

Glossary and references

CA	Competent Authority. Note: MHRA is the interim Competent Authority in the UK
EU Blood Safety	Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 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.
MHRA	Medicines and Healthcare products Regulatory Agency
Quality system	Based on the principles of good practice. See EU Directive Article 11(1) and UK Legislation Citations 7(1)(b), 9(1)(b)
SABRE	Serious Adverse Blood Reactions and Events.
SAE	Serious Adverse Event. Defined in EU Directive Article 3 Definitions para (g) and identically in UK Legislation Citation 1 – commencement and interpretation (3)
SAR	Serious Adverse Reaction. Defined in EU Directive Article 3 Definitions para (h) and identically in UK Legislation Citation 1 – (3)
SHOT	Serious Hazards Of Transfusion
UK legislation	Statutory Instrument 2005 No 50 – The Blood Safety and Quality Regulations 2005.

All italicised quotes have been derived from the UK legislation.

Contact Information

MHRA		SHOT	
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Reports of Serious Adverse Events and Serious Adverse Reactions should only be submitted via SABRE, the MHRA's online reporting system for blood safety.

Other means of submission should only be considered if SABRE is temporarily unavailable and the report is urgent. In such cases MHRA should be contacted for guidance on how to report.

UK Blood Safety and Quality Regulations 2005

Implementation of the EU Blood Safety Directive

Background and Guidance on reporting Serious Adverse Events & Serious Adverse Reactions



MHRA – the UK Competent Authority for Blood Safety

Report Serious Adverse Events & Serious Adverse Reactions online:
Log on to SABRE via the MHRA website: www.mhra.gov.uk
email: sabre@mhra.gsi.gov.uk tel: 020 7084 3336

Introduction

EU Blood Safety Directive and the Competent Authority The *EU Blood Safety Directive* introduces a legal requirement for *serious adverse reactions* (SAR) and *serious adverse events* (SAE) occurring within EU Member States to be reported to the relevant *Competent Authority*. The Department of Health has designated the MHRA as the interim UK Competent Authority. It is, therefore, the MHRA's responsibility to put in place by 8 November 2005, a mechanism for the reporting and recording of these incidents. For this purpose the MHRA has developed a new online reporting system: *SABRE* (Serious Adverse Blood Reactions & Events).

Haemovigilance in the UK Haemovigilance comprises organised surveillance procedures relating to serious adverse or unexpected events or reactions in blood donors or recipients, and the epidemiological follow-up of donors. The UK was one of the first countries to implement such a system and since 1996 the Serious Hazards of Transfusion (*SHOT*) scheme has successfully undertaken those aspects of haemovigilance relating to recipients. Implementation of the EU Blood Safety Directive has provided an opportunity to strengthen and further develop haemovigilance in the UK, the aim of which is to improve transfusion safety.

This document describes the requirements of the Directive and also, in order to assist reporters of adverse events and reactions, includes guidance and flowcharts to help identify what constitutes a serious adverse reaction and a serious adverse event and, therefore, what is or is not reportable to the Competent Authority (MHRA) under the EU Blood Directive and UK legislation. A list of typical scenarios and frequently asked questions has been compiled and is available on SHOT's website. However, this is not exhaustive and does not provide a definitive list of what does and what does not constitute a reportable incident. As well as consulting these documents you may also contact the MHRA or SHOT for advice, as appropriate. As a general rule, in cases of doubt, a report should be submitted.

Investigation and corrective/preventive action It is not the purpose of this document to provide guidance on how to investigate incidents, nor on how to implement effective corrective and preventive actions.

SABRE - online reporting to MHRA and SHOT In addition to satisfying the requirements of the EU Directive for reporting to MHRA, SABRE has been developed to facilitate SHOT reporting by incorporating SHOT questionnaires. This provides a single reporting route for UK haemovigilance. MHRA has also created a system for SHOT to review and then extract data for detailed manipulation and analysis. Guidance on the new SABRE online reporting system is being issued separately by the MHRA. This will explain: how to register as a SABRE user; how to complete the simple online report forms; and how to optimise SABRE use with existing local reporting arrangements.

Annual summary reports The Directive also requires that each reporting establishment submit to the Competent Authority an annual summary report of serious adverse reactions and serious adverse events. SABRE will support this process. The Competent Authority must, in turn, submit an annual summary report to the EU Commission.

Reporting to SHOT – Serious Hazards Of Transfusion Reporting to SHOT remains voluntary, but is required for compliance with HSC/2004/009 'Better Blood Transfusion' and is a standard for the Clinical Negligence Scheme for Trusts in England. Active participation in SHOT by **all** hospitals was recommended by the CMO for England in his 2003 annual report. A number of blood safety initiatives depend on continuity of SHOT data for monitoring and evaluation and it is therefore vital that hospitals use the SABRE system to continue to report to SHOT. The spectrum of events and reactions reportable to SHOT has not changed and SHOT data will continue to be used as a benchmark for the joint Blood Safety Project between the National Patient Safety Agency, SHOT and the National Blood Transfusion Committee.

Serious adverse reactions (SAR)

Definition '*an unintended response in a donor or in a patient that is associated with the collection, or transfusion of blood or blood components that is fatal, life-threatening, disabling or incapacitating, or which results in or prolongs hospitalisation or morbidity*'

These are:

- Immunological haemolysis due to ABO incompatibility
- Immunological haemolysis due to other allo-antibody
- Non-immunological haemolysis
- Transfusion-transmitted bacterial infection
- Anaphylaxis / hypersensitivity
- Transfusion related acute lung injury (TRALI)
- Transfusion-transmitted viral infection (HBV)
- Transfusion-transmitted viral infection (HCV)
- Transfusion-transmitted viral infection (HIV-1/2)
- Transfusion-transmitted viral infection, other (specify)
- Transfusion-transmitted parasitological infection (Malaria)
- Transfusion-transmitted parasitological infection, other (specify)
- Post-transfusion purpura
- Graft-versus host disease
- Other serious reaction(s) – specify (e.g. transfusion associated circulatory overload)

SHOT agreed definitions of these reactions can be found on the SHOT website together with standards for investigation.

As soon as a transfusion transmitted infection (TTI) due to viruses, bacteria or parasites is suspected it should be reported to MHRA. Once the investigation of the suspected TTI is concluded a confirmatory report should then be submitted to the MHRA. SABRE includes a reminder that all suspected TTIs and TRALIs should be reported immediately to the relevant blood establishment.

It must be emphasised that the robust systems currently in place for rapid notification of suspected TTI to the national blood services are unchanged.

Using SABRE to report serious adverse events and serious adverse reactions to MHRA and SHOT

Reporting requirements

'blood establishments and the person responsible for the management of a hospital blood bank shall notify the Secretary of State (Competent Authority) of any serious adverse reactions observed during or after transfusion which may be attributable to the quality or safety of blood or blood components –

(i) collected, tested, processed, stored or distributed by the blood establishment, or

(ii) issued for transfusion by the hospital blood bank'

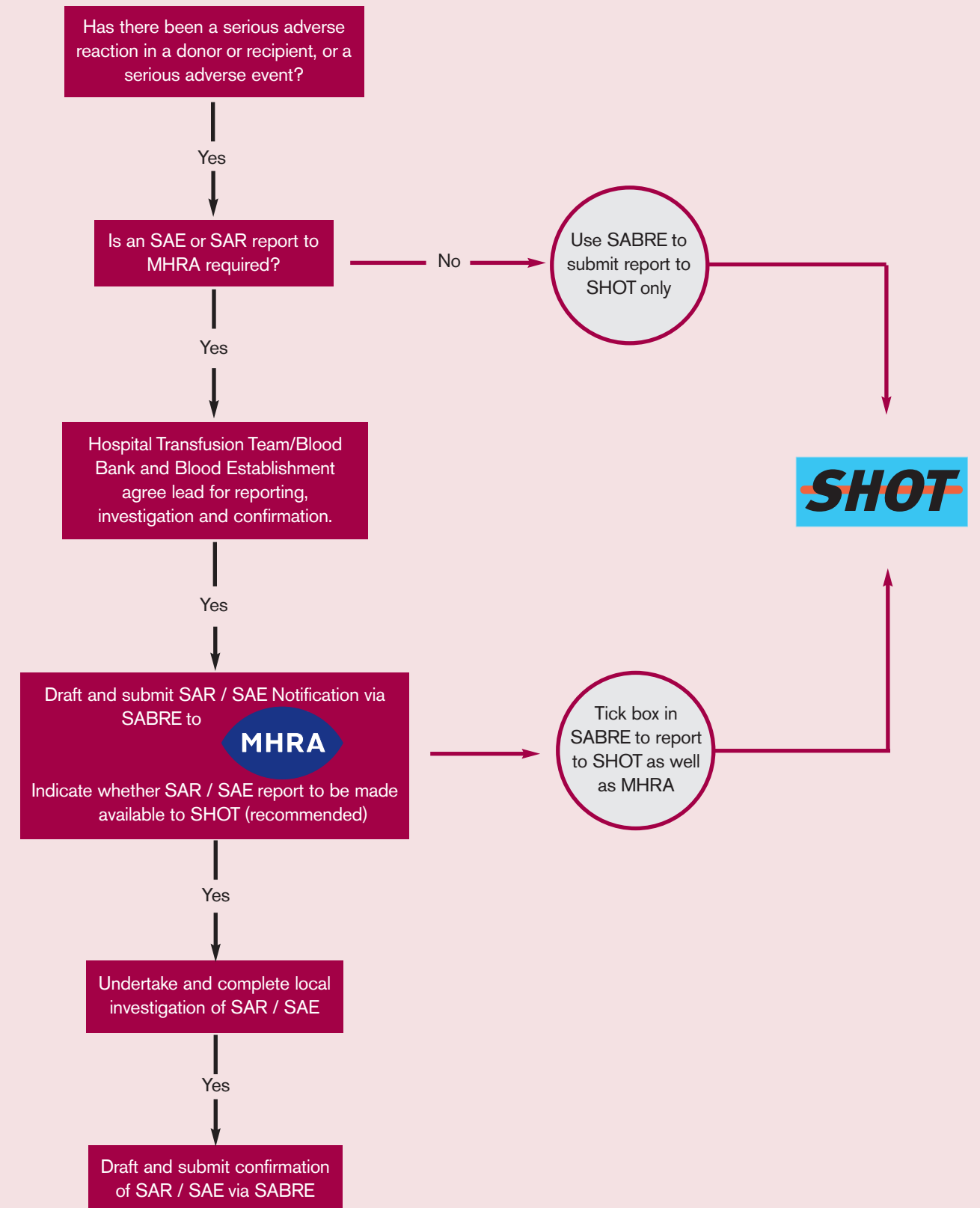
Many serious adverse reactions are related to patient factors, consequently the same blood component, if given to another patient, would not cause a problem. If a serious reaction may be attributable to the quality or safety of blood, **for the patient to whom it is given**, it must be reported to the Competent Authority. Concluded local investigations, including an assessment of the likelihood of the reaction being attributable to the quality or safety of blood or blood components (the Imputability Level) must subsequently be confirmed, and the information held on SABRE must be updated appropriately. For Imputability Levels 2 and 3 the confirmation should include a full account of the symptoms, investigation, root cause analysis (outcome of investigation) and corrective and preventive action taken.

If any associated products were required to be recalled and/or investigated as a result of the serious adverse reaction, the report should also include explicit reference to the fate of those products and any subsequent actions taken for blood components that had been distributed for transfusion.

Donors For serious adverse reactions of a donor, the blood establishment must notify the Competent Authority only where the quality and safety of the blood may be compromised.

Imputability Levels 'Imputability' means the likelihood that a serious adverse reaction in a recipient can be attributed to the blood or blood component transfused or that a serious adverse reaction in a donor can be attributed to the donation process. The table below defines the imputability levels.

N/A	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 causes other than the blood or blood components.
	Unlikely	When the evidence is clearly in favour of attributing the adverse reaction to causes other than the blood or blood components.
1	Possible	When the evidence is indeterminate for attributing the 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	Certain	When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to the blood or blood component.



Serious adverse events (SAE)

Definition

'any untoward occurrence associated with the collection, testing, processing, storage and distribution, of blood or blood components that might lead to death or life-threatening, disabling or incapacitating conditions for patients or which results in, or prolongs, hospitalisation or morbidity.'

Reporting requirements

'Blood establishments shall notify... any serious adverse events related to the collection, testing, processing, storage and distribution of blood or blood components by the blood establishment which may have an influence on their quality and safety, and;

the person responsible for the management of a hospital blood bank shall notify... any serious adverse events related to the testing, storage and distribution of blood or blood components by the hospital blood bank which may have an influence on their quality and safety.'

Distribution

'the act of delivery of blood and blood components to other blood establishments, hospital blood banks and manufacturers of blood and plasma derived products. It does not include the issuing of blood or blood components for transfusion'

The following terms, though used, are not defined within the EU Directive. Reporters in the UK should be guided by the following definitions to help in determining the reportability of an SAE.

'Testing' means the mandatory or discretionary testing of the donation by the blood establishment. It also includes tests done by the blood bank on processed components or the recipient sample to determine compatibility.

'Processing' means manipulation of the blood donation or other blood components for further manufacturing or subsequent administration to humans. Note: under the UK legislation only a blood establishment can undertake processing.

'Storage' means safe husbandry of the blood at all stages of the cold chain and is undertaken by blood establishments and also by hospital transfusion laboratories. Blood leaves the control of the hospital transfusion laboratory at the point where it is issued for transfusion or transferred to a satellite refrigerator that is not within the control of the laboratory (it is arguable that all blood storage refrigerators should be within laboratory control).

What constitutes a Serious adverse event (SAE)?

