable to further characterise the case.
- vii. Perform clinical investigation and consult transfusion specialists for assistance as necessary.



4.1.3 Responsibilities of the Hospital Blood Bank (HBB)

The Hospital Blood Bank or any facility performing pre-transfusion testing and distribution of blood and blood components is central to the reporting and investigation of transfusion related ARs and AEs.

HBB responsibilities include:

- i. Performing pre-transfusion testing and issuing compatible blood and blood components for transfusion.
- ii. Performing transfusion reactions investigations in accordance with laid down procedures.
- iii. Reporting results of AR laboratory investigations to the hospital transfusing ward and to the Haemovigilance Focal Person.

4.1.4 Responsibilities of the Haemovigilance Focal Person

Specific responsibilities include:

- i. Completing and sending initial report of suspected transfusion reaction to the Provincial Blood Centers and to ZAMRA within stipulated time frames: (as soon as possible for all serious AEs & ARs and monthly for all other). Refer to Section 7 of this guideline.
- ii. Consolidating AR investigation reports and other AR relevant information from other departments (Transfusing Ward, Blood Bank, Other laboratories, Radiology etc).
- iii. Reporting details of reported ARs to the HTC.
- iv. Completing and sending the final report of AR to the PBC and ZAMRA.
- v. Custodian of the facility AR and AE registers.
- vi. Reports monthly statistics of blood and blood components receipt and usage to the Blood Establishment (Provincial Blood Center) as per prescribed form.
- vii. Submits statistics on blood and blood components usage + collated monthly AEs and recipient ARs reports annually to the PBC and ZAMRA (refer to section 7 of this guideline).

4.1.5 Responsibilities of the Hospital Transfusion Committee (HTC)



HTC is responsible for reviewing all reported transfusion ARs/AEs and develop/recommend corrective and preventive actions as per institutional policy and terms of reference of the HTC.

4.2 Provincial Blood Centers

Provincial Blood Centers are the users of the materials, disposables, reagents and equipment manufactured by the industry. At the same time, they are also the producers of labile blood components of all types, as well as the providers of transfusion related services. In this way, they play a key role in haemovigilance.

Blood Centers are responsible for protecting donor health and for product safety and quality. Adverse events, incidents and near misses are identified, managed and reported as part of the institutional quality management system. Blood establishments are typically required to report defined categories of donor and product safety events to ZNBTS (NHO) and ZAMRA at the national level. The Provincial Blood Centers responsibilities include:

- i. Identify, record and report all adverse donor reactions and AEs during manufacturing processes to the ZNBTS (NHO) within the stipulated time frames (as soon as possible for all serious AEs & ARs and monthly for the rest).
- ii. Manages all cases of donor adverse reactions according to institution's established procedures.
- iii. Receive reports of AEs and recipient ARs from transfusing facilities and forward these to the ZNBTS (NHO).
- iv. Investigation of all local AEs and donor ARs.
- v. Coordination with hospital personnel where labile blood products are issued.
- vi. Supporting transfusing facilities and ZNBTS (NHO) with investigation of AEs and ARs (donor + recipient).
- vii. Provide feedback on reporting haemovigilance data to transfusing facilities.
- viii. Assist capacity building for Transfusing facilities.
- ix. Submit blood statistics information monthly to ZNBTS (NHO) and annually to ZAMRA: total blood & blood component collected, type & number of blood component produced, number. used, number discarded, number of tested & reactive units, number recalled, quarantined etc.
- x. Submit monthly report on AEs + donor ARs to ZNBTS (NHO) and ZAMRA.



4.3 Zambia National Blood Transfusion Services (NHO)

ZNBTS (NHO) responsibilities include:

- i. Lead investigations at PBCs and transfusing facilities.
- ii. Submit all SARs (donor and recipient) and SAEs to ZAMRA as soon as possible
- iii. Collation of preliminary annual HV reports and submission to ZAMRA for publishing.
- iv. Support development of different guidelines for transfusion e.g. SOPs, clinical use guideline, etc. for hospitals in relation to the use of blood components.
- v. Support the audit function of hospitals in relation to transfusion practice.
- vi. ZNBTS (NHO) should communicate to all reporting facilities on a periodic basis with a view to developing national best transfusion practice.
- vii. Report blood statistics information received from all Blood Establishments (PBC) and transfusing facilities to ZAMRA annually.
- viii. Training and education of all haemovigilance stakeholders.

4.4 Zambia Medicines Regulatory Authority

ZAMRA is responsible for taking regulatory action on haemovigilance findings. The development, recommendation and implementation of regulatory interventions are fundamental, in addition to monitoring through a quality systems approach. The ultimate outputs from haemovigilance systems are the 'learnings' and recommendations for clinicians, policymakers and the community.

Specific ZAMRA responsibilities include:

- i. Ensure the quality and safety of blood and blood components used in hospitals, blood banks and other transfusing facilities in Zambia.
- ii. Inspect and authorize all blood establishments in Zambia to ensure compliance with national legislation.
- iii. Collaborate with the ZNBTS (NHO) to review and evaluate serious adverse reactions and events related to the collection and transfusion of blood and blood components.
- iv. Perform imputability assessment and allocation.



- v. Collaborate with the ZNBTS (NHO) to review and publish annual HV report.
- vi. Formulation of regulatory decisions.
- vii. Responsible for effective leadership and governance via monitoring and controlling blood transfusion activities: legislating, inspecting and licensing.
- viii. Review completeness, quality check and causality assessment of AE reports.
- ix. Collection of all data on blood transfusion chain complications in a central database.
- x. Use haemovigilance data for improving blood safety through policy changes and quality management.
- xi. Data analysis.
- xii. Provide feedback on reporting haemovigilance data to ZNBTS, PBCs and Transfusing facilities.
- xiii. Awareness, training and education.
- xiv. Regular communication with Haemovigilance stakeholders and the general public on blood safety.
- xv. Regular review and updating of standards and risk minimization measures (e.g. TTI testing requirements, donor selection and deferral criteria) in line with current science and epidemiological situation or emerging diseases.

4.5 Ministry Responsible for Health

The Ministry responsible for Health is ultimately responsible for the national blood system and for the quality, safety and sufficiency of the supply of blood products. Therefore, government plays key policy and operational roles for provision of governance and reporting structures. These include provision of adequate human and financial resources for haemovigilance programmes.



5. Haemovigilance Methods

5.1 Spontaneous Reporting System (Passive)

Spontaneous reporting system is a haemovigilance method that solely relies on the health care professionals in transfusing facilities, blood establishments and patients (patients and donors should also be educated on the need to report any AR experienced to the respective transfusing facilities and blood establishments) to detect and take the initiative to report adverse reactions and adverse events. There are no active measures taken to look for adverse effects other than encouraging health care professionals to report to the haemovigilance centre or national regulatory authority. This is the most used method in haemovigilance and reporting can be either voluntary or mandatory.

a) Advantages of Spontaneous Reporting System

- i. Administratively easiest to establish and least labour intensive
- ii. Relatively inexpensive
- iii. Covers the whole population and includes all blood components/products
- iv. There is continual monitoring throughout life-cycle of product
- v. Detects signals of new, rare or serious adverse reactions/events

b) Disadvantages of Spontaneous Reporting System

- i. Usually associated with gross under-reporting
- ii. Captures only suspected ARs/AEs
- iii. Denominator unknown
- iv. There is strong bias in reporting
- v. Risk factors cannot be identified with certainty due to absence of rates

5.2 Active Methods

5.2.1 Intensified Spontaneous Reporting

This is an extension of the Spontaneous Reporting System used to enhance the reporting of ARs/AEs of specific blood components and blood products in early post-approval phase.

Generally, the advantages and disadvantages of spontaneous reporting apply.



5.2.2 Targeted Spontaneous reporting

This is intensified ARs/AEs reporting within a defined cohort. Specific targets are defined such as specific population, specific clinics, and specific blood components/products, all ARs or specific ARs.

a) Advantages of Targeted Spontaneous Reporting

- i. Can utilize existing ARs/AEs reporting infrastructure
- ii. Possible to implement monitoring programme that targets specific issue of concern (AR/AE, product, patient group)
- iii. Captures useful information; less “background noise”

b) Disadvantages of Targeted Spontaneous Reporting

- i. Under-reporting remains a problem
- ii. Captures only suspected ARs/AEs
- iii. May limit reporting only to specific ARs/AEs
- iv. Relies on competency of the reporter

5.2.3 Cohort Event Monitoring

Cohort event monitoring (CEM) is a prospective observational cohort study of adverse events associated with one or more blood component/product. It is useful for gathering more information on the safety profile of a new blood component/product in the post-approval phase thereby acting as an early warning system.

Enrolled patients are actively followed up during treatment to record all adverse events.

a) Advantages of Cohort Event Monitoring

- i. Identify risk factors for adverse reactions
- ii. Able to produce rates
- iii. Produce a near complete profile of the adverse events and/or adverse reactions for the blood component/product of interest
- iv. Very effective in identifying signals at an early stage



b) Disadvantages of Cohort Event Monitoring

- i. More labour intensive and more costly than spontaneous reporting
- ii. Requires more training of the health workers who will implement

5.2.4 Retrospective Studies

These involve review and analysis of historical information on ARs and AEs.

a) Advantages of Retrospective Reporting

Makes use of already existing data.

b) Disadvantages of Retrospective Reporting

Reliant on old data which may not have captured information of interest.



6. Traceability

A traceability system should enable complete look-back and trace-back procedures, if possible through a computer database. Collected blood as well as manufactured components and issued units should be traceable from donor to recipient and *vice versa*. It is important to be able to identify previous donations or related blood components or recipients of units from donors that e.g. have been tested positive for TTI. Further, it is necessary to trace issued units that e.g. caused an AR back to the original donation/ associated donor to identify other recipients of those blood components.

6.1 Identification of Donor, Donation, and Recipient

There should be a system in place to uniquely identify each donor, donation, testing samples, resulting blood components, and the recipient of such products.

6.1.1 Donor identification

Identification of a donor should take place before the donation via an official identification document, such as a national registration card, passport or a driver's licence. The requirements for identification processes should be laid out in SOPs at every donation site. Entering donor data into a database should be covered by an SOP for copying critical data, including descriptions of practical execution following GMP standards (e.g. four-eye-principle). Before donation, donor data on the questionnaire and donation form must be cross-checked with the ID card and/or the donor database.

6.1.2 Identifying donation and blood products/units

The system must allow to uniquely identify a donation and any resulting products. The labelling system should have the following minimal requirements:

- i. Product Description
- ii. Date of collection
- iii. Storage and transport temperature
- iv. Titres (where applicable)
- v. Expiration date



- vi. Blood group (ABO/RhD)
- vii. Product Number/Donation Identification Number
- viii. Facility
- ix. Name and volume of anticoagulant (where applicable)
- x. Preservative used

6.1.3 Recipient identification

All Transfusing facilities must have SOPs and guidance documents in place that have requirements for recipient and product identification. Recipient data shall be available for health care workers to cross-check patient's identity with recipient data on product label directly before transfusion.

6.2 Record Keeping

A system of record keeping should be in place that covers the complete transfusion chain from donor to recipient. Linkages between the different information should be clear and traceable: donor, donation, and questionnaire; donation number, test results, and product unit ID; product unit ID and recipient. These linkages may be maintained in databases and reporting forms (e.g. donation form, manufacture report, transfusion report).

6.2.1 What needs to be captured and by whom?

Data must be recorded by appropriate stakeholders at different stages throughout the transfusion chain. All acquired data should be handled following national requirements for data protection and access to the information should be restricted to authorized personnel.

6.3 Blood Establishments

Blood Establishments that collect donations are required to store identification data of donors, reports of donations that contain the donor ID and the donation number, and the completed questionnaires.

Testing establishments have to store reports of testing results that are unmistakably linked to the donation number and test tubes.



Establishments that process blood and blood components are required to keep records about the origin of the blood, about the quality of the manufactured products (compliance) including storage conditions, and about the destination of the products. The final unit/product ID must be linked to the original donation ID.

6.4 Facilities that Store and Transport Blood and Blood Components

Facilities that store and/or transport blood and blood component units must keep records about storage and transport conditions, following the respective guidance documents.

6.5 Transfusing Facilities

All Transfusing facilities must have a system recording the origin of the units and final destination which is either 'issue for a patient' or 'disposal'. Further, the facilities are required to keep transfusion records that contain the product unit ID as well as the patient identification information.

6.6 Retention period

It should be clear for all stakeholders involved in the transfusion chain how long to store records about the different activities and processes. The respective minimum retention periods of the documentation as stated below:

RECORDS	TIME	RESPONSIBLE
Transfusion Records	10 years	Transfusing facilities, hospitals
Donation Records	10 years	Blood Establishments
Laboratory Testing Records	10 years	Testing facilities, Blood Establishments
Manufactured Products/Units	10 years	Blood Establishments
Issued Units	10 years	Transfusing facilities (for recipients); and Blood Establishments (for delivered units to Transfusing facilities)
Haemovigilance Reports	10 years	All involved parties



6.7 Critical Data

Data that must under all circumstances be transcribed correctly, such as laboratory test results, are 'critical data'. Manual entry of critical data should be verified by a second authorised person. There should be secure methods for transcription in place.

6.8 Look-Back and Trace-Back

6.8.1 Look-back

A blood establishment must initiate Lookback investigations on recognition that there may have been risk of transmitting an infection from a donor to a recipient.

Look-back is required under the following circumstances:

- i. When a donor has undergone seroconversion during their blood donation career.
- ii. Donors identified to be infected and reported to the Blood Establishment from an outside source.
- iii. Donors identified as infected by a TTI through the introduction of a new, more sensitive screening test applied to all donation.

General Principles for Look-Back Investigations

Look-back investigations should be managed through a generic system which incorporates the following steps at the BE and Transfusing Facility:

a) At the Blood Establishment:

- i. Identification of potentially infectious donations.
- ii. Identification of all blood components prepared from those donations and their immediate quarantine and/or recall of unused products.
- iii. Documentation of the fate of the blood components.
- iv. Retest of retained samples from the potentially infectious donation.
- v. Notification of compatibility testing laboratory in receipt of involved blood components.



- vi. Notification of ZNBTS (NHO) and ZAMRA through completion of **forms 3a and 3b**

b) At the Transfusing Facility:

- i. Identification of the fate of the component, including details of any identified recipient.
- ii. For recipients not known to be dead, a procedure for notification, generally following notification of the treating physician.
- iii. A protocol for management of recipient notification and testing (if required).
- iv. Notification of case details to blood establishment and ZNBTS (NHO) and ZAMRA.

6.8.3 Trace-back

Trace-back is required when a recipient of blood or blood components has been identified to be infected with a transfusion transmissible infection for which another more likely cause is not apparent.

General principles for Trace-back investigations

Trace-back investigations should be managed through a generic system which incorporates the following steps at the Transfusing Facility and Blood Establishment:

a) At the Transfusing facility:

- i. Identification of recipients potentially infected through transfusion via patient reports or routine patient management and testing.
- ii. Identification of unit numbers of all blood components transfused to the recipient.
- iii. Notification to respective blood establishments who supplied the transfused products.
- iv. Notification of recipient of outcome of investigations.
- v. Notification of blood establishment and ZAMRA through completion of **form 2**.

b) At the Blood Establishment:

- i. Forwarding of reports received from Transfusing Facilities to ZNBTS (NHO) as soon as possible.



- ii. Identification of components from implicated donations and quarantine and/or recall them if not used.
- iii. Retest of retained samples from the respective donations.
- iv. Identification of respective donors of implicated of blood and blood components.
- v. Follow-up on donors and obtain samples for testing as appropriate.
- vi. Where an infection similar to that identified in recipient is detected in any donor of the transfused products, perform phylogenetic testing to verify/confirm TTI transmission where possible.
- vii. Notification of transfusing facility of the outcome of investigations.
- viii. Notification of ZNBTS (NHO) and ZAMRA through completion of **form 2**.



7. Reporting and Investigation of Adverse Reactions and Adverse Events

7.1 Reporting Process

The main method used in Zambia for blood safety monitoring is spontaneous reporting. However, ZAMRA or the ZNBTS (NHO) may implement active reporting for specified products or AEs and/or ARs. The spontaneous method is described below.

7.2 What to Report?

In accordance with the National Haemovigilance Framework for Zambia, all suspected adverse events and adverse reactions related to the whole transfusion chain must be reported to ZAMRA and to the National Haemovigilance Office at the ZNBTS HQ. Adverse reactions and adverse events are defined in Annex I of these guidelines.

7.3 Reportable Data

The following data must be reported for each adverse event as applicable:

Table 2. Overview of reportable data

Patient/Donor	Blood Products/Procedure	Adverse Event	Facility
Patient/Donor initials	Product type and modification	Type of adverse event	Reporting jurisdiction
Date of birth	Product ID and donation date	Date and time of transfusion /event	Contact details of reporter/reporting facility
Age	Manufacturer/origin blood establishment	Symptoms and suspected diagnosis	
Gender	Concomitant blood products/medication	Contributing factors	
Blood type	WB/Apheresis donation	Outcome	



7.4 Who should report?

7.4.1 Transfusing Facilities

All transfusing facilities in Zambia are required to report transfusion related AEs and ARs. Any health professional in a Transfusing facility who identifies a suspected AE or AR should report.

7.4.2 Blood Establishments

All blood establishments in Zambia are required to report transfusion related AEs and ARs. Any health professional in a blood establishment who identifies a suspected AE or AR should report.

Where an AE or AR is identified by the patient, donor or any other person, the health professional who is informed shall facilitate reporting.

7.5 When to report?

7.5.1 Reporting Timelines

Transfusing facilities should report **all serious** AEs and recipient ARs to the Blood Establishment and ZAMRA **as soon as possible** following occurrence and **all other** AEs and ARs **monthly**.

Blood Establishments are required to report **all serious** AEs and donor ARs to the ZNBTS (NHO) **as soon as possible** following occurrence and **all other** AEs and ARs **monthly**. Further, Blood Establishments should forward to the ZNBTS (NHO) **all serious** AEs and recipient ARs received from Transfusing Facilities **as soon as possible** and **all other** AEs and ARs **monthly**.

The ZNBTS (NHO) reports **all serious** AEs and ARs (donor + recipient) **as soon as possible** to ZAMRA and **all other** AEs and ARs **monthly**.

If the reporting transfusing facility, Blood Establishment or ZNBTS (NHO) becomes aware of relevant additional information about a serious AE or AR they have previously submitted to the ZNBTS (NHO) or ZAMRA they can submit a follow-up report whenever the information becomes available or include the information in the final report.



7.5.2 How and where to report?

a) Reporting Forms

Form X is used for reporting acute transfusion reactions to the Compatibility Testing Laboratory by the transfusing ward. AE and AR reporting forms have been developed for reporting transfusion reactions (initial and final report: **forms 1a and 1b**, respectively), suspected TTIs (**form 2**), donor lookback procedures (initial and final report: **forms 3a and 3b**, respectively), donor reactions (**form 4**), and incidents (such as adverse events during manufacture, transport, storage, handling and near misses: **form 5**). These capture the minimum information considered important in order to fully understand the AE or AR. Additionally, **forms 6 and 7** have been developed to capture annual statistics on blood usage and on blood activities (collection, production, distribution etc.) at transfusing facilities and blood establishments respectively. These forms are available in Annex II of these guidelines.

Transfusing facilities should submit AEs and ARs reports to the blood establishments and ZAMRA. Blood establishments should submit AEs and ARs reports to the ZNBTS (NHO). The ZNBTS (NHO) should submit AEs and ARs reports to ZAMRA using any one of the following methods:

b) Online Reporting

Complete and submit the report using the online reporting platform available on the ZAMRA website.

c) Email

Complete the prescribed available hard copy reporting form or download and fill out the appropriate form available on the ZAMRA website, complete all required sections of the form and send via email to: *ZAMRA at npvu@zamra.co.zm; pharmacy@zamra.co.zm and the ZNBTS (NHO).*

d) Post

Complete the prescribed reporting form or download and print the prescribed form available on the ZAMRA website, complete all required sections of the form and send via post to:

ZAMRA at P. O. Box 31890, Lusaka and ZNBTS (NHO).



7.6 Investigation of ARs and AEs

All ARs and AEs must be investigated to further characterise them as well as determine the root causes to facilitate implementation of appropriate corrective and preventive actions.

7.6.1 Who Should Investigate?

Transfusing facilities should investigate all ARs and AEs that occur in their facilities in accordance with Guidelines on Appropriate Clinical Use of Blood Products in Zambia and Standards for Blood Donation, Processing and Clinical Transfusion in Zambia. Investigation procedures include administrative checks, clinical, laboratory and radiology investigations as applicable.

Blood Establishments should investigate all donor ARs and any AEs that occur in their facilities following defined procedures.

In addition, blood establishments should investigate all cases reported to them by the transfusing facilities where a blood bag they supplied is implicated for example in cases of suspected TRALI, bacterial contamination or suspected TTI transmission.

7.6.2 Follow-up on Reports Submitted to ZAMRA and ZNBTS (NHO)

Transfusing facilities and Blood Establishments should be aware that they may be contacted as necessary for additional information in regards to the (serious) AE or AR reports submitted to ZAMRA and to ZNBTS (NHO). When a follow-up is required, ZAMRA, or ZNBTS (NHO) will contact the contact person indicated on the report via email or telephone.

Reasons for follow-up by ZAMRA and/or ZNBTS (NHO) may include but not limited to the following:

- i. Missing important information
- ii. Contradicting information provided
- iii. Legibility issues requiring clarification

7.7 Haemovigilance process flow

The process flow of reporting adverse events and reactions in Zambia is depicted in figure 2 below.

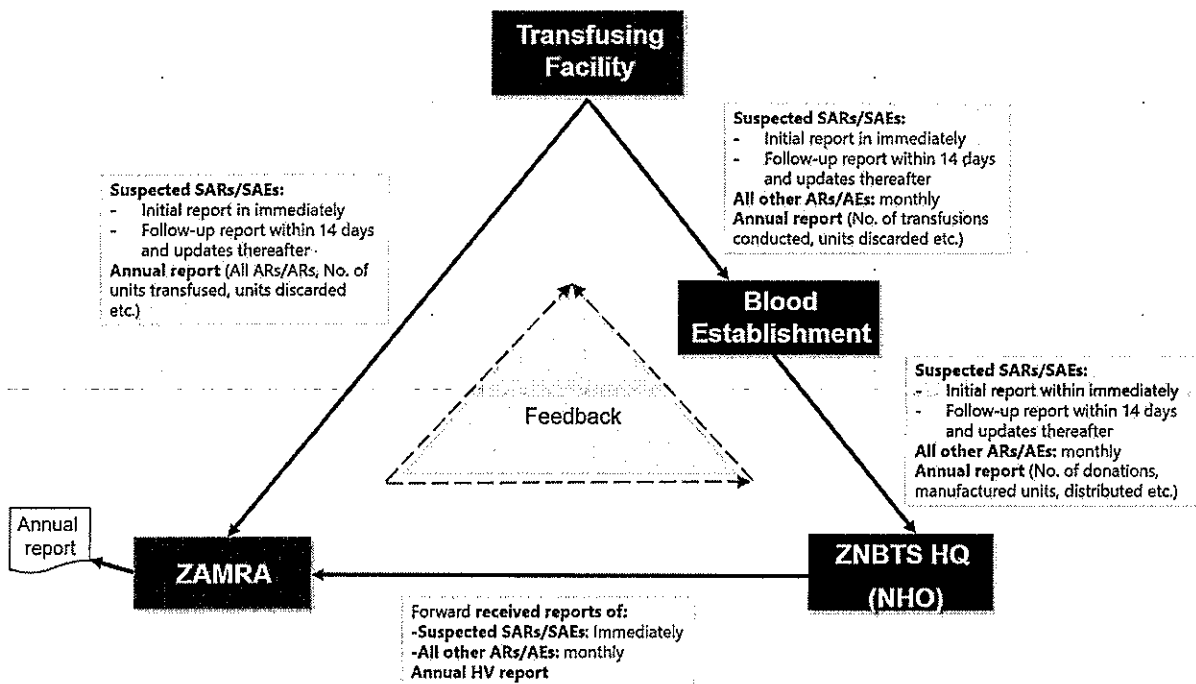


Figure 2. Reporting Flowchart Zambia (source: National Haemovigilance Framework for Zambia)

The reporting process flow for suspected adverse transfusion reactions is as shown in [Annex IV](#).

7.8 Haemovigilance Data Collection

7.8.1 Reportable Blood-Related Adverse Events

For an event to be deemed as valid it must reflect the prescribed definition. Definitions of blood-related adverse event types to be reported for haemovigilance reporting are provided in [Annex I](#). ZAMRA is responsible for amending and updating the agreed dataset and associated definitions to align with changes at the national and international levels.



7.9 Imputability Scoring System

Reported adverse reactions should be accompanied by an imputability score such as described by the Commission Directive 2005/61/EC of the European Union (4) and the “Proposed Standard Definitions for Surveillance of Non-Infectious Adverse Transfusion Reactions” from ISBT in 2011 (5). The imputability is the assessment of the strength of relation between transfusion/blood donation and observed adverse reaction in recipient/donor respectively. The imputability is scored once the investigation is completed. In table 2 the imputability scoring system, amended after the ISBT proposal (incl. 2005/61/EC values), is described:

Table 3. Imputability Assessment Criteria (adapted from EU Directive 2005/61/EC (4) and ISBT (5))

VALUE	ASSESSMENT	CRITERIA
3	Definite (certain)	When there is conclusive evidence beyond reasonable doubt that the AR can be attributed to the transfusion/blood donation
2	Probable (likely)	When the evidence is clearly in favour of attributing the AR to the transfusion/blood donation
1	Possible	When the evidence is indeterminate for attributing the AR to the transfusion/blood donation or an alternate cause
0	Unlikely (doubtful)	When the evidence is clearly in favour of attributing the AR to causes other than the transfusion/blood donation
	Excluded	When there is conclusive evidence beyond reasonable doubt that the AR can be attributed to causes other than the transfusion/blood donation
NA	Not assessable	Insufficient data available

7.10 Outcome Severity Scoring System

Reported AEs and ARs should be accompanied by an outcome severity score. A Table for severity grading of adverse transfusion reactions amended from the ISBT Working Party on Haemovigilance is provided below (see Table 4):



Table 4. Severity Grading System for Adverse Transfusion Reactions (adapted from the ISBT (5))

VALUE	CRITERIA
Grade 1 (Non-Severe)	The recipient may have required medical intervention (e.g. symptomatic treatment) but lack of such would not result in permanent damage or impairment of a body function
Grade 2 (Severe)	The recipient required in-patient hospitalization or prolongation of hospitalization directly attributable to the event; and/or The AR resulted in persistent or significant disability or incapacity; or The AR necessitated medical or surgical intervention to preclude permanent damage or impairment of a body function
Grade 3 (Life threatening)	The recipient required major intervention following the transfusion (vasopressors, intubation, transfer to intensive care) to prevent death
Grade 4* (Death)	The recipient died following an adverse transfusion reaction
Outcome not available	The clinical outcome might be pending or is not final yet
<i>*Grade 4 severity should only be attributed to an AR when the imputability score is 2, 3 or 4</i>	

Kindly refer to [Annex III](#) for an example of how imputability and severity scoring of transfusion adverse reactions is performed.

The table below shows the severity grading system for adverse donor reactions.

Table 5 Grading system for adverse donor reactions (adapted from ISBT/IHN (8))

VALUE	CRITERIA
Grade 1	No Outside Medical Care AND Short duration ≤ 2 weeks AND No limitation on Activities of Daily Living AND Resolved with no or minimal intervention



VALUE	CRITERIA
Grade 2	Outside Medical Care, no hospitalization <i>OR</i> Duration >2 weeks- ≤ 6 months <i>OR</i> Limitations on Activities of Daily Living for ≤2 weeks
Grade 3	Not life-threatening <i>AND any of the following</i> Hospitalization <i>OR</i> Duration >6 months <i>OR</i> Limitations on Activities of Daily Living >2 weeks <i>OR</i> Require surgery <i>OR</i> Other serious complications
Grade 4	Immediate medical intervention required to prevent death
Grade 5	Death



7.11 Potential Severity of Transfusion Errors

Potential severity is a measure of the harm that the error may cause to the patient if the error is **NOT** detected. High severity level is assigned to errors that have potential to cause serious injury (including fatal outcome), whereas low and medium severity levels are assigned to errors with potential to cause no or minor/transient injury, respectively.

Table 6 Potential Severity of Transfusion Errors (adapted from TESS Report (11))

TYPE OF ERROR	DESCRIPTION
Product Request	Order for wrong patient Sample labelled with wrong patient identification Not labelled Wrong patient collected (not from intended patient)
Sample Collection	Label incomplete/illegible for key patient identifiers (e.g., name, identification, birthdate) Armband incorrect/not available
Sample Handling	Paperwork and sample ID do not match
Sample Receipt	Sample accepted in error
Sample Testing	Sample labelled with incorrect accession label Sample/test tubes mixed up/mislabeled
Request for Pick-Up	Request for pick-up on wrong patient
Unit Issue	Product issued to wrong patient LIS warning overridden (in error or outside SOP) Wrong type/dose of product issued to right patient
Unit Transfusion	Administered product to wrong patient Administered wrong type/dose of product to patient
Miscellaneous	Patient registration incomplete/incorrect



8. Data Management and Use of Haemovigilance Data

A successful national haemovigilance programme requires an effective data management system with clearly documented definitions, policies and procedures as well as defined roles and responsibilities. A comprehensive data collection network should be established to ensure data can be collected from all Transfusing facilities. The type of information collected should be scalable; to allow the scope and the level of detail to be extended as the system matures. A stable and secure database is required for receipt, management and analysis of reports. A computer-based system is ideal; however, a simple but accurate reporting and analysis of manually collected data is equally effective. Both methods of data collection should ensure collection of the same quality of data. Furthermore, it is fundamental to have effective traceability. Haemovigilance data received from blood establishments and Transfusing facilities shall be retained for at least 10 years in an appropriate and readable storage medium in order to ensure traceability.

Reports should be scrutinized to ensure that they are correctly categorized, and that all relevant information has been documented, such as results of laboratory investigations in the case of adverse reactions, or root cause analysis of errors. This may require dialogue between the national haemovigilance officers and the reporter.

- a) A national haemovigilance data management system requires the following:
 - i. confidentiality and anonymity for donors and patients.
 - ii. data security and compliance with applicable regulations on data protection.
 - iii. minimal impact of data collection on the working methods of the transfusing facility or health care system.
 - iv. expert and non-judgemental advice and guidance on investigation, management, reporting and follow-up of adverse events.
 - v. expert analysis of events and trends and provision of clear recommendations for improvement.
- b) A critical process in haemovigilance is the flow of data between the local (including institutional), regional, and national levels as illustrated in Figure 2. The rigorous and transparent management of information generated through this system has a key role in introducing amendments in blood policies and guidelines that lead to improvements in processes and practices in donation and transfusion.



8.1 Privacy and Security of Data

Adverse event reports to the national system should not include information that could identify the patient or donor but should include a unique identifier enabling the national haemovigilance officers to request further details if necessary. Any database of haemovigilance reports must operate in compliance with applicable regulations on the confidentiality of individual recipient and donor data.

No patient or donor will be identified in the data sent by transfusing facilities or blood establishments to the ZAMRA and/or ZNBTS (NHO). The identities of the reporters and institutions are never revealed to third parties.

8.2 Data Storage

A reliable system for information storage with an appropriate backup system should be in place to retain reports for traceability purposes. The system should be qualified to store data over long periods. The storage period for certain reports and data should be according to national requirements. See also **chapter 6. Traceability**. The system must meet national security standards for confidential data.

8.3 Data analysis

Haemovigilance data received from all over the national territory shall be analysed centrally by ZNBTS (NHO) and ZAMRA. Data on adverse events including transfusion reactions reported through the reporting system shall be analysed with regard to the following parameters:

a) For transfusion reactions:

- i. Type of blood component transfused
- ii. Type of transfusion reactions
- iii. Clinical diagnosis of the patient, age, and gender
- iv. Seroprevalence of transfusion-transmitted infections
- v. First time or repeat transfusion
- vi. Clinical outcome
- vii. Imputability assessment

b) For donor reactions:

- i. Type of donation
- ii. Type of reaction



- iii. First time or repeat donation
 - iv. Outcome
 - v. Imputability assessment
- c) For other AEs Collection Testing (donations)
- i. Processing
 - ii. Storage
 - iii. Distribution
 - iv. Materials
 - v. Near-misses

Specifications for the above-mentioned topics:

- a. Product defect
- b. Equipment failure
- c. Human error

A panel of experts at ZAMRA and ZNBTS (NHO) will be entrusted with the following defined responsibilities regarding analysis of data:

- a. Review quality and completeness of data.
- b. Collation and analysis of information from the adverse events data submitted.
- c. Define bio-statistical methods to be used for the analysis.
- d. Create standardized post analytical reports that will help understand the information that is derived from adverse reaction data.
- e. Make evidence-based recommendations and devise formats and guidance documents for follow-up actions after implementation of recommendations.

8.4 Examples of practical considerations for haemovigilance data analysis

Annex V gives examples of practical considerations for haemovigilance data analysis. These include:

- i. Assessing the probability that an adverse event will occur
- ii. Vigilance for patients (recipients)
- iii. Vigilance for donors



9. Feedback on reported Adverse Reactions and Adverse Events

Haemovigilance data should be analysed centrally by ZAMRA and the ZNBTS (NHO) and an aggregate feedback report should be compiled and distributed to all the relevant stakeholders. The feedback report should include recommendations for implementation of corrective and preventive actions (this could be by transfusing facilities, blood establishments, ministry responsible for health or other relevant stakeholders) and it should be issued **no later than fourteen (14) days for defined emergencies and ninety (90) days for all other reports**, to ensure effective use of the data to improve practice and to encourage submission of data. Generic template reporting forms listed in Annex II and attached to this guideline provide a resource to assist in designing the national feedback report.

Benchmarking and comparison of haemovigilance data between transfusing facilities, blood establishments and even countries require reliable and correct denominator data. **(1)**

10. Annual Haemovigilance Reports

The Annual Haemovigilance Report is published each year by ZAMRA in collaboration with the ZNBTS (NHO). The report contains information including but not limited to:

- a) Blood and blood component production and usage statistics.
- b) Analysis of reported adverse reactions (donor + recipient) and events
 - i. Reporting denominator for AEs - total units (blood + blood components) processed.
 - ii. Reporting denominators for ARs - units issued, units transfused, recipients transfused.
- c) Bacterial monitoring of platelet concentrates.
- d) Donor infectious disease testing.
- e) Adverse events associated with blood donation.
- f) Trends in blood and blood component transfusion.
- g) Recipients of blood and blood component transfusions (i.e., gender, age).

Documented feedback on reported AEs and ARs can be made via email or post or via any agreed national shared haemovigilance database used in Zambia.



11. Rapid Alert Systems

The haemovigilance system in Zambia includes a Rapid Alert System (RAS), which is an early warning mechanism for the rapid dissemination of information on important events, emerging hazards or trends. This system is not a replacement for urgent notifications to the blood establishment, but it is an information channel enabling rapid diffusion of important information concerning emerging threats of whatever kind. It typically works via telephone, WhatsApp, e-mail and in advanced settings, a protected website. Quick transmission of information potentially important for the safety, quality and efficacy in a structured predefined way is needed to inform actors in the transfusion chain.

The main objective of a RAS is to enable the taking of corrective actions in the shortest period of time. RAS in haemovigilance are used to signal the appearance of clusters of clinical signals after transfusion. A good RAS permits quick and safe transmission of correct and precise data to quality assurance responsible persons in blood transfusion centres and to competent authorities, allowing a decision on possible action(s) in order to maintain or improve safety in blood transfusion.

In principle, the three types of rapid alert systems are:

- a) **Quality and Safety Defects** are understood as alerts requiring field corrective and preventive actions (e.g. recall, quarantine, discard, etc.) for the blood or blood components that might impact patient safety after collection, preparation, and during usage of these products.
- b) **Information Notices** are defined as alerts related to field corrective actions performed in the medical device sector, medicinal products sector or other sector(s), which are of relevance to the blood and blood components sector.
- c) **Epidemiological Notices** are alerts related to important epidemiological developments (e.g. disease outbreaks) which may have cross-border implications in the field of blood donation and transfusion.

Because of the importance of the message and the preciseness of the information to prevent unnecessary and unjustified actions, several practical aspects should be considered.



a) Before using the Rapid Alert System:

- i. The pertinent information has to be brought to an official qualified person (e.g. a blood safety officer);
- ii. The information has to be checked to be correct, and as far as possible complete, in case a manufacturer of a device is implicated, written information and/or confirmation should be requested from the manufacturer.

NB: An emphasis should be placed on avoidance of transmitting unverified information.

b) Using the Rapid Alert System:

- i. An Alert Report Form should be used;
- ii. The requested information should be filled in with special care to lot and batch numbers (medical devices), and other reference numbers needed for traceability, actions considered, suggested, or requested should be described;
- iii. Additional information should be attached, such as written information and/or confirmation from the manufacturer;
- iv. The information should be dispatched in an authorised predefined way to reach the department responsible for blood safety at ZAMRA.

c) After using the Rapid Alert System:

- i. Investigations on the adverse event should continue; additional information should be dispatched concerning outcome, impact, consequences, etc.;
- ii. where applicable, reactions from other informed parties like expert committees, blood establishments from other countries should be collected, compiled and disseminated in order to ensure an overview of actions taken and the follow-up thereafter.



12. Training and Capacity Building

Successful National Haemovigilance Systems demonstrate some common characteristics including education and training. All personnel involved in the blood transfusion chain, from the blood transfusion service, the hospital blood bank through to the clinical areas, should be trained in safe handling and administration of blood products and in haemovigilance. National coordination of training and standardization of forms, procedures, reports and educational materials is necessary, as this will be cost-effective and will help ensure a consistent approach to haemovigilance at the national level.

Staff training, education and competence assessment are the responsibility of ZAMRA, ZNBTS HQ, PBC and transfusing facilities. ZAMRA and ZNBTS shall organize haemovigilance trainings regularly. All relevant stakeholders involved in the transfusion chain should be trained and documentation of training should be kept. Training should include the general principles of haemovigilance, its objectives and benefits, and individual roles and responsibilities. At all levels, trainings shall be regularly updated in response to haemovigilance reports and practice guidelines to ensure improvements to the practice.

Training and capacity building is a continuous process that should include:

- a) role-specific training for all staff involved in the transfusion chain and for management of donor and patient complications availability of current standard operating procedures and practice guidelines
- b) documentation of training
- c) competency assessment

Education and training activities shall include:

- a) Pre-service training of responsible stakeholders in:
 - i. appropriate prescribing
 - ii. safe bedside procedures, correct patient identification and pre-transfusion sampling and labelling
 - iii. safe administration of blood and blood products
 - iv. recognising, investigating and managing adverse reactions and events in patients or donors



- v. quality data collection and processing
 - vi. the practice of haemovigilance in general
- b) In-service training in good working practices, including an understanding of quality systems and the need to follow standard operating procedures
- c) Haemovigilance-specific training that ensures a good understanding of:
- i. the rationale and concept of haemovigilance
 - ii. the national haemovigilance programme
 - iii. detecting, recognizing, investigating and reporting adverse events
 - iv. conducting root cause analysis
 - v. applying corrective and preventive actions to improve practice
- d) Addressing common concerns arising from the practice of haemovigilance e.g. barriers to reporting adverse events and communication-related issues.
- e) Specific trainings for staff with lead or coordination roles in haemovigilance since they require more, such individuals will require a broad knowledge of evidence-based transfusion practices and technical skills related to transfusion safety, together with leadership qualities, effective communication and teaching skills, and ability to influence practice and effect change. Further skills needed by staff in lead positions will include:
- i. developing tools for data collection
 - ii. characterizing adverse events
 - iii. verifying reports
 - iv. advising on investigation and root cause analysis of events
 - v. analysing and managing data
 - vi. producing annual feedback reports and educational material
 - vii. liaising with professional groups and stakeholder organizations
- f) Regular competence assessments carried out and documented to ensure that staff retain the necessary skills and knowledge for their specific roles in the transfusion chain.

All training materials developed by ZAMRA and/or ZNBTS HQ (NHO) will be made available to all relevant stakeholders.



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Annex I – Adverse Event Definitions

The following information is based on the ‘Proposed Standard Definitions for Surveillance of Non-Infectious Adverse Transfusion Reactions’ from ISBT (5). Additional events were adopted from the Western Australia Haemovigilance Reporting Guideline (7) and the “Standard for Surveillance of Complications Related to Blood Donation” from the ISBT, AABB IHN (10). The dataset of reportable adverse events for haemovigilance reporting is as follows:

Hemolytic Transfusion Reactions (ISBT)

AE TYPE	DEFINITION
Acute hemolytic transfusion reaction (AHTR)	An AHTR has its onset within 24 hours of a transfusion. Clinical or laboratory features of hemolysis are present. Common signs of AHTR are: – Fever – Chills/rigors – Facial flushing – Chest pain – Abdominal pain – Back/flank pain – Nausea/vomiting – Diarrhea – Hypotension – Pallor – Jaundice – Oligoanuria – Diffuse bleeding – Dark urine Common laboratory features are: – Hemoglobinemia – Hemoglobinuria – Decreased serum haptoglobin – Unconjugated hyperbilirubinemia – Increased LDH and AST levels – Decreased hemoglobin levels Not all clinical or laboratory features are present in cases of AHTR. Blood group serology usually shows abnormal results but absence of immunological findings does not exclude AHTR. AHTR may also be due to erythrocyte auto-antibodies



AE TYPE	DEFINITION
	in the recipient or to non immunological factors like mechanical factors inducing hemolysis (malfunction of a pump, of a blood warmer, use of hypotonic solutions, etc.).
Delayed hemolytic transfusion reaction (DHTR)	A DHTR usually manifests between 24 hours and 28 days after a transfusion and clinical or laboratory features of hemolysis are present. Signs and symptoms are similar to AHTR but are usually less severe. DHTR may sometimes manifests as an inadequate rise of post-transfusion hemoglobin level or unexplained fall in hemoglobin after a transfusion. Blood group serology usually shows abnormal results.
Delayed serologic reaction (DSTR)	There is a DSTR when, after a transfusion, there is demonstration of clinically significant antibodies against red blood cells which were previously absent (as far as is known) and when there are no clinical or laboratory features of hemolysis. This term is synonymous with alloimmunization.

Non-Hemolytic Transfusion Reactions (ISBT)

AE TYPE	DEFINITION
Febrile non hemolytic transfusion reaction (FNHTR)	There is a FNHTR in the presence of one or more of: – fever ($\geq 38.0^{\circ}\text{C}$ oral or equivalent and a change of $\geq 1.0^{\circ}\text{C}$ from pre-transfusion value), – chills/rigors This may be accompanied by headache and nausea. occurring during or within four hours following transfusion without any other cause such as hemolytic transfusion reaction, bacterial contamination or underlying condition. FNHTR could be present in absence of fever (if chills or rigors without fever). For the purpose of international comparison only the most serious cases of FNHTR should be accounted for: – fever ($\geq 39^{\circ}\text{C}$ oral or equivalent and a change of $\geq 2^{\circ}\text{C}$ from pre-transfusion value) and chills/rigors
Allergic reaction	An allergic reaction may present only with mucocutaneous signs and symptoms: – Morbilliform rash with pruritus – Urticaria (hives) – Localized angioedema – Edema of lips, tongue and uvula – Periorbital pruritus, erythema and edema



AE TYPE	DEFINITION
	– Conjunctival edema occurring during or within 4 hours of transfusion. In this form it usually presents no immediate risk to life of patient and responds quickly to symptomatic treatment like antihistamine or steroid medications. This type of allergic reaction is called ‘minor allergic reaction’ in many haemovigilance systems. For the purpose of classification this type of allergic reaction would be graded as 1, i.e. non-severe. An allergic reaction can also involve respiratory and/or cardiovascular systems and present like an anaphylactic reaction. There is anaphylaxis when, in addition to mucocutaneous systems there is airway compromise or severe hypotension requiring vasopressor treatment (or associated symptoms like hypotonia, syncope). The respiratory signs and symptoms may be laryngeal (tightness in the throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing/bronchospasm, hypoxemia). Such a reaction usually occurs occurring during or very shortly after transfusion. For the purpose of classification this type of allergic reaction would be graded as 2 (severe), 3 (life-threatening) or 4 (death) depending on the course and outcome of the reaction. An allergic reaction classically results from the interaction of an allergen and preformed antibodies. A rise of mast cell tryptase can support the diagnosis of an allergic reaction. IgA deficiency and/or anti-IgA in the recipient has been associated with severe allergic reactions but is only one infrequent cause out of many others.
Transfusion-associated graft-versus-host disease (TA-GVHD)	TA-GVHD is a clinical syndrome characterised by symptoms of fever, rash, liver dysfunction, diarrhoea, pancytopenia and findings of characteristic histological appearances on biopsy occurring 1-6 weeks following transfusion with no other apparent cause. The diagnosis of TA-GVHD is further supported by the presence of chimerism.
Post transfusion purpura (PTP)	PTP is characterized by thrombocytopenia arising 5-12 days following transfusion of cellular blood components with findings of antibodies in the patient directed against the Human Platelet Antigen (HPA) system.
Transfusion-related acute lung injury (TRALI)	In patients with no evidence of acute lung injury (ALI) prior to transfusion, TRALI is diagnosed if a new ALI is present (all five criteria should be met): – Acute-onset – Hypoxemia ○ $PaO_2 / FiO_2 < 300$ mm Hg or



AE TYPE	DEFINITION
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	○ Oxygen saturation is < 90% on room air or ○ Other clinical evidence – Bilateral infiltrates on frontal chest radiograph – No evidence of left atrial hypertension (i.e. circulatory overload) – No temporal relationship to an alternative risk factor for ALI, during or within 6 hours of completion of transfusion. Alternate risk factors for ALI are: – Direct Lung Injury ○ Aspiration ○ Pneumonia ○ Toxic inhalation ○ Lung contusion ○ Near drowning – Indirect Lung Injury ○ Severe sepsis ○ Shock ○ Multiple trauma ○ Burn injury ○ Acute pancreatitis ○ Cardiopulmonary bypass ○ Drug overdose It has been suggested by the Toronto TRALI Consensus Panel to add a category of possible TRALI that would have the same definition as TRALI except for the presence of a temporal relationship to an alternative risk factor for ALI (as described above). In such a circumstance TRALI should be indicated with a possible imputability to transfusion. TRALI is therefore a clinical syndrome and neither presence of anti-HLA or anti-HNA antibodies in donor(s) nor confirmation of cognate antigens in recipient is required for diagnosis
Transfusion-associated dyspnea (TAD)	TAD is characterized by respiratory distress within 24 hours of transfusion that does not meet the criteria of TRALI, TACO, or allergic reaction. Respiratory distress should be the most prominent clinical feature and should not be explained by the patient's underlying condition or any other known cause.
Transfusion-associated circulatory	TACO is characterized by any 4 of the following: – Acute respiratory distress – Tachycardia



AE TYPE	DEFINITION
overload (TACO)	– Increased blood pressure – Acute or worsening pulmonary edema on frontal chest radiograph – Evidence of positive fluid balance occurring within 6 hours of completion of transfusion. An elevated BNP is supportive of TACO.
Hypotensive transfusion reaction	This reaction is characterized by hypotension defined as a drop in systolic blood pressure of ≥ 30 mm Hg occurring during or within one hour of completing transfusion and a systolic blood pressure ≤ 80 mm Hg. Most reactions do occur very rapidly after the start of the transfusion (within minutes). This reaction responds rapidly to cessation of transfusion and supportive treatment. This type of reaction appears to occur more frequently in patients on ACE inhibitors. Hypotension is usually the sole manifestation but facial flushing and gastrointestinal symptoms may occur. All other categories of adverse reactions presenting with hypotension, especially allergic reactions, must have been excluded. The underlying condition of the patient must also have been excluded as a possible explanation for the hypotension.
Other transfusion reactions	a) Haemosiderosis Transfusion-associated haemosiderosis is being defined as a blood ferritin level of ≥ 1000 micrograms/l, with or without organ dysfunction in the setting of repeated RBC transfusions. b) Hyperkalemia Any abnormally high potassium level (> 5 mmol/l, or ≥ 1.5 mmol/l net increase) within an hour of transfusion can be classified as a transfusion- associated hyperkalemia. c) Unclassifiable Complication of Transfusion (UCT) Occurrence of an adverse effect or reaction temporally related to transfusion, which cannot be classified according to an already defined ATE and with no risk factor other than transfusion and no other explaining cause.



Other Transfusion Related Adverse Events and Transfusion Reactions (from WA Haemovigilance Reporting Guideline (7) and Swissmedic Haemovigilance Annual Report 2020 (12))

AE TYPE	DEFINITION (FROM ISBT)
Incorrect blood component transfused (IBCT)	All reported episodes where a patient was transfused with a blood component that did not meet the appropriate requirements or that was intended for another patient. Include even if any of the following apply: – the component was ABO compatible (e.g. an immune compromised patient requires irradiated cellular products but receives non- irradiated blood instead) – only a small quantity of blood was transfused and/or – there was no adverse reaction Further examples: – WBT (Wrong Component Transfused e.g. non-allo-antibody-compatible blood product, HLA-incompatible, wrong product, transfusion of avoidable untested O negative blood products etc.), – SRNM (Specific requirements not met e.g. non-irradiated/non-washed blood products, phenotype not observed, SOP not followed etc.), – HSE (Handling and storage errors) e.g. wrong equipment used, transfusion after expiry of type and screen validity, incorrect storage of blood product etc, – ADU (Avoidable, delayed or under-/over-transfusion) e.g. transfusion volume not adapted, delayed transfusion, transfusion rate not adapted etc., RBRP (Right blood right Patient e.g. incorrect blood product ID
Anaphylactoid or anaphylactic reaction	An allergic reaction can also involve respiratory and/or cardiovascular systems and present like an anaphylactic reaction. There is anaphylactic reaction when, in addition to mucocutaneous symptoms, there is airway compromise or severe hypotension requiring vasopressor treatment (or associated symptoms like hypotonia, syncope). The respiratory signs and symptoms may be laryngeal (tightness in the throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnoea, cough, wheezing/ bronchospasm, hypoxemia). Such a reaction usually occurs occurring during or very shortly after transfusion.
ABO incompatibility	All cases where a blood component was transfused which was ABO incompatible. Include all such events even if: – only a small quantity of blood was transfused, and/or – no adverse reaction occurred



AE TYPE	DEFINITION (FROM ISBT)
	All cases are to be included, whether the first error occurred in Lifeblood, the hospital transfusion laboratory or in clinical areas. Note that these events are a subgroup of the IBCT category. Transfusion of ABO incompatible products to a patient is considered a 'sentinel event' and is also subject to other reporting channels outside of local and National Haemovigilance Programs.
Near Misses	Deviation discovered before the transfusion has taken place Discrepancies relating to patient identification, sample tubes or the prescribing of blood products Examples of Near Misses: - Order form not initialled - Sample tubes not labelled correctly or order form incomplete - Minor discrepancy between tubes and order form - Another patient's date of birth - Labels missing from sample tubes - Handling & storage with products discarded - Wrong sample tubes retrieved - Different patient identification on sample tubes/form - Blood taken from wrong patient and only discovered because of discrepancy in blood group / wrong blood in tube (WBIT) - Blood product orders for the wrong patient - Wrong blood product ordered Blood products ordered on the basis of haemoglobin, platelet or coagulation values that are wrong due to pre-analytical factors
Transfusion transmitted infection (TTI)	The recipient had evidence of infection following transfusion of blood components and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection. Transfusion transmitted bacterial infection Transfusion transmitted bacterial infection should be clinically suspected if: - fever $>39^{\circ}\text{C}$ or a change of $>2^{\circ}\text{C}$ from pre-transfusion value and - rigors and



AE TYPE	DEFINITION (FROM ISBT)
	- tachycardia >120 beats/min or a change of >40 beats/min from pre- transfusion value or a rise or drop of 30mmHg in systolic blood pressure within 4 hours of transfusion are present <u>Possible transfusion transmitted bacterial infection:</u> - detection of bacteria by approved techniques in the transfused blood component but not in the recipient's blood or - detection of bacteria in the recipient's blood following transfusion but not in the transfused blood component and no other reasons are ascertainable for the positive blood culture. <u>Confirmed transfusion transmitted bacterial infection:</u> - detection of the same bacterial strain in the recipient's blood and in the transfused blood product by approved techniques. Transfusion transmitted viral infection Following investigation, the recipient has evidence of infection post transfusion and no clinical or laboratory evidence of infection prior to transfusion and either, at least one component received by the infected recipient was donated by a donor who had evidence of the same infection, or, at least one component received by the infected recipient was shown to have been contaminated with the virus. Reports should at least consider HIV, Hepatitis B, Hepatitis C and Cytomegalovirus. Transfusion transmitted parasitic infection Detection of the same parasite in the recipient's blood and parasite or specific antibodies in the donor blood.
Wrong Blood In-Tube (WBIT)	WBIT means that the patient identification on the tube and order form does not match the patient whose blood is in the tube

Classification of Other Adverse Events as per Activity Steps and Specification – Blood Establishment (European Commission SARE report 2019 (13))

ACTIVITY STEPS	SPECIFICATIONS OF AEs
- Donor Selection - Whole Blood Collection - Apheresis Collection - Testing Of Donations - Processing	- Detection of blood borne infection in a blood donor - Safety risks for blood donors (incidents that pose a threat to the health of blood donors) - Component Defect - Equipment Failure



ACTIVITY STEPS

SPECIFICATIONS OF AEs

– Issue – Compatibility Testing/ Cross-Matching – Storage – Distribution/Transport – Other Activity Step (Please Specify)	– Human Error: e.g. donor and donation mix-ups, incorrect release, incorrect labels, release of out-of-specification blood products, incorrect testing, incorrect packaging of product for transport, transport delayed / sent to wrong location, recall process not / incorrectly followed, order incompletely / incorrectly filled, Look-back / trace-back issues etc. – Materials: e.g. suspected quality defects, defective materials, reagents) – Other
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Donor Adverse Events

The ISBT Working Group on Donor Vigilance has published together with the AABB Donor Haemovigilance Working Group and the International Haemovigilance Network, a Standard for Surveillance of Complications Related to Blood Donation (10). Below is a list of possible complications related to blood donations (10).

AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
A. Complications mainly with local symptoms These complications are directly caused by the insertion of the needle. Some of these are mainly characterized by occurrence of blood outside vessels, whereas others are mainly characterized by pain.	A1. Complications mainly characterized by the occurrence of blood outside the vessels.	Haematoma (bruise) <u>Definition:</u> a haematoma is an accumulation of blood in the tissues outside the vessels. <u>Mechanism:</u> the symptoms are caused by blood flowing out of damaged vessels and accumulating in the soft tissues. For apheresis procedures, haematomas may also be caused by infiltration of the soft tissues by red cells during the return phase of the procedure. Large haematomas, particularly those in deeper layers of the forearm, put pressure on surrounding tissues and may contribute to other complications such as nerve irritation and injury and more rarely compartment syndrome. <u>Signs and symptoms:</u> bruising, discolouration, swelling and local pain. Accumulation of blood in deeper tissues may result in more serious pain and pressure syndromes listed below. Arterial puncture <u>Definition:</u> arterial puncture is a puncture of the brachial artery or of one of its branches by the needle used for bleeding the donor.



AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
		<u>Mechanism</u>: because of the rapid blood flow, the risk of a large haematoma is increased and thereby risks of more serious pain and pressure syndromes listed below. <u>Signs and symptoms</u>: a lighter red colour than usual of the collected blood can be seen. The needle and tubing may appear to pulsate; the blood bag fills very quickly. There may be weak pain localized to the elbow region. Delayed bleeding (re-bleeding) - optional category <u>Definition</u>: leakage of blood from the venipuncture site after the initial bleeding has stopped. <u>Mechanism</u>: re-bleeding may be related to pressure not being applied to the correct location or for an adequate duration, or premature removal of the bandage. After the donor has left the clinic, re-bleeding may be related to heavy lifting or strain to the donor's arm. Donors on certain medications, such as autologous donors on anticoagulants, may be at higher risk to re-bleed. <u>Signs and symptoms</u>: spontaneous recommencement of bleeding from the venipuncture site, after pressure has been applied and the initial dressing has been removed, or leaking through the dressing.
	A2. Complications mainly characterized by pain	Nerve injury/irritation <u>Definition</u>: injury or irritation of a nerve <u>Mechanism</u>: a nerve may be hit directly by the needle at insertion or withdrawal, or there may be pressure on a nerve due to a haematoma or inflammation of the soft tissues. Include medically diagnosed cases, as well as cases reported on the basis of documented 'nerve' type symptoms. <u>Signs and symptoms</u>: radiating, often 'electrical' sharp pain moving away from the venepuncture site, and/or paraesthesias such as tingling, burning sensations in the hand, wrist or shoulder area but away from the venepuncture site. Symptoms may arise immediately when the needle is inserted or withdrawn. In cases associated with a haematoma, pain may not be apparent at the time and may start when the haematoma has reached a sufficient size, some time after insertion of the needle. Symptoms may be



AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
		worse in certain positions or with certain arm motions. Rarely, weakness of the arm may develop. <i>Optional split by duration of symptoms:</i> <i>Symptoms resolving within 12 months: symptoms usually resolve within days, but rarely may persist for months or become permanent.</i> <i>Symptoms lasting more than 12 months.</i> Other painful arm – optional category <u>Definition:</u> pain in the arm is the primary symptom, without the characteristics of nerve irritation outlined above, or the presence of a large hematoma or other defined complications that may be painful. <u>Mechanism:</u> pain may be related to tissue injury, possibly due to hematoma in the deeper tissues. <u>Signs and symptoms:</u> pain in the arm, without characteristics of nerve irritation. May be described as an ache or heaviness in the arm, similar to that experienced after vaccination. Include all cases where arm pain is the main symptom, unless a diagnosis of nerve injury/irritation is suspected in the presence of nerve type symptoms recognised by trained staff.
	A 3. Localised infection/inflammation	Localised infection/inflammation <u>Definition:</u> inflammation along the course of a vein, which may progress to localised infection several days after phlebotomy. There may be clotting in the vein. <u>Mechanism:</u> tissue damage and introduction of surface bacteria into the deeper tissues with venepuncture. The superficial vein itself (thrombophlebitis) or the surrounding subcutaneous tissue (cellulitis) may be predominantly affected. <u>Signs and symptoms:</u> warmth, tenderness, local pain, redness and swelling at the site of phlebotomy. The site and the vein may feel tender, firm, and warm to the touch. Fever may be present. <i>Optional split into 2 categories:</i> <i>Thrombophlebitis: the redness, swelling, and tenderness extend along the course of the vein.</i> <i>Cellulitis: the redness, swelling and tenderness affect the soft tissues, and are not localised to the course of the vein.</i>



AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
	A4. Other major blood vessel injury.	Deep Venous Thrombosis (DVT) <u>Definition:</u> thrombosis of a deep vein in the donor's phlebotomy arm. <u>Mechanism:</u> superficial venous thrombosis may progress into the deeper veins of the donor's arm. DVT may also rarely occur without previous signs and symptoms of superficial thrombosis. An additional risk factor for thrombosis, in particular, the use of oral contraceptives, may be present in these donors. <u>Symptoms and signs:</u> swelling and pain in the upper arm. May be accompanied by symptoms of superficial inflammation and thrombosis (see above).
		Arteriovenous fistula <u>Definition:</u> acquired connection between the vein and artery due to venepuncture lacerations. <u>Mechanism:</u> a channel forms between the lacerated vein and artery immediately post-venepuncture, or in the healing process. May be related to arterial puncture. <u>Signs and symptoms:</u> pulsating mass with a palpable thrill and associated bruit. The affected area may be warm, and the distal part of the arm may be cool if significant shunting of blood is present. The distal veins may be dilated and may pulsate
		Compartment syndrome <u>Definition:</u> increased intracompartment pressure leading to muscle and soft tissue necrosis. <u>Mechanism:</u> blood may accumulate in the frontal deep areas of the forearm, closing small blood vessels and resulting in muscle and nerve tissue necrosis. May be related to arterial puncture. <u>Signs and symptoms:</u> painful arm, particularly on movement; swelling, paresthesias and partial paralysis.
		Brachial artery pseudoaneurysm <u>Definition:</u> collection of blood outside an artery, contained by adventitia or the surrounding tissues alone. <u>Mechanism:</u> after a traumatic arterial puncture, blood may leak out of the artery and accumulate in the surrounding space.



AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
B. Complications mainly with generalized symptoms: vasovagal reactions	/	<u>Signs and symptoms:</u> pulsating mass in the arm. May be accompanied by pain and paraesthesias. May be preceded by a large hematoma following arterial puncture Vasovagal reaction <u>Definition:</u> a vasovagal reaction (VVR) is a general feeling of discomfort and weakness with anxiety, dizziness and nausea, which may progress to loss of consciousness (faint). It is the most common acute complication related to blood donation. <u>Mechanisms:</u> both physiologic and psychological factors may be important. The reaction is generated by the autonomic nervous system and further stimulated by psychological factors and the volume of blood removed, relative to the donor's total blood volume. <u>Signs and symptoms:</u> usually several of the following: discomfort, weakness, anxiety, light-headedness/dizziness, nausea, chills, sweating, vomiting, pallor, hyperventilation, rapid or a slow pulse. Hypotension and loss of consciousness (LOC) may occur and can be accompanied by loss of bladder or bowel control or convulsive movements. Reactions may occur before phlebotomy (rare), during phlebotomy or immediately after phlebotomy, when the donor stands up, in the refreshment area, or after the donor has left the collection site. Most reactions occur within 12 hours of phlebotomy. Reactions accompanied by LOC carry a risk of injury, particularly if they occur once the donor has left the collection site (delayed vasovagal reactions). Vasovagal reactions are divided in two main subgroups: - Without loss of consciousness (LOC) - the donor does not faint - With loss of consciousness (LOC) - the donor faints for a period of time Optional subdivision for donors with LOC: LOC < 60 seconds - without other signs and symptoms LOC ≥ 60 seconds - or with complications of convulsive movements, urinary or faecal incontinence



AE SUB-CATEGORY		AE TYPE AND DEFINITION
C. Complications related to apheresis	/	Optional subdivision: With injury - injury caused by falls or accidents in donors with a vasovagal reaction without injury Optional subdivision: Location of reaction: – On collection facility*- symptoms occurred before donor has left the donation site – Outside collection facility - symptoms occurred after donor has left the donation site *in area within which staff can observe the donor and be responsible for the care of donors with complications
		Citrate reaction <u>Definition:</u> neuromuscular hyperactivity related to reduced ionized calcium levels. <u>Mechanism:</u> infusion of citrate anticoagulant during apheresis causes a fall in ionised calcium levels, leading to neuromuscular hyperactivity. If untreated, symptoms may progress to tetany and severe cardiac arrhythmias, including cardiac arrest. Operator error with mix up of saline and citrate bags may occur with some apheresis equipment, and lead to rapid citrate infusion. <u>Symptoms and signs:</u> numbness or tingling of lips, feelings of vibrations, numbness or tingling in the fingers, metallic taste, chills, shivering, light-headedness, feeling of tightness, muscle twitching, rapid or slow pulse, shortness of breath. Symptoms may progress to carpopedal spasms and vomiting, and in severe reactions, to generalised muscle contractions (tetany), shock, irregular pulse and cardiac arrest. Haemolysis <u>Definition:</u> donor red cells may be damaged, releasing haemoglobin. <u>Mechanism:</u> there may be malfunctioning valves, kinks or obstruction of the tubing, incorrect installation of equipment, or other equipment failures affecting the extracorporeal circuit.



AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
		Incompatible replacement fluids, such as 5% Dextrose , may be used in error. <u>Signs and symptoms:</u> pink or red plasma, blood in lines or filter may appear dark. The donor may notice pink or red urine after collection. Air embolism <u>Definition:</u> air bubble introduced into the donor's circulation. <u>Mechanism:</u> air may enter into the lines due to incomplete priming of lines, as a result of a machine malfunction or defective collection kits or through incorrect manipulation by staff. Air in the donor's pulmonary circulation may occlude the pulmonary arteries in the lung and cause cardiopulmonary symptoms. Air may pass to the arterial circulation through an atrial septal defect, and reduce blood flow to the brain. <u>Signs and symptoms:</u> bubbling sound or feeling at the venipuncture site. Cough, dyspnea, apprehension, sweating, chest pain, confusion, tachycardia, hypotension, nausea and vomiting. Optional category: infiltration <u>Definition:</u> intravenous solute (saline solution) enters the extravascular tissues during volume replacement (generally only applicable to double red cell procedures). <u>Mechanism:</u> the needle is no longer positioned in the intravascular space, so fluids enter the surrounding tissues. <u>Signs and symptoms:</u> swelling of the tissues at the venipuncture site.
D. Allergic reactions	/	Allergy (local) <u>Definition:</u> red or irritated skin at the venipuncture site. <u>Mechanism:</u> reaction caused by allergens or irritants in solutions used for disinfection of the arm (such as iodine or chlorhexidine) or in manufacture of the collection set. Irritation may also occur due to application of the adhesive bandage (bandage adhesive dermatitis). An allergic reaction to latex that may be in supplies such as gloves may also occur. <u>Signs and symptoms:</u> itching and redness at the venepuncture site, the bandage site, or the entire skin disinfection area. In a true



AE CATEGORY	AE SUB-CATEGORY	AE TYPE AND DEFINITION
E. Other serious complications related to blood donation	/	allergic reaction, there may be a raised rash or hives in these areas that may expand to cover a larger area of the arm. The reaction may occur soon after donation or in the hours to days post-donation.
		Generalised allergic reaction (anaphylactic reaction) <u>Definition:</u> anaphylactic type reactions usually starting soon after the procedure is begun and may progress rapidly to cardiac arrest. <u>Mechanism:</u> extremely rare reactions, attributed to donor sensitivity to ethylene oxide gas used to sterilize some collection kits.
E. Other serious complications related to blood donation	/	<u>Signs and symptoms:</u> apprehension, anxiousness, flushing, swelling of eyes, lips or tongue, cyanosis, cough, wheezing, dyspnea, chest tightness, cramps, nausea, vomiting, diarrhoea, tachycardia, hypotension, and altered mentation Major Cardiovascular Event (MCE) Acute cardiac symptoms (other than myocardial infarction or cardiac arrest). Myocardial infarction Cardiac arrest Transient ischemic attack Cerebrovascular accident Death
		Reporting is encouraged of MCE or death from any cause up to 24 hours after donation, with an assessment of imputability. Only cases with definite, probable or possible imputability should be included in international reporting. Major cardiovascular events, including death, may occur in the hours after attending the collection centre for blood donation. This can occur without any relation to the donation (for deaths, this is described by the term Actuarial deaths).
F. Other complications	/	Other systemic reactions or complications that do not fit into the above, such as chest pain that may have been investigated as angina, but was actually musculoskeletal, or transmission of infection to a donor through erroneous re-use of equipment.



Annex II – Haemovigilance Reporting Forms

Reporting should not excessively affect the work of health care professionals, thus, reporting forms should be as brief as possible and as comprehensive as necessary for adequate assessment of cases. Providing different reporting forms fit to the event or reaction to be reported allows the form to focus on only the specific event required information and, thus, keeps forms short and reduces the risk of reporting errors such as insufficient data transmission.

Overview of the reporting forms:

	Form X	Ward Transfusion Reaction Report form
1.	Form 1a	Transfusion reaction – initial report
2.	Form 1b	Transfusion reaction – final report
3.	Form 2	Suspected TTI/Trace-back
4.	Form 3a	Donor look-back – initial report
5.	Form 3b	Donor look-back – final report
6.	Form 4	Donor reaction
7.	Form 5	Incidents (AEs – manufacture, transport, storage, handling, near-misses)
8.	Form 6	Annual blood usage statistics – Transfusing Facilities
9.	Form 7	Annual Activity Summary Report - Blood Establishment



Annex III – Example of Imputability and Severity Scoring of Adverse Reactions

Allergic Reaction (CDC - 2021 HV Module Protocol (14))

Case Definition	Severity	Imputability
Definitive: 2 or more of the following occurring during or within 4 hours of cessation of transfusion: – Conjunctival edema – Edema of lips, tongue and uvula – Erythema and edema of the periorbital area – Generalized flushing – Hypotension – Localized angioedema – Maculopapular rash – Pruritus (itching) – Respiratory distress; bronchospasm – Urticaria (hives)	Severe, Life-threatening, Death: Involves respiratory and/or cardiovascular systems and presents like an anaphylactic reaction. There is anaphylaxis when, in addition to mucocutaneous symptoms, there are airway symptoms, hypotension or associated symptoms like hypotonia and syncope. The respiratory signs and symptoms may be laryngeal (tightness in the throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing, bronchospasm, hypoxemia). Such a reaction usually occurs during or shortly after cessation of transfusion.	Definite: Occurs during or within 2 hours of cessation of transfusion AND No other evidence of environmental, drug or dietary risks.
Probable: ANY 1 of the following occurring during or within 4 hours of cessation of transfusion: – Conjunctival edema – Edema of lips, tongue and uvula – Erythema and edema of the periorbital area – Localized angioedema – Maculopapular rash – Pruritus (itching) – Urticaria (hives)	Death should be used if death is possibly, probably or definitely related to transfusion. If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction.	Probable: Occurs during or within 2 hours of cessation of transfusion AND There are other potential causes present that could explain symptoms, but transfusion is the most likely cause.
		Possible: Occurs 2 - 4 hours after cessation of transfusion OR Other present causes are most likely, but transfusion cannot be ruled out
OPTIONAL Possible: N/A	OPTIONAL Non-severe: There is no immediate risk to the life of the patient, and the patient responds quickly to symptomatic treatment.	OPTIONAL



Annex IV - Flow Chart for Reporting and Investigation of Transfusion Adverse Reactions

Transfusing ward:

- i. Suspected AR/AE identified by Nurse/Physician
- ii. Immediate management of patient and notification of Physician



Transfusing ward:

Fills out Transfusion Reaction Form X and sends along with the following to the Compatibility testing laboratory

- i. Blood bag with transfusion form attached
- ii. Post-transfusion blood samples
- iii. Sample of first urine after identification of reaction.
As necessary:
- iv. Sends blood samples to the laboratory for FBC, Coagulation screen, renal function tests, liver function tests.
- v. Sends post transfusion blood sample to Microbiology laboratory for blood culture.
- vi. Sends patient for chest x-ray.



Compatibility Testing Laboratory:

- i. Investigates transfusion reaction as per established procedures.
- ii. Reports results and inferences to the Transfusing Ward.
- iii. Submits investigation report to HV Focal Person



Haemovigilance Focal Person:

- i. Fills out Initial Report form 1a and sends to BE and ZAMRA
- ii. Consolidates reports from other departments (Transfusing Ward, Blood Bank, other laboratories, Radiology etc)
- iii. Fills out Final Report Form 1b and sends to BE and ZAMRA



Blood Establishment :

- i. Immediately forwards AR reports (either Initial 1a or Final 1b) to ZNBTS (NHO)
- ii. Investigates reactions which could possibly be caused by blood and blood componentss (e.g. suspected TRALI, bacterial contamination, improper labelling)



ZNBTS (NHO):

- i. Immediately forwards all reports of serious ARs to ZAMRA
- ii. Performs imputability assessment
- iii. Reviews, records and analyses all reports and compiles monthly/annual reports



ZAMRA:

- i. Receives, reviews and analyses all reports
- ii. Performs imputability assessment
- iii. Publishes annual report in collaboration with ZNBTS (NHO) and disseminate to



Annex V – Examples of practical considerations for haemovigilance data analysis

Assessing the probability that an adverse event will occur

It is necessary to know both the number of occasions on which the adverse event has occurred (so-called numerator data) and the number of times the associated procedure or process has occurred in total (so-called denominator data). For example, if a blood centre sends three reports of virus transmission in a year and the total volume of blood provided by that centre is 120,000 units, then the risk of transmission is 1 in 40,000. However, if the total volume of blood provided is 6000 units, the risk of transmission is 1 in 2000.

Vigilance for patients (recipients)

The ideal denominator here is the number of units of the relevant blood product transfused and the number of patients receiving the blood product. However, accurate data on products transfused may not be available and in such cases, a surrogate, such as the number of units of blood products distributed from the blood transfusion service to the hospital or issued from the hospital blood bank to the clinical area, can be used. Demographic and clinical data (e.g. sex, age, disease or indication for transfusion) for transfused patients can help identify patients at higher risk of an adverse event.

Vigilance for donors

The denominator data may be the number of donations collected or the number of times potential donors present. Adverse events may thus be expressed as, for example, number per 100,000 whole blood donations. Where possible, both adverse reactions or complications and collections should be broken down into the main collection types - whole blood donation versus apheresis, first-time donors versus repeat donors.



14. Amendment Sheet

Date identified	Amendment identified by	Short description of the changes proposed to the document	Review of proposed amendment