Aim of document

1. This document provides guidance on serious adverse event (SAE) and serious adverse reaction (SAR) reporting under the Quality and Safety of Organs Intended for Transplantation Regulations 2012 (the Regulations). The Regulations transpose into UK law the requirements of EU Directive 2010/53/EU on standards of quality and safety of human organs intended for transplantation.

2. It includes guidance on the definitions of reportable events and reactions, the roles and responsibilities of the organisations involved, algorithms for notification and management, and examples of SAEs and SARs.

3. Further information on the statutory requirements relating to SAEs and SARs can be found in the Human Tissue Authority’s (HTA) framework document.

4. The requirement to report SAEs and SARs applies to all UK establishments licensed under the Regulations, regardless of geographical location or whether they are a private or an NHS organisation.

5. This resource is not exhaustive and other events and reactions not included as examples here may fall within the definitions. If in doubt, we would always encourage establishments to contact NHS Blood and Transport (NHSBT) for further advice.

6. Effective systems for adverse event and reaction reporting rely on reports by the professionals involved in organ donation and transplantation. Retrieval teams, transplant centres (private or NHS), donor hospitals, testing laboratories, NHSBT Specialist Nurses Organ Donation (SNODs) and other NHSBT staff, and the HTA should foster a culture of reporting SAEs and SARs. **It is important to acknowledge that the reporting of SAEs and SARs is not associated with blame.**

7. The serious adverse event and reaction (SAEAR) system has two roles:
   
   - To raise the alert if there is any unexpected complication, particularly if other recipients may be at risk.
To ensure the quality and safety of organs during the entire chain from donation to transplantation by requiring serious adverse events and reactions to be reported, investigated and management measures implemented.

Definitions of serious adverse event and reaction

8. A serious adverse event (SAE) is defined in the Regulations as ‘any undesired and unexpected occurrence associated with any stage of the chain from donation to transplantation that might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients or which results in, or prolongs, hospitalisation or morbidity’.

9. SAEs that may influence the quality and safety of an organ and that may be attributed to the testing, characterisation, procurement, preservation and transport of organs must be reported and investigated.

10. The HTA also requires that any SAEs which occur at a transplant centre which may influence the quality and safety of an organ must be reported and investigated.

11. A serious adverse reaction (SAR) is defined in the Regulations as ‘an unintended response, including a communicable disease, in the living donor or in the recipient that might be associated with any stage of the chain from donation to transplantation that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity’.

12. SARs observed during or after transplantation which may be connected to the testing, characterisation, procurement, preservation and transport of organs must be reported and investigated.

The SAEARs system

13. NHSBT will be managing the system for reporting and managing SAEARs on behalf of the HTA as one of a series of assisted functions. Reports of SAEs and SARs should therefore be made to NHSBT following their current incident reporting procedure [link to be inserted]. This will be part of NHSBT’s wider clinical incident reporting system, and a continuation of current practice for NHS establishments.

14. NHSBT will notify HTA of any SAEARs that have been reported, the steps being taken to manage the SAEAR and confirmation that all actions associated with the SAEAR have been concluded.

15. There will therefore be no requirement for licence holders to report directly to the HTA. However, if the licence holder or any party involved has
concerns relating to conflict of interest with NHSBT and a specific event or reaction, then they should contact the HTA. The HTA will take responsibility for overseeing the investigation where such a conflict of interest is identified.

16. All SAEARs should be reported within 24 hours of the discovery by the licence holder. In cases where an urgent notification is required, the establishment must telephone the NHSBT Organ Donation and Transplantation (ODT) Directorate duty office on 01179 757575 immediately upon discovery. Such urgent notification would include cases where there are potential implications for other recipients. The telephone call should be followed up with the submission of a report form.

17. The roles and responsibilities of organisations involved in the chain from donation to transplantation are outlined in paragraphs 19 - 38 below.

18. Licence holders are expected to collaborate fully in the investigation of a suspected SAEAR, and to submit a follow up report. This must normally be provided within 90 days and should include the corrective and preventative actions taken or planned to prevent reoccurrence. It is a condition of a licence to report on the management measures taken with regards to SAEARs.

Roles and responsibilities

19. A route map for reporting is included in the appendix to this guidance [to be inserted when NHSBT’s IT system completed].

Persons working under the licence (retrieval teams / private and NHS transplant centres / NHSBT staff)

20. It is a condition of the licence that SAEARs are reported. In practice, organisations will need to ensure procedures are in place for this obligation to be met. Licence holders need to ensure that the procedures show clearly who is responsible for submitting notifications to NHSBT.

21. Policies, procedures and staff training arrangements should be updated, as required, to include the relevant requirements, to ensure that SAEARs are reported and within the required timescales.

22. A SAEAR may have implications for other transplant centres or tissue establishments. In this case it is the responsibility of NHSBT to ensure that all those affected are informed, and not the duty of the licence holder.

23. Licence holder should consider providing information to living donors and recipient referral centres on how to identify and report any event or serious adverse reaction that may result from the donation or transplant. Living donors should be encouraged to discuss this information with their families and GPs, where appropriate. This is particularly relevant for donors from overseas who travel to the UK to donate.
24. Any SAEARs relating to SNOD activities should also be reported to NHSBT. In cases where there is perceived to be a conflict of interest, then HTA will oversee the investigation, and review any management measures taken.

**Laboratories**

25. Although not licensed by the HTA, laboratories will be able to report SAEARs directly to NHSBT.

26. Any SAEAR discovered by a licence holder, which involves a testing laboratory, should also be reported to NHSBT.

**Donor hospitals**

27. Although not licensed by the HTA, donor hospitals will be able to report SAEARs directly to NHSBT.

28. Any SAEAR discovered by a licence holder, which involves a donor hospital, should also be reported to NHSBT.

**NHSBT (acting on behalf of the HTA)**

29. NHSBT will manage a system for reporting, investigating, registering and transmitting information about SAEARs as part of their system for receiving wider incident reports. This is a continuation of current practice for NHS establishments, but this will now include reporting from private hospitals licensed by the HTA for organ donation and transplantation.

30. NHSBT will rapidly notify SAEARs information to any affected person or organisation, including facilitating the transfer of information between transplant centres and tissue establishments when an organ donor is also a tissue donor.

31. Upon receiving a report, NHSBT will assign a case number and carry out an assessment, including grading the incident using a risk matrix. NHSBT will investigate where it considers that an investigation will promote the quality and safety of organs.

32. NHSBT will register the information on SAEARs and keep it for 30 years.

33. NHSBT will inform HTA of any SAEARs that have been reported, the steps being taken to manage the SAEAR and confirmation that all actions associated with the SAEAR have been concluded.
As the Competent Authority, HTA will maintain oversight of the SAEARs system. In addition to being notified of any SAEARs reported to NHSBT, an HTA representative will attend NHSBT’s Donation and Transplantation Care meetings where all reported clinical incidents are discussed.

Specifically, HTA will superintend investigations involving NHSBT staff, or where there is a perceived conflict of interest.

As one of the Competent Authorities for tissues and cells, the HTA will ensure interconnection with the SAEARs reporting system for tissues and cells, and will ensure NHSBT are informed of any SAEARs reported by a tissue establishment which may have relevance to transplant centres.

In certain cases, and where justified on the basis of risk to the quality and safety of organs, the HTA may initiate an audit of a licence holder following a report of a SAEAR. In any event, the HTA will ensure that information received regarding SAEARs is available to inform the audit teams.

The HTA will be responsible for liaising with other organisations, including other competent authorities and government agencies, as necessary and will retain responsibility for issuing any regulatory alerts to licence holders, however they may be assisted in this regard by NHSBT as appropriate.

Organs sent overseas

Organs sent overseas should be accompanied by information for the receiving establishment on how to report any SAEARs relating to donation, characterisation, retrieval, preservation or transport carried out in the UK.

Triggers for reporting – serious adverse reactions in recipients

Clinical symptoms or situations suggesting that any of the following reactions might have occurred in an organ recipient should be seen as triggers for a serious adverse reaction report. Please note that the list is not exhaustive.

- Infections possibly transferred from the donor to the recipient (e.g. viral, bacterial, prion) that were not known at the time of transplantation.
- Infections possibly transferred due to contamination or cross-contamination by an infectious agent on the organ or associated materials from procurement to transplantation.
- Malignant disease possibly transferred from the donor to the recipient that was not known at the time of transplantation.
- Any unintended consequence for the recipient, including early failure or delayed graft function, which may be connected to the testing, characterisation, procurement, preservation and transport of the organ.
• Unexpected immunological reactions that were not anticipated and may be connected to the testing, characterisation, procurement, preservation and transport of the organ.

• Aborted transplantation procedure due to any issue with the organ supplied, discovered after recipient is anaesthetised, where the issue may be attributable to the testing, characterisation, procurement, preservation and transport of the organ.

41. The HTA recognises that organs may have early graft failure for a number of reasons, and a specific cause may be difficult to determine. Early graft failure should only be reported as a serious adverse reaction when there are grounds for suspecting that the failure may be connected to the testing, characterisation, procurement, preservation and transport of the organ, or a serious adverse event.

42. Evaluation of the risks is inherent in organ donation and transplantation, and there may be cases where a certain risk is known and taken by clinicians after discussion with the recipient. In such cases there is no requirement to report as a serious adverse event or reaction.

**Triggers for reporting – serious adverse reactions in living donors**

43. Donor adverse reactions with a possible direct effect on the quality and safety of the donated organ, or that may have resulted from the donation must be reported as a serious adverse reaction.

44. These may be immediate, i.e. occurring at the time of donation or within a few days post-donation, or they may be delayed, i.e. identified after the donation (possibly even many years later). The licence holder must report the suspected SAR within 24 hours of its discovery.

**Triggers for reporting – serious adverse events**

45. Deviations from standard operating procedures, or other adverse events, should be reported as a serious adverse event when one or more of the following criteria applies:

• The event could have implications for the quality and safety of organs.
• The event could have implications for other patients, recipients or donors because of shared practices, services, supplies or donors.
• The event resulted in the loss of any organs.

46. Events that are commonly referred to as ‘near misses’ are included in the above categories.

47. The table of examples in the appendix to this guidance includes reference to these criteria.
Glossary


**Disposal** means the final placement of an organ where it is not used for transplantation.

**Donor** means a person who donates one or several organs, whether donation occurs during lifetime or after death.

**Donor selection** means a process by which consent or authorisation is obtained or verified, and a potential donor is identified.

**Donation** means donating organs for the purposes of transplantation.

**Donor characterisation** means the collection of relevant information on the characteristics of the donor needed to evaluate the donor’s suitability for donation, in order to undertake a proper risk assessment and to minimise the risks for the recipient, and optimise organ allocation.

**Implantation** means the activity of transferring an organ into a recipient.

**Licence holder** means a person who holds a licence under Schedule 1 to the Regulations.

**Licensed activity** in relation to a licence, means an activity which the licence authorises under Schedule 1 to the Regulations. Such an activity will either be a procurement activity or a transplantation activity.

**NHSBT** means NHS Blood and Transplant.

**Organ** means a differentiated part of the human body, formed by different tissues, that maintains its structure, vascularisation, and capacity to develop physiological functions with a significant level of autonomy. A part of an organ is also considered to be an organ if its function is to be used for the same purpose as the entire organ in the human body, maintaining the requirements of structure and vascularisation.

**Organ characterisation** means the collection of the relevant information on the characteristics of the organ needed to evaluate its suitability for transplantation, in order to undertake a proper risk assessment and minimise the risks for the recipient, and optimise organ allocation.
**Operating procedures** means written instructions describing the steps in a specific process, including the material and methods to be used and the expected outcome.

**Person** means an individual or corporate body.

**Procurement** means a process by which a donated organ becomes available for transplantation.

**Procurement activity** means any of the following licensable activities, undertaken for the purposes of procurement:

a) donor characterisation;

b) organ characterisation;

c) preservation of an organ;

d) making arrangements to transport an organ; or

e) retrieval of an organ.

**Preservation** means the use of chemical agents, alterations in environmental conditions or other means to prevent or retard biological or physical deterioration of organs from procurement to transplantation.

**Recipient** means a person who receives a transplant of an organ.

**Regulation 6** means regulation 6 of the Quality and Safety of Organs for Transplantation Regulations 2012 (SI 2012 No. xxx), authorising the HTA to give directions to a licence holder to ensure compliance with the Directive.

**Regulation 11** means regulation 11 of the Quality and Safety of Organs for Transplantation Regulations 2012 (SI 2012 No. xxx), authorising the HTA to give directions to a licence holder as prescribed in Schedule 2 of the Regulations.

**Retrieval** means the activity of removing an organ from a donor.

**Schedule 2** means Schedule 2 of the Quality and Safety of Organs for Transplantation Regulations 2012 (SI 2012 No. xxx), requiring the HTA to give specific directions to ensure consistent compliance with the licensing conditions prescribed in Schedule 1 of those Regulations.

**Serious adverse event** means any undesired and unexpected occurrence associated with any stage of the chain from donation to transplantation that might lead to the transmission of a communicable disease, to death or life-
threatening, disabling or incapacitating conditions for patients or which results in, or prolongs, hospitalisation or morbidity.

**Serious adverse reaction** means an unintended response, including a communicable disease, in the living donor or in the recipient that might be associated with any stage of the chain from donation to transplantation that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity.

**Tests** means laboratory-based tests for the purposes of donor and organ characterisation, including microbiological and virology screening, human leukocyte antigen (HLA) typing and cross-matching, and ABO blood grouping.

**Traceability** means the ability to locate and identify the organ at each stage in the chain from donation to transplantation or disposal, including the ability to:

a) identify the donor and the licence holder who retrieved the organ from the donor;

b) identify the licence holder who implanted the organ into the recipient;

c) identify the recipient at the premises that the organ is implanted into the recipient; and

d) locate and identify all relevant non-personal information relating to products and materials coming into contact with that organ.

**Transplantation** means a process which is intended to restore certain functions of the human body by transferring an organ from a donor to a recipient.

**Transplantation activity** means any of the following licensable activities, undertaken for the purposes of transplantation:

a) organ characterisation;

b) preservation of an organ;

c) making arrangements to transport an organ; or

d) implantation of an organ.

**UK Transplant Registry** means the register of organ donation and transplantation activities as held by NHSBT.
## Appendix – examples of SAEARs

<table>
<thead>
<tr>
<th>Description</th>
<th>Reportable as a SAE/SAR?</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Transcription error when recording test results.</td>
<td>Yes as a SAE.</td>
<td>Report to ODT Duty Office asap.</td>
</tr>
<tr>
<td>Positive virology result post-transplantation that was not known at the time of donation and has implications for recipients of organs or tissues and cells.</td>
<td>Yes as a SAE.</td>
<td>Report to ODT Duty Office asap.</td>
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<tr>
<td>Mis-labelling of organ boxes resulting in wrong organs being delivered to the transplant centre.</td>
<td>Yes as a SAE.</td>
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<tr>
<td>Tumour discovered that was not known or communicated at the time of donation.</td>
<td>Yes as a SAE.</td>
<td>Report to ODT Duty Office asap.</td>
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<tr>
<td>Damage to organ, during retrieval or transplant, which resulted in an impact on recipient (significant delay/unable to transplant/graft failure) or loss of the organ.</td>
<td>Yes as a SAE.</td>
<td>Graft failure caused by damage to organ should be reported as suspected SAR.</td>
</tr>
<tr>
<td>Problems with transport or arranging transport resulting in loss of organ due to prolonged cold ischaemic time.</td>
<td>Yes as a SAE.</td>
<td></td>
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<tr>
<td>Donor or recipient data reporting incident</td>
<td>Yes as a SAE.</td>
<td>Report to ODT Duty Office asap if there are implications for recipients.</td>
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<tr>
<td>Suspected transfer of infection or malignant disease from donor to recipient, that was not known at the time of transplantation</td>
<td>Yes as a SAR.</td>
<td>Report to ODT Duty Office asap.</td>
</tr>
<tr>
<td>Suspected transfer of infection to a recipient due to contamination by an infectious agent in the preservation fluid.</td>
<td>Yes as a SAR.</td>
<td>Report to ODT Duty Office asap.</td>
</tr>
<tr>
<td>Aborted transplantation procedure where the recipient is already anaesthetised, due to an issue with the organ supplied that may be attributable to the testing, characterisation, procurement, preservation and transport of the organ.</td>
<td>Yes – as a SAR as there is an impact for the recipient, but likely to have been</td>
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<tr>
<td>Event</td>
<td>SAE/SAR</td>
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<tr>
<td>Aborted transplantation procedure where the recipient is already anaesthetised due to an issue at the transplant centre which affected the quality and safety of the organ.</td>
<td>Yes – as a SAR.</td>
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<tr>
<td>Equipment malfunction or iatrogenic damage during living laparoscopic donor nephrectomy requiring conversion to an open operation and consequent delayed graft function.</td>
<td>Equipment malfunction would be an SAE. Any clinical consequences for the donor or recipient would be an SAR.</td>
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</tr>
<tr>
<td>Damage to an organ which has no consequence for the recipient.</td>
<td>Not an SAE.</td>
<td></td>
</tr>
<tr>
<td>Post operative infection which is not suspected to be attributable to the testing, characterisation, procurement, preservation and transport of the organ.</td>
<td>Not an SAR.</td>
<td></td>
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<tr>
<td>Early graft failure or delayed graft function which is not suspected to be attributable to the testing, characterisation, procurement, preservation and transport of the organ.</td>
<td>Not an SAR.</td>
<td></td>
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</table>
Serious adverse event and reaction reporting – Summary

Criteria for reporting SAEs:
- The event could have implications for the quality and safety of organs;
- The event could have implications for other patients, recipients or donors because of shared practices, services, supplies or donors;
- The event resulted in the loss of any organs.

Criteria for reporting SARs in recipients:
- Infections possibly transferred from the donor to the recipient (e.g. viral, bacterial, prion) that were not known at the time of transplantation;
- Infections possibly transferred due to contamination or cross-contamination by an infectious agent on the organ or associated materials from procurement to transplantation;
- Malignant disease possibly transferred from the donor to the recipient that was not known at the time of transplantation;
- Any unintended consequence for the recipient, including early failure or delayed graft function, which may be connected to the testing, characterisation, procurement, preservation and transport of the organ;
- Unexpected immunological reactions that were not anticipated and may be connected to the testing, characterisation, procurement, preservation and transport of the organ;
- Aborted transplantation procedure due to any issue with the organ supplied, discovered after recipient is anaesthetised, where the issue may be attributable to the testing, characterisation, procurement, preservation and transport of the organ.