Irish Blood Transfusion Service
Seirbhís Fuilaistriúcháin na hÉireann

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National Haemovigilance Office

REQUIREMENTS FOR REPORTING SERIOUS ADVERSE REACTIONS AND EVENTS TO THE NATIONAL HAEMOVIGILANCE OFFICE

TITLE: REQUIREMENTS FOR REPORTING SERIOUS ADVERSE REACTIONS AND EVENTS TO THE NATIONAL HAEMOVIGILANCE OFFICE

Change description:

1. Expire BT - 0459 [1] & BT - 0566 [6] and add all required information to new IBTS/HV/CM/0001. Write new customer manual/handbook for the NHO.

Reason for change

1. CC 253/23/IBTS

Referenced Documents

IBTS/QA/POL/0007
IBTS/QA/UG/0001
IBTS/QA/UG/0002

SmartSolve Roles

HV HVO NBC	MED CON MSD IBTS
HV CO NBC	

Training Type

All Roles
Read and Understand

SmartSolve Document Category

Category	**Mobile**	**Cryobiology**	**Website**	**GDP**
Yes / No	Yes	No	Yes	No

Contents

GLOSSARY OF TERMS

AHTR:	Acute Haemolytic Transfusion Reactions	NBUG:	National Blood Users Group
BNP:	B Natriuretic Peptide	NHO:	National Haemovigilance Office
CMV:	Cytomegalovirus	PUCT:	Previously unreported (undescribed) complications of transfusion.
DAT/DCT:	Direct Antiglobulin Test / Direct Coombs Test	SAE:	Serious Adverse Event
DHTR:	Delayed Haemolytic Transfusion Reaction	SAR:	Serious Adverse Reaction
FNHTR:	Febrile Non-Haemolytic Transfusion Reaction	SD plasma:	Solvent Detergent Plasma
Hb	Haemoglobin	SHOT:	Serious Hazards of Transfusion
HBB	Hospital Blood Bank	sTTI:	Suspected Transfusion Transmitted Infection
HBV	Hepatitis B Virus	TACO:	Transfusion Associated Circulatory Overload
HCV	Hepatitis C Virus	TAD:	Transfusion Associated Dyspnoea
HDU	High Dependency Unit	TA-GVHD:	Transfusion-associated graft-versus-host disease
HIV	Human Immune Deficiency Virus	TRALI:	Transfusion Related Acute Lung Injury
HLA	Human Leucocyte Antigen	TTP:	Thrombotic Thrombocytopenic Purpura
HTLV	Human T-cell Lymphotropic Virus	Rh D:	Rhesus D
IBCT	Incorrect Blood Component/Product Transfused		
IBTS:	Irish Blood Transfusion Service		

HPRA:	Health Products Regulatory Authority			
ISBT:	International Society of Blood Transfusion			
LDH:	Lactic Dehydrogenase			

1 BACKGROUND

1.1 Legal Framework

The European Communities (Quality and Safety of Human Blood and Blood Components) Regulations 2005 Statutory Instrument (SI) No. 360 of 2005 as amended became effective for the purposes of regulation on 8 November 2005.

These regulations transpose the requirements of the following EC Legislation into national law.

Directive 2002/98/EC – setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC.

Directive 2004/33/EC – implementing Directive 2002/98/EC as regards certain technical requirements for blood and blood components.

Two further technical Directives were adopted by the European Commission on 30 September 2005.

Directive 2005/61/EC – implementing Directive 2002/98/EC as regards traceability requirements and notification of serious adverse reactions and events, transposed into national law by S.I. No.547 of 2006.

The European Communities (Human Blood and Blood Components Traceability Requirements and Notification of Serious Adverse Reactions and Events) Regulations.

Directive 2005/62/EC - implementing Directive 2002/98/EC as regards Community standards and specifications relating to a quality system for blood establishments, transposed into national law by S.I. No. 562 of 2006, The European Communities (Quality System for Blood Establishments) Regulations.

1.2 Scope of Reporting

The Blood Directive provides that reportable information concerns only serious adverse reactions observed in patients during or after transfusion which may be attributable to the “quality and safety of blood and blood components” (article 5.1 of Directive 2005/61/EC) and "any serious adverse events which may affect the quality or safety of blood and blood components" (article 6.1 of Directive 2005/61/EC).
The above regulations apply to serious adverse reactions and serious adverse events occurring in blood establishments, hospital blood banks and facilities as defined in Directive 2002/98/EC and 2005/61/EC.

'The NHO also collates reactions and events reports which fall beyond the legislative scope i.e. non-mandatory case reports.

1.3 Definitions

Serious Adverse Reaction (SAR)

An unintended response in a patient associated with the collection or transfusion of blood or blood components that is:

- Fatal
- Life-threatening
- Disabling,
- Incapacitating, Or
- Results in, or prolongs, hospitalisation or morbidity.

Mandatory SAR are those that meet the criteria as defined in legislation. For more detailed explanations for individual mandatory and non-mandatory reactions please refer to Appendix 1.
Non-mandatory SAR are those not meeting the criteria set by legislation but can be still reported to the NHO.

Serious Adverse Event (SAE)
Any untoward occurrence associated with the collection, testing, processing, storage and distribution of blood and blood components that might:

- Lead to death,
- Be life-threatening,
- Causes disabling or incapacitating conditions for patients,
- Results in, or prolongs, hospitalisation or morbidity.

Mandatory SAE are those that meet the criteria as defined in legislation for more detailed explanations for individual mandatory and non-mandatory events please refer to Appendix 3.

Non-mandatory SAE are those not meeting the criteria set by legislation but can be still reported to the NHO.

Near Miss SAE
'Is defined as an error or deviation from standard procedures or policies that is discovered before the start of the transfusion and that could have led to a wrong transfusion or a reaction in a recipient if transfusion had taken place.' (SHOT 2022)

Clinical near misses are currently not accepted by the NHO.

Wrong blood in tube (WBIT) events are defined as events where:

- Blood sample is taken from the wrong patient and labelled with the intended patient's details ('mis collected').
- Blood sample is taken from the intended patient, but labelled with another patient's details (in other schemes 'mislabelled')

Reporting Establishment is the blood establishment, the hospital blood bank or facilities where the transfusion takes place that reports serious adverse reactions and/or serious adverse events to the competent authority.

Blood Establishment (BE) is any structure or body involved in any aspect of the collection, testing, processing, storage and distribution of blood and blood components.

Hospital Blood Bank (HBB) is a hospital unit which stores and distributes and may perform compatibility tests on blood and blood components exclusively for use within hospital facilities.

Facility means hospitals, clinics, manufacturers, and biomedical research institutions to which blood or blood components may be delivered.

'**Haemovigilance**' shall mean a set of organised surveillance procedures relating to serious adverse or unexpected events or reactions in donors or recipients, and the epidemiological follow-up of donors.

1.4 Roles of the Parties Responsible for Haemovigilance

1.4.1 The Role of the National Haemovigilance Service (NHO)

The National Haemovigilance Office (NHO) established in 1999 by the Department of Health was set up at the National Blood Centre in the IBTS and launched by the Minister for Health and Children in the same year. The purpose of the haemovigilance programme is to identify unexpected or undesirable effects of transfusion of blood components by ensuring they are reported in a timely and reliable manner.

With the transposition of the EC Blood Directives into Irish law, the NHO has a statutory obligation to collect, evaluate and convey reports of SARs attributed to and SAEs which may affect the quality and safety of blood, to the Health Products Regulatory Authority (HPRA) (S.I. No. 547 of 2006).
The NHO was also tasked with the promotion of best transfusion practice in hospitals throughout Ireland, through the provision of advice, guidelines and education. Further information regarding the role of the NHO is available at:
https://healthprofessionals.giveblood.ie/clinical-services/reporting-to-nho/

1.4.2 The Role of the Irish Blood Transfusion Service (IBTS)

The National Haemovigilance Office (NHO) is staffed and administered by the IBTS pursuant to its function under Article 4(k) of the Blood Transfusion Service Board (Establishment) Order 1965 as amended.

The IBTS has a separate role as a reporting establishment and submits reports to the NHO, both mandatory (as required by the legislation) and non-mandatory which meet the reporting criteria as defined in this handbook.

1.4.3 The Role of the hospital based Haemovigilance Officer in reporting SARs and SAEs

The Haemovigilance Officer should review all suspected reaction /event reports. The Haemovigilance Officer should communicate with clinical and laboratory staff and review the patient's clinical notes to assess all suspected reactions and events.

The Haemovigilance Officer should ensure that appropriate investigation forms are completed (as per local hospital policies) and should present the results of the investigation along with a history for review by the Consultant Haematologist/Physician prior to the confirmation of the reaction / event.

- in the case of a Serious Adverse Reaction, it is important to exclude any underlying illness or concomitant medication, which may have contributed to the reaction.
- in the case of a Serious Adverse Event, the Haemovigilance Officer should contact and work with appropriate staff to review, investigate and where appropriate to undertake a root cause analysis of the error. Follow-up action, whether corrective or preventative should be agreed following review with the Consultant Haematologist.

A summary report on all serious adverse reactions and events investigated along with accompanying blood transfusion documentation should be returned to the patient's chart. The Haemovigilance Officer should retain a copy of this report in the hospital based Haemovigilance office.

The Haemovigilance Officer should submit reports to the NHO, both mandatory (as required by the legislation) and non-mandatory which meet the reporting criteria as defined in this handbook. All Haemovigilance reports should be discussed with the hospital Haemovigilance team before submission to the NHO.

1.4.4 Health Products Regulatory Authority

The Health Products Regulatory Authority (HPRA) is the national competent authority for implementation of blood legislation in Ireland. The HPRA liaises with the NHO in relation to the review and evaluation of cases and provides guidance related to mandatory SAR and SAE associated with blood and blood components. The HPRA is also responsible for the submission of cumulative, national SAR/E data to the EC Commission on an annual basis. Further information regarding the role of the HPRA is available on the HPRA website at www.hpra.ie

2 REPORTING PROTOCOLS

This section will outline the following:

- Classification of reports into mandatory and non–mandatory reporting as required by the legislation
- The reporting process to the NHO
- Clinical inquiries to the NHO
- Management of reports relating to blood derived medicinal products

2.1 Reporting to the NHO

The blood and blood components covered by legislation for mandatory reporting are the following:

- Whole blood
- Red blood cells
- Platelets
- Plasma

While reporting of SARs involving SD plasma and other blood derived medicinal products is covered by pharmaceuticals legislation and does not fall within the blood and blood components legislation, the NHO collects and reports on any such cases, along with SAEs involving SD plasma.

Mandatory Reporting (as required in the legislation)

- **Mandatory SARs** observed in patients, attributable to the quality and safety of the blood/blood components transfused (Refer to Appendix 1)
- **Mandatory SAEs**, including near-miss events which may affect the quality or safety of blood and blood components occurring in the reporting establishments (Refer to Appendix 3)
- **A Near Miss SAE** is an error or deviation from standard procedures or policies that is discovered before the start of the transfusion and that could have led to a wrong transfusion or a reaction in a recipient if transfusion had taken place. (SHOT 2022)

Clinical near misses are not accepted by the NHO. (Clinical near misses are near-miss events occurring within the clinical sphere where the unit was issued but not transfused e.g. prescription errors) SAEs can occur at:

- Donor Selection (Blood Establishment (BE) activity)
- Whole Blood and Apheresis collection (BE activity)
- Testing (BE activity)
- Processing (BE activity)
- Storage (BE or Hospital Blood Bank (HBB) activity step)
- Distribution (BE activity)
- Component selection (BE or HBB activity step)
- Compatibility testing/Crossmatching (BE or HBB activity step)
- Issue (BE or HBB activity step)
- Other

Non-Mandatory Reporting (as required by the NHO)

- **Non-mandatory SARs** – The NHO accepts reports of SAR related to SD plasma and blood components where the EC reporting requirements are not met (Refer to Appendix 1).

- **Non-mandatory SAEs** - These fall outside the scope of the mandatory SAEs however the NHO collect (Refer to Appendix 3). These include:
  - events occurring in the clinical area,
  - events relating to SD plasma,
  - events relating to anti-D Ig and factor concentrates.

- **Wrong Blood in Tube Events**

Note for reporting (mandatory and/or non-mandatory reactions):

- **SAR linked to SAE** should be reported systematically as SAR, as they are due to the quality and safety of blood component,

- **Each individual** adverse reaction in an individual recipient following the application of blood or blood components, and where the reaction is 'serious' and can be linked to the quality and safety of the blood component, should be counted as **1 adverse reaction report**.

- **Multiple reactions in the same recipient**, even if they occurred in association with the same transfusion episode, should be reported as multiple SARs i.e. one report for each relevant category of SAR (see Annex 1 table of reportable reactions). Example: a finding of TACO and a finding of viral infection associated with a single transfusion episode should be assessed (imputability) and reported separately.

2.2 Completing the report forms

This section is designed to aid hospital staff when submitting reports to the NHO. Table 2.1 includes an index of all report forms used by reporting establishments.

Table 2.1: Index of NHO report forms used for reporting from reporting establishments.

BT FORM NUMBER	TITLE
IBTS/HV/FORM/0001	INITIAL REPORT FORM
BT- 0414	DETAILED FORM: MANDATORY / NON-MANDATORY SERIOUS ADVERSE EVENT DETAILED QUESTIONNAIRE
BT - 0415	DETAILED FORM: INCORRECT PRODUCT ADMINISTRATION /OMMISION
BT - 0416	DETAILED FORM: DETAILED TRANSFUSION REACTION FORM
BT- 0417	DETAILED FORM: DETAILED BACTERIAL SUSPECTED TRANSFUSION TRANSMITTED INFECTION
BT - 0418	DETAILED FORM: DETAILED VIRAL SUSPECTED TRANSFUSION TRANSMITTED INFECTION
BT - 0419	DETAILED FORM: DETAILED PARASITIC/OTHER SUSPECTED TRANSFUSION TRANSMITTED INFECTION
BT - 0420	DETAILED FORM: DETAILED POST TRANSFUSION PURPURA
BT - 0421	DETAILED FORM: DETAILED GRAFT VERSUS HOST DISEASE
BT - 0422	DETAILED FORM: DETAILED PRE-DEPOSIT AUTOLOGOUS DONOR INCIDENT
WBIT	WRONG BLOOD IN TUBE (CLINICAL NEAR MISS) REPORT FORM
Notification NM	HOSPITAL BLOOD BANK: NOTIFICATION OF A NEAR MISS EVENT TO THE NATIONAL HAEMOVIGILANCE OFFICE
Confirmation NM	HOSPITAL BLOOD BANK: CONFIRMATION OF A NEAR MISS EVENT TO THE NATIONAL HAEMOVIGILANCE OFFICE

- Hospital HVOs/ appropriate designated person should use the initial report form (IBTS/HV/FORM/0001) –to report SAR and both mandatory and non-mandatory SAEs involving blood components and products.
- The NHO will send the reporting establishment an appropriate detailed report form (DRF) – BT - 0414 to BT - 0422.
- Hospital HVOs / appropriate designated person should use the notification and confirmation forms when submitting a report of a mandatory near miss event in the hospital blood bank.
- Hospital HVOs / appropriate designated person should use Wrong Blood in tube Form when submitting a report of this nature.

2.2.1 Initial Report Form (IBTS/HV/FORM/0001)

Incidents (SAR & SAE) which fulfil the reporting criteria (apart from Near-miss events and Wrong Blood in Tube Events) should be submitted to the NHO on

IBTS/HV/FORM/0001 which is available on the website:
https://www.giveblood.ie/clinical-services/reporting-to-nho/initial-report-form-v4-.pdf
or can also be obtained by directly contacting the NHO.

- It is essential that **all sections** are completed fully. If *Not Applicable,* write *N/A* in the relevant section. Omissions in form filling cause delay and information may be misinterpreted
- IBTS/HV/FORM/0001 should be completed and returned to the NHO as soon as possible after the occurrence of a reaction or event.
- It is important to inform the NHO if this report has been submitted from another reporting establishment e.g. IBTS.
- The following information is required when completing IBTS/HV/FORM/0001. This is necessary to gain a complete understanding of the reported reaction or event. The nature of the report i.e. SAR or SAE will determine which questions should be answered (See Table 2.3 (A) for SAR and Table 2.3 (B) for SAE).

Table 2.2 Completing IBTS/HV/FORM/0001

Essential Information	Question Number
Age	1
Gender	1
Reporting establishment (hospital)	1
Component / product	2
Unit number	2
Patient's primary diagnosis	5
Has this report has been submitted to the NHO from another reporting establishment e.g. IBTS or hospital?	15
If yes, state name of reporting establishment	
If yes, what is unique incident number from that reporting establishment?	

<u>And</u>

Table 2.3 (A): Information required when reporting SAR.

Essential Information	Question Number
Interval between commencing transfusion and onset of symptoms	12
Symptoms	13
Date reaction occurred	3
Time reaction occurred	3
Classification of Serious Adverse Reaction	Nature of Incident
Imputability	SAR

<u>Or</u>

Table 2.3 (B): Information required when reporting SAE.

Essential Information	Question Number
Date error occurred	3
Time error occurred	3
Date error discovered	3
Time error discovered	3
Was vitamin K administered (plasma events)?	9
Emergency transfusion	11
Classification of SAE	Nature of Incident

If there are any difficulties encountered while completing this form, contact the NHO for assistance.

2.2.2 The role of the NHO on receipt of IBTS/HV/FORM/0001

- On receipt of IBTS/HV/FORM/0001 the NHO will review the information and enter this information in the haemovigilance database.
- A unique haemovigilance identifier is assigned to each individual report received to the NHO as follows; HV/Sequence/Year.
- The NHO will select and send a suitable DRF to the reporting hospital, where appropriate. The choice of DRF is dependent on the classification of the submitted report. This report will include the unique NHO identifier.
- A copy of all mandatory reports (IBTS/HV/FORM/0001 and Near Misses) is sent to the HPRA on a weekly basis.

2.2.3 Detailed Report Form (DRF) (BT - 0414 – BT -0422)

- It is essential that all relevant sections are completed fully. Pay particular attention to **'Required Information for Inclusion in Reports to the NHO'** sections for each category as highlighted throughout this handbook.
- In the case of adverse events, it is often useful to attach a summary of the event to aid interpretation of the form.
- All *DRFs* should be returned as soon as possible but no later than **four weeks** following receipt from the NHO.
    - Where a DRF is not received within 42 days the NHO will contact the reporting hospital for an update on the status. Failure to return forms relating to mandatory SARs and SAEs can be notified to the HPRA.

2.2.4 The role of the NHO on RECEIPT OF A DRF

On receipt of the D*RF* the NHO will review the information and enter this information in the haemovigilance database.

Following this, NHO staff will either request further information or send a letter confirming "close-out" of the report. This letter will inform the reporting hospital/HVO of the final designation of the report. Where the report is a mandatory report, this information is very useful when submitting the Annual Notification Form at the end of the reporting year.

The NHO will where possible close out reports within 60 days of receipt of the DRF. Where there is a delay in closing the investigation e.g. suspected TRALI or TTI, the NHO will inform the reporting hospital / HVO.

2.2.5 Reports which are not progressed

Reports not meeting the criteria for reporting will not be progressed. The criteria for "not progressing" a report are outlined in Appendix 4. This can occur following review of either IBTS/HV/FORM/0001 or both the IBTS/HV/FORM/0001 and DRF. A letter informing the reporting hospital / HVO of this is sent by the NHO.

2.2.6 Reporting of a near miss SAE

Submitting a report of a near miss SAE

- Events which fulfil the reporting criteria should be submitted to the NHO on the Notification Near Miss and Confirmation Near Miss Report forms separately or at the one time. These forms are available on the NHO webpage:
  https://www.giveblood.ie/clinical-services/reporting-to-nho/hospital-blood-bank-sae-near-miss-notification-report-form.pdf
  https://www.giveblood.ie/clinical-services/reporting-to-nho/hospital-blood-bank-sae-near-miss-confirmation-report-form.pdf

- All questions should be completed to facilitate an exploration of the reported event and meet the requirements of the legislation.

Table 2.4 Near Miss SAE

Questions	Questions explained	Form
Reporting Establishment	Name of hospital	Notification Near Miss
Report identification	Identifier in hospital	Notification Near Miss
Reporting date	Date Near Miss SAE reported in hospital	Notification Near Miss
Dare of serious adverse event	Date Near Miss SAE occurred in hospital	Notification Near Miss
Deviation in / Specification	Part of work process where near miss SAE occurred / pre-determined categories of	Notification Near Miss
Further details	A short description of near miss SAE	Notification Near Miss
Root Cause analysis	Cause of adverse event	Confirmation Near Miss
Corrective measures	A short description of actions taken following event.	Confirmation Near Miss

- All form/s are reviewed on receipt and entered on to a database. The NHO assigns a unique identifier to each near miss SAE report as follows; HV/NM/Sequence/Year.
- Both forms are reviewed at an internal case meeting. Following this, NHO staff will either request further information or send an email confirming "close-out" of the report. This will inform the reporting hospital/HVO of the final designation of the report which can be useful when submitting the Annual Notification Form at the end of the reporting year.

2.2.7 Reporting of a Wrong Blood in Tube (Clinical Near Miss)

Submitting a report of a Wrong Blood in Tube (Clinical Near Miss):

Events which fulfil the reporting criteria should be submitted to the NHO on the Wrong Blood in Tube Report Form which is available on the NHO webpage: https://www.giveblood.ie/clinical-services/reporting-to-nho/wrong-blood-in-tube-clinical-near-miss-report-form.pdf

2.2.8 Reporting timelines

- Reports relating to mandatory *serious adverse reactions* and *serious adverse events should be submitted to the* NHO as soon as possible after the reaction or event has occurred.
- Reports relating to mandatory *serious adverse reactions* and *serious adverse events,* and which have occurred after the introduction of mandatory reporting in November 2005 will be accepted at any time by the NHO and included in the figures for the year of reporting.

- Non-mandatory SAEs will still be collected and should be sent to the NHO as soon as possible after the event discovery. The NHO recognises that audit findings may identify multiple similar reports which may affect yearly reporting trends, and therefore such reports will be accepted if submitted within one year of occurrence of SAE.

- Initial reports of SAR and SAE occurring during the previous reporting period (i.e. to end of year) will be accepted if received prior to 7th January, for inclusion in the annual report figures for the preceding year. Initial reports received after 7th January will be included in the annual report figures for the current year.

2.3 Clinical Enquiries

- Enquiries to the NHO relating to incidents which may or may not fulfil the reporting criteria and are not accompanied by an appropriate form will be filed as 'Clinical Enquiries' by the NHO.
- However, if a subsequent report form is received, the case will be managed appropriately.

2.4 Non-Mandatory Reporting relating to medicinal products

This includes reports relating to Solvent Detergent (SD) plasma, medicinal products (both plasma derived and recombinant) and Anti D Ig. (This is summarised in Table 2.5).

2.4.1 Reporting SARs and SAEs associated with SD plasma.

While reporting of SARs involving SD plasma is covered by pharmaceuticals legislation and does not fall within the blood and blood components legislation, the NHO collects and reports on any such cases, along with SAEs involving SD plasma.

- *Serious adverse reactions* associated with SD plasma should be reported in the usual manner to the NHO on *IBTS/HV/FORM/0001*
  - The Quality Assurance Department of the IBTS forwards all relevant reports to the manufacturer.

In addition, SARs associated with the use of SD plasma should be reported to the HPRA via the spontaneous reporting system using the 'Human Medicines Adverse Reaction' i.e. human pharmacovigilance reporting options, via the HPRA website at www.hpra.ie

- *Serious adverse events* associated with SD plasma should be reported to the NHO on IBTS/HV/FORM/0001 and are captured as non-mandatory SAE. These events reflect the safety of the overall transfusion process. Serious adverse events associated with SD plasma are not reported to the HPRA.

Suspected quality defects e.g. pinhole perforations of the bag suspected to be caused by the manufacturing process should be reported to the Quality Department of the IBTS and to the HPRA via the 'Medicine Quality Issue/Defect (Patients and Healthcare Professionals)' options (see www.hpra.ie)

2.4.2 Reports associated with anti–D Ig and plasma derived & recombinant medicinal products.

Adverse reactions (AR)

Reporting of *adverse reactions* (AR) involving medicinal products is covered by pharmaceuticals legislation and therefore does not fall within the blood and blood components legislation. Suspected adverse reactions associated with medicinal products including those relating to anti D Ig, factor concentrates, albumin or other immunoglobulin should be reported directly to HPRA via the pharmacovigilance reporting system using the 'Human Medicines Adverse Reaction' options, via the HPRA website at www.hpra.ie

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Adverse events (AE)

Adverse events (AE) associated with these medicinal products i.e. anti D Ig and factor concentrates should be reported to the NHO on an HV FORM 1.

Reports of adverse events associated with albumin or other immunoglobulin should not be reported to the NHO. These should be investigated and followed up within the hospital quality system.

Any incidents related to an actual or suspected quality defect that may affect the quality safety and/or efficacy of the product, e.g. mislabelled products, should be reported as Quality Defects to the HPRA.

Table 2.5: Non-Mandatory Reporting relating to medicinal products

Medicinal Products		
	Non-mandatory SAE	**Non-mandatory SAR**
Anti D IG	NHO	HPRA
SD Plasma	NHO	NHO and HPRA
Plasma derived coagulation factor concentrates		
Specific coagulation factor concentrates	**Non-mandatory SAE**	**Non-mandatory SAR**
Fibrinogen concentrate	NHO	HPRA
von Will brand Factor/Factor VIII Complex (Dilate)	NHO	HPRA
Others	NHO	HPRA
Factor XI concentrate	NHO	HPRA
Factor XIII concentrate (Fibrogammin P)	NHO	HPRA
Anti-thrombin III concentrate (Kiernan P500)	NHO	HPRA
Multiple coagulation factor concentrates	**Non-mandatory SAE**	**Non-mandatory SAR**
Octaplex (Prothrombin Complex)	NHO	HPRA
Others	NHO	HPRA
Factor II IX X concentrate (Prothromplex TIM 4)	NHO	HPRA
(Non- Pdr) Recombinant Factor concentrates	**Non-mandatory SAE**	**Non-mandatory SAR**
rFVIII concentrate (Advate)	NHO	HPRA
rFIX concentrate (BeneFix)	NHO	HPRA
NovoSeven	NHO	HPRA

*Please report both serious and non-serious suspected adverse reactions associated with medicinal products to the HPRA. Reports can be submitted atwww.hpra.ie using the using the 'Human Medicines Adverse Reaction' i.e. human pharmacovigilance reporting options.

3 Serious Adverse Reactions

3.1 Introduction

This section clarifies the reporting requirements for reporting establishments with regards to serious adverse reactions (SARs).

- With the introduction of European and National legislation on Blood and Blood Components, reporting of SARs, which are attributable to the quality and safety of the blood components, is now mandatory.
- Reports relating to SD plasma are also accepted by the NHO.
- The NHO continue to accept non-mandatory SAR.

Serious Adverse Reactions (SAR)

An unintended response in a patient associated with the collection or transfusion of blood or blood components that is:

- Fatal
- Life-threatening
- Incapacitating

Or

- Results in, or prolongs, hospitalisation or morbidity.

3.2 SARs to be reported to the NHO

Table 3.1 outlines the types of SARs which should be reported as specified in Commission Directive 2005/61/EC.

Table 3.1: Table of Reportable serious adverse reactions

Directive 2005/61/EC categories	Reportable reactions
Immunological haemolysis due to ABO incompatibility	Acute haemolytic transfusion reaction (AHTR according to ISBT) due to ABO-incompatibility
Immunological haemolysis due to other allo-antibody	Acute haemolytic transfusion reaction (AHTR according to ISBT) due to irregular antibodies Delayed haemolytic transfusion reaction (DHTR according to ISBT) due to irregular antibodies
Non-immunological haemolysis	Acute haemolytic transfusion reaction (AHTR according to ISBT) due to physical, chemical or biological (but non-immune) reasons (for example mechanical stress, temperature, osmotic pressure, pH, drugs etc.)
Transfusion-transmitted bacterial infection (TTBI)	Sepsis due to TTBI (according to SHOT definition of transfusion-transmitted infections)
Anaphylaxis / hypersensitivity	Severe allergic reaction (according to ISBT)
Transfusion related acute lung injury (TRALI)	TRALI (according to ISBT)
Transfusion-transmitted viral infection (HBV, HCV, HIV-1/2, others)	T-t viral infection (according to SHOT definition of transfusion-transmitted infections)
Transfusion-transmitted parasitical infection (malaria, others)	T-t parasitical infection (according to SHOT definition of transfusion-transmitted infections)
Transfusion-transmitted fungal infection	T-t fungal infection (according to SHOT definition of transfusion-transmitted infections)
Post-transfusion purpura	Post transfusion purpura (PTP according to ISBT)
Graft versus host disease	Transfusion associated graft versus host disease (TA-GVHD according to ISBT)
Other serious reactions (specify)	• Febrile non haemolytic transfusion reactions (FNHTR according to ISBT) • Severe reaction due to transfusion associated circulatory overload (TACO according to ISBT) as well as cases occurring after 6 hours if clinically confirmed • Severe reaction due to transfusion associated dyspnoea (TAD according to ISBT Definition) • Hypotensive transfusion reaction according to ISBT) • Transfusion-transmitted prion infection • Others (including previously uncategorised complications)

*The reporting requirements are continuously updated by the EC Commission. The NHO reviews all case reports. Case reports which do not fulfil the current EC recommendations will not be included in the ANSAR. However, an analysis of all reports accepted by the NHO will be included in the NHO annual report.

- For the most up to date definitions please visit the website at: https://www.isbtweb.org/

3.3 Imputability of SARs

'Imputability' means the likelihood that a SAR in a recipient can be attributed to the blood or blood component transfused or that a SAR in a donor can be attributed to the donation process (Commission Directive 2005/61/EC).

Table 3.2 outlines the levels of imputability. While imputability may be determined at hospital level at the time of investigation of the reaction, these will be reviewed by the NHO. The reporting hospital will be notified of any change of assessment in imputability.

Table 3.2 Imputability level

NA	Not assessable	When there is insufficient data for imputability assessment
0	Excluded	When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to alternative causes
		When the evidence is clearly in favour of attributing the adverse reaction to causes other than the blood or blood components
1		When the evidence is indeterminate for attributing adverse reaction either to the blood or blood component or to alternative causes.
2	Likely, probable	When the evidence is clearly in favour of attributing the adverse reaction to the blood or blood component.
3		When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to the blood or blood component

3.4 Clinical Outcome

The NHO and the HPRA have developed a definition of clinical outcome, and an explanation for the classification for the categories laid out in the Directive.
Clinical Outcome refers to the effect of the precipitating SAR on the patients' clinical condition.

Table 3.3 Clinical Outcome

Clinical outcome categories (Directive 2005/61/EC)	Degree of harm (WHO,2009)
Complete recovery	Patient outcome is not symptomatic or no symptoms detected, but may have signs of an SAR and no treatment is required. Or Patient outcome is symptomatic, symptoms are mild, loss of function or harm is minimal or intermediate but short term, and no or minimal intervention (e.g., extra observation, investigation, review or minor treatment) is required.
Minor Sequelae	Patient outcome is symptomatic, requiring intervention (e.g. additional operative procedure; additional therapeutic treatment) or an increased length of stay.
Serious Sequelae	Patient outcome is symptomatic, requiring lifesaving intervention or major surgical/medical intervention, shortening life expectancy or causing major permanent or long-term harm or loss of function.
Death	On balance of probabilities, death was caused or brought forward in the short term by the SAR.

(Adapted from The Conceptual Framework for the International Classification for Patient Safety Version 1.1 FINAL TECHNICAL REPORT January 2009 World Health Organisation, 2009).

3.5 Reportable SAR's

SAR in recipients that fulfil the SAR definition from the legislation and the ISBT definitions for non-infectious adverse transfusion reactions, with an imputability of possible, likely probable, or certain are reportable to the NHO.

Reports of any SAR that fulfil the seriousness criteria below will be reportable to the EU Commission. Furthermore, where a SAR does not fulfil ISBT classification for a particular type of reaction but there is outcome for the patient as per table – these reports will now be captured as *Other Serious Reaction – Unclassified SAR.*
This does not change local reporting to the National Haemovigilance Office or local classification of a Serious Adverse Reaction. It is only to facilitate reporting to the EU Commission.

Each individual adverse reaction in an individual recipient following the application of blood or blood components, and where the reaction is 'serious' and can be linked to the quality and safety of the blood component should be reported as **1 adverse reaction report**

When a SAR results from an SAE it should be reported **only** as SAR. The following seriousness assessment table should be applied when reviewing all reactions.

Table 3.4 Serous Assessment Table

NOT REPORTABLE	**Insignificant**	No harm to the recipient or donor
	Non-serious	Mild clinical consequences. No hospitalisation. No anticipated long-term consequence/disability.
TO BE REPORTED	**Serious**	Adverse reaction resulted in: - hospitalisation[1] or prolongation of hospitalisation and/or - persistent or significant disability or incapacity[2] and/or - intervention to preclude permanent damage or impairment of a body function and/or - evidence of transmission of a serious communicable disease
	Life-threatening [9]	- major intervention [3] to prevent death and/or-evidence of a life-threatening communicable disease
	Fatal	Death in a recipient (transfused patient) or a donor: report if you suspect that the death was an outcome of the adverse reaction. Provide relevant information in the comments box. *Recipient SAR:* Deaths that are possibly, likely/probable or certain to be attributable to the transfusion should be reported. Deaths associated with a patient's underlying conditions, or any other cause should not be included in this category. *Donor SAR:* this applies to all fatalities where a link cannot be excluded, i.e. imputability possible, probable or certain.

[1] **Hospitalisation:**

• Report if overnight admission to the hospital or prolongation of hospitalization was a result of the adverse reaction, even if the admission was precautionary. The criterion of hospitalisation also applies in the case of a donor.

• Emergency room visits that do not result in admission to the hospital should be evaluated for other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

[2] **Disability, incapacity, or prolongation of morbidity**:

• Report if the adverse reaction resulted in prolongation of morbidity or a substantial disruption of a person's ability to conduct normal life functions, i.e., the reaction resulted in persistent or significant disability or incapacity or significant disruption in the patient or donor's physical activities or quality of life

[3] **Life-threatening**:

Report if suspected that the patient or donor was at substantial risk of dying as a result of the adverse reaction or medical intervention was necessary to prevent death. Report major interventions including vasopressor, intubation, and transfer to intensive care

4 Serious Adverse Events

4.1 Introduction

This section describes the reporting requirements for hospitals regarding mandatory serious adverse events (SAEs), mandatory near miss SAE, non-mandatory SAE and Wrong Blood in Tube (WBIT) events.

Following the introduction of European and National legislation on Blood and Blood Components, reporting of specific SAEs and near miss SAEs, which may have an influence on their quality and safety, is now mandatory. The NHO will collect these mandatory SAEs along with all other non-mandatory events.

4.2 Mandatory SAE

Definition

A Serious Adverse Event (SAE) is defined as any untoward occurrence associated with the collection, testing, processing, storage and distribution of blood and blood components that might:

- Lead to death,
- Be life-threatening,
- Causes disabling or incapacitating conditions for patients,
- Result in, or prolong, hospitalisation or morbidity.

Not all adverse events are considered 'serious'. In the sense intended in the Annual (ANSARE) reporting exercise, adverse events are considered serious and reportable to the European Commission, when they may put in danger blood donors or recipients of blood or blood components, or they may have a negative impact on blood donation or on transfusion of patients.

When a SAE results in a reportable SAR in a blood recipient or donor, only the SAR, not the SAE, should be reported.

Deviations from standard operating procedures in reporting establishments, or other adverse events which have implications for the quality and safety of blood/blood components, should be reported to the Commission only when one or more of the following criteria applies:

Table 4.1

Inappropriate blood/blood components have been issued/distributed for use, even if not used.
For instance: - blood components distributed for use with incorrect blood group labels, - blood components distributed for use without the mandatory donor testing results, - blood components issued with incorrect cross-matching information, - blood components distributed for use despite a post-donation notification from the donor implying a disease transmission risk, - blood components distributed/issued for use despite having been stored at temperatures outside the required range, - blood components issued by the HBB without specific characteristics requested by the treating physician (e.g. irradiation, CMV negative).
The adverse event resulted in loss of any irreplaceable highly matched (i.e. recipient specific) blood/blood component
For instance: - blood components prepared for a patient with highly specific and urgent needs lost due to a storage or processing error, - blood components of a very rare group collected for a specific recipient and lost due to a storage or processing error.
The adverse event resulted in the loss of a significant quantity of unmatched blood or blood components – a significant quantity is considered a loss that will have a negative impact (delay or cancellation) on treatment or surgery,
For instance: - in a BE, an undetected cold-room break down with the consequent discard of number of red cell concentrates creating a problem to respond to requests for RCC from hospitals, - a failure of the virology testing equipment results in 50% of a large blood establishment (supplying many hospitals) platelet stock expiring without being cleared for issue.
The adverse event could have implications for other patients or donors because of shared practices, services, supplies or donors (e.g. repeat event inside or outside the BE/HBB),
For instance: - a defect is detected in a haemoglobin testing device known to be used by other blood establishments – no harm caused to donors due to parallel testing by a different method[15].
The adverse event could significantly impact the blood transfusion system (e.g. by jeopardising the confidence of blood donors or recipients).
For instance: - confidential donor information is accidentally made publicly accessible, - donations are collected, in error, from underage donors.

The term **"near miss event"** is not defined in the Blood Directive but is a commonly used term. Near miss events are adverse events and, if they meet the criteria listed above, they are reportable as SAE.

SAE which are not reportable include:
• an incorrect result of compatibility testing performed by the BE/HBB due to a misidentification of the recipient's blood sample (e.g. wrong blood in tube from a clinical area and detected in the lab) is not reportable as the error falls within the "clinical practice" scope and is not covered by the Blood Directives.
• correctly cross-matched and labelled blood components that are issued for the correct patient and transfused to the wrong patient are not reportable as the error falls within the "clinical practice" scope and is not covered by the Blood Directives
4.3 Reporting Mandatory SAE Reports to the NHO
The Legislation covers the quality and safety of blood components extending from the blood establishment to the hospital blood bank (HBB) and other facilities. It does not extend to clinical aspects of the transfusion chain.

These activity steps where a **deviation** may occur are as follows:

- **Donor Selection**- Not applicable to the Hospital Blood Bank (HBB).
  Donor selection or evaluation is performed in order to avoid collecting blood from donors with increased risk of complications and to avoid risk of transfusion-transmitted infectious diseases or other adverse reactions in the recipient (exclusive to blood establishment).
- **Whole blood and apheresis collection** refers to the act of collection of whole blood or apheresis donations (exclusive to blood establishments).
- **Testing of donations –**refers to the act of testing blood donations in the blood establishments to meet the requirements of Directive 2002/98/EC Annex IV, as well as supplementary national requirements (exclusive to blood establishments). This includes donor testing as well as blood component testing. Compatibility testing or Cross-matching is **not** included in testing.
- **Processing**-is the process of transforming donations of whole blood and apheresis donations into issuable components intended for transfusion (exclusive to blood establishment). This also involves secondary processing such as irradiation.
- **Storage**- Storage refers to the act of storing blood or blood components at blood establishments or hospital blood banks and to procedures to ensure maintenance of quality and safety from the time blood and blood components are released from a Blood Establishment and distributed to a hospital blood bank in accordance with relevant rules and written SOPs. Annex IV of Directive 2004/33/EC lays down requirements for both storage temperature and length.
- **Distribution-** Distribution is the act of delivery of blood and blood components to other blood establishments, hospital blood banks and manufacturers of blood and plasma derived products (exclusive to blood establishment). It does not include the issuing of blood or blood components for transfusion.
- **Component Selection-** (Blood Establishment (BE) or HBB activity step) means the selection of the appropriate component by a blood establishment or hospital blood bank based on the recipient’s needs. This occurs before issue.
- **Compatibility testing/Crossmatching-** (BE or HBB activity step) refers to procedures of blood group serological investigations of the intended recipient and compatibility testing with donor red cells, carried out before transfusion by

a blood establishment or a hospital blood bank. This includes procedures for (electronic) compatibility verification in facilities where "Type and Screen" is used for eligible patients.

- **Issue-** (BE or HBB activity step) means the provision of blood or blood components by a blood establishment or a hospital blood bank for transfusion to recipient (Directive 2005/61/EC), i.e. the process of linking the correctly selected component to the correct patient and patient records and the labelling of that component, to maintain traceability.
- **Other-** Other refers to any other activity or parameter in the process that can affect the quality and safety of the component that may harm a patient.

Activity steps where a **Specification error** may occur:

- **Component defect**
  An SAE, meeting the criteria should be included in the **Product Defect** category when the blood or a blood component that has been issued for use does not meet the quality and safety requirements in table of this document due to an undetectable parameter.
- **Equipment Failure**
  An SAE, meeting the criteria defined in this document should be included in the **Equipment Failure** category when it was caused by any material, instruments or machinery that did not function as required at any stage from the collection to the distribution of blood and blood components. If the equipment failed because of inappropriate use, or the failure was not detected/prevented by an incorrect human action, these should be reported as human error.
  Note: Failures of medical devices, whether they met the criteria for SAE notification or not, should be reported via the medical devices reporting procedure.

- **Materials**
  An SAE, meeting the criteria in this document should be included in the **Materials** category when it was caused by any material (bags, preservation solutions etc.) from collection to distribution of blood or blood component. If the SAE was caused by inaccurate human handling of the material, these should be reported as human error.
  It should be noted that medical device defects should also be reported under Medical Device

- **System Failure**
  - Training or education
  - Staffing, workload or skill-mix
  - Inadequate process, procedures or documentation

  An SAE, meeting the criteria defined in this document, should be included in the **System Failure** category when the quality management system fails.

Insufficient training or education, high workload or pressure, incompetent staffing or insufficient skill-mixes of staffing, inadequate processes, procedures or documentation are examples of System failure.

- **Human Error**
  - Incorrect decision or omission following the correct procedure.
  - Following the wrong procedure.

  An SAE, meeting the criteria defined in this document, should be included in the **Human Error** category when it resulted from an inappropriate or undesirable human decision or behaviour that reduces, or has the potential of reducing, effectiveness, quality, safety, or system performance. SAEs should only be categorised as human error once investigation has ruled out failure of the system. Slips and lapses can be categorised as human errors.

- **Other (Specify)**
  Any SAE, meeting the criteria defined in this document should be included in the **Other** category when it cannot be classified in the already listed specifications.

  'Please note that these are not legal definitions but rather guidance aimed at facilitating case processing' as they are taken from the Common approach Document 2023 https://health.ec.europa.eu/publications/blood-common-approach-definition-reportable-serious-adverse-events-and-reactions-sare_en

4.4 Required Information on Mandatory, Non-Mandatory SAE and Near Miss SAE for inclusion in reports to the NHO

Mandatory SAE and Non-Mandatory SAE

Reports of both mandatory and non-mandatory SAE relating to blood and blood components are collected on the same forms (HV FORM 1 and DRF). This section outlines fields on the detailed report form which should be completed to facilitate full exploration of the reported event.

Table 4.2 Mandatory & Non-Mandatory SAE

Essential information	Question Number
Who discovered error?	1
Where error discovered (clinical area)?	2
Describe error type?	3
Step in the work process error discovered?	4
Stage in work process where error occurred	6
Area where error occurred	7
Personnel involved	8
Root Cause	9
Does the Medical Scientist normally work in transfusion?	16
Unit and patient identification	28, 29
Indications for transfusion within guidelines	34
Follow-up action (changes to practice) to incident	36

Near Miss SAE

Refer to Chapter 2.2.6 where the fields on both the Notification form - and the Confirmation form which should be completed are outlined and explained on Table 2.4.

4.5 NHO risk assessment of Mandatory and Non-Mandatory SAEs

The NHO has implemented a risk impact score used by the Office of Quality and Risk at Health Services Executive (2017). This impact scale has been adapted to the requirements of this reporting system.

The NHO classifies both mandatory SAE and non-mandatory SAE on actual or potential harm to the patient. This focuses only on the patient.

- If a patient develops an SAR directly as a result of an SAE involving a blood component this should be reported to as an SAR, while an SAE which has posed a risk, but has not, or not yet, caused harm is reported as an SAE.
- This risk assessment is currently not applied to near miss SAE.

This assessment should be carried out in the hospital by the haemovigilance team and should consider consultation with the patient's primary care team.

Table 4.3 Risk Impact Table

Impact /Consequence	Numerical Value	Description
Negligible	0	No obvious potential for harm.
Minor	1	Potential for minor harm which may require first line treatment. Could potentially result in < 3 days extended hospital stay.
Moderate	2	Potential for significant harm, requiring immediate and possibly ongoing treatment. Could potentially result in 3-8 days extended hospital stay.
Major	3	Potential for major / catastrophic harm. Could potentially be life threatening, could potentially result in long term incapacity requiring medical treatment or death.

- Events with no obvious potential for harm (Negligible Impact) should be collected and followed up at hospital level as they indicate defects in the quality of the service delivered. Trends identified are useful for both report writing and teaching. The NHO does not normally capture these incidents unless multiple errors are reported. These may be indicative of system failures.

4.6 Examples of adverse events which are generally not reportable to the NHO.

- Lack of traceability - Failures of traceability should be captured as non-conformances within the local reporting establishment quality system. Such failures should not be reported to the NHO but will be assessed at inspection.
- Transfusion of red cells which had been cross matched on a sample > 72 hours (but less than five days old).
- Supply problems/ lack of stock.

These are generally not reportable to the NHO if they are sole occurrences and should be captured by the Hospital Blood Bank Quality System.

4.7 Near Miss SAE

Since the beginning of 2010 the NHO has commenced collation of reports of mandatory near miss events. These will be reported as SAE to the HPRA and on to the EC.

Definition

A near miss is an error or deviation from standard procedures or policies that is discovered before the start of the transfusion and that could have led to a wrong transfusion or a reaction in a recipient if transfusion had taken place (SHOT 2022).

Reporting Near Miss SAE

Serious adverse events where the blood components have not been transfused because the error was discovered should be reported in this category.

It is important to clarify when a report is a near miss SAE (See Appendix 4) and when it becomes serious and reportable to National Haemovigilance Office (Section 4.4).

EC Notification Category

Near Miss SAE are reported as SAE under the following categories: Storage, Distribution, Component Selection, Compatibility testing/Crossmatching, Issue and Other.

4.8 Reporting SAE and Near Miss SAE

It is important to clarify when a report of an SAE or a Near Miss SAE becomes serious and reportable to NHO.

Deviations from standard operating procedures in reporting establishments or other adverse events which have implications for the quality and safety of blood or blood/ components, should be reported to NHO when one or more of the criteria discussed in table 4.1 may apply.

4.9 Non–mandatory SAE

Reporting Non-Mandatory SAE from clinical area

The NHO continues to collect reports relating to all adverse events occurring in the clinical area e.g. initial clerking, sampling, prescription/request, and retrieval of blood from fridge by clinical staff and administration. While provision of these reports is not mandatory under the blood and blood components legislation, the collection and analysis of these reports contributes to continuous improvement of transfusion practice.

Definitions of Non–mandatory SAE which should be submitted to the NHO.

These are defined as follows:

- **Incorrect Blood Component Transfused:**
  Where a patient was transfused with a blood component of an incorrect blood group, or which was intended for another patient and was incompatible with the recipient, which was intended (the occurrence of this error would be in the clinical area)

- **Incidents involving Anti–D Immunoglobulin or Medicinal Products:**
  Incidents involving delays, omissions, unnecessary administration relating to anti D Ig and serious adverse events associated with SD plasma (where transfusion has occurred) or other medicinal products are captured as non-mandatory SAE.

EC Notification Category:

Not applicable to reports of adverse events in the clinical area.

4.10 Wrong Blood in Tube (Clinical Near Miss) Events

Wrong blood in tube' (WBIT) may be defined as events where:

1. Blood sample is taken from the wrong patient and labelled with the intended patient's details ('miscollected').
2. Blood sample is taken from the intended patient, but labelled with another patient's details (in other schemes 'mislabelled')

Please note where a mismatch between the paperwork request and specimen is not identified on receipt in the Hospital Blood bank *and*/*or* the patient has a previous history on the Laboratory Information System and the invalid sample is not identified and subsequently processed – this now becomes a mandatory Near Miss SAE and should be reported accordingly.

Completion of reporting form: For guidance please refer to Document Detail

5 RAPID ALERT NOTIFICATION SYSTEM BETWEEN FACILITIES AND THE SUPPLYING BLOOD ESTABLISHMENT OR HOSPITAL BLOOD BANK

This section relates to the Rapid Alert Notification System between Facilities and the supplying Blood Establishment or Hospital Blood Bank. It is aimed at hospital practitioners who:

- Must initiate a rapid alert notification to the blood establishment.
- Participate in a recall following a rapid alert from the blood establishment.

This is included to help the HVO or other relevant personnel on the rare occasion where such a process may need to be initiated. **As the Rapid Alert Process may result in the recall of any other blood components from that donor/donation, the decision to initiate it must follow careful clinical assessment of the patients' symptoms in relation to the transfusion.**

5.1 Definition

The Rapid Alert Notification System between Facilities and the supplying Blood Establishment or Hospital Blood Bank is the immediate urgent notification to the supplying Blood Establishment or Blood Bank to initiate a recall of blood components, or to prevent the issue of blood components from a donor which may remain in stock. The aim is to protect the blood supply and any potential recipients. This system should be activated in the following circumstances:

- Suspected bacterial infection.
- Viral, parasitic or other post transfusion infection.
- TRALI.
- Failure in blood processing/ equipment in blood establishments e.g. failure of irradiation.
- Any situation with a potential risk to others.

5.2 Responsibilities of Various Parties

5.2.1 Hospital where Rapid Alert Notification occurs.

- Where any of the above there is a suspected TTI or a suspected TRALI careful clinical assessment of the patient should take place.
- **A decision to initiate a rapid alert should be taken following review with a consultant haematologist or the patient's primary physician**. This decision

should be taken at hospital level. If a Hospital Consultant is unavailable or if further assistance is needed, an IBTS Consultant Haematologist may be contacted (via switch board -Tel No. 01 4322800 / 021 4807400).

- Following this clinical review where the symptoms are deemed to be related to the transfusion, the hospital should contact the blood establishment where the blood was issued. Rapid Alert Notification may be initiated by telephone contact:
  - To the QA department of the IBTS at 01 4322800 / 021 4807400,
  - Through a Consultant Haematologist or Medical Officer in the IBTS, 01 4322800
  - Through the Medical Scientist on duty at the IBTS or supplying Blood Establishment / Hospital Blood Bank, 01 4322800
  - To the NHO at 01 432 2825 /432 2741 /432 2731
- An Initial Report Form (HV Form 001) should also be completed and submitted in the usual manner to the NHO.

5.2.2 IBTS

The IBTS will take action to recall products or defer donors where appropriate.

5.2.3 Hospital where a recall occurs

- Where a recall involves blood components which have been transfused, hospitals should have a system in place which includes a review of a patient to ensure a complete follow-up.
- Following this review, there needs to be clear evidence that the patient:
  - developed symptoms of bacterial infection suspected to be related to the transfusion following a BacT Alert (**Confirmed or Unconfirmed**) at the IBTS, this should be reported to the NHO as a suspected bacterial transfusion transmitted infection.
  - remained asymptomatic but was commenced on antibiotics or their antibiotic is changed as a result of the recall (due to a False Positive, Confirmed or Unconfirmed BacT Alert), this will be collected as an **SAE.**
  - had increased donor exposure as a result of resulting from a False Positive BacT Alert, this will be collected as ***SAE - Incorrect Component Transfused***

If there are no sequelae for the patient i.e. any reaction or event as detailed, arising from the BacT Alert and recall, then no report is required to the NHO. See Appendix 5 for further information on reporting SAR and SAE involving BacT Alerts.

5.2.4 NHO

- The NHO will process the report in the usual manner.
- Where there is a delay in closing the investigation the reporting establishment will be informed.

6 ANNUAL NOTIFICATION OF SERIOUS ADVERSE REACTIONS /EVENTS

6.1 Introduction

Article 8 of EC Directive 2005/61/EC states the Competent Authority of Member States must submit an annual report to the Commission by a pre-defined date for the preceding reporting year.

The Competent Authority in Ireland (HPRA) has designated the NHO to collect and collate these reports prior to submission to the HPRA.

Each hospital must submit an annual report known as the Annual Notification of Serious Adverse Reactions and Events (ANSARE) to the NHO. This section of the handbook is to assist reporters from hospitals in completing the ANSARE form.

6.2 Collation of the ANSARE

The format of the Annual Notification Form is set out in the Directive 2005/61/EC and SI 547 of 2006. The NHO, in consultation with the HPRA, has devised an Annual Notification Form based on this format and in line with the common approach document https://health.ec.europa.eu/publications/blood-common-approach-definition-reportable-serious-adverse-events-and-reactions-sare_en

Reports of Serious Adverse Reactions (SAR) and Serious Adverse Events (SAE) are separately compiled on this Annual Notification Form (See Appendix 7).

- Each year reporting establishments receive an email and an electronic copy of the ANSARE form from the NHO.
- Reporters receive two attachments:
  - One attachment used to report mandatory SARs labelled ANSAR (Annual Notification of Serious Adverse Reactions
  - One attachment used to report mandatory SAEs labelled ANSAE (Annual Notification of Serious Adverse Events
- ANSARE forms will be issued at the end of January each year. The data to be entered relates to transfusion activity for the preceding year.
- Reporters unable to return the form in the electronic format can request a hardcopy by contacting the NHO.
- The completed form must be either posted or e-mailed to the NHO at: haemovigilance@ibts.ie, by the date stipulated in the e-mail sent to all reporting establishments.
- Reporters using the electronic option will receive an acknowledgement e-mail. This only states the data has been imported into a database used to collate all data from reporting establishments.
- While the NHO makes every effort to verify information on individual forms with SARs and SAEs reported to the NHO during the preceding calendar year, reporting establishments are responsible for data entered on forms.

6.3 Completing the Annual Notification Form

This section gives advice on how to complete the form. If any section of the form is difficult to interpret, contact the NHO for advice.

6.3.1 Reporting Serious Adverse Reactions.

- All mandatory SARs relating to blood components reported to the NHO during the preceding calendar year should be reported on the ANSAR form.
- There is a separate page for each blood component:
  - Red blood cells.
  - Platelets.
  - Fresh Frozen Plasma.
  - Other e.g. granulocytes or cryoprecipitate.
- SARs relating to SD plasma and blood products e.g. anti D Ig and cases which ***'Did not Progress'*** are ***not*** reportable on the Annual Notification Form.
- Only include information on the selected component on each table.
- In the electronic format the reporting year will be set to the default year. Those reporters completing a hard copy must enter the reporting year: i.e. the preceding calendar year.
- In the section ***"Reporting Establishment"*** enter the name of the reporting establishment. In the electronic format a drop-down list of reporting hospitals is displayed. Select the name of the appropriate reporting establishment.
- For the HBB the section "***Number of units issued…."*** refers to the number of units issued from the laboratory which were transfused together with wastage occurring only in clinical areas.

  - Each unit should only be counted ***once***. Handling of a unit to perform compatibility testing so that a unit is available for transfusion is not considered issued and should remain part of the laboratory inventory until it is actually taken to the clinical area.
- The section ***"Number of recipients transfused……" (if available)*** refers to the number of individual patients' transfused in each reporting establishment in the reporting year (every effort should be made to obtain this information which may be available from the Laboratory Information System). Please note each patient should only be counted once irrespective of the number of times transfused in the preceding calendar year.
- The section ***"Number of units transfused" (if available)*** refers only to the number of units transfused. This differs from the number issued because it specifically excludes clinical wastage (every effort should be made to obtain this information which may be available from the Laboratory Information System).
- The form includes a grid which plots the category of reactions and the imputability of each reaction. Refer to Chapter 3 for a description of categories.
- On each component page there are columns labelled ***'A'*** and '***B'*.** Please only use the 'A' column at this time. In the A column enter the ***'Imputability'*** of each reaction.
  - Each SAR reported within the category must have an assigned imputability level.
- SARs involving multiple components should be reported on the relevant component sheet. Each component sheet has a column labelled ***"single"***

and ***"multiple"***. If the SAR is associated with only one component e.g. red blood cells, then enter the total number of SARs for each reporting category in the ***"single"*** column. If the SAR involves more than one component, then enter the number of SARs involving more than one component in the ***"multiple"*** column. E.g. SAR involving red blood cells and platelets.

- This should be done on each page for those components implicated in the SAR. For example, if a SAR occurred during a transfusion of red blood cells and platelets then the reaction would be entered in the "multiple" column on both pages.

- The section **"*Other Serious Reactions (Please specify)"*** captures:
  - Febrile Non-Haemolytic Transfusion Reactions (FNHTR).
  - Transfusion Associated Circulatory Overload (TACO).
  - Transfusion Associated Dyspnoea (TAD).
  - Hypotensive Reaction
  - Unclassified Reaction
  - Previously Uncategorised Complications
  - Other Serious Reaction (Specify) of Transfusion
- Each component report sheet has two ***"Totals".***
  - The section ***"Total number reported"*** refers to the total number of reactions within the specified component. It is the sum of the SARs reported within the component sheet. The number of SARs reported within the grid on each page must be equal to the total number of reactions on that page. For those reporters using the electronic format a warning box in red will appear if the total of SARs on that page does not equal those reported within the spread sheet and the data must be re-entered.
- Each reporting category has a section ***"Death"***. This refers to the number of deaths within the specified category. This only includes deaths occurring as an outcome of an SAR. It does not include deaths associated with the patient's underlying condition. Therefore, only deaths with an imputability of ***'definite, highly likely, or possible'*** should be reported.
  - In the section ***"Number of deaths"***, enter the sum of the number of deaths reported within each component page. In the electronic format if the total number of deaths reported on each page does not equal the number of deaths reported within the reporting grid this will be indicated by a red box and the data must be re-entered.
- Only SAR reactions which occurred in the calendar year beginning on 1st January and ending on 31st December should be reported on the ANSAR. The investigations must be completed and confirmation received by the hospital reporter by the cut-off date of 31st March for the year immediately following the SAR.

- For those SARs where the investigations are not completed and a 'close-out' letter has not been received from the NHO then the SAR should be reported for the following year.

- To facilitate reconciliation of the Annual Notification Form, the NHO can issue a summary of reported cases for the reporting year on request.
- SARs involving aliquots for neonatal or paediatric transfusion should be considered as one incident if the aliquots are all from one donor.
- In the electronic format there is a blank column beside each reporting category that allows a limited amount of free text. To enable the NHO to reconcile cases reported on the Annual Notification Form, reporting establishments should indicate the HV number of SARs. Those reporters completing a hard copy please indicate the HV numbers of SARs on each page beside the relevant category.

6.3.2 Reporting Serious Adverse Events

- SAEs including near miss events relating to blood components (as outlined in sections 4.2 and 4.3) should be reported on the Annual Notification of Serious Adverse Events (ANSAE) Form.
- All mandatory SAEs reported and accepted by the NHO in the preceding year must be reported on the Annual Notification Form.
- At the top of the Serious Adverse Events page (known as ANSAE) fill in the following:
  - ***Reporting establishment:*** name of reporting establishment (select from a drop-down list in the electronic format).
  - The reporting period: this is the preceding calendar year (1st January to 31st December).
  - The ***"Total number of blood and blood components issued.*** This information is used to provide denominator data. This includes any *step in the preparation of a blood component that is carried out between the collection of blood and the issuing of a blood component.* HBB do not perform processing (Directive 2002/98/EC). For the purposes of completing this form, reporters should incorporate the number of blood components received from a BE or another HBB in this section.
- The first column relates to the steps in the work process where the SAE occurred.
  - HBBs should complete only the relevant areas. These will be highlighted on the form.
- In each row fill in the number of SAEs *(if applicable).*
  - For examples of mandatory and non-mandatory SAEs, refer to Table 4.1.
- The ***'close-out'*** letter issued by the NHO during the reporting year will indicate if the incident is reportable under the EC Blood Directive.

7 References

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Article 15 (Notification of Serious Adverse Reactions and Events) of EC Directive 2002/98/EC. (IBTS/EXT/DOC/0017)Available at: https://www.inab.ie/inab-documents/mandatory-international-standard/minimum-requirements-for-blood-bank-compliance-with-article-14-traceability-and-article-15-notification-of-serious-adverse-reactions-and-events-of-eu-directive-2002-98-ec-.pdf (Accessed on 18/10/2022).

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8 Appendices

Appendix 1: Serious Adverse Events
Appendix 2: Current IHN/SHOT Classification of Acute Transfusion Reactions
Appendix 3: Serious Adverse Events: Description of current NHO SAE categories
Appendix 4: Criteria for not progressing cases
Appendix 5; Reporting SAR and SAE from HBB involving False Positive/Unconfirmed Positive/Conformed Positive Bac T Alerts
Appendix 6: Flow Chart from Hospitals to NHO
Appendix 7: Annual Notification form
Appendix 8: National Haemovigilance Office Organogram

9 Attachments

9.1 TACO Checklist

Appendix 1

Serious Adverse Reactions

Acute haemolytic transfusion reaction (AHTR) (ISBT definition)

An AHTR has its onset within 24 hours of a transfusion. Clinical or laboratory features of haemolysis are present.
Common signs of AHTR are:

- Fever
- Chills/rigors
- Facial flushing
- Chest pain
- Abdominal pain
- Back/flank pain
- Nausea/vomiting
- Diarrhoea
- Hypotension
- Pallor
- Jaundice
- Oligoanuria
- Diffuse bleeding
- Dark urine

Common laboratory features are:

- Haemoglobinaemia
- Haemoglobinuria
- Decreased serum haptoglobin
- Unconjugated hyperbilirubinaemia
- Increased LDH an AST levels
- Decreased haemoglobin 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 in the recipient or to non-immunological factors like mechanical factors inducing haemolysis (malfunction of a pump, of a blood warmer, use of hypotonic solutions, etc.).

Reporting Criteria for Mandatory Reactions
Reactions meeting the definition should be reported to the NHO. Only reactions where there is an outcome to the patient will become mandatory (Please refer to serious assessment table 3.4)

Investigations for AHTR

- Clerical check; recheck the identity of the patient and the implicated unit(s).
- Visual check of transfused units to ascertain any signs of deterioration (BSH 2023).
- Recheck ABO and D type.
- IAT antibody screen and cross match the of implicated units (if available) using post transfusion sample and retrospectively using the pre- transfusion sample (BSH 2023)
    - The use of a serum sample is recommended for post transfusion antibody investigation (BSH 2023)
- Look for evidence of haemolysis.
    - Direct Antiglobin /Coombs Test (DAT/DCT)- (this should be checked in a well-mixed sample as transfused cells are older and most likely
      denser than the patient's own cells and may consequently sit at the bottom of a centrifuged sample (BSH 2023).
    - Bilirubin, LDH, Urinary Urobilinogen, Haptoglobins.
    - Where a clinically significant red cell antibody is detected on the post transfusion sample which was not detected on the original pre-transfusion sample, pre and post transfusion samples should be sent to the reference center for investigation as it suggests that the original testing technique may have been insufficiently sensitive to detect the antibody.
    - Further guidance on serological investigations to be carried out in specific situations and referral to a reference laboratory, can be found in the recently published guidelines on pre –transfusion compatibility procedures in blood transfusion laboratories.
- Where clinical symptoms suggest the possibility of bacterial contamination, the following microbiological investigations should be carried out:
    - Blood cultures on patients should be taken from a peripheral and any central line in situ.
    - When possible, culture the pack contents and the pack segment line. The administration set may be cultured, as this is helpful to evaluate the possibility of contamination. It is unnecessary to culture the outside of the blood bag.
    - If clinically indicated other cultures may be necessary to out rule other causes.

EC Notification Category:

The term AHTR now incorporates the following EC categories, which are now mandatory for reporting.

- Immunological haemolysis due to ABO incompatibility
- Immunological haemolysis due to other alloantibody
- Non –immunological haemolysis.

Required Information on AHTR for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 416) which should be completed in relation to AHTR. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Essential Information	Question Number
Evidence of haemolysis	6, 15, 16
Antibodies detected	17,18
Evidence of bacterial contamination	20, 21
Treatment	33, 34, 35
Clinical outcome and timeframe of recovery	36

Delayed Haemolytic Transfusion Reactions

Delayed haemolytic transfusion reaction (DHTR) (ISBT definition)

DHTR usually manifests between 24 hours and 28 days after a transfusion and clinical or laboratory features of haemolysis are present. Signs and symptoms are similar to AHTR but are usually less severe. AHTR may sometimes manifest as an inadequate rise of post-transfusion haemoglobin level or unexplained fall in haemoglobin after a transfusion. Blood group serology usually shows abnormal results.

Reactions meeting the definition should be reported to the NHO. Only reactions where there is an outcome to the patient will become mandatory (Please refer to serious assessment table 3.4)

Investigations for DHTR

- Very often HBB will identify a new antibody in a patient transfused in the previous 28 days. Where this occurs a full clinical and laboratory review of patient's history and results should be undertaken to out rule a DHTR (Davenport, 2012).
- Investigations for haemolysis to include:
  - Hb,
  - LDH,
  - Bilirubin,
  - Haptoglobin
- Serological investigations e.g. direct antiglobulin test (DAT), detection of red cell antibodies.

Reporting DHTR

Detection of red cell antibodies within 28 days should be reported to the NHO.

For the purpose of analysis, the NHO grades such reactions by severity using current IHN/SHOT/B(C) SH Classification of Acute Transfusion Reactions criteria– See Appendix 2.

EC Notification Category:

- The term DHTR is incorporated in the following EC category - Immunological haemolysis due to other alloantibody.

Required Information on DHTR for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 416) which should be completed in relation to DHTR. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Essential information			Question Number
Investigations	Hb	Pre-transfusion	9
		Post-transfusion	6
	Bilirubin	Pre and Post –transfusion (**up to peak)**	6
	LFT	Pre and Post transfusion LDH (**up to peak**)	6
	DAT	Pre and Post transfusion	6
	Renal impairment	Pre and Post transfusion **(up to peak)**	6
	Other	Haptoglobins	6
Antibodies pre transfusion			11, 12,13
Antibodies post transfusion			17, 18, 19
Clinical outcome and timeframe of recovery			36
Future transfusion requirements			38

Febrile Non-Haemolytic Transfusion Reactions

- There is a FNHTR in the presence of one or more of:

• Fever (≥39ºC oral or equivalent and a change of ≥2ºC from pretransfusion value),

And/or

• Chills/rigors , myalgia, nausea or vomiting and/or loin pain (BSH 2023)

- (ISBT Definition -https://health.ec.europa.eu/publications/blood-common-approach-definition-reportable-serious-adverse-events-and-reactions-sare_en)
- This may be accompanied by headache and nausea occurring during or within four hours following transfusion without any other cause such as haemolytic transfusion reaction, bacterial contamination or underlying condition.
- FNHTR could be present in absence of fever (if chills or rigors without fever).

Laboratory Investigations for FNHTR

- Clerical check; recheck the identity of the patient and the implicated unit(s).
- Visual check of transfused units to ascertain any signs of deterioration (BSH 2023).
- Recheck ABO and D type
- IAT antibody screen and cross match of the implicated units (if available) using post transfusion sample and retrospectively using the pre- transfusion sample (BSH 2023).
    - The use of a serum sample is recommended for post transfusion antibody investigation (BSH 2023)
- Laboratory testing is required to exclude haemolysis due to transfusion of incompatible red cells or other causes. The following should be carried out:
    - DAT, bilirubin, LDH, urinary urobilinogen and haptoglobins.
- ABO type and re-crossmatch the units using pre and post transfusion samples.
- Where clinical symptoms suggest the possibility of bacterial contamination the following microbiological investigations should be conducted:
    - Blood cultures on patients should be taken from a peripheral and any central line in situ (BSH 2023).
    - Culture pack segment line, pack contents and administration set. It is unnecessary to culture the outside of the blood bag.

Reporting FNHTR to NHO

- The NHO will accept reports of FNHTR meeting the definition outlined in this handbook.
- Where symptoms of FNHTR are considered possible, likely-probable or certainly associated with transfusion and lead to increased morbidity or prolonged hospitalisation for patients, these reactions should be reported to the NHO (including incidents where day ward patients require admission overnight).
- Cases where the symptoms are considered due to the patient's primary diagnosis and not due to the transfusion i.e. imputability unlikely or excluded should not be reported

Criteria for reporting to EC

For the purpose of international comparisons and reporting to the EC, only the most serious cases of FNHTR will be reported as follows:

- Where an SAR includes **fever** (≥39˚C oral or equivalent and a change of ≥2˚C from pre-transfusion value) **and chills/rigors** (ISBT, 2011; EC, 2012). Reports meeting this criterion will be deemed as mandatory FNHTR reports and will be reported to the EC on ANSAR form.

EC Notification Category:

Reports of mandatory FNHTR are incorporated in the following EC category: Other - Febrile Non-Haemolytic Transfusion Reactions.

Required Information on FNHTR for Inclusion in Reports to NHO

This section outlines the fields on the DRF (BT 416) which should be completed in relation to FNHTR. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Table 3.7: FNHTR

Essential information	Question Number
Evidence of haemolysis	6, 15, 16,
Antibodies detected	17,18
Evidence of bacterial contamination	20, 21
Treatment	34, 35
Clinical outcome and timeframe of recovery	36

Anaphylaxis / hypersensitivity

An allergic reaction may present only with mucocutaneous signs and symptoms:

- Morbilliform rash with pruritus
- Urticaria (hives)
- Localized angioedema
- Oedema of lips, tongue and uvula
- Periorbital pruritus, erythema and oedema
- Conjunctival oedema

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 (dyspnoea, 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.

PLEASE NOTE: The NHO do not collect allergic reactions where Urticaria is the sole symptom.

Investigations for Allergic Reactions

- Frequently, investigations carried out do not elucidate a cause. In some cases, the reactions are related to drug/food allergy and unrelated to transfusion.
- IgA levels should be checked in patients with a severe allergic reaction or with a history of repeated allergic reactions to exclude IgA deficiency with anti IgA antibodies (McClelland, 2001).
- Mast cell tryptase (MCT) levels rise within 30-60 minutes of onset of anaphylaxis, peak at 3-4 hours and return to normal levels at 6-8 hours. This test is useful only to confirm that the SAR was anaphylactic, rather in treatment or future management of the patient. Blood samples should be taken immediately post the reaction, then at 3 and 24 hours (BSH 2023]).
    - ***Note:*** Persistent elevation of MCT may occur in patients with myleodysplastic syndrome, systemic mastocytosis, chronic renal syndromes and pruitis (BCSH, 2012 [a]).

Reporting Anaphylaxis /Hypersensitivity Reactions

- Allergic type reactions (except for pruritus, mild rashes and urticaria) which are considered possible, likely probable or certainly associated with transfusion should be submitted to the NHO.

- **Non-Severe Allergic Reactions**

  Where the presentation is of two symptoms i.e. urticaria / hives and oedema, this should be reported to the NHO.

- **Severe, Life –threatening or Death- Allergic Reactions**

  All allergic SAR classified as being severe, life-threatening or causing death should be reported to the NHO.

Anaphylaxis / Hypersensitivity which may be non-mandatory in terms of definition but however meet criteria as discussed in the Risk Assessment table (Please refer serious assessment table 3.4) may also be deemed mandatory following individual assessment.

EC Notification Category:

Allergic SAR is incorporated in the following EC category: Anaphylaxis / hypersensitivity.

Required Information on Anaphylaxis /Hypersensitivity Reactions for Inclusion in Reports to NHO

This section outlines the fields on the DRF (BT 416) which should be completed in relation to AA. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Table 3.8: Allergic SAR

Essential information	Question Number
Investigations; IgA MCT	6
Treatment	34, 35

Essential information	Question Number
Clinical outcome and timeframe of recovery	36

Transfusion Associated Circulatory Overload (TACO)

ISBT Mandatory Definition
Patients classified with a TACO (surveillance diagnosis) should exhibit at least one required criterion* with onset during or up to 12 hours after transfusion and a total of **3 or more** criteria:
* Required Criteria

A. Acute or worsening respiratory compromise *and/or*

B. Evidence of acute or worsening pulmonary oedema based on:
o clinical physical examination, *and/or*
o radiographic chest imaging and/or other non-invasive assessment of cardiac function

Additional Criteria
C. Development of cardiovascular system changes not explained by the patient's underlying medical condition, including development of tachycardia, hypertension, jugular venous distension, enlarged cardiac silhouette and/or peripheral oedema.

D. Evidence of fluid overload including any of the following: a positive fluid balance; clinical improvement following diuresis.
E. Supportive result of a relevant biomarker, e.g. an increase of B type natriuretic peptide levels (BNP or NT-pro BNP) above the age group-specific reference range and greater than 1.5 times the pre-transfusion value.

*and/or B, and total of at least 3 (A to E)

Please note the NHO accept reports of TACO where one or more of the symptoms below may occur as a non-mandatory TACO.

<u>Clinical Signs & Symptoms</u>
The signs and symptoms of TACO may include any or all of the following:
- dyspnoea,
- orthopnoea,
- cyanosis,
- tachycardia,
- hypertension
- pulmonary and/or peripheral oedema.
- There may be evidence of positive fluid balance.
- Chest auscultation usually reveals crepitations.
- Chest x ray shows evidence of pulmonary oedema. The heart size may be normal or enlarged and there may be pleural.

Investigations for TACO

- Careful clinical assessment of cardiovascular status.
- Assessment of fluid balance and response to diuretics.
- Pre and post transfusion Brain Natriuretic Peptide (BNP) and/or NT- pro BNP, may be of help when differentiating TACO from other causes of respiratory distress i.e. TRALI. The post–transfusion sample should wherever possible be taken within two hours of the suspected reaction.
- Troponin levels may be helpful in differentiating TACO from acute myocardial ischemia.
- Chest x-ray.

Reporting TACO

- TACO considered possible, likely probable or certainly associated with a transfusion should be reported to the NHO.
- The NHO will continue to collect reports of TACO where patients exhibit clinical signs and symptoms of overload following transfusion and which do not meet the very strict criteria of the ISBT definition either in terms of the timeline or evidence of three characteristics. The NHO will review all case reports and an analysis of all reports accepted by the NHO will be included in the NHO annual report.
- Reports meeting the strict ISBT definition will be deemed as mandatory TACO reports and will be reported to the EC on ANSAR form.

Transfusion Associated Circulatory Overload (TACO) reactions which may be non-mandatory in terms of definition but however meet criteria as discussed in the Risk Assessment table (Please refer serious assessment table 3.4) may also be deemed mandatory following individual assessment.

EC Notification Category

TACO is incorporated in the following EC category: Other – TACO

Required Information on TACO for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 416) which should be completed in relation to TACO. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Table 3.9: TACO

Essential information		Question Number
Investigations: Chest X ray		6
Auscultation of chest		6
BNP		6
Weight of patient		27
Pre-existing cardiac condition		28
Pre-existing respiratory condition		28
Pre-existing Renal failure		28
Fluid Balance		29
Diuretic	**Pre *transfusion*:**	30
Diuretic	***During transfusion:***	30
Diuretic	***Post transfusion:***	30
Clinical outcome and timeframe of recovery		36

Essential information		Question Number
Investigations: Chest X ray		6
Auscultation of chest		6
BNP		6
Weight of patient		27
Pre-existing cardiac condition		28
Pre-existing respiratory condition		28
Pre-existing Renal failure		28
Fluid Balance		29
Diuretic	**Pre *transfusion*:**	30
Diuretic	***During transfusion:***	30
Diuretic	***Post transfusion:***	30
Clinical outcome and timeframe of recovery		36

Transfusion Associated Dyspnoea (TAD)

TAD is characterized by respiratory distress within 24 hours of transfusion that do not meet the criteria of TRALI, TACO, or allergic reaction. Respiratory distress should not be explained by the patient's underlying condition or any other known cause. (ISBT Definition)

Investigations for TAD

- Careful clinical assessment to out rule Allergic SAR and both TACO and TRALI (Refer to Sections 3.6.2, 3.7.1 and 3.7.2).

Reporting TAD

TAD considered possible, likely, probable or certainly associated with a transfusion should be reported to the NHO.

EC Notification Category

TAD is incorporated in the following EC category: Other – TAD.

Required Information on TAD for Inclusion in Reports to NHO

This section outlines the fields on the DRF (BT 416) which should be completed in relation to TAD. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Transfusion Associated Dyspnoea (TAD)reactions which may be non-mandatory in terms of definition but however meet criteria as discussed in the Risk Assessment table (Please refer serious assessment table 3.4) may also be deemed mandatory following individual assessment.

Table 3.11: TAD

Essential information		Question Number
Investigations: Chest X ray		6
Auscultation of chest		6
BNP		6
Other –ECG, Troponin, Arterial blood gas		6
Weight of patient		27
Pre-existing cardiac condition		28
Pre-existing respiratory condition		28
Pre-existing Renal failure		28
Fluid Balance		29
Diuretic	***Pre transfusion*:**	30
Diuretic	***During transfusion:***	30
Diuretic	***Post transfusion:***	30
Other symptoms supporting diagnosis of TRALI		32
Treatment		34,35
Clinical outcome and timeframe of recovery		36

TAD considered possible, likely, probable or certainly associated with a transfusion should be reported to the NHO.

Suspected Transfusion Transmitted Infection (sTTI)

Include as a TTI if, following investigation the recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion, and no evidence of an alternative source of infection.

Plus:

Either at least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection.

Or at least one component received by the infected recipient was shown to contain the agent of infection.

- Bacterial transmission from blood components, where cultures from the patient's blood match cultures from the component bag and/or from the donor
- Transmissions of viruses, whether routinely tested for by the Blood Services or not
- Transmissions of other agents such as prions, protozoa and filarial
  (SHOT Definition)

Investigations for Suspected Transfusion Transmitted Viral Infection (Patient)

- Reports of possible viral transfusion infection should be based on confirmed positive results (e.g. HCV EIA +RIBA or EIA +PCR), as screening tests may give false positive results.
- Previous archived samples of patients should be identified if possible as they may be valuable in pinpointing the timing of infection and out-ruling transfusion as a source of the infection.

Investigations for Suspected Transfusion Transmitted Viral Infection (Donor)

Donor investigations are carried out by the IBTS. Investigation of markers of infection in an implicated donation, or in subsequent samples from the donors of implicated donations, can confirm transfusion as the probable cause of infection, or identify the need to investigate other possible sources. Such investigations may involve testing of considerable numbers of donors and may take months to complete.

Reporting Transfusion Transmitted Viral Infections

The NHO collects and investigates reports on the following:

- All suspected transfusion-transmitted viral infections relating to blood components which have been transfused after the introduction of mandatory testing for that virus i.e. HIV 1 + 2 (October1985), HCV (October 1991), HBV (June 1973), HTLV I&II (November 1996).
- Viral infections which are not covered by mandatory testing, e.g. hepatitis A virus, cytomegalovirus (CMV) and parvovirus, but are suspected to be associated with a blood transfusion.
- Isolated findings of hepatitis B core IgG antibody and/or e antibody and/or surface antibody in a transfusion recipient who has had no clinical or biochemical evidence of hepatitis within 6 months of transfusion, and where there is no prior patient sample, and where the donations have been core antibody tested (since January 2002) will not be further investigated by the NHO.
- Where the donor has not been tested for core antibody (e.g. donation prior to January 2002), review of donor records will be undertaken and a decision to undertake any active donor investigation e.g. donor recall will depend on evaluation of the clinical circumstances.

EC Notification Category

These infections are incorporated in the following EC categories:

- Transfusion Transmitted Viral Infection (HBV, HCV, HIV-1/2, Other)

Required Information on Suspected Transfusion Transmitted Viral Infections for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (418) which should be completed in relation to Suspected Transfusion Transmitted Viral Infection. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Suspected Transfusion Transmitted Viral Infection

Essential Information	Question Number
Year of implicated transfusion	2
Year of confirmation of infection	3
Viral Markers; HIV 1 or 2	4
HBV	4
HCV	4
Other	4
Patient risk factors	8
Clinical Outcome	10
Donor investigations	11 (Completed in IBTS)

Transfusion Transmitted Parasitic Infection

Investigations for Suspected Transfusion Transmitted Parasitic Infection (Patient)

Investigations to be undertaken are dependent on the type of parasite and will be decided on following discussions between the IBTS and the hospital.

Investigations for Suspected Transfusion Transmitted Parasitic Infection (Donor)

Reports are passed on to the QA Department of IBTS for investigation and follow up as appropriate.

Reporting Transfusion Transmitted Parasitic Infection

The NHO collects and investigates reports on the following:

- All suspected transfusion transmitted parasitic infections, which have occurred since 1st October 1999 e.g. malaria and toxoplasmosis.

EC Notification Category

These infections are incorporated in the following EC categories:

- Transfusion Transmitted Parasitical Infection (Malaria, Other)

Required Information on Suspected Transfusion Transmitted Parasitic Infection for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 419) which should be completed in relation to Suspected Transfusion Transmitted Parasitical Infection. This information is necessary to gain

a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Suspected Transfusion Transmitted Parasitic Infection

Essential Information	Question Number
Symptoms	4
Year of implicated transfusion	2
Year of confirmation of infection	3
Investigations conducted	5
Patient risk factors	7
Clinical Outcome	9
Donor investigations	11 (Completed in IBTS)

Transfusion Transmitted Bacterial Infection

Investigations for Suspected Transfusion Transmitted Bacterial Infection (Patient)

- Blood cultures from the patient should be taken from a peripheral and any central line in situ (BSH 2023).
- Culture of the **segment line and pack contents** is recommended.
- The administration set may be cultured as this is helpful to evaluate the possibility of contamination.
- It is unnecessary to culture the outside of the blood bag.
- Out rule other sources of sepsis in patient e.g. sputum, urine, wound swab or other if clinically indicated.

Investigations for Suspected Transfusion Transmitted Bacterial Infection (Donor/Donors)

Upon receipt of the report the NHO will consult with the Quality Assurance department in the IBTS, where investigations of the implicated pack or other components from the same donation and the donor will be initiated if indicated (see rapid alert notification system between facilities and the supplying blood establishment or hospital blood bank).

Reporting Suspected Transfusion Transmitted Bacterial Infection

The NHO investigates reports where a patient.

- Develops signs and symptoms of bacterial infection suspected to be related to the transfusion. Results from both the patient and pack should be available, and both should be positive.
  Or
- Develops symptoms of bacterial infection suspected to be related to the transfusion, and there is a positive Bacterial Contamination Alert (BacT Alert) (Confirmed /Unconfirmed) at the IBTS.

Reports meeting the criteria outlined in definition (SHOT 2022) will be accepted by the NHO.

The following should NOT be reported FROM HOSPITALS

- Where a patient is asymptomatic following a transfusion and there is a BacT Alert (False Positive, Unconfirmed or Confirmed) on the component.

- Where there is a confirmed positive BacT Alert on a unit distributed and recalled from the blood establishment irrespective of whether it has been transfused. This will be reported from the blood establishment as an SAE.

Further information on reporting SAR arising from BacT Alerts, see Appendix 5.

EC Notification Category

These infections are incorporated in the following EC categories:

- Transfusion Transmitted Bacterial Infection

Required Information on Suspected Transfusion Transmitted Bacterial Infection for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 417) which should be completed in relation to Suspected Transfusion Transmitted Bacterial Infection. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Suspected Transfusion Transmitted Bacterial Infection

Essential Information	Question Number
Investigation: Culture of patient	1
Culture of pack	3
Treatment	5, 6
Clinical Outcome	7

Suspected transfusion transmitted prion infection

Definition Variant CJD

vCJD is one of a group of diseases known as transmissible spongiform encephalopathies (TSEs), or prion diseases. (Johnson, 2005) These are rare, progressive and fatal non-inflammatory degenerative diseases of the brain which can affect both humans and animals. They are caused by an abnormal form of a naturally occurring protein in the brain (the prion protein) that can be acquired through infection (HIQA, 2011).

Reporting suspected transfusion transmitted prion

The NHO collects and investigates reports on the following:

- All suspected / confirmed transfusion transmitted prion infection, where the patient has a history of receiving a blood transfusion.

EC Notification Category

Suspected transfusion transmitted prion infection is incorporated in the EC category – Other serious reaction.

Required Information on suspected transfusion transmitted prion infection for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 419) which should be completed in relation to suspected transfusion transmitted prion infection. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Suspected Transfusion Transmitted Parasitic Infection

Essential Information	Question Number
Symptoms	4
Year of implicated transfusion	2
Year of confirmation of infection	3
Investigations conducted	5
Patient risk factors	7
Clinical Outcome	9
Donor investigations	11 (Completed in IBTS)

Transfusion Associated Graft-versus-Host Disease (TA-GvHD)

Definition

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 (ISBT, 2011).

It occurs where viable donor lymphocytes transfused in a blood component attack recipient tissue in immunosuppressed or immunodeficient patients (Webb and Anderson, 2001). It rarely occurs in transfusion recipients who have no evidence of immunodeficiency and where HLA haplotypes are shared between donor and recipient. The incidence appears reduced since the introduction of universal leucodepletion of blood components.

Clinical Signs & Symptoms and Laboratory Findings

TA-GvHD is characterised by:

- Fever, rash, liver dysfunction, diarrhoea, and pancytopenia occurring 1-6 weeks post transfusion with no other apparent cause.
- Supported by characteristic histological appearances on skin and bone marrow biopsy (ISBT, 2011).

Confirmed by:

- Evidence of donor derived lymphocytes circulating in blood or tissues (chimerism**).**

Investigations for TA-GvHD

- Skin and bone marrow biopsy, chimerism studies.
- Contact IBTS for further investigation which may be required.

Reporting TA-GvHD

Where TA-GvHD is considered possible, likely, probable or certain, a report should be sent to the NHO. This information is passed on to the Quality Department of IBTS for further investigations.

EC Notification Category

TA-GvHD is incorporated in the EC category: Graft versus host disease.

Required Information on TA-GvHD for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 421) which should be completed in relation to TA-GvHD. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Transfusion Associated Graft Versus Host Disease

Essential Information	Question Number
Clinical features	2
Investigations	4
Concurrent drug/radiotherapy	6
Irradiation of blood components?	13-16
Clinical Outcome	17

Post-Transfusion Purpura (PTP)

Definition

Post-Transfusion Purpura (PTP) is characterised 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.
(ISBT, 2011), usually anti HPA 1a but antibodies against other platelet antigens may be involved.

It is a rare condition occurring usually in female patients who have been immunised to platelets by a history of pregnancy or transfusion in the past. The incidence of this condition appears reduced since introduction of red cell leucodepletion which also removes platelets from red cell components, thereby reducing the risk of secondary alloimmunisation.

Clinical Signs & Symptoms and Laboratory Findings

PTP is characterised by:

- Thrombocytopenia often associated with bleeding and poor response to platelet transfusion.

Investigations for PTP

- Platelet antibodies and platelet genotyping (Samples to be sent to HLA laboratory at the IBTS).
- HLA type of the patient (samples to be sent to IBTS HLA Laboratory).

Reporting PTP

PTP considered possible, likely, probable or certain should be reported to NHO.

EC Notification Category

Post Transfusion Purpura (PTP) is an EC Notification Category.

Required Information on PTP for Inclusion in Reports to the NHO

This section outlines the fields on the DRF (BT 420) which should be completed in relation to PTP. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Post Transfusion Purpura

Essential Information	Question Number
Symptoms	3
Investigations: Anti platelet allo-antibody /platelet genotyping	8, 9
Clinical outcome	11

Reporting to the NHO

This section outlines the fields on the DRF (BT 420) which should be completed in relation to PTP. This information is necessary to gain a complete understanding of the reported reaction. If there are any difficulties encountered while completing these forms, please contact the NHO.

Unclassified Serious Adverse Reaction

Definition

Unclassified SAR is the occurrence of an adverse symptom / sign with no risk factor other than the transfusion and which on its own does not allow the reaction to be classified within the defined categories of SAR (i.e. such as those outlined in this handbook).

This category differs from PUCT and captures these adverse symptoms, which have been previously reported (in the literature) as associated with an SAR, but which do not fulfill the criteria of an already defined SAR. An example may be the occurrence of an isolated hypertension or bradycardia, which is attributed to the transfusion.

Out rule other causes of reaction such as haemolysis, bacterial contamination or respiratory distress i.e. TACO or TRALI.

Where the signs and symptoms are recognised as associated with an SAR but cannot be classified within an already defined category of SAR, such as those outlined in this handbook this should be reported as an "Unclassified SAR".

If an "Unclassified SAR" is considered *possible, likely- probable* or *certainly* related to the transfusion this should be reported to the NHO.
Any queries relating to reactions which may be suspected to be Unclassified SAR should be directed to the NHO.

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. (ISBT Definition)

Hypotensive reactions which are considered likely probable or certainly associated with transfusion should be submitted to the NHO.

Others (including uncommon and previously uncategorized reported complication of transfusion). Reports of new previously unreported signs and symptoms temporally related to transfusion and with no other risk factor other than transfusion e.g. like the red eye syndrome associated with some leucodepletion filters or in future if new reactions occur related to psoralene or prion filters.

Transfusion Related Acute Lung Injury TRALI (ISBT definition incorporating 2013 correction)

In patients with no evidence of acute lung injury (ALI) prior to transfusion, TRALI is diagnosed if a new ALI is present:

- Acute onset
- Hypoxemia
  - o Pa02 / Fi02 < 300 mm Hg or
  - o Oxygen saturation is < 90% on room air or
  - o 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*

o Aspiration
o Pneumonia
o Toxic inhalation
o Lung contusion
o Near drowning

Indirect Lung Injury
o Severe sepsis
o Shock
o Multiple trauma
o Burn injury
o Acute pancreatitis
o Cardiopulmonary bypass
o 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.

Appendix 2: Current IHN/SHOT Classification of Acute Transfusion Reactions

	1=Mild	**2=Moderate**	**3=Severe**	
Febrile type reaction	A temperature > 38^{o}C and a rise between 1^{o}C and 2^{o}C from pre-transfusion values, but no other symptoms/signs	A rise in temperature of 2^{o}C or more, or fever 39^{o}C or over and/or rigors, chills, other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion	A rise in temperature of 2^{o}C or more, and/or rigors, chills, or fever 39ºC^{o} or over, or other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion, prompt medical review AND/OR directly results in, or prolongs hospital stay	Other/Febrile Non-Haemolytic Transfusion Reaction (FNHTR)
Allergic type reaction	Transient flushing urticaria or rash	Wheeze or angioedema with or without flushing/urticaria/rash but without respiratory compromise or hypotension	Bronchospasm, stridor, angioedema or circulatory problems which require urgent medical intervention AND/OR, directly result in or prolong hospital stay, or **Anaphylaxis** (severe, life-threatening, generalised or systemic hypersensitivity reaction with rapidly developing airway AND/OR breathing AND/OR circulation problems, usually associated with skin and mucosal changes)	Anaphylaxis /Hypersensitivity /Allergic

Reaction with both allergic and febrile features	Features of mild febrile **and** mild allergic reactions	Features of both allergic and febrile reactions, at least one of which is in the moderate category	Features of both allergic and febrile reactions, at least one of which is in the severe category.	Other /Mixed febrile /Allergic FNHTR
Hypotensive reaction		Isolated fall in systolic blood pressure of 30 mm Hg or more occurring during or within one hour of completing transfusion **and** a systolic blood pressure 80 mm or less in the absence of allergic or anaphylactic systems. No/minor intervention required.	Hypotension, as previously defined, leading to shock (e.g., acidaemia, impairment of vital organ function) without allergic or inflammatory symptoms. Urgent medical intervention required	Other /Hypotensive FNHTR

SEVERITY GRADES FOR HAEMOLYTIC TRANSFUSION REACTIONS			
1=Positive DAT without haemolysis	**1 =Mild**	**2=Moderate**	**3=Severe**
Not reportable	• Falling haemoglobin • Positive DAT • Spherocytes	• Falling haemoglobin • Rise in bilirubin • + positive DAT • + spherocytes	• Falling haemoglobin • Rise in bilirubin • Renal Impairment • +/- positive DAT • + /-spherocytes

Appendix 3: Serious Adverse Events: Descriptions of current NHO SAE categories

Category	Descriptor
Blood to wrong patient (if no reaction)	All adverse events where a patient was transfused with a blood component or SD plasma which was intended for another patient.
Incorrect ABO and Rh D group transfused (if no reaction)	All adverse events where a patient receives an incorrect ABO or Rh D group and does not have an adverse reaction to the transfusion.
Incorrect ABO group transfused (if no reaction)	All adverse events where a patient receives an incorrect ABO group and does not have an adverse reaction to the transfusion.
Incorrect Rh D group transfused (if no reaction)	All adverse events where a patient receives an incorrect Rh D group and does not have an adverse reaction to the transfusion.
Transfusion of other incorrect antigen /incompatible antigen RCC (if no reaction)	All adverse events where a patient receives an incorrect antigen typed component and does not have an adverse reaction to the transfusion.
Incorrect component/product transfused	All adverse events where a patient receives an incorrect component /SD plasma, when another component would have been more appropriate. E.g. 1: Patient is transfused SD plasma where it would be more appropriate to receive Prothrombin Complex (Octaplex) E.g. 2: Aliquots transfused to a baby from paedi-pack which subsequently had been cross matched and allocated and transfused to another baby due to an error in the clinical area. E.g. 3: Neonatal patient exposed to a second paedi-pack where aliquots from a previously cross matched paedi-pack remain available.
Inappropriate (Unnecessary) transfusion	All adverse events where a patient is transfused with a blood component / SD plasma which was not required by the patient. This may occur due to an error in clinical decision making or failure to verify blood results.
Failure to give an irradiated component	All adverse events where a patient who required an irradiated blood component or FFP was transfused with a blood component that was not irradiated.
Failure to give CMV negative component	All incidents where a patient who required a CMV negative blood component or FFP was transfused with a blood component that was not CMV negative. (also please refer to NTAG CMV Guidelines (https://hse-ie.libguides.com/Covid19V2/transfusions)
Transfusion of an incorrectly labelled component	Adverse events where a patient was transfused correctly despite one or more serious labelling errors which in other circumstances might have led to an incorrect component /SD plasma being transfused e.g. a transposition of labels in a cross match.
Transfusion of expired component	Transfusion of a correct component to an

Category	Descriptor
	intended patient but where the component is commenced after expiry time.
Transfusion of incorrectly stored component	Transfusion of a correct component to an intended patient, when storage errors may have rendered the component less safe for transfusion. E.g. 1: Units returned to controlled storage after 60 minutes, subsequently removed and transfused greater than four hours after initial removal from controlled storage E.g. 2: Units stored in uncontrolled storage E.g.3: Problems with controlled storage
Transfusion of incorrectly distributed component	SAE involving distribution of blood components between HBBs e.g. during re-routing of blood components.
Failure to administer product (Anti-D Ig)	Adverse events resulting in an omission. Anti D -Ig is not administered to a patient who should have received it.
Delay in giving product (Anti -D Ig)	Adverse events resulting in a delay in administration of Anti D Ig greater than 72 hours to patients, but the patient receives anti -D Ig 10 days post sensitising event. Adverse events associated with delays, omissions and inappropriate administrations of anti-D occurring in the RAADP Program e. Due to variation in local practice in reporting establishments the NHO have defined late administration of RAADP as after 34 weeks of gestation
Other	Examples of reports categorised as Other include: • Red cell transfusion exceeding 6 hours, where the unit was transfused following initial removal from the fridge. • Components administered too quickly in patients at risk of developing a reaction e.g. patients with cardiac failure. • Components transfused through a non-filtered giving set. • Over transfusion of a neonate or infant • Where an asymptomatic patient is commenced on antibiotics following a false positive BacT alert from IBTS • Transfusion of red cells cross matched on a sample which is 5 days or older. • Unnecessary administration of anti- D Ig • Incorrect dose of coagulation factor concentrates with potential to result in severe under/over dosage to patient.

Events to be reported to NHO as SAE, Near Miss SAE or Non-Mandatory SAE

NHO Category of SAE report	
Blood to wrong patient (if no reaction)	***Mandatory SAE Report:*** Details of sample incorrectly entered on LIS resulting in wrong patient receiving blood ***Mandatory Near Miss SAE:*** Details of sample incorrectly entered on LIS resulting in blood being issued to wrong patient (but not transfused).
• Incorrect ABO and Rh D group transfused (if no reaction) • Incorrect ABO group transfused (if no reaction) • Incorrect Rh D group transfused (if no reaction) Transfusion of other antigen incompatible RCC (if no reaction	***Mandatory SAE Report:*** Details of sample incorrectly entered on LIS resulting in patient receiving an incompatible ABO, Rh D or other antigen component Error made • **at sub-sampling** where the wrong sample is tested • **in unit selection** • **in grouping** • **in unit labelling** resulting in incompatible ABO, Rh D or other antigen blood components being transfused to the patient ***Mandatory Near Miss SAE:*** Details of sample incorrectly entered on LIS resulting in incompatible ABO, Rh D or other antigen blood components being issued to the patient Error made • **at sub-sampling** where the wrong sample is tested • **in unit selection** • **in grouping** • **in unit labelling** Resulting in incompatible ABO, Rh D or other antigen blood components being issued to the patient (but not transfused). ***Non-Mandatory SAE:*** Example 1- Where an error at sampling (i.e. sample taken from wrong patient) leading to the provision of a wrong ABO /Rh D /both /antigen incompatible group by the HBB Example 2: Transfusion of an ABO/ Rh D or other incompatible unit, which was collected and administered by a doctor/nurse or clinical staff. **The Blood Directive does not apply** in these cases as the error involves the clinical use of blood components by clinical staff (Principle of subsidiarity).

Incorrect component/product transfused	***Mandatory SAE Report:*** Error made in unit selection resulting in patient receiving an incorrect unit. Error made in unit labelling resulting in transfusion of incorrect unit to patient due to transposition of labels in a crossmatch or between two cross matches. False positive BacT Alert where a recall causes transfusion of a second pedipack to an infant resulting in increased donor exposure. ***Mandatory Near Miss SAE:*** Error made in unit selection resulting in the incorrect unit being issued to the patient (but not transfused). Error made in unit labelling resulting in the incorrect unit being issued to the patient due to transposition of labels in a crossmatch or between two cross matches (but not transfused). ***Non-Mandatory SAE:*** Where the error occurred in the clinical area or by a clinician e.g. at collection, prescription/request resulting in a patient receiving a component or SD plasma or other blood product which was not appropriate to their needs. Example 1: patient is transfused SD plasma where it would be more appropriate to receive Prothrombin Concentrate (Octaplex) Example 2: second paedipack or unit of red cells transfused to infant, where paedipack available, resulting in increased donor exposure. In this case there would be a clinical error perhaps during collection/selection of the unit by the clinical staff

Inappropriate (Unnecessary) transfusion	***Mandatory SAE Report:*** N/A ***Mandatory Near Miss SAE:*** N/A ***Non-Mandatory SAE:*** Where the error occurred outside the HBB, either in the clinical area or in another laboratory e.g. haematology laboratory resulting in an unnecessary transfusion of blood components or SD plasma
DELAYED: Where a transfusion of a blood component was clinically indicated but was not undertaken or non-availability of blood components led to a significant delay (e.g., that caused patient harm, resulted in admission to ward or return on another occasion for transfusion).	***Mandatory SAE Report:*** N/A ***Mandatory Near Miss SAE:*** N/A ***Non-Mandatory SAE:*** Delays• Situations where transfusion would have been clinically appropriate but could not be given due to lack of availability of a suitable component (e.g., rare component, recognised blood shortage) • Delays in provision of blood components in an emergency, including delays in clinical recognition of major haemorrhage or need for blood components (e.g., transfusion in sickle cell patients) • Delays where specialist testing is required (e.g., monoclonal antibody therapy, complex antibodies) • Cases where a delay in transfusion affected the patient's health/wellbeing, for example: o An out-patient who must return to hospital the next day as components were not available at the allotted time o Delayed treatment
• Failure to meet patient's special requirements	***Mandatory SAE Report:*** Error made in unit selection resulting in a patient being transfused blood components which did not meet individual special requirements (e.g. CMV negative, Irradiated, HLA matched, and this error occurred in the Hospital Blood Bank). ***Mandatory Near Miss SAE:*** Error made in unit selection resulting in a patient being issued blood components which did not meet individual special requirements e.g. CMV negative, Irradiated, HLA matched (but not transfused) and this error occurred in the Hospital Blood Bank.

	Non-Mandatory SAE: Where an error occurred in the clinical area for example at prescription or at request results in a transfusion where the patient does not receive the special requirements ***(Also please refer to NTAG CMV Guidelines*** ncd19-038-001_071220.pdf ***s)***
• Transfusion of expired component/product	***Mandatory SAE Report:*** Expired components i.e. red cells, platelets transfused to patients, where transfusion is commenced after expiry time due to an error in the HBB. ***Mandatory Near Miss SAE:*** Expired components i.e. red cells, platelets issued to patients, where a component is issued to clinical area after expiry time due to an error in the HBB (but not transfused). ***Non-Mandatory SAE:*** Expired components i.e. red cells, platelets transfused where a unit is commenced after expiry time [1]
• Transfusion of incorrectly stored component	***Mandatory SAE Report:*** Errors surrounding storage of blood /blood components; where storage incidents involve the breakdown / malfunction of a controlled fridge and where a number of units are transfused. Transfusion of red cells returned to storage that were out of controlled storage for greater than 60 minutes and subsequently reused for transfusion. • Yes - where the transfusion time exceeds 4 hours from the time the red cells were initially removed from controlled storage and the RCC were re-issued by staff from the HBB [2]. • Yes- if RCC were subsequently taken back into stock and reissued for another patient. Incorrect storage i.e. red cells in non-blood fridge or platelets in fridge. Failure in agitation of platelets according to Council of Europe guidelines. ***Mandatory Near Miss SAE:***

	Errors surrounding storage of blood /blood components, where storage incidents involve the breakdown / malfunction of a controlled fridge resulting in the loss of a significant quantity of blood and blood components. Re-issue of red cells returned to storage that were out of controlled storage for greater than 60 minutes. Where the RCC were taken back into stock and the unit was re-issued to a different patient (but not transfused). ***Non-Mandatory SAE:*** • Incorrect storage of. SD plasma in a monitored / unmonitored fridge post thawing
• Failure to administer product • Delay in giving product	***Mandatory SAE Report:*** N/A ***Mandatory Near Miss SAE:*** N/A ***Non-Mandatory SAE:*** Failure to administer Anti D Ig Delay in administering Anti D Ig > 72 hours following sensitising event. RADDP event leading to delay
• Other	***Mandatory SAE Report:*** BacT Alert (Confirmed, Unconfirmed and False Positive) where the blood component has been transfused and the patient remains asymptomatic but is commenced on antibiotics or antibiotic treatment is changed following the recall. Transfusion of red cells cross matched on a sample which is 5 days or older. Acceptance & testing of an incorrectly labelled sample in the HBB, but the component issued is correctly labelled with details from the Laboratory Information System. ***Mandatory Near Miss SAE:*** Issue of red cells cross matched on a sample which is 5 days or older. ***Non-Mandatory SAE:*** Red cell transfusion exceeding 6 hours, where the unit was transfused following initial removal from the fridge. [3] Components administered too quickly in patients at risk of developing a reaction e.g. patients with cardiac failure.

	Components transfused through a non-filtered giving set. Over transfusion of a neonate or infant due to a clinical error Unnecessary administration of Anti D Ig

[1]The NHO does not accept reports relating to components commenced prior to expiry time completed within recommended transfusion time, but transfusion completed after expiry time.
The NHO does not accept reports where there is a clear clinical rationale for commencing a transfusion after expiry time e.g. massive bleeding scenario or transfusion of rare cross matched units not readily available in the HBB.

[2] Where the decision to return and subsequently remove the RCC was a clinical decision, and if units were transfused within four hours of initial removal from fridge to the patient for whom they were cross matched, this is not reportable as a non-mandatory SAE.

[3] The NHO does not accept reports of prescription of red cells for six hours, where there is a clear clinical indication for extending the transfusion time over four hours. The safety of the patient is the primary objective, and extending the transfusion time to six hours must be balanced against either transfusing a unit over four hours or stopping one unit after four hours and commencing another unit for a further two hours.

Appendix 4: Criteria for not progressing cases.

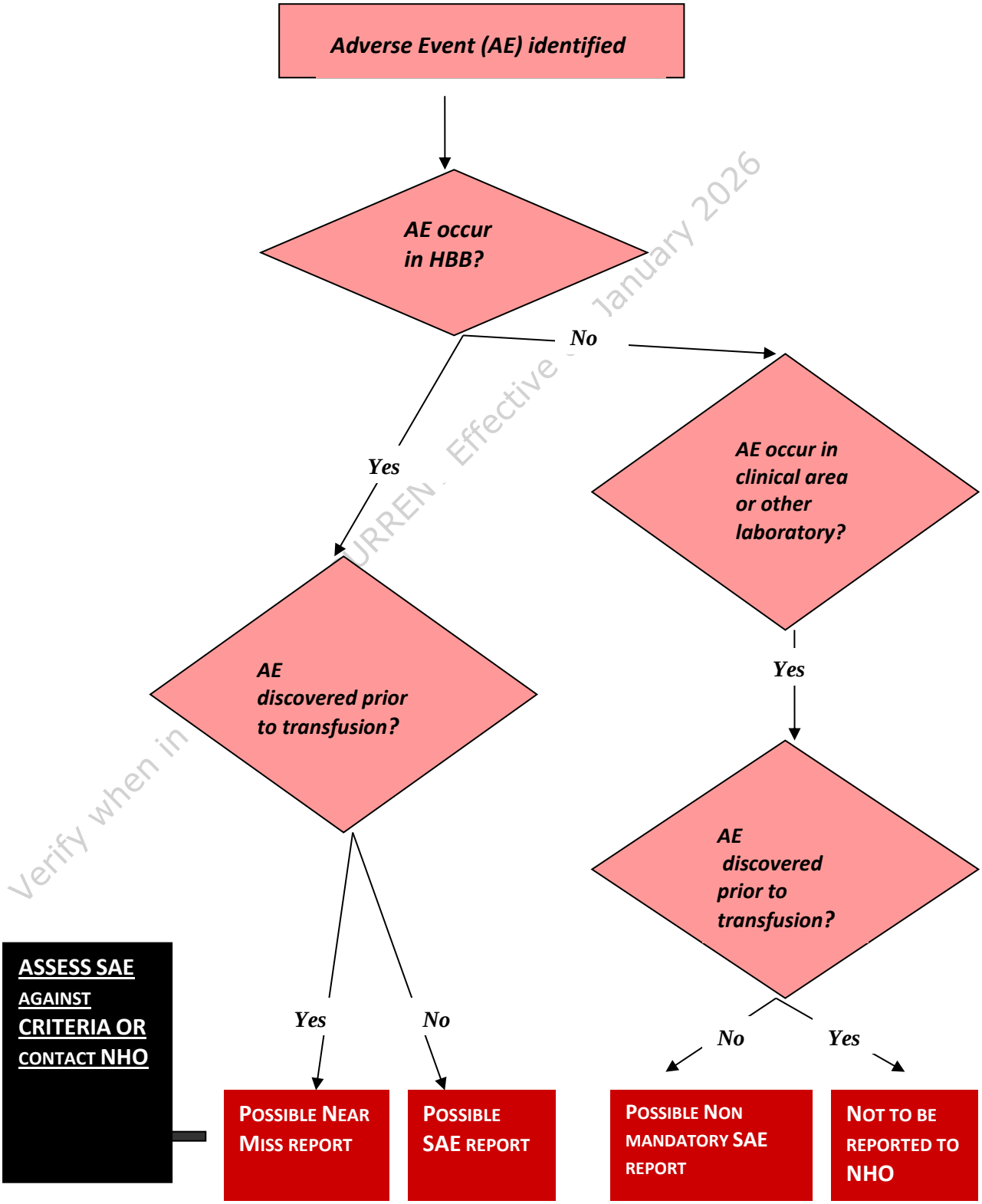
SAR following transfusion of blood components and SD plasma are assigned a DNP status. • Where the symptoms are / can be attributed to patients underlying condition (Imputability – Excluded /Unlikely/Not Assessable) And / Or • Investigations out rule transfusion associated reaction And /Or • Where the report does not meet the reporting criteria as outlined in the Haemovigilance Handbook And /Or • Where these cases have been reviewed by Consultant Haematologist /Treating Physician in the reporting establishment and the Director of NHO. And /Or • Other (Please provide details)
Reports of STTI following transfusion of blood components and SD plasma are only assigned a DNP status • When there is clear evidence of infection prior to transfusion. And /Or • Other (Please provide details)
SAE to blood components and SD plasma are assigned a DNP status where an event • Has a low risk /potential to cause harm to patients as defined in the haemovigilance handbook And / Or • Does not meet the criteria as set out in the 'Common Approach for definition of reportable serious adverse events and reactions as laid down in the blood directive 2002/98/EC and Commission Directive 2005/61/EC'. And /Or • Other (Please provide details)
SAR to blood products (except SD plasma) are not accepted by NHO • Therefore, all such reports are assigned a DNP status And /Or • Other (Please provide details)
SAE to blood products (except SD plasma) • Where adverse events fall outside the criteria outlined in the haemovigilance handbook i.e. delays, omissions or other administration errors relating to anti-D Ig and serious adverse events associated factor concentrates And /Or • Other (Please provide details)

Appendix 5: Reporting SAR and SAE from HBB involving False Positive/Unconfirmed Positive/Confirmed Positive BacT /Alerts

This table outlines how reports relating BacT/Alerts are reported to the NHO and subsequently at the end of year to the EC on the ANSAR/E report. It does not cover the Rapid Alert reporting requirement to the blood establishment

Type of BacT Alert	Patient outcome	Category of NHO Report	EC classification (ANSAR/E Report)
False positive BacT Alert	where the patient is commenced on antibiotics, or their antibiotic is changed as a result of the recall	*SAE – Other*	*SAE –Testing of Donations / Other*
False positive BacT Alert	where there is increased donor exposure as a result of the BacT Alert	*SAE - Incorrect Component Transfused*	*SAE –Testing of Donations / Other*
False positive BacT Alert	No sequelae for the patient	Not to be reported to NHO from HBB	Not to be reported to EC
Confirmed and Unconfirmed positive BacT Alert	Where patient develops signs and symptoms of a reaction	*SAR - STTI Bacterial.*	*SAR - STTI Bacterial where report has met the criteria for STTI (section 3.8)*
Confirmed and Unconfirmed Positive BacT Alert	Where the patient is • commenced on antibiotics or their antibiotic is changed as a result of the recall. • but there is no reaction detected	SAE -Other	*SAE –Testing of Donations / Other*
Confirmed and Unconfirmed Positive BacT Alert.	No sequelae for the patient	Not to be reported to NHO from HBB	Not to be reported to EC from HBB

Appendix 6: Flow-Chart from hospitals to NHO



Appendix 7: Annual notification form
Annual notification for serious adverse reactions

Reporting establishment	
Reporting period	

This table refers to: **RED BLOOD CELLS** (use separate tables for each component)	Number of units issued (total number of units issued with a given number of blood components) *****								
	Number of recipients transfused (total number of recipients transfused with a given number of blood components) (*if available)*								
	Number of units transfused (the total number of blood components (units) transfused over the reporting period) (*if available)*								
	Total number reported	Number of serious adverse reactions with imputability level 0 to 3 after confirmation (see Annex IIA)							
	Number of deaths								
		Components			not assessable	Level 0	Level 1	Level 2	Level 3
			Single	Multiple	A	A	A	A	A
Immunological Haemolysis	Due to ABO incompatibility	Total							
		Deaths							
	Due to other allo-antibody	Total							
		Deaths							
Non-immunological haemolysis		Total							
		Deaths							
Transfusion-transmitted bacterial infection		Total							
		Deaths							
Anaphylaxis/ Hypersensitivity		Total							
		Deaths							
Transfusion related acute lung injury		Total							
		Deaths							

		Components			not assessable	Level 0	Level 1	Level 2	Level 3
			Single	Multiple	A	A	A	A	A
Transfusion-transmitted viral Infection	HBV	Total							
		Deaths							
	HCV	Total							
		Deaths							
	HIV-1/2	Total							
		Deaths							
	Other (specify)	Total							
		Deaths							
Transfusion-transmitted parasitical infection	Malaria	Total							
		Deaths							
	Other (specify)	Total							
		Deaths							
Transfusion-transmitted prion infection		Total							
		Deaths							
Post-transfusion purpura		Total							
		Deaths							
Graft versus host disease		Total							
		Deaths							
Other serious reaction (FNHTR)		Total							
		Deaths							
Other serious reaction (TACO)		Total							
		Deaths							
Other serious reaction Transfusion Associated Dyspnoea (TAD)		Total							
		Deaths							
Other serious reaction Hypotensive Transfusion Reaction		Total							
		Deaths							
Other serious reaction (Unclassified)		Total							
		Deaths							
Other serious reaction (PUCT)		Total							
		Deaths							
Other serious reaction (please specify)		Total							
		Deaths							

Reported by: _____

(*Please print name)*

Signed: _____ Date: _____

Note: There are separate pages for reporting SAR related platelets, whole blood, cryoprecipitate and other components covered under the Directive

Appendix 8: Annual notification for serious adverse events

Reporting establishment

Reporting period | 1 January-31 December (year)

	Blood establishments	**Hospital blood bank**
Total number of blood and blood components processed[1]		Not applicable
Total number of units of blood and blood components issued[2]		

[1]Refers to units processed in a blood establishment

[2]Refers to units issued in a hospital blood bank

To be completed by hospital blood banks

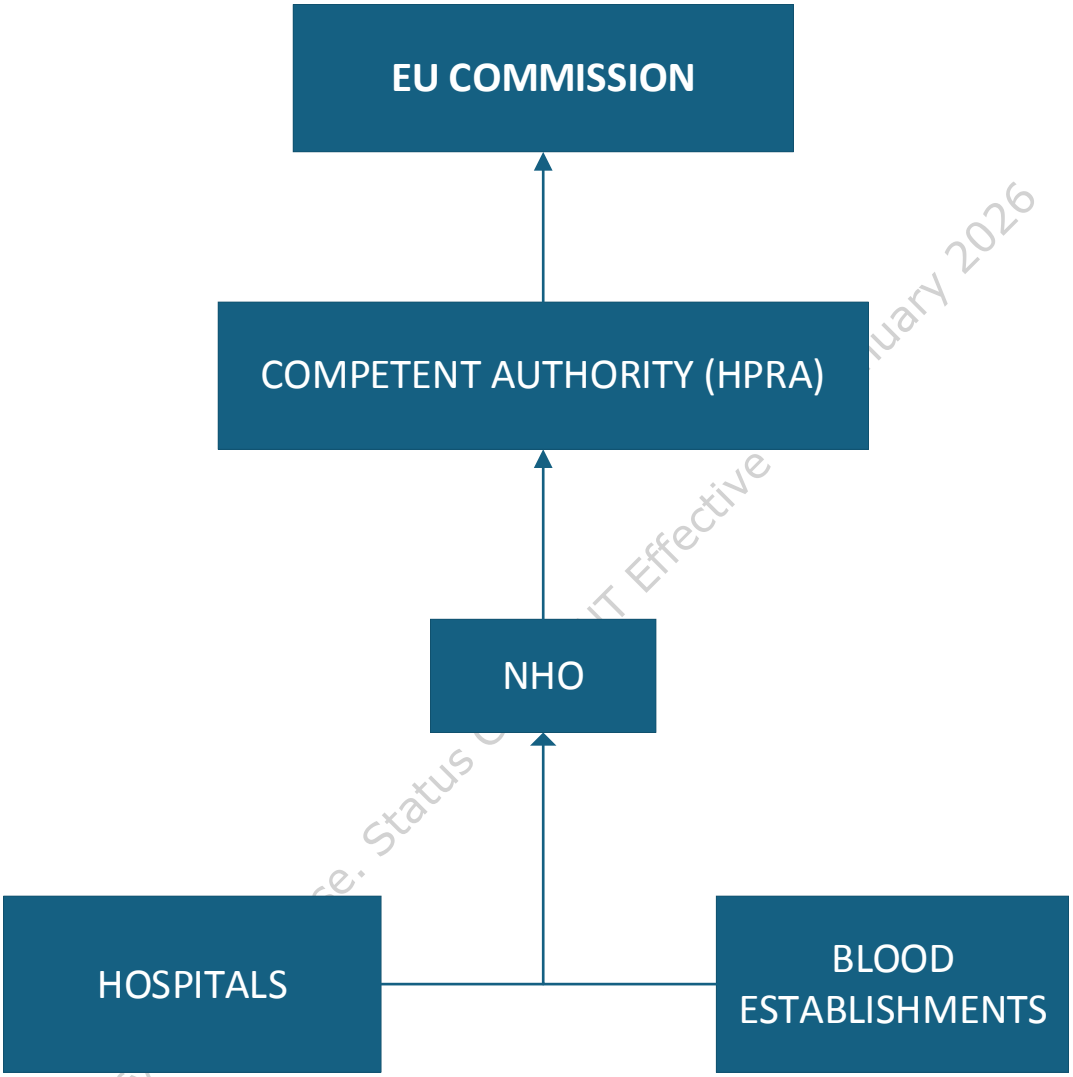
Serious adverse event, affecting quality and safety of blood component due to a deviation in:	**Total Number**	**Specification**					
		Component defect	Equipment failure	Materials	System Failure	Human error	Other (*specify*)
Whole blood collection							
Apheresis collection							
Donor Selection							
Testing of donations							
Processing							
Storage							
Distribution							
Component Selection							
Compatibility Testing/Cross-Matching							
Issue							
Other							

Reported by: _____

(*please print name)*

Signed: _____ Date: _____

Appendix 9: National Haemovigilance Office Organogram



TACO Checklist

	Patient Risk Assessment	Yes	No
Cardiac	Does the patient have any pre-existing co-morbidities i.e. Cardiac Failure, Hypertension, Severe aortic stenosism or moderate or severe left ventricular dysfunction?		
	Is this patient on regular Diuretics?		
	Does the patient have severe anaemia?		
Pulmonary	Is the patient known to have Pulmonary Oedema		
	Has the patient respiratory symptoms		
Fluid Therapy	Is the pre-transfusion fluid balance positive?		
	What other fluids is the patient receiving		
	Is there peripheral oedema present: Does the patient have significant renal impairment?		

If any of the above risks have been identified, PLEASE:

	Yes	No
Review the patients need for Transfusion		
Can the transfusion be safely deferred		

If Proceeding with the transfusion, please ensure the following steps are completed:

- Body Weight of patient and correct component dosing
- Transfuse a single unit of RCC and review
- Monitor Fluid Balance
- Is prophylactic Diuretics required?
- Monitor observations closely