

SaBTO

Advisory Committee on the
Safety of Blood, Tissues and Organs

MICROBIOLOGICAL SAFETY GUIDELINES

PREVIOUSLY KNOWN AS

**GUIDANCE ON THE MICROBIOLOGICAL SAFETY
OF HUMAN ORGANS, TISSUES
AND CELLS USED IN TRANSPLANTATION**

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1 Introduction

- 1.1 This guidance updates and replaces the 'Guidance on the Microbiological Safety of Human Organs, Tissues and Cells used in Transplantation' issued in February 2011.
- 1.2 SaBTO's role is to advise Ministers of the UK Government and the Devolved Administrations as well as UK Health Departments on the most appropriate ways to ensure the safety of blood, cells, tissues and organs for transfusion and transplantation.
- 1.3 This guidance should be read with reference to other current SaBTO guidance.
- 1.4 This guidance has been written by a working group. Members are listed in [Annex 1](#). Other publications on this subject were taken into consideration during the preparation of this document.
- 1.5 The underlying principle running through this guidance is that the risk of an infection being passed on through transplanted organs, tissues and cells be kept to an *acceptable minimum*. What constitutes an acceptable minimum is dependent on the balance of risk and benefit for the potential recipient in terms of either receiving the proposed transplant or going without that specific transplant. In urgent life-preserving situations, a higher risk of infection may be acceptable whilst stricter controls are needed in non-urgent situations and for transplants aimed at improving a patient's quality of life rather than saving it. In all situations the potential recipient, or their proxy, should provide full informed consent that must include discussions regarding the potential for transmission of infection.
- 1.6 Table 1 contains a list of most of the organs, tissues and cells (haematopoietic, reproductive and other cells) covered by this guidance.
- 1.7 The broad principle regarding minimisation of transmission of infection also applies to the source human tissues and cells cultured in a laboratory before transplantation and to manufactured products or services that use human cells or tissues.
- 1.8 Reproductive cells, embryos and embryonic stem cells and haematopoietic stem and progenitor cells are within the remit of this guidance. However, the microbiological safety and quality of human blood and blood components and blood products, is covered elsewhere (<http://www.transfusionguidelines.org/>).
- 1.9 The Guidelines set out the main recommendations covering microbiological screening of organ, tissue and cell donors together with resulting actions to take following the identification of an infected (or potentially infected) donor.
- 1.10 For organ donors and deceased tissue donors, the information required for assessing an organ donor's risk of harbouring an infection are set out in the NHS Blood and Transplant Patient Assessment Form (PA1)¹.

¹ <http://www.odt.nhs.uk/donation/deceased-donation/organ-donation-services/role-of-specialist-nurse/patient-assessment.asp>

- 1.11 For haematopoietic and therapeutic cell donors, guidance on the minimum requirements for assessment of suitability to donate can be found in the current edition of the FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (<http://www.factwebsite.org> and <https://www.jacie.org>). The World Donor Marrow Association provides guidance on the minimum standards by which unrelated haematopoietic stem and progenitor cell donors should be assessed (<https://www.wmda.info>). Neither set of guidelines is intended to supersede local laws or requirements of national legislative bodies.
- 1.12 The recommendations and guidance contained within this document reflects good practice in accordance with available evidence, supplemented by expert opinion where published evidence is lacking. It is also acknowledged that the advice contained within may need to be modified as a consequence of clinical developments or emerging infections.
- 1.13 This document will only be published in electronic format. Sub-sections will be revised at intervals to reflect changes in knowledge and perceived risk of transmission of infection. Clinicians should consult the most up to date version available on the SaBTO website (<https://www.gov.uk/government/groups/advisory-committee-on-the-safety-of-blood-tissues-and-organs>) and web at other sites including NHS Blood & Transplant (<http://www.nhsbt.nhs.uk/> and <http://www.odt.nhs.uk/>).

Table 1: Examples of human substances covered by this guidance

Organs	Tissues and cells	Haematopoietic stem and progenitor cells (HSPC) and therapeutic cells (TC)*	Reproductive cells
Bowel Heart Kidney Liver Lung Pancreas Composite tissue transplants, e.g. face, hands Regenerated organs	Bone Cartilage Cornea/sclera Heart valves Skin Tendons Vascular tissue Amnion Menisci Pancreatic islet cells** Ocular stem cells, i.e. limbal*** Chondrocytes Keratinocytes*** Induced pluripotent stem cells (iPS) Immature ovarian or testicular tissue	Haematopoietic stem and progenitor cells collected from bone marrow (HSPC, marrow) Haematopoietic stem and progenitor cells collected from peripheral blood (HSPC, apheresis) Haematopoietic stem and progenitor cells collected from umbilical cord blood (HSPC, cord blood) Donor lymphocyte infusions and other therapeutic cells (TCs) Embryonic stem cell lines derived from human embryos created for treatments excluding fertility. Embryonic stem cell lines intended for clinical use derived from human embryos initially created for fertility treatment.	Gametes (sperm and eggs) Embryos created <i>in vitro</i>

*TCs include a wide range of selected and cultured products including T-cells, Natural killer cells, mesenchymal stem cells, cytotoxic T-lymphocytes, T-regulatory cells, tumour derived cells.

**Although islet cells are processed (isolated and purified) they are subject to time constraints akin to organs

***Limbal stem cells, keratinocytes, chondrocytes, iPS and embryonic stem cells may be cultured and expanded in the laboratory and should be considered as tissues for the purposes of microbiological testing. Cells used as feeder layers at any stage in the process are considered to fall within this guidance and also require microbiological testing including for potential zoonotic infections where feeder cells are of non-human origin. In addition, some of these materials may also be considered Advanced Therapeutic Medicinal Products (ATMPs) and are therefore regulated by the appropriate guidelines. In addition, the statutory requirements set out in the [Human Tissue \(Quality and Safety for Human Application\) Regulations 2007](#) still apply to the procurement, donor selection and testing of the starting tissue.

2 Legislation and accountability

Legislation

- 2.1 We have endeavoured to align our advice in this guidance with the regulatory framework in this field, whilst remaining mindful of the clinical need for transplantation. In some respects, the recommendations in this guidance may exceed the requirements of statutory regulations, and in doing so are believed to reflect consensus views for good practice. This is particularly true for the implementation of routine molecular testing, where techniques of nucleic acid test (NAT) and antigen detection testing offer a significant advantage in terms of both sensitivity and specificity, as well as reducing the window period of for the detection of pathogens, but may not be immediately accessible. Where newer protocols for testing can replace existing protocols and give operational advantages with no impact upon microbiological safety this has been addressed. Tissue and transplant establishments receiving donations from outside the UK should ensure that donor testing meets the requirements of relevant European Union Directives and recommendations within these guidelines either at retrieval or on receipt in the UK.
- 2.2 The standards for the quality and safety of organs for transplantation are set according to the European Union Organ Donation Directive 2010/53/EU (EUODD) which has been enacted into UK law through the through [The Quality and Safety of Organs Intended for Transplantation Regulations 2012](#) and [The Quality and Safety of Organs Intended for Transplantation \(Amendment\) Regulations 2014](#). This Act allows for the establishment of a Competent Authority for the regulation of organ transplantation. In the UK the Competent Authority is the Human Tissue Authority, which has published the "[The Quality and Safety of Organs Intended for Transplantation : a documentary framework](#)" which details mandatory requirements as well as guidance on how those requirement may be met.
- 2.3 Tissue and cell donation and use is undertaken according to the European Union Tissue and Cells Directives (EUTCD 2004/23/EC, 2006/17/EC and 2006/86/EC) which were implemented into UK law through the [Human Tissue \(Quality and Safety for Human Application\) Regulations 2007](#). These regulations require for a Competent Authority to regulate activities. In the UK the Human Tissue Authority (HTA) is the Competent Authority for regulating tissues and cells (other than gametes and embryos) for human applications. The HTA has published the '[Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatment](#)' as implemented by Directions 003/2010 detailing the requirements for the use of tissues and cells (other than gametes and embryos) for human applications.

- 2.4 For establishments procuring or processing tissue intended for clinical use it is a statutory requirement to be licensed and inspected by the Competent Authority in the UK, the HTA, and to comply with their Codes of Practice' - Establishments should comply with the standards which are detailed in the HTA's '[Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatment](#)' as implemented by Directions 003/2010.
- 2.5 The [Human Fertilisation and Embryology Authority \(HFEA\)](#) is the Competent Authority that has responsibility for gametes and embryos for human application.
- 2.6 The HFEA is responsible for regulating the procurement of gametes and the associated processing involved in the creation of an embryo. This falls under the [Human Fertilisation and Embryology Act 1990](#) (as amended in [2008](#)) and guidance on regulation is available through its code of practice. The HFEA's remit includes the use of embryos in the derivation of stem cell lines, but does not extend to the regulation of these stem cell lines themselves.
- 2.7 During the cell line derivation process the embryo is dissociated and it is at this processing stage that the HTA regulatory remit begins and the HFEA's regulatory remit ceases. During the processing / derivation phase, stem cell lines do not come within medicines regulation. However, once Master Cell Banks have been created with a reasonable expectation of clinical utility in a medicinal product, they fall within the remit of the [Medicines and Healthcare products Regulatory Agency \(MHRA\)](#).
- 2.8 The MHRA regulates medicines, medical devices and blood components for transfusion in the UK. This includes the regulation of [advanced therapeutic medicinal products](#) (ATMPs) that may be derived from tissues and cells including gametes and embryos. In this case the activities of procurement and testing would be regulated by HFEA and/or the HTA.
- 2.9 Cross-regulatory advice on the development of stem cell lines and other regenerative medicines can be obtained from the [Regulatory Advice Service for Regenerative Medicine](#).
- 2.10 Microbiological testing includes screening tests that are mandated by statutory requirements in the European Union Tissue and Cells Directives (2004/23/EC, 2006/17/EC and 2006/86/EC) and the EU Directive on organ transplantation ([2010/53/EU](#)).

Accountability

- 2.11 In the case of organ donation, the ultimate responsibility for use of a donated organ lies with the surgeon undertaking the transplant.
- 2.12 The legal responsibility for donor assessment and testing lie with the Designated Individual of the tissue or stem cell laboratory or storage facility, the Assisted Conception Unit or HSPC clinical collection facility. These units are collectively referred to as the tissue establishments. There are well defined roles for tissue establishments in national legislation for which the HTA is the Competent Authority. The Designated Individual may be supported a Medical Advisor providing advice and guidance.

- 2.13 In the case of donated tissues and cells, the Designated Individual of the cord blood bank, tissue establishment or bone marrow registry has legal responsibility for making sure the risk of infection is assessed as accurately as possible. All of this information should be retained in the donor's record at the tissue establishment. All donations should be coded to allow recipient hospitals to maintain a two-way audit trail between donors and recipients to facilitate traceability. Full traceability from donor to recipient must be retained according to [HTA Directions 003/2010](#) and the necessary anonymisation, to prevent identification of the donor by the recipient, should not compromise this requirement.
- 2.14 In the case of gametes and embryos, the requirements for Assisted Conception Units for the creation, storage and use of embryos for both fertility treatment and stem cell derivation are covered in the [HFEA Code of Practice](#). The Person Responsible for the Licence is accountable under the terms of the Human Fertilisation and Embryology Act.
- 2.15 Unrelated donor registries should also conform to all relevant national and international requirements and guidance. Traceability and responsibility for reporting adverse events to the Competent Authority lies with the HTA and HFEA licensed establishments and their designated individuals for the licences.

3 Overview of the principles underpinning these guidelines

- 3.1 Transplantation has been one of the great success stories in health care. However, there have been reports of transmissions of viruses, bacteria, fungi, protozoa, nematodes and prions following transplantation of organs, tissues and cells. These infections may be difficult to manage in the setting of immunosuppression, which may increase morbidity and mortality.
- 3.2 The risk of infection due to transplantation can never be completely removed. This guidance sets out precautions that should help to keep the risk as low as is reasonably possible whilst at the same time facilitating the maximum clinical benefit from transplantation.
- 3.3 Transplants have many benefits, whether life-preserving (such as heart or HSPC transplants), life-producing (such as in-vitro fertilisation – IVF), or aimed at improving the quality of life (such as bone grafts). Consequently, the risk of infection from a particular donor may be an absolute contra-indication to accepting a bone donation but only a relative contra-indication for liver donation where the potential recipient might otherwise die from liver failure. For this reason, the criteria used to accept a tissue donor are stricter than those for organ donors.
- 3.4 In cases where unusual (e.g. Trypanosoma cruzi, malaria etc) or extra risks (e.g. donation from a person who injects drugs, commercial sex worker etc) of infection are identified with a particular donation, these should be discussed before transplantation with the person who would receive the organ(s), with the parent or legal guardian in the case of a child who lacks capacity to consent, and with the family or carer(s) where appropriate. The discussion and the consent if given should be recorded in the patient's clinical notes. Specific treatment or prophylaxis of the recipient and appropriate close contacts may be offered to mitigate risks.

- 3.5 In the situation where the potential recipient lacks capacity for decision making for whatever reason then transplantation may be undertaken in accordance with existing legal frameworks.
- 3.6 Infection may also result from transplant material becoming contaminated from organisms in the environment. Contamination may occur while the material is being collected, processed, packed, tested, stored, transported and/or transplanted. Standard procedures for all these activities should include a microbiological risk assessment as part of a quality assurance programme.
- 3.7 A continuing audit of the outcome of tissue and organ transplantation is an essential part of maintaining and improving safety. The reporting of adverse outcomes of such treatment is an important component of this strategy and is discussed in more detail in Sections 16 and 17.

4 Referral for donation

Deceased donors

- 4.1 The donor's family and/or the most relevant life partner should be interviewed, and supporting information obtained from relevant health professionals such as the donor's GP. Standard questionnaires are used to seek relevant information and should be kept as part of the donor record. Wherever possible any post mortem findings will need to be available to ensure that an appropriate risk assessment is complete and that all information pertaining to the cause of death is taken into account.
- 4.2 Current microbiological results on the donor should be available from the donor's clinician and must be included in the comprehensive patient assessment process conducted by the trained Health Care Professional. Where circumstances dictate, the risk arising from the use of materials from potentially infected, or known-to-be-infected, donors should be discussed with a consultant or specialist with relevant knowledge regarding and expertise regarding that infectious risk. Advice from a specialist centre may be required for defining the balance between risk and benefit. Such discussion is normally between medical staff in the transplant unit receiving the organ and the relevant consultant infection specialist.
- 4.3 The information gathered by the trained Health Care Professional must include the relevant microbiological findings.
- 4.4 Assessment of donor risk does not end at the time of retrieval of tissues and organs. Important information relating to the risk of transmission of infection may become available after transplantation. This information must be made available by the organ donation team or Tissue Establishment to the recipient centres for appropriate management of the recipient.

Living donors

- 4.5 Some people wish to donate an organ to a relative, to another person they are close to or to an individual they do not know. The latter situation may occur in the setting of paired donation, pooled donation and non-directed altruistic donation. Others may agree to donate surplus tissue, such as heart valves from the replaced heart after heart transplantation, bone following hip-replacement surgery, or

umbilical cells to a cord blood bank. The information needed to assess any risk should be gathered from the potential donor or, in the case of child donors too young to understand the issues, from the adult with parental responsibility for that child as specified by the [Human Tissue Act 2004](#)² and the current HTA [Code of Practice on consent](#).

- 4.6 Autologous tissue donation is a special example of living donation where tissue or cells previously taken from an individual is transplanted to meet that same individual's clinical needs. Where tissues and cells for autologous donation are removed and are to be stored and, or cultured, then microbiological screening of the donor prior to the procedure is a requirement of the [Human Tissue \(Quality and Safety for Human Application\) Regulations 2007](#). The HTA has a statutory requirement that whilst awaiting microbiological testing results, tissues and cells are quarantined regardless of ultimate destination. An autologous donation from an infected donor must be stored securely in a way that does not pose an infection risk to other donations stored in the same facility.

Donors of gametes (spermatozoa or eggs) and embryos

- 4.7 The various uses of gametes and embryos for reproductive purposes have additional considerations to organ or tissue transplantation. Their use in the human body carries a small risk of infection transmission not only to recipients, but also to any child that might result from fertility procedures.
- 4.8 Partner donation is defined as a procedure that intends to produce a pregnancy in a woman who is in an intimate relationship with a man who is providing the spermatozoa. In relation to infection risk it may be considered to be similar to autologous donation.
- 4.9 Donation of gametes or embryos to a non-partner recipient requires further assessments and testing. The definition of such donors is given in <http://www.hfea.gov.uk/498.html#guidanceSection4293>. Where cryopreserved embryos are donated to a third party, there may be a period of several years between the embryo creation and donation.
- 4.10 Embryonic stem cell (ESC) lines for therapeutic use may be derived from embryos created for treatment of infertility that are surplus to clinical requirements. Similar criteria apply as for other stem cell lines taking account of the potential time interval between embryo creation and donation. If the embryos are created for the purpose of creation of ESCs rather than fertility, the same criteria will apply as for tissue and cell donation. Further guidance relating to the regulatory requirements for conducting human stem cell research can be obtained via the [UK Stem Cell Tool Kit](#)
- 4.11 SaBTO has previously published a review considering risks of infection from cell based advanced therapies (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/326823/Cellular_Therapy.pdf)

² Donation in Scotland is undertaken according to the Human Tissue (Scotland) Act 2006

Table 2 gives examples of donations relevant to these guidelines.

Table 2 – Examples of donors and circumstances of donation.

Type of donor		Circumstances surrounding the donation	Example
Deceased	DBD (Donation after brain stem death)	Retrieval from donor certified as dead by brain stem testing while on respiratory and circulatory support.	All organs and tissues
	DCD (Donation after circulatory death)	Retrieval of organs usually within one hour of circulatory arrest.	Kidney Liver Lung Pancreas and islet cells Heart
		Donations of tissues up to 48 hours after death.	Eye/cornea* Heart Valves Bone Tendons Skin Cartilage
Living Allogeneic	Directed	A donation from a living relative or someone emotionally related. Related Haematopoietic progenitor cells (HSPC) donors e.g. a sibling or parent.	Kidney Liver, Lung Pancreas Small bowel Limbal stem cells HSPC-marrow HSPC-apheresis HSPC-cord blood
	Voluntary unrelated donation of organ or tissues to an unknown individual	Altruistic donation of organs and tissues. Large registries are now available nationally and internationally in order to select volunteer unrelated HSPC for transplantation.	Kidney Liver Bone Reproductive cells Amniotic membrane HSPC-marrow HSPC-apheresis HSPC-cord blood hESCs iPS
Autologous	Tissues and cells	Procedures involving retrieval of tissues and cells for use in the donor.	Skin Bone Keratinocytes Limbal stem cells HSPC-marrow HSPC-apheresis HSPC-cord blood Cartilage Reproductive cells

*Donation for corneas should take place within 24 hours of death

5 Donor assessment

- 5.1 Requirements for donor assessments are contained in the HTA's 'Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatment' and EU Organ Donation Directives.
- 5.2 Once a donor has been identified there are three principal components to assessing suitability as a source of human materials for clinical use.
- 5.3 The first component comprises a clinical risk assessment based upon an interview, which addresses the likelihood of a donor having been exposed to a variety of infection risks. This interview is an opportunity to explain the consequences of making a donation, including testing, possible results and the impact of positive results on the contacts of the donor. In the case of deceased donors, the most relevant life partner or close relative should be interviewed to ascertain the required medical, behavioural and travel history. Additional information may be available from the referring clinician, the primary healthcare practitioner, the donor's GP, post-mortem examination and/or examination at the time of tissue procurement or organ retrieval. The information needed for assessing the infection risk from donors is also set out in the NHS Blood and Transplant Patient Assessment Form (PA1), or equivalent. This information does not necessarily exclude donation but is required to inform the final risk and benefit analysis prior to transplantation. Guidance on the assessment of donors of gametes and embryos is outlined in Guidance note 11 (Donor recruitment, assessment and screening) of the [HFEA Code of Practice](#). Donors of gametes must be selected for testing on the basis of a questionnaire and through a personal interview performed by a qualified and trained healthcare professional.
- 5.4 Detailed information is needed on the following:
 - 5.4.1 Treatment received in the illness before donation (including duration and dose of antimicrobial and other drug therapy);
 - 5.4.2 Vaccination history and immunisation status
 - 5.4.3 History of receipt of blood, blood components, blood products, tissue or organ graft.
 - 5.4.4 If large volume intravenous fluid administration has occurred, then consideration needs to be given to the effects of haemodilution when interpreting test results.
 - 5.4.5 Previous or current immunosuppression (by disease or drugs) as this may affect the interpretation of test results or the donor's suitability.
 - 5.4.6 Travel history or domicile outside of the UK. Infections may be acquired during travel outside the UK that have the potential for transmission through transplantation. These infections include Malaria, West Nile Virus, and Rabies. In addition to the well-documented infectious risks, there must be on-going vigilance for the possibility of infection with a pathogen demonstrating geographic epidemiology or an emerging infection. Information regarding infectious risks associated with travel or domicile outside the UK may be sought from the [Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee \(JPAC Geographical Disease Risk Index \(<http://www.transfusionguidelines.org/dsg/gdri>\)\)](#) but also [National Travel Health Network & Centre website \(NaTHNaC, <http://travelhealthpro.org.uk/>\)](#), [Health Protection Scotland Fit For Travel website \(<http://www.fitfortravel.nhs.uk/home.aspx>\)](#), and the [European](#)

[Centre for Disease Control](http://ecdc.europa.eu/en/Pages/home.aspx) (ECDC
<http://ecdc.europa.eu/en/Pages/home.aspx>)

- 5.4.7 History of contact with animals and other vectors. Transplantation may transmit zoonotic infections.
 - 5.4.8 History that may have put the donor at increased risk of transmissible spongiform encephalopathies (TSEs). See Section 12.
 - 5.4.9 History of malignancy, recent infectious disease or exposure to an infectious disease.
 - 5.4.10 Behavioural history that could have put the donor at risk of transmissible pathogens This will include questions about risk behaviours such as recreational drug use, men who have sex with men (MSM), sex with commercial sex workers, sex with a partner know to have a sexually transmissible disease, acupuncture, tattooing and body piercing.
 - 5.4.11 Results of any recent microbiological tests should be reviewed.
- 5.5 The second component is a physical examination of the potential donor that should be undertaken at the time of organ donation or tissue retrieval. This may indicate extra risks of infection and should be taken into account when assessing the donor suitability. For example, needle marks on the potential donor could indicate possible injecting drug use risk behaviour. In the case of potential deceased organ or tissue donation, a physical assessment body map is completed by the SNOD or the Tissue Establishment retrieval team.
- 5.6 The third component comprises microbiological testing. Whilst medical and behavioural assessment will be similar for all donors, the actual microbiological assessment will vary for different types of donors but must include those that are mandatory under current regulations. The results of the donor-suitability assessment will inform the balance of risk and benefit in deciding whether a donor is suitable in particular transplant situations.

6 Collection of blood samples for donor testing.

Blood samples should be collected that are appropriate for the required tests. Mandatory tests as required by EUTCD and EUODD and other other recommended standard donor screening tests are summarised in Table 3.

Deceased organ and tissue donors

- 6.1 Accurate testing of donor blood samples requires high quality samples of sufficient volume to allow primary testing, confirmation and archiving. In all situations ante-mortem blood samples are preferable.
- 6.2 Where ante-mortem blood samples taken for other purposes exist, these samples (taken up to seven days preceding death and appropriately stored) are usually preferable to post-mortem samples if samples specifically for the purpose of donor testing cannot be obtained prior to death. Appropriate systems should be in place to make sure samples can be uniquely identified and stored in optimum conditions.
- 6.3 Deceased donor blood sampling and retrieval of tissue for transplantation may happen many hours after circulatory arrest. With time after a donor's heart stops beating the quality of blood deteriorates, potentially impairing the performance of tests. Post-mortem blood samples should therefore be collected as soon as

possible after the donor's death and, as required by the Quality and Safety Regulations within 24 hours following circulatory arrest.

- 6.4 In order to maximise the quality of the blood samples obtained for testing, they should only be taken by trained staff. The site from which the sample was obtained and the time of sampling must be documented in the donor's file. Preferred sites for taking samples include cardiac or subclavian puncture and femoral vessel puncture. It is essential to avoid sites close to intravenous lines. The time of death must be recorded.

Table 3– Mandatory and recommended screening of organ, tissue and cell donors

Infection	Serological Test	Organs*	Tissues**	Haematopoietic progenitor cells (HSPC), therapeutic cells (TC) and human embryonic stem cells**	Gametes and embryos***
HIV1/2	Anti-HIV1/2Ab/HIV Ag combo	M	M	M	M
HBV	HBsAg	M	M	M	M
	Anti-HBc	M	M	M	M
HCV	Anti-HCV IgG	M	M	M	M
HTLV1/2	Anti-HTLV1/2****	R	M	M	M
Syphilis	Anti- <i>T. pallidum</i> antibody	R	M	M	R
<i>Toxoplasma gondii</i>	Anti- <i>T. gondii</i> IgG	R	NR	R*****	NR
CMV	Anti-CMV IgG	R	NR	R	R
EBV	Anti-EBV IgG	R	NR	R	NR
HEV	HEV RNA	R	R	R	NR
<i>Chlamydia trachomatis</i>	n/a	NR	NR	NR	M
<i>Neisseria gonorrhoea</i>	n/a	NR	NR	NR	M

M = Mandatory Tests as required by EUODD and EUTCD

R = Recommended tests

NR = not required; n/a = not applicable;

*NAT tests for HIV, HBV and HCV are not mandatory for organ transplantation. Pre-donation NAT testing may help reduce the residual risk of infection during the serological window period and may be done on an individual basis.

** NAT testing is not mandatory for deceased donors of tissues, nor for living donors of tissue and HSPC, but it replaces the need for quarantine and the follow-up serological screening.

*** Partner donation with direct use (donation and use without any banking) does not require microbiological testing.

**** HTLV is not mandatory for all donors of tissues and cells but is for donors living in, or originating from high-prevalence areas, or with sexual partners originating from those areas or where the donor's parents

originate from those areas. There are also requirements for the repeat testing after at least 180 days for those donors at risk of HTLV infection

(https://www.hta.gov.uk/system/files/HTA%2520Policy%2520on%2520HTLV%2520testing%2520requirements_0.pdf).

*****T. gondii IgM and IgG required

Living donors

- 6.5 A blood sample that has been taken up to 30 days before organ donation is considered to meet the requirements for testing, as long as the donor's risk status has not changed in the time between the sample being taken and the donation.
- 6.6 For tissues, serological testing of a sample taken on the day of donation or up to 7 days post-donation, and of a subsequent sample taken 6 months later for donors of tissues which may be stored before use, is considered to meet the requirements for testing. In the circumstances of repeat testing, the donation sample can be taken up to 30 days prior to and 7 days post donation. Negative results on NAT testing for HBV, HCV and HIV of a blood sample taken on the day of donation, or up to 7 days after donation, from a seronegative individual abrogate the need to quarantine cryopreserved donations and retest donors after six months.
- 6.7 HSPC-cord donations are usually initially stored un-tested, under conditions that prevent cross-contamination. Cord donations should be quarantined if cryopreservation precedes microbiological testing. A maternal sample taken at the time of donation or up to 7 days prior to donation or up to 7 days post-donation may be used for serological and NAT testing. Donations from infected mothers should be removed from the storage facility as soon as the infection risk is identified. In the case of cord blood banks, if NAT is not performed on the initial maternal sample then it should be policy to retest for relevant microbiological markers before issuing a cord blood unit. In the absence of NAT testing (HIV, HBV and HCV) on the original maternal sample taken at the time of delivery the antibody tests should be repeated on a repeat sample taken at least 180 days/six months after delivery. NAT testing can be done on the archived maternal donation sample prior to releasing cord blood unit as an alternative to antibody testing at six months. Cord blood donations themselves should undergo microbiological testing prior to use.
- 6.8 For microbiological testing of donors in the setting of HSPC- apheresis or bone marrow donation, a sample from the donor is required on the day of donation or up to 30 days prior to donation.
- 6.9 For partner donation of gametes and embryos serological testing of a sample taken within 2 years of the procedure is required. (http://www.hfea.gov.uk/docs/EU_Directive_2012_39_EU_on_26_November_2012.PDF). Positive tests do not preclude donation.
- 6.10 For non-partner donation sperm, samples must either be stored and repeat serological tests carried out after a minimum of 180 days, or can be released for donation if both the serology and NAT tests for HIV, HBV and HCV are negative (<http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32006L0017> Annex 3, 4.3). For non-partner donation of eggs, serological testing up to 7 days prior to donation is required. For non-partner donation of embryos for fertility treatment or stem cell derivation, there may have been several years between the embryo creation and donation as the embryos are usually cryopreserved. Tests and history

at the time of creation are relevant but further testing may be required at the time of donation.

Testing of the neonate and infant

- 6.11 When assessing infection status in a deceased donor less than 18 months of age, or older children who have been breastfed within 12 months of donation, the testing requirements depend on the age and any intervention risk that may have led to acquisition of an infection by the neonate/infant:
- 6.11.1 If the death of the neonate falls within 48 hours of birth, full microbiological screening of the mother is required.
 - 6.11.2 For death between 48 hours and 28 days of birth, if there has been no identifiable intervention in the neonate, the same microbiological screening of the mother applies. If, however, there are identifiable risks (eg. transfusion of blood components/products or undergoing a surgical procedure) then a full microbiological testing of the mother and NAT testing of the neonate are required.
 - 6.11.3 From 28 days of age up to 18 months or within 12 months of breast feeding full microbiological screening of both the infant and the mother are required.

7 Haemodilution, Transfusion and Donor Testing

- 7.1 Large volume blood loss requiring intravenous fluid replacement therapy has the potential to lead to false negative screening test results owing to dilution of specific antibody or antigen below the lower limit of detection of the test.
- 7.2 The volume of fluid that may be infused before false negative results may occur depends on the size of the individual, amount of blood loss and the nature of the infused fluid, as well as the initial concentration of the analyte being tested for and the diagnostic test characteristics. A number of algorithms exist that allow for the estimation of haemodilution. Estimated haemodilution greater than 50% indicates that testing of pre-infusion samples should be undertaken for greater accuracy.
- 7.3 If the donor has been transfused with blood or blood products in the immediate pre-donation period (within 48 hours of donation) then the sample obtained prior to transfusion should be sought and tested. If a pre-transfusion sample is not available for testing, then this should be recorded and reported to clinicians responsible for transplantation.
- 7.4 Where a donor has received blood products or components in the preceding 3 months, the interpretation of serological results should take into account the possibility of the individual having acquired antibody passively from the blood product or component.
- 7.5 Consideration may be given to NAT testing where concern exists regarding haemodilution affecting serology based tests, although the precise role of these tests is not yet known.

8 Handling and transportation of samples for testing

- 8.1 Standard clinical procedures must exist to minimise the potential for contamination of blood and tissues samples for microbiological testing during the collection of the sample. Appropriate processes allowing for the monitoring and review of these standard procedures should be in place.
- 8.2 The sample should be transported to the laboratory as soon as possible and marked urgent, preferably with prior notice given to laboratory staff. Prolonged transportation or storage should be at 4°C, but not frozen.
- 8.3 Blood samples taken for specific purposes of discretionary testing (such as malaria and Chagas) are handled according to separate instructions, since whole blood is required for testing at a central reference laboratory.
- 8.4 For NAT testing, EDTA anti-coagulated whole blood is the sample type of choice.

9 Laboratory Requirements for the Microbiological Screening of Donors

- 9.1 Microbiology laboratories that test serum or plasma samples from organ donors should:
 - 9.1.1 Be UK Accreditation Service ISO15189 accredited.
 - 9.1.2 Have a Consultant microbiologist/virologist available at all times for the interpretation of laboratory results.
 - 9.1.3 Have appropriately trained Health and Care Professions Council (HCPC) registered Biomedical Scientists on call at all times for testing.
 - 9.1.4 Have full quality assurance procedures in place for all tests in routine use.
- 9.2 All blood samples taken for testing must be accurately identified and labelled with records retained to ensure continuing linkage of donor details with the donor sample(s).
- 9.3 The tests used for testing donors of cells, tissues and organs should be CE marked.
- 9.4 Tests validated for deceased donor blood samples should be used if available. Inhibitors to NAT tests in deceased donor samples may generate false negative results but may be detected by the incorporation of appropriate internal controls in the assays.
- 9.5 The principles for determining the infection status of donors of organs, tissues and cells are based on the strategies that have been established for screening blood donors. Laboratory screening can take the form of serological testing for antibody, for antigen, and molecular testing for the DNA or RNA sequences of infectious agents. The EU Directive currently requires serological testing of donors irrespective of NAT testing. Whilst antibody detection relies on the host response, antigen and molecular assays directly detect components of the infectious agent.

- 9.6 Laboratories undertaking donor testing should archive donor blood/plasma samples for a minimum period of 10 years and should keep testing records, whether as paper or electronic reports, for a period of 30 years³. Maintaining the potential for retesting can also help prevent donated and archived tissue and cells being discarded unnecessarily because novel risks of infection cannot otherwise be assessed.

10 Microbiological testing of donations prior to transplantation

Organs

- 10.1 Donor organs are removed under the sterile conditions of a surgical operation and transported cooled and bathed in fluid. Contamination of the organ and, or the preservation fluid with a pathogen may occur at any point of the organ retrieval and transplant process. Standard operating procedures (SOPs) must exist to minimise the potential for contamination of organs and preservation fluids. Appropriate processes allowing for the monitoring and review of these standard operating procedures must be in place.
- 10.2 If there is particular concern for the contamination of organ and or preservation fluid, for example if the donor was known to have had a bacteraemia, or enteric injury has occurred during the retrieval procedure, then culture of the preservation fluid surrounding the organs should be undertaken. A positive culture will inform recipient management and clinically significant results, as assessed by the recipient centre infection specialists, must be communicated to NHSBT-ODT to ensure this information is conveyed to clinicians involved in the care of recipients of other organs and tissue from the same donor.

Tissues

- 10.3 Tissues must be procured in a suitable and appropriately risk-assessed facility, which must be either a HTA licensed premises or operate under the authority of a licensed establishment under a third party agreement. The licensed establishment must have written agreements with the staff or clinical teams responsible for tissue and cell procurement, unless they are employed by the same establishment. Where procurement premises are not specified *a priori* as part of an existing licence or third- party premises, tissue retrieval may occur following a documented risk assessment in respect of contamination and health and safety risks carried out by the procurer prior to each procurement episode. This risk assessment can be undertaken and documented with the help of a proforma authorised by the Designated Individual.
- 10.4 Tissues should be retrieved as soon after death as possible, and within 12 hours if the body is not refrigerated. If the body has been refrigerated within six hours of death, retrieval of tissue must be completed within 48 hours of death. The exception is eye retrieval which must be undertaken within 24 hours of death, because of the need to preserve viability of corneal cells.

³ <https://www.rcpath.org/resourceLibrary/the-retention-and-storage-of-pathological-records-and-specimens--5th-edition-.html>

- 10.5 Tissues should be recovered using local sterile fields to minimize cross contamination with microbes from other body sites. Where possible, sterile single-use instruments and equipment should be used with a minimal number of appropriately gowned and masked retrieval staff in attendance. Where re-usable instruments are used, these should be cleaned, sterilised and fully traceable to allow a record of which specific instruments were used on any given donor.
- 10.6 Retrieval should preferably precede any post mortem examination of the donor and no other activities (embalming, autopsy or other tissue donor recovery) should occur at the same time in the facility. However, on occasion, and subject to an appropriate risk assessment, tissues outside the abdominal cavity (e.g. heart, eyes and skin) may be retrieved at, or after, post-mortem examination.
- 10.7 Tissues should be processed and screened for microbial contamination by validated methods, the mandatory requirements of which are outlined in the [HTA Directions 003/2010](#).
- 10.8 Representative pre-processing samples (e.g. bone or bone chips, pieces of tissue or swabs of tissues) should be transferred aseptically into appropriate culture media at the time of processing. Pre-processing microbiological testing is not required for eye donation.
- 10.9 Controlled work areas in tissue processing facilities should be monitored by air, settle plate, contact plate and glove print sampling to ensure that bacterial counts fall within the defined air quality grade for the type of process being undertaken.
- 10.10 Samples of the tissue must be taken before and after the tissue is exposed to decontamination agents. Enrichment cultures should be used to maximize the recovery of aerobic and anaerobic bacteria and fungi.
- 10.11 Tissues which cannot be terminally sterilized must be discarded if post-decontamination culture tests are positive: an exception is cryopreserved skin allografts which can be transplanted if only non-pathogenic bacteria in low numbers are present.
- 10.12 If an individual tissue fails bacteriological testing and is therefore required to be discarded, a risk benefit analysis must be undertaken to determine whether other tissues from the same donor must also be discarded because of the risk of contamination.
- 10.13 The acceptance criteria for specified tissues, and the identification of organisms which are also considered acceptable at the various stages of processing, should be documented in written policies through consultation with a designated microbiologist. Advice should be sought for tissues that give equivocal or inconsistent bacteriological test results.
- 10.14 Bioburden estimations of marrow-depleted bone are not considered to be of value as the process of removing marrow effectively reduces microbial load. Similarly, estimation of bioburden of skin and amnion is not recommended as the former carries a substantial bioburden and the latter is surgically recovered under aseptic conditions. However, a heavy growth of bacteria from pre-process samples may signify gross contamination and the tissue should not be released unless able to be terminally sterilized by gamma irradiation or other techniques. The potential

damage to the integrity of the tissue by the high numbers of bacteria should also be considered before it is used for transplantation.

10.15 To preserve cell viability a number of tissues, including cryopreserved cardiovascular allografts, menisci or osteochondral grafts, cannot be irradiated. These may be decontaminated with mixtures of antibiotics. The antibiotic solutions used should be validated to be effective against the range of bacterial species normally recovered from such tissues and the tissue bank should develop a list of species exclusion criteria based on an assessment of the clinical risk of serious infection in the recipient. Cardiovascular tissues must also be tested for *Mycobacterium* spp., and fungal contamination using validated techniques. Where corneas are stored by organ culture, samples of the medium should be tested during storage for bacterial and fungal contamination. If contamination is detected, the tissue should be discarded. The opportunity for detecting contamination of corneas stored by hypothermia is limited and typically testing is not undertaken.

Gametes and embryos

10.16 Appropriate skin cleansing procedures must be carried out prior to the provision of semen samples, surgically retrieved sperm and eggs but sterility cannot be guaranteed for gametes.

10.17 *In vitro* fertilisation and embryo culture carries a risk of microbiological contamination. Laboratory procedures must include procedures to minimise this risk and subsequent loss of embryos. This includes consideration of both endogenous and exogenous contamination. Embryos found to be growing in contaminated medium should not be transferred.

10.18 Full quality assurance procedures should be in place.

10.19 HFEA guidance is provided in the [HFEA Code of Practice](#).

11 Microbiological risk of cryopreservation of donations.

11.1 Tissues, cells and gametes may be subject to long-term cryopreservation prior to use.

11.2 In the past, storage in the fluid phase of liquid nitrogen has afforded the opportunity for pathogenic contaminants to gain ingress to the stored materials. In one unit, this led to a series of HBV infections in recipients whose bone marrow autografts were stored in a contaminated tank. As a result of this a series of recommendations for cryopreservation were made. These apply to the storage of tissues retrieved for use as allografts by third parties as well as tissues stored for subsequent use as autografts.

11.3 It is appropriate to reduce the contamination risk by routinely storing donations in the vapour rather than the liquid phase of nitrogen, and considerable validation of this has been carried out by NHSBT. Where this is not considered possible, donations should be stored in a primary container into which access by liquid nitrogen is prevented. A secondary container should enclose the primary container, further reducing the likelihood of liquid nitrogen washing material in and out of the primary container. Once validated, such a process can be deemed to isolate an unscreened sample within the storage tank, and complies with the need

for quarantine before test results are available. This may be desirable but prove not to be possible for very delicate tissues, such as human embryos and hESCs cryopreserved by vitrification and stored in open pulled straws, although sealed straws and closed systems are preferable.

- 11.4 In view of the recognised potential for contamination of material with adventitious agents, local risk assessments must be used to guide best practice. Contamination in this way may become a concern for the repeated cryopreservation of derived cell lines. Where it is not possible to store donations in a manner which prevents contamination, it is advisable to have separate storage facilities for each known infectious risk. Storage tanks should be cleaned and decontaminated in the event of thawing. If it is found that an infectious unit has inadvertently been placed in the routine storage facility, a risk assessment should be undertaken to define any potential hazard for recipients of materials who have received material from the tank or may receive material in the future.
- 11.5 To preserve the integrity of storage tanks in use, only donations known to have come from uninfected donors should be placed in the tank. If the timing of procedures is such that cryopreservation is required before the results of microbiological testing can be made available, the use of a holding tank should be considered in which cryopreservation can be performed before long-term storage. This applies unless the conditions of storage can be expected to prevent the possibility of contamination.
- 11.6 Donors of materials intended for cryopreservation should be screened as for donors of tissue, cells or gametes.
- 11.7 Quarantine of samples until testing results are available is a requirement of the [Human Tissue \(Quality and Safety for Human Application\) Regulations 2007 and subsequent HTA Directions](#).
- 11.8 Where automated platforms are used for cryopreservation, donations identified to come from infected donors should be removed after cryopreservation to a separate long-term storage facility. The geographical separation from the routine storage facility to a secure site for infectious donations which cannot be discarded, for example an autologous bone marrow or a semen donation from a person about to undergo radiotherapy, removes the possibility of a third party being put at infection risk from mislabelling or the use in error of a wrong donation. It also reduces possible contamination of the storage facility.

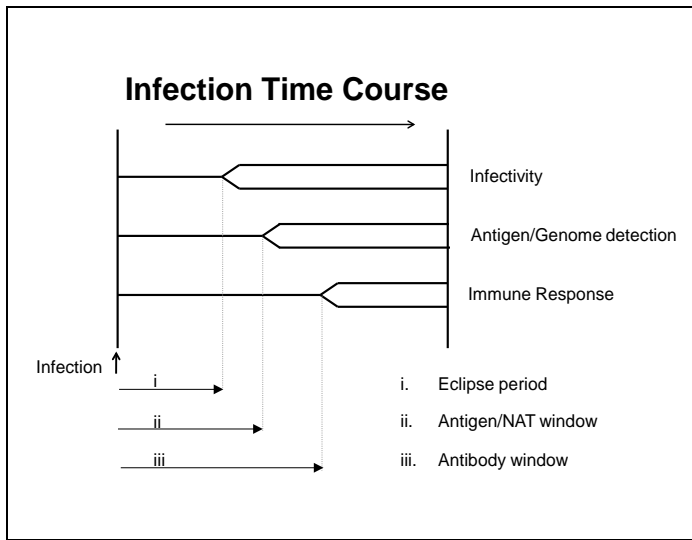
12 Interpreting donor test results

Time course of an infection

- 12.1 Following exposure to, and infection by, a microbiological agent there is a period of time during which no microbe can be readily recovered from the host; this is classically called the eclipse period (Figure 1). Donations taken during this period are unlikely to be infectious but in practice this would not be safe and should be avoided.
- 12.2 The time from infection to the onset of detectable infectivity depends upon the method used for detection of infection. This period of infectivity which cannot be detected is colloquially called a “window” and represents the duration of

undetectable infectivity. This “window” is shortest for genomic (nucleic acid technology testing, NAT) and antigen tests, and longest for antibody tests. For practical purposes, the time from infection to first detection of a marker is referred to as the “window period”.

Figure 1: Diagrammatical representation of the eclipse and window



Risk Assessment

12.3 The risk of transmitting an infection where microbiological antibody tests are negative may be quantified and is termed the residual risk. The residual risk for transmitting an infection is not solely dependent on the characteristics of the specific test used (sensitivity and specificity) but is also dependent on the incidence of infection within a defined population and the length of the window period.

12.4 The calculated residual risk estimates for the transmission of HBV, HCV and HIV in solid organ donors in the United Kingdom are included in Table 4. These figures have been calculated from results of microbiological testing in 8272 potential solid organ donors in the United Kingdom for the period 2010-2014⁴. Calculated residual risk estimates are provided for screening protocols utilising antibody based testing and those that would incorporate NAT testing.

Table 4: Residual risk estimates for undetected blood borne virus infection in those testing negative at the time of solid organ donation using either standard serological tests or with the addition of nucleic acid testing (NAT).

Figures are number of undetected cases per 100,000 donors (95% confidence intervals).

	Antibody alone	Antibody + Antigen	Addition of NAT
Hepatitis B Virus	NR	0.55 (0.27-0.92) ¹	0.30 (0.15-0.51) ²
Hepatitis C Virus	5.96 (5.58-6.33) ³	0.71 (0.66-0.75) ⁴	0.30 (0.28-0.32) ⁵
HIV	NR	0.08 (0.04-0.12) ⁶	0.04 (0.02-0.06) ⁷

NR – Not relevant. Antibody alone test not performed for donor characterisation

¹ Anti-HBc antibody + HBsAg

² Anti-HBc antibody + HBsAg + HBV DNA PCR

⁴ Infection and risk behaviours among UK organ donors. Su Brailsford,^{1,2} Katy Davison,¹ Marcus Lawrance¹ and Ines Ushiro-Lumb² December 2015 (final revisions January 2017) ¹NHSBT/PHE Epidemiology Unit, ²NHSBT Microbiology Services

- ³ Anti-HCV antibody
- ⁴ Anti-HCV antibody + HCV antigen
- ⁵ Anti-HCV antibody + HCV NAT
- ⁶ Anti-HIV + HIV antigen (combo test)
- ⁷ HIV combo test + HIV RNA PCR

Positive screening tests and confirmatory tests

- 12.5 Standardised terminology must be adopted by all involved in the donation process regarding terminology used during donor testing.
- 12.6 Positive test results on microbiological screening tests require that further confirmatory testing be undertaken. The nature of that confirmatory testing is dependent on the pathogen being tested for. The time-scale in which confirmatory testing will be carried out is dependent on the nature of the planned donation and the confirmatory tests required.
- 12.7 It is recognised that confirmatory testing of initial reactive tests may not be available at the time of transplantation following deceased organ donation. Similarly results of other specialised microbiological tests may not be available at the time of donation and transplantation. In these circumstances, transplantation of organs may be undertaken if the benefits are deemed greater for the patient than the risk of remaining on the waiting list but only after due consideration of the available results including, where necessary, specialist advice and after informed patient consent.
- 12.8 Centres receiving solid organs for transplantation are not required to repeat the donor microbiological screening tests. When microbiological testing is repeated by recipient centres or tissue establishments, any and all discordant results obtained following repeat testing must be made available to other centres that have accepted material from that donor. Results must also be communicated to the ODT Duty Office, NHSBT so that all interested parties are informed in a timely manner.
- 12.9 The donor testing laboratory has responsibility for ensuring that confirmatory testing of positive screening tests is completed.
- 12.10 The organ, donor or tissue procurement organisation has responsibility for the communication of the confirmatory testing results to relevant individuals and organisations.
- 12.11 Centres or organisations accepting material from donors for whom confirmatory testing is required also have a responsibility and must ensure that the results of confirmatory testing are known and that patient management is modified as appropriate.
- 12.12 Where organs, tissues or cells from a donor have been sent to other tissue establishments or centres, these must be told about repeat reactive and positive test results. This is to prevent unsuitable tissues or cells being transplanted as it often takes a considerable time to get definitive results from confirmatory testing. For tissues with a long shelf-life, no material should be released until all confirmatory testing for a mandatory marker is complete and shown to be negative.

12.13 In the case of a deceased donor, there must be an operating policy detailing measures that ensure that close contacts of the deceased donor are appropriately informed of results that may have implications for close contacts of the donor. The responsibility for ensuring that close contacts are informed rests with the organisation that obtains consent or authorisation for donation. There is a need to ensure at a local level that appropriate counselling of affected persons can and will take place if desired by close contacts of the donor. This is considered a duty of care to the donor and /or donor's family. The need to inform close contacts of relevant results also highlights the importance of completion of all testing for all potential donors tested regardless of whether or not donation and/or transplantation occurred.

Decisions based on specific test results

12.14 Cytomegalovirus (CMV)

Table 5: – Positive serological result in an ALLOGRAFT donor – CMV

Test result(s) suggesting possible donor CMV infection	Organs	Tissues	HSPC, TC and Human embryonic stem cells*	Gametes and embryos
Anti-CMV IgG positive	Donation permitted. Informs need for post transplant CMV monitoring and management	Donation permitted	Donation permitted. Informs need for post transplant CMV monitoring (CMV NAT positive donor is unsuitable for use**)	Donation permitted. Match serology status to donor if possible

*All umbilical cord donations are tested prior to issue by CMV NAT. In exceptional circumstances a life preserving donation containing CMV DNA might be used for a recipient whose serum contains anti-CMV antibody in accordance with Section 15. Routine CMV prophylaxis should be administered post-transplant and/or routine CMV viral load surveillance instituted.

**Defer donor until NAT negative

12.15 Epstein-Barr virus (EBV)

Organs, HSPC and TC from an EBV seropositive donor may transmit infection to a seronegative recipient. EBV may also reactivate in sero-positive recipients

Table 6: – Positive serological result in an ALLOGRAFT donor – EBV

Test result(s) suggesting possible EBV infection of donor	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
Anti-EBV IgG	Donation permitted. Informs need for post transplant EBV monitoring.	Donation permitted	Donation permitted. Informs need for post transplant EBV monitoring	EBV testing not required.

12.16 Hepatitis B Virus (HBV)

- 12.16.1 Screening for HBV infection must include testing for HBsAg and anti-HBc (total antibodies).
- 12.16.2 Samples giving repeat reactivity for HBsAg should undergo a confirmatory test and additional markers performed
- 12.16.3 HBV DNA PCR and anti-HBs should be undertaken where screening tests suggest current or past HBV infection in order to inform management of the recipient. The results should be available within 72 hours of initial testing.
- 12.16.4 The detection of confirmed HBsAg and/or HBV DNA indicates current infection.
- 12.16.5 Detection of anti-HBc in the absence of HBsAg indicates past hepatitis B virus infection, however donations from a proportion of individuals whose sera contain anti-HBc in the absence of anti-HBs may still be infectious. Although this is unlikely, the EU Tissue Directives require testing tissue donors for anti-HBc.
- 12.16.6 Detection of anti-HBs and the absence of anti-HBc suggests previous immunisation.
- 12.16.7 Proven acute or chronic HBV infection is a contra-indication to tissue donation.
- 12.16.8 Organ transplantation and cell transplantation may be undertaken after consideration of the following and with the informed consent of the potential recipient. Relevant specialist advice must be sought.
- 12.16.8.1 Status of HBV infection in potential donor – acute or chronic infection, previous infection.
- 12.16.8.2 Nature of proposed transplant – liver transplant, non-liver transplant.
- 12.16.8.3 HBV anti-viral therapy use in recipient.
- 12.16.8.4 HBV immunisation status of recipient.
- 12.16.9 Hepatitis B virus has been contracted from contaminated liquid nitrogen tanks. If cells, gametes or tissues requiring long term cryopreservation from an unscreened donor or an HBV-infected donor are to be stored, see Section 11.

Table 7: – Positive serological and/or positive NAT result in an ALLOGRAFT donor – HBV

Test result(s) suggesting possible donor HBV infection	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
HBsAg positive	Relative contraindication to donation*	Contraindication to donation	Contraindication to donation	Contraindication to donation
HBV DNA NAT positive	Relative contraindication to donation*	Contraindication to donation	Contraindication to donation*	Contraindication to donation
Anti-HBc positive HBsAg	Donation permitted*	Donation permitted**	Donation permitted**	Contraindication to donation

negative and/or NAT negative				
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*See 12.16.8 above

** If HBV NAT is not performed, then donation is permitted if anti HBs over >100 IU/l

12.17 Hepatitis C Virus (HCV)

- 12.17.1 Screening for HCV infection employs either an antibody-only assay or a combined HCV antigen/antibody assay and molecular tests for HCV RNA
- 12.17.2 Positive samples should undergo confirmatory testing. The detection of confirmed anti-HCV antibody indicates past or current infection. Confirmed HCV antigen or and/or RNA detection indicates current infection.
- 12.17.3 Effective anti-viral therapy resulting in sustained virological response for HCV is now available.
- 12.17.4 Effective treatment for HCV infection in the recipient may be undertaken either before or after transplantation.
- 12.17.5 Re-infection with HCV can occur in patients with a previous sustained virological response following HCV treatment.
- 12.17.6 HCV infection in the potential donor does not amount to an absolute contra-indication to donation of material for life-preserving transplantation, however the net benefit of transplantation must be considered against the risk of not receiving that specific transplant. This risk/benefit analysis allows for the potential use of a transplant from a HCV infected donor to a non-infected recipient.

Table 8: – Positive serological and/or positive NAT result in an ALLOGRAFT donor – HCV

Test result(s) suggesting possible donor HCV infection	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
HCV IgG antibody	Relative contraindication to donation	Absolute contraindication to donation*	Relative contraindication to donation*	Absolute contraindication to donation**
HCV RNA NAT or HCV combination Ab/Ag ("combo") test	Relative contraindication to donation	Absolute contraindication to donation*	Relative contraindication to donation*	Absolute contraindication to donation**

* EUTCD prohibits donation from individuals with a "history, clinical evidence, or laboratory evidence of HIV, acute or chronic hepatitis B (except in the case of persons with a proven immune status), hepatitis C and HTLV I/II, transmission risk or evidence of risk factors for these infections", unless justified on the basis of a documented risk assessment approved by the responsible person as defined in Article 17 of Directive 2004/23/EC. The categorisation of a relative contraindication for HCV is indicative of the current knowledge of treatments for this virus.

**EUTCD states that for "donation other than by partner" of gametes and embryos the donor "must be negative" for HCV

12.18 Human immunodeficiency virus (HIV)

- 12.18.1 Screening for HIV infection must include a combined HIV antigen/antibody assay.
- 12.18.2 Samples giving repeat reactivity in antibody or combined antigen/antibody assays must undergo additional testing to confirm HIV infection including nucleic acid tests (NAT) for HIV RNA.
- 12.18.3 Confirmed detection of specific anti-HIV 1/2 antibodies and/or HIV RNA and/or HIV antigen indicates current infection.
- 12.18.4 HIV infection is an absolute contraindication for tissue transplantation.
- 12.18.5 The use of organ and cells from HIV-infected individuals may be considered in the setting of HIV-infected recipients. Assessment of the potential donor must include details of previous HIV assessment and management in that individual. Specialist advice in the management of HIV must be sought to inform the decision making process.
- 12.18.6 The intentional use of organs and cells from an HIV-infected individual in a non-infected patient is considered to be contraindicated. However, it is recognised that effective treatment for HIV exists in the form of Highly Active Anti-Retroviral Therapy (HAART), with life expectancy of successfully treated individuals being comparable to those without HIV infection. Therefore, the possibility may arise where transplantation of organs or cells from an HIV-infected donor is considered for a non-HIV infected recipient following an opinion from a clinician with expertise in the management of HIV infection allowing for HIV management after transplantation and with the full informed consent of the potential recipient.

Table 9: – Positive serological and/or positive NAT result in an ALLOGRAFT donor – HIV

Test result(s) suggesting possible donor HIV infection	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
HIV 1/2 antibody/antigen	Relative contraindication to donation	Absolute contraindication to donation	Absolute contraindication to donation	Absolute contraindication to donation
HIV RNA NAT	Relative contraindication to donation	Absolute contraindication to donation	Absolute contraindication to donation	Absolute contraindication to donation

12.19 Human T cell Lymphotropic Virus (HTLV)

- 12.19.1 Screening for HTLV infection employs an antibody-only assay.
- 12.19.2 Positive samples should undergo confirmatory testing. Confirmation of specific anti-HTLV antibodies indicates current infection. Reference NAT testing may be used to confirm HTLV infection.
- 12.19.3 Material from donors with repeat positive anti-HTLV antibody testing can be released for clinical use providing the antibody reactivity is shown to be non-specific in confirmatory testing.
- 12.19.4 Although confirmation of HTLV status can be completed prior to use of tissues and cells, in the setting of deceased organ donation

confirmatory results are unlikely to be available. In this situation specialised advice should be sought to help provide an assessment as to the likelihood that an initial reactive results represents a true infection, the probability of which will depend on the details obtained in the donor assessment. The decision to proceed with solid organ transplantation following an initial reactive HTLV antibody test is dependent on an assessment of the net benefit of receiving that transplant when compared to the risk of not receiving that specific transplant.

Table 10: – Repeat reactive result in an ALLOGRAFT donor – HTLV

Test result(s) suggesting possible donor HTLV 1/ 2 infection	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
Anti-HTLV 1/2 IgG	Relative contraindication to donation	Absolute contraindication to donation	Absolute contraindication to donation	Absolute contraindication to donation

12.20 Toxoplasma gondii

12.20.1 Although the results of serological tests demonstrating past or current *Toxoplasma gondii* infection will be available in the setting of live donation, serological evidence of infection may only be available after deceased-donor solid organ transplantation and can therefore only inform post surgical management.

Table 11 – Repeat reactive serological result in an ALLOGRAFT donor – *Toxoplasma gondii*

Test result(s) suggesting possible <i>T. gondii</i> infection of donor	Organs*	Tissues	HSPC, TC and Human embryonic stem cells **	Gametes and embryos
Anti- <i>T. gondii</i> IgG positive; (IgM should also be tested for in the setting of HSPC and TC donation)	Donation permitted Informs need for prophylaxis in heart recipients	Donation permitted	Inform need for prophylaxis and donor deferral if recent acute infection	Not required

*The risk of acquiring *T. gondii* infection from the transplant, rather than developing *T. gondii* disease from endogenous reactivation in the recipient under immunosuppression, results from a serological mismatch between an infected donor (antibody positive) and a naïve seronegative recipient in the absence of prophylaxis

**Avoid donors with evidence of recent/acute infection (e.g. IgM positive).

12.21 Hepatitis E Virus

12.21.1 SaBTO has recently published guidance recommending HEV NAT testing for donors of organs, tissues and cells⁵.

12.21.2 Results of donor HEV testing may not be available prior to the use the transplantation of organs but will usually be available before the use of tissues and cells.

Table 12 – HEV Nucleic Acid Testing in an ALLOGRAFT donor

Test result(s) suggesting possible donor HEV infection	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
HEV NAT	Donation permitted. Informs post transplant management	Donation permitted	Donation permitted. Informs post transplant management	Donation permitted

⁵ <https://www.gov.uk/government/publications/protecting-patients-from-getting-hepatitis-e-through-transfusion-or-transplantation>

12.22 Treponema pallidum (Syphilis)

12.22.1 The interpretation of syphilis serology can be difficult, and may require help from an experienced clinician.

12.22.2 Serological tests for are not specific for *Treponema pallidum* subspecies *pallidum* (syphilis) and may detect any of the trypanomatoses (syphilis, yaws, pinta and bejel), and therefore when positive, correlation of test results with the history, epidemiological exposure and clinical features is required.

Table 13: – Positive syphilis serology in an allograft donor.

Test result	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
Syphilis EIA positive (initial screen)	Donation permitted	Relative contraindication to donation **	Donation permitted	Relative contraindication to donation **
Non treponemal test positive ^o (i.e. VDRL or RPR)	Donation permitted*	Relative contraindication to donation	Donation permitted*	Relative contraindication to donation
Treponemal test positive†(i.e. TPPA or THPA)	Donation permitted*	Relative contraindication to donation **	Donation permitted*	Relative contraindication to donation

^o A high non-treponemal test titre (>1:16) is suggestive of a recent or active infection, in the absence of a clear history of treatment. However a low titre does not out-rule active infection

† Treponemal specific tests can remain positive indefinitely despite adequate treatment

*Where a recipient has been exposed to a potentially infectious donation a risk assessment must be undertaken, and expert advice sought from an Infectious Diseases or Genitourinary Medicine physician to ensure administration of timely and adequate antimicrobial therapy, and to guide serological follow up

**A donation from a positive donor, may be considered following careful consideration of the risk/benefit ratio of the transplant, taking into account which tests are reactive and the donor's treatment history if applicable, and the informed consent of the intended recipient

12.23 Transmissible Spongiform Encephalopathies (TSEs)

- 12.23.1 TSEs (otherwise known as prion diseases) are a group of fatal transmissible neurodegenerative disorders that in humans occur in sporadic, genetic and acquired forms. The commonest human TSE, Creutzfeldt-Jakob disease, occurs in all three forms: genetic (gCJD), sporadic (sCJD) and acquired (Variant CJD, vCJD, and iatrogenic CJD, iCJD). The transmissible agent (or prion) is presently not fully characterised but is generally considered to be composed principally of a misfolded form (designated PrP^{S^c}) of the normal prion protein (designated PrP^C)
- 12.23.2 sCJD has been transmitted from one patient to another through medical or surgical procedures involving neurosurgical instruments, brain electrodes, tissue (human cornea and dura mater grafts) and tissue extracts (human pituitary hormones). There have been no known transmissions of vCJD via surgery or use of tissues or organs to date; however there has been transmission of vCJD infection via transfusion of blood (non-leucodepleted red cells) and, in one instance, probably by a blood product (factor VIII)
- 12.23.3 Donor deferral issues centre around the potential for transmitting TSEs during organ and tissue transplantation and the administration of blood/blood products. Deferral of donors is complex. An effective practical screening test for the detection of misfolded prions in donor blood, or other tissues, is not available at present. The prevalence of asymptomatic infected persons in the UK is uncertain (although, for public health purposes, it is presently considered to be around 1:2000⁶) and there is additional uncertainty as to the infectivity potential of those presumed to be asymptotically infected
- 12.23.4 There are a number of risk factors for human TSEs that have been identified, aside from age, geographical residence and genetic factors, including prior exposure to human blood, dura mater grafts, pituitary-derived hormones and contaminated surgical instruments. In addition, a number of individuals have been notified that they are at increased risk of CJD/vCJD for public health purposes, due to their exposure to one or more risk factors. Guidance from the Advisory Committee on Dangerous Pathogens (ACDP) TSE Working Group is available from <https://www.gov.uk/government/publications/guidance-from-the-acdp-tse-risk-management-subgroup-formerly-tse-working-group>. Concerns have also been raised of a theoretical transmission risk from human urine-derived gonadotrophins (Metrodin HP). There is no evidence that donated human eggs can transmit CJD
- 12.23.5 Individuals with a confirmed or suspected TSE, a neurological disease of unknown aetiology or those who are blood relatives of persons with genetic CJD cannot be accepted as donors of organs or tissues. However, if a donor has had two or more blood relatives develop a prion-associated disease and, following genetic counselling and/or testing they have been informed they are not at risk, they may be accepted for donation

⁶ Gill et al. Prevalent abnormal prion protein in human appendixes after bovine spongiform encephalopathy epizootic: large scale survey. *BMJ*. 2013 Oct 15;347:f5675. doi: 10.1136/bmj.f5675.

- 12.23.6 Pre-exposure to human dura mater grafts, human pituitary-derived growth hormone and/or gonadotrophin excludes the donation of tissues, and should be taken into account when assessing any donor for their suitability for organ donation. There is no good evidence of transmission by organs or tissues other than by those of the central nervous system, the cornea or, in the case of vCJD, blood/blood products.
- 12.23.7 For lifesaving organ and bone marrow transplantation only, donor exposure to risk factors for CJD and vCJD should be taken into account in the risk assessment, but does not necessarily preclude donation
- 12.23.8 The potential for transmission of the aetiological agent of TSE has generated a need for tests to identify infected donors . Presently blood tests of sufficient sensitivity, specificity and practical utility for donor screening are not available.
- 12.23.9 Table 14 gives a summary of the exclusions from organ and/or tissue donation, based on possible TSE exposure.
- 12.23.10 Level of risk or exposure should be clarified and weighed, on an individual basis, against the expected benefit of the transplant and the availability of alternative donors. The recipient (and/or relatives) should be informed of the nature of the estimated risk of vCJD transmission.
- 12.23.11 Definite transfusion is defined as at least one of the following:
- 12.23.11.1 Recorded in medical notes available to clinical staff at time of donation;
 - 12.23.11.2 Documented during interview;
 - 12.23.11.3 Reported by GP;
- 12.23.12 For tissue and organ donors, probable transfusion is defined as:
- 12.23.12.1 Previous major surgery; and/or
 - 12.23.12.2 Previous major accident.
- 12.23.13 Ocular tissue donors should not be excluded if they have a history of definite or probable transfusions, in view of supply issues. However it is essential that: donors excluded on the basis of public health measures are not accepted as ocular tissue donors.

Table 14: – Exclusions from organ and/or tissue donation based on possible TSE exposure

	Solid Organ Donors	Live tissue donors			Deceased tissue donors			
		Bone	HSPC	Gametes & embryos	Musculo-skeletal (ligaments, tendons & cartilage)	Bone & processed bone	Ocular	Skin/ Heart Valve/ Pancreatic islets/ Hepatocytes
Definite, probable or possible case of human TSE, including CJD and vCJD	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
Individual with a neurological disease of unknown aetiology	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
Individual whose blood relatives have had familial CJD ¹	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
Individual “presumed infected” with vCJD ²	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
Individual “at increased risk of CJD/vCJD” (for public health purposes) ³	Individual assessment required ⁴	Absolute contra-indication	Individual assessment required ⁴	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
History of definite ⁵ or probable ⁶ blood transfusion since 1980	Individual assessment required ⁴	Absolute contra-indication	Individual assessment required ⁴	Individual assessment required ⁴	Absolute contra-indication ⁸	Absolute contra-indication	Accept ⁷	Accept
History of receipt of <i>dura mater</i> graft	Individual assessment required ⁴	Absolute contra-indication	Individual assessment required ⁴	Individual assessment required ⁴	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
History of definite receipt of tissue since 1980	Individual assessment required ⁴	Absolute contra-indication	Individual assessment required ⁴	Individual assessment required ⁴	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Accept
History of receipt of pituitary derived growth hormone and/or gonadotrophin	Individual assessment required ⁴	Absolute contra-indication	Individual assessment required ⁴	Individual assessment required ⁴	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication
History of receipt of organ	Individual assessment required ⁴	Absolute contra-indication	Absolute contra-indication	Individual assessment required ⁴	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication	Absolute contra-indication

- 1 However, if a donor has had two or more blood relatives develop a prion-associated disease and, following genetic counselling, they have been informed they are not at risk, they may be accepted for donation
- 2 Donors who have received blood components, tissues and/or organs from donors who have gone on to develop vCJD.
- 3 Donors who have been notified that they are at increased risk of vCJD/CJD (for public health purposes) due to possible exposure.
- 4 Level of risk or exposure should be clarified and weighed, on an individual basis, against the expected benefit of the transplant and the availability of alternative donors. The recipient (and/or relatives) should be informed of the nature of the estimated risk of vCJD transmission.
- 5 Definite transfusion is defined as at least one of the following:
- Recorded in medical notes available to clinical staff at time of donation;
 - Documented during interview;
 - Reported by GP;
- 6 For tissue and organ donors, probable transfusion is defined as:
- previous major surgery; and/or
 - previous major accident.
- 7 Ocular donors should not be excluded if they have a history of definite or probable transfusions, in view of supply issues. However it is essential that:
- donors excluded on the basis of public health measures are not accepted as ocular donors.
- 8 Do not exclude if transfusion is within 1 week prior to death

13 Infections present at the time of donation.

This section relates to organ and tissue donors only.

13.1 At the time a deceased donor is being considered for suitability there may be co-incident infections which may have a bearing on safety. Diagnosed acute infections, and undiagnosed presumed acute infectious disease, in a potential donor do not necessarily preclude donation, but any such illness should be discussed as early as practicable with the local consultant microbiologist/virologist.

13.2 Abscesses

13.2.1 Organ donors with abscesses occurring in the preceding 5 days and at a distance from the organ to be retrieved are acceptable for donation if appropriate recipient antibiotic prophylaxis covering the causative organism is given.

13.2.2 *Staphylococcus aureus* and *Streptococcus pyogenes* are more likely to spread to distant organs and cause infection in a recipient.

13.2.3 Transmission of infection is unlikely after effective drainage of an abscess and adequate antimicrobial treatment of the donor.

13.2.4 If the clinician caring for the potential donor believes that therapy given for a localised infection has successfully cleared the infection, tissues may be retrieved. Otherwise, the donation of tissues (other than cornea donation) is contraindicated unless life-preserving.

13.2.5 Advice within this document regarding bacteraemia and drug resistant bacteria may also pertain for those potential donors with an abscess.

13.3 Malaria

13.3.1 The donation of organs, tissues, other than corneas, from donors with active malarial infection and no curative chemotherapy is contraindicated. Corneal tissue, but not other ocular tissue, is acceptable as corneas are avascular and not considered to be a risk of transmitting protozoal infections.

13.3.2 Acellular or decellularised tissues from a donor with a history of malaria may be accepted for transplantation.

13.3.3 Patients with a history of travel to a malaria-endemic area more than one year ago, but afebrile at the time of assessment, can be accepted as donors.

13.3.4 Febrile donors with a recent travel history to a malaria-endemic country require a malarial screen (blood film) before donation.

13.3.5 If a donor was born or has lived in a malarious area for more than 6 months at any time of life, a validated anti-malarial antibody test should be performed but in the case of deceased organ donors, donation may proceed pending the results. In very special circumstances e.g. where the donor is the only match for a bone marrow transplant, expert advice should be sought to inform a risk assessment.

13.3.6 If the return to the UK from a malaria-endemic area is within 4 months, defer the living donor. For deceased donors, the organs may be used but a validated malarial antibody and NAT test of the donor should be done.

13.3.7 If return to the UK from a malaria-endemic area is between 4 months and 1 year, a validated anti-malarial antibody test should be performed. Organs may be used before the serological result is available. If a positive result for malarial antibodies is obtained, testing for malaria DNA should be done. A

risk assessment should be carried out and follow up of the recipients undertaken.

- 13.3.8 Gamma irradiation offers a method for tissue sterilisation for those tissues able to withstand this process and offers an alternative to malarial antibody testing of tissue donors with relevant travel history.
- 13.3.9 When a recipient has been found to have received a donation from a donor whose serum contains malarial antibody, a risk analysis must be undertaken with the assistance of the PHE Malaria Reference Laboratory and a clinician experienced in parasitology or tropical medicine. Recipients should be advised of the potential risk of contracting malaria and clinicians should consider the diagnosis if the recipients subsequently becomes ill with pyrexia.

13.4 Fungal Infection

- 13.4.1 Fungal infection should be distinguished from colonisation.
- 13.4.2 Where there is localised fungal infection, specialist microbiological advice should be sought ahead of careful consideration of the benefits from transplantation and with recipients receiving appropriate antifungal prophylaxis.
- 13.4.3 Systemic infection defined by fungaemia may be associated with mycotic aneurysm at vascular anastomoses. On-going fungaemia is an absolute contra-indication to donation of organs and tissues but specialist microbiological advice should be sought for an accurate risk assessment to be made.
- 13.4.4 Organs and tissues from donors with superficial fungal infection of the skin or mucosa due to candida species are acceptable for donation.
- 13.4.5 Organs from a patient with a blood stream infection or abscess due to yeast or filamented fungi species are acceptable for donation providing appropriate recipient antimicrobial prophylaxis covering the donor organism is given. The potential for transmission of fungal infection and the development of a mycotic aneurysm at the vascular anastomoses must be considered.

13.5 Aspergillosis

- 13.5.1 Aspergillosis or other systemic fungal infections are contraindications for transplantation unless a specific risk assessment is carried out and appropriate recipient antifungal prophylaxis is prescribed.

13.6 Unusual bacterial/fungal/protozoal infections

- 13.6.1 Specialist microbiological advice should be sought when considering using organs and tissues from donors who have had unusual infections in the past, including those acquired outside of Western Europe. This should include infections common in immuno-compromised patients (e.g. listeriosis, nocardiosis) or infections which lie dormant or may be difficult to eradicate (e.g. brucellosis, Lyme disease, typhoid).

13.7 Endemic mycoses

- 13.7.1 There are no uniform recommendations for donor screening for endemic mycoses such as histoplasma, blastomycosis and coccidioidomycosis.
- 13.7.2 Evidence of active systemic fungal infection in the donor is a contraindication to transplantation. Evidence of active infection may include, but is not limited

to the detection of antigenemia, antigenuria, H and/or M precipitin bands, and complement fixation titers of $\geq 1:32$.

- 13.7.3 Most reports of infections with these fungi within transplant recipients are in those individuals who have resided in endemic areas. Diagnosis can be difficult as mycotic infection may be dormant.
- 13.7.4 Transmission of histoplasmosis by transplantation has been described, but most cases appear to be the result of reactivation of past infection in the recipient. In many individuals from the Midwestern United States, calcified pulmonary, hilar and splenic granulomata are the radiographic residua of old *Histoplasma* infection, but such signs have not traditionally been considered a contraindication to donation. Antifungal prophylaxis is recommended for lung transplant recipients whose donors have positive serology or incidental *H. capsulatum* detection in the donor lung. There is currently no consensus on, whether recipients of other organs from sero-positive donors should receive prophylaxis.
- 13.7.5 Transmission of coccidioidomycosis by lung transplantation has been reported in the Southwestern United States, this has also been described in kidney and liver recipients. Although reactivation of coccidioidomycosis in the previously infected recipient appears to be far more common. Antifungal prophylaxis is recommended for recipients of sero-positive donors. Post-transplant clinical and serologic monitoring of at-risk patients should be performed periodically to assess for evidence of reactivation infection.
- 13.7.6 At this time primary or secondary antifungal prophylaxis for blastomycosis after solid organ transplantation is not recommended

13.8 Trypanosoma cruzi (Chagas Disease)

- 13.8.1 *T. cruzi* antibody screening should be undertaken in donors that meet any of the following criteria:
 - 13.8.1.1 Born in Latin America (South America, Central America or Mexico).
 - 13.8.1.2 Received blood components or products while resident in Latin America (South America, Central America or Mexico).
 - 13.8.1.3 Lived in rural subsistence farming communities for a continuous period of 4 weeks or more in Latin America (South America, Central America or Mexico).
 - 13.8.1.4 Individuals whose mothers were born in Latin America (South America, Central America or Mexico).
- 13.8.2 Presently, *T. cruzi* antibody testing is limited to a small number of laboratories in the United Kingdom and consequently results may not be available at the time of retrieval and implantation of solid organ transplants.
- 13.8.3 For those potential organ donors meeting any of the above criteria, transplant centres should be made aware at the time of offering of the potential for *T. cruzi* infection in that donor. Organs can be accepted for transplantation provided recipients are appropriately informed and consented as to the risk and consequences of *T. cruzi* infection.
- 13.8.4 If donor serology is subsequently shown to be positive, specialist microbiological advice should be sought and an appropriate post-transplant management plan instituted.
- 13.8.5 Transmission rates from seropositive donors to seronegative recipients have been reported to be approximately 13-20% for kidney transplants, 20–29%

for liver transplants and 75% for heart transplants. Transmission rates for other organs (lung, pancreas and intestine) are not well defined.

13.8.6 Donors with positive *T. cruzi* serology should not donate tissues other than corneas.

13.9 Strongyloides stercoralis

13.9.1 Asymptomatic carriage with *strongyloides stercoralis* has been reported most often in donors who were both born in and lived for some while in endemic areas which include most of the Tropics and Sub-tropics. An Eosinophilia may or may not be present. Transmission to immuno-compromised recipients is often associated with significant morbidity and a high mortality rate.

13.9.2 Pre-donation identification from stool sampling and serology, most practicable for a live donor allows for effective recipient prophylaxis.⁷

13.10 Bacillus anthracis (anthrax)

13.10.1 Infection is an absolute contraindication to solid organ and tissue donation

13.11 Sexually Transmitted Infections

13.11.1 For those pathogens not otherwise specified, STIs are

13.11.1.1 Not a contra-indication to donation of solid organs for transplantation.

13.11.1.2 A marker of increased risk of transmissible disease.

13.12 Influenza

13.12.1 Lungs and bowel should not be used from donors with confirmed influenza infection.

13.12.2 Other organs may be offered, and the final decision lies with the transplanting surgeon weighing the balance of risks for the recipient.

13.12.3 SaBTO has issued [advice](#) concerning organ donation and seasonal influenza

(https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216780/dh_129670.pdf).

13.12.4 While there is no specific guidance for tissue donors, the criteria for blood donation as described in the Change Notifications 14 and 15 in 2009 issued by JPAC: <http://www.transfusionguidelines.org.uk/document-library/change-notifications/change-notifications-issued-in-2009>

13.13 Tuberculosis

13.13.1 Donation of organs and tissues is contraindicated from donors with active disease or within the first six months of anti-tuberculosis treatment.

⁷Abanyie FA, Gray EB, Delli Carpini KW, Yanofsky A, McAuliffe I, Rana M, Chin-Hong PV, Barone CN, Davis JL, Montgomery SP, Huprikar S. Donor-derived *Strongyloides stercoralis* infection in solid organ transplant recipients in the United States, 2009-2013. *Am J Transplant*. 2015 May;1

- 13.13.2 However, organs can be considered for transplant if a recipient has received a 6 month course of chemotherapy, unless the isolate is found to be resistant to anti-tuberculous drugs.
- 13.13.3 If there is a past history of tuberculosis at the site of the organ to be used for donation, use of that organ is contraindicated if there is evidence of organ damage but the donation of other organs is acceptable.
- 13.13.4 Advice should be sought from a microbiology, respiratory or infectious disease specialist in tuberculosis.

13.14 Current Infective Endocarditis

- 13.14.1 Is not a contraindication to solid organ transplantation;
 - 13.14.1.1 If organ does not have features of sepsis.
 - 13.14.1.2 If the organism is known.
 - 13.14.1.3 There has been adequate microbiological treatment. What constitutes adequate microbiological treatment will be dependent on knowledge of the identified organism.
- 13.14.2 Is a contraindication to tissue donation (cornea donation permitted).
- 13.14.3 Specialist microbiological advice should be sought.

13.15 Drug resistant bacteria e.g. methicillin resistant Staphylococcus aureus (MRSA), vancomycin resistant Enterococcus (VRE), carbapenemase-producing Enterobacteriaceae (CPE)

- 13.15.1 Drug resistant bacteria can be transmitted from donor to recipient. Transmitted infections are difficult to treat and are associated with poorer outcome in the recipient.
- 13.15.2 The presence of drug resistant bacteria in the donor.
 - 13.15.2.1 Is a relative contraindication to solid organ transplantation.
 - 13.15.2.2 Specialist microbiological advice must be sought.
 - 13.15.2.3 Careful consideration of benefits from transplant is required.
 - 13.15.2.4 Is an absolute contraindication to tissues unless life preserving.
- 13.15.3 Gamma irradiation offers a method for tissue sterilisation for those tissues able to withstand this process.

13.16 Urinary Tract Infection

- 13.16.1 A localised urinary tract infection may be transmitted to the recipient in the setting of renal transplantation. Urinary tract infections may also result in a bacteraemia which can lead to transmission of a donor derived infection.
- 13.16.2 Is not a contraindication to donation of solid organs for transplantation;
 - 13.16.2.1 If the organ is healthy.
 - 13.16.2.2 Organism known.
 - 13.16.2.3 Treated appropriately in donor.
 - 13.16.2.4 Antibiotics continued in recipient especially in renal transplantation.
- 13.16.3 Is a relative contraindication to tissues unless clinicians caring for patient feel that adequate treatment has been provided.
- 13.16.4 Is not a contraindication to cornea donation
- 13.16.5 Gamma irradiation offers a method for tissue sterilisation for those tissues able to withstand this process.

13.17 Lyme Disease

- 13.17.1 Lyme disease-associated myocarditis is a rare cause of cardiac death in areas where Lyme disease is prevalent.
- 13.17.2 At the time of writing there were no reported cases of donor-derived transmission in the literature.
- 13.17.3 Organism can be found in tissues so transplant-related transmission is possible.
- 13.17.4 Case reports of corneal transplant from donors that were later found to be infected with *Borrelia burgdorferi* but no evidence of transmission of disease was found.
- 13.17.5 Specialist microbiological advice must be sought.
- 13.17.6 Careful consideration must be given to the potential benefits from transplant.
- 13.17.7 Lyme disease is a relative contraindication for donation of solid organs for transplantation.
 - 13.17.7.1 Lyme disease-associated myocarditis in the donor is an absolute contra-indication for cardiac transplantation.
 - 13.17.7.2 Lyme disease-associated myocarditis in the donor is a relative contra-indication for other allografts.
- 13.17.8 Is an absolute contraindication to tissues unless transplant is life preserving.

13.18 Dengue Virus

- 13.18.1 Dengue virus is a common insect borne human disease and occurs in tropical and sub-tropical countries worldwide.
- 13.18.2 The majority of Dengue virus infections are asymptomatic. The possibility of infection should be considered in individuals recently returned (less than 28 days) from countries in which Dengue virus exists. Information regarding infection outbreaks may be found at the the National Travel Health Network & Centre website (NaTHNaC, <http://travelhealthpro.org.uk/>), Health Protection Scotland Fit For Travel website (<http://www.fitfortravel.nhs.uk/home.aspx>), JPAC Geographical Disease Risk Index (<http://www.transfusionguidelines.org/dsg/gdri>) and the ECDC (<http://ecdc.europa.eu/en/Pages/home.aspx>)
- 13.18.3 Case reports confirm that Dengue virus may be transmitted by by solid organ transplants.
- 13.18.4 Known Dengue virus infection
 - 13.18.4.1 Is a contraindication to donation of Solid Organs for Transplantation.
 - 13.18.4.2 Is a contraindication to tissue donation. Advice has been given by JPAC [http://www.transfusionguidelines.org/document-library/documents/jpac-position-statement-for-dengue-november-2015/download-file/JPAC Position Statement for Dengue - November 2015.pdf](http://www.transfusionguidelines.org/document-library/documents/jpac-position-statement-for-dengue-november-2015/download-file/JPAC%20Position%20Statement%20for%20Dengue%20-%20November%202015.pdf)
- 13.18.5 Donation may be considered 6 months after recovery from infection with Dengue virus.
- 13.18.6 For asymptomatic organ donors returning from affected areas, an individual risk assessment is required before donation.

13.19 Chikungunya Virus

- 13.19.1 Chikungunya virus may be found worldwide including parts of Europe

- 13.19.2 The majority of infections are symptomatic.
- 13.19.3 Although theoretically possible, transmission from the transplantation of tissues or organs has not been reported.
- 13.19.4 The possibility of infection should be considered in individuals recently returned from countries in which Chikungunya virus exists. Information regarding infection outbreaks may be found at the the National Travel Health Network & Centre website (NaTHNaC, <http://travelhealthpro.org.uk/>), Health Protection Scotland Fit For Travel website (<http://www.fitfortravel.nhs.uk/home.aspx>), JPAC Geographical Disease Risk Index (<http://www.transfusionguidelines.org/dsg/gdri>) and the ECDC (<http://ecdc.europa.eu/en/Pages/home.aspx>)
- 13.19.5 Known Chikungunya virus infection
 - 13.19.5.1 Is a contraindication to donation of Solid Organs for Transplantation
 - 13.19.5.2 Is a contraindication to tissue donation. Advice has been given by JPAC (<http://www.transfusionguidelines.org.uk/document-library/documents/jpac-position-statement-chikungunya-virus-august-2015/download-file/JPAC%20Position%20Statement%20Chikungunya%20Viruses%20-%20August%202015.pdf>)
- 13.19.6 Donation may be considered 6 months after recovery from infection with Chikungunya virus.
- 13.19.7 For asymptomatic organ donors returning from affected areas, an individual risk assessment is required before donation.

13.20 Zika Virus

- 13.20.1 Zika virus is a common mosquito borne human disease and occurs in tropical and sub-tropical countries worldwide. Since 2015, an outbreak of Zika virus has been occurring in the he Caribbean, Central and South America, Oceania and some parts of Asia. In addition to vector transmitted infection, both sexual and vertical transmission of Zika virus can occur.
- 13.20.2 The majority of Zika virus infections are asymptomatic. The possibility of infection should be considered in individuals recently returned (less than 28 days) from countries in which Zika virus exists. Information regarding infection outbreaks may be found at the the National Travel Health Network & Centre website (NaTHNaC, <http://travelhealthpro.org.uk/>), Health Protection Scotland Fit For Travel website (<http://www.fitfortravel.nhs.uk/home.aspx>), JPAC Geographical Disease Risk Index (<http://www.transfusionguidelines.org/dsg/gdri>) and the ECDC (<http://ecdc.europa.eu/en/Pages/home.aspx>).
- 13.20.3 Due to the possibility of sexual transmission by semen, consideration should be given to the possibility of Zika virus infection (asymptomatic or otherwise) in potential donors whose sexual partner has been in an area affected by Zika virus.
- 13.20.4 Case reports confirm that Zika virus can be transmitted by blood transfusion but to date transmission through solid organ, tissue and cell transplantation has not been reported.
- 13.20.5 The virus has a clear neurotropism, as evidenced by congenital Zika Syndrome and other CNS presentations, but the course of Zika virus infection in the immunocompromised host has not been well documented thus far. It is not known whether there is a risk of prolonged viraemia or virus compartmentalization after disappearance in blood.
- 13.20.6 Known Zika virus infection

- 13.20.6.1 Is a contraindication to donation of Solid Organs for Transplantation except in exceptional circumstance.
- 13.20.6.2 Is a contraindication to tissue donation.
- 13.20.7 Donation may be considered 6 months after recovery from infection with Zika virus.
- 13.20.8 For asymptomatic organ donors returning from affected areas, an individual risk assessment is required before donation.
- 13.20.9 Advice for organ donation has also been given by NHSBT http://www.odt.nhs.uk/pdf/Zika_virus_and_Transplantation_of_Solid_Organs_from_Deceased_Donors.pdf
- 13.20.10 Advice for tissue donation has also been given by JPAC <http://www.transfusionguidelines.org.uk/document-library/documents/jpac-position-statement-on-zika-virus-april-2016/download-file/JPAC%20Position%20Statement%20on%20Zika%20Virus%20April%2016.pdf>

13.21 West Nile Virus

- 13.21.1 West Nile Virus is a mosquito borne zoonotic infection that is currently not indigenous to the UK at present, but is endemic in many countries in Southern Europe, North America and Australia.
- 13.21.2 The majority of West Nile virus infections are asymptomatic, although a minority can develop neuroinvasive disease. The possibility of infection should be considered in individuals recently returned (less than 28 days) from countries in which West Nile virus exists. Information regarding infection outbreaks may be found at the the JPAC Geographical Disease Risk Index (<http://www.transfusionguidelines.org/dsg/gdri>), National Travel Health Network & Centre website (NaTHNaC, <http://travelhealthpro.org.uk/>), Health Protection Scotland Fit For Travel website (<http://www.fitfortravel.nhs.uk/home.aspx>) and the ECDC (<http://ecdc.europa.eu/en/Pages/home.aspx>).
- 13.21.3 Known West Nile virus infection
 - 13.21.3.1 Is a contraindication to donation of Solid Organs for Transplantation.
 - 13.21.3.2 Is a contraindication to tissue donation.
- 13.21.4 For asymptomatic donors returning from affected areas, an individual risk assessment is required before donation.
- 13.21.5 Donor transmission may occur from an asymptomatic individual or from a donor who died of unrecognised and therefore undiagnosed West Nile Neuroinvasive Disease. SaBTO has considered the implications should an organ and tissue donor test positive for WNV infection posthumously following the transplantation of an organ and published guidance: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/224546/SaBTO_Position_Statement_-_West_Nile_Virus_and_Solid_Organ_Transplantation.pdf

13.22 Progressive Multifocal Leukoencephalopathy

- 13.22.1 Is a rare progressive CNS disorder caused by the JC virus.
- 13.22.2 Previous JC virus infection is not a contraindication to donation of tissues or organs.
- 13.22.3 A confirmed diagnosis of progressive multifocal leukoencephalopathy is an absolute contra-indication to donation of tissues or organs.

13.23 Listeria monocytogenes

- 13.23.1 May cause meningitis/septicaemia.
- 13.23.2 Although the potential for disease transmission exists there are no reported cases
- 13.23.3 Is a relative contraindication to donation of solid organs for transplantation
- 13.23.4 May be considered if adequate antimicrobial treatment in the donor
- 13.23.5 Specialist microbiological advice must be sought
- 13.23.6 Careful consideration of benefits from transplant
- 13.23.7 Is an absolute contraindication to donation of tissues unless life preserving.

13.24 Mumps, measles and rubella

- 13.24.1 No reported transmission.
- 13.24.2 Acute disease is a relative contraindication to donation of solid organs for transplantation
- 13.24.3 Specialist microbiological advice must be sought
- 13.24.4 Careful consideration of benefits from transplant
- 13.24.5 Acute disease is an absolute contraindication to donation of tissues unless life preserving.

13.25 Middle East Respiratory Syndrome – coronavirus (MERS-CoV)

- 13.25.1 Where acute disease is confirmed, there is no evidence base to support safe use of substances of human origin..
- 13.25.2 Is an absolute contraindication to donation of solid organs for transplantation
- 13.25.3 Is an absolute contraindication to donation of tissues

13.26 Severe Acute Respiratory Syndrome (SARS)

- 13.26.1 Where acute disease is confirmed, there is no evidence base to support safe use of substances of human origin.
- 13.26.2 Is an absolute contraindication to donation of solid organs for transplantation.
- 13.26.3 Is an absolute contraindication to donation of tissues.

13.27 Rabies

- 13.27.1 Is an absolute contraindication to donation of solid organs for transplantation.
- 13.27.2 Is an absolute contraindication to donation of tissues.

13.28 Yellow Fever

- 13.28.1 Is an absolute contraindication to donation of solid organs for transplantation.
- 13.28.2 Is an absolute contraindication to donation of tissues.

13.29 Viral Haemorrhagic Fevers (VHF)

In general;

13.29.1 Acute disease is an absolute contraindication to donation of solid organs for transplantation

13.29.2 Acute disease is an absolute contraindication to the donation of tissues.

14 Clinical conditions present at the time of death

Conditions which may not necessarily be due to infection require careful consideration.

14.1 Hepatitis

- 14.1.1 Infectious hepatitis may be due to viral (hepatitis A-E viruses, CMV, EBV, Yellow fever), bacterial (legionella, leptospira, coxiella) and protozoal (toxoplasma) infections. Some cases of hepatitis are non-infectious.
- 14.1.2 The presence of a hepatotropic pathogen is not in itself an absolute contraindication to donation but careful consideration is required.
- 14.1.3 Donation for liver transplantation may be undertaken depending on the pathogen involved, the presence or absence of chronic liver disease in the potential donor and the recipient need for transplantation. Liver allografts may be used from individuals who have HBV and HCV infection.
- 14.1.4 Acute liver failure due to pathogen:
 - 14.1.4.1 Is a contra-indication to liver transplantation.
 - 14.1.4.2 Is a contra-indication to solid organ transplantation (other than liver) unless life preserving.
- 14.1.5 Specialist microbiological advice must be sought.
- 14.1.6 Careful consideration of benefits from transplant.

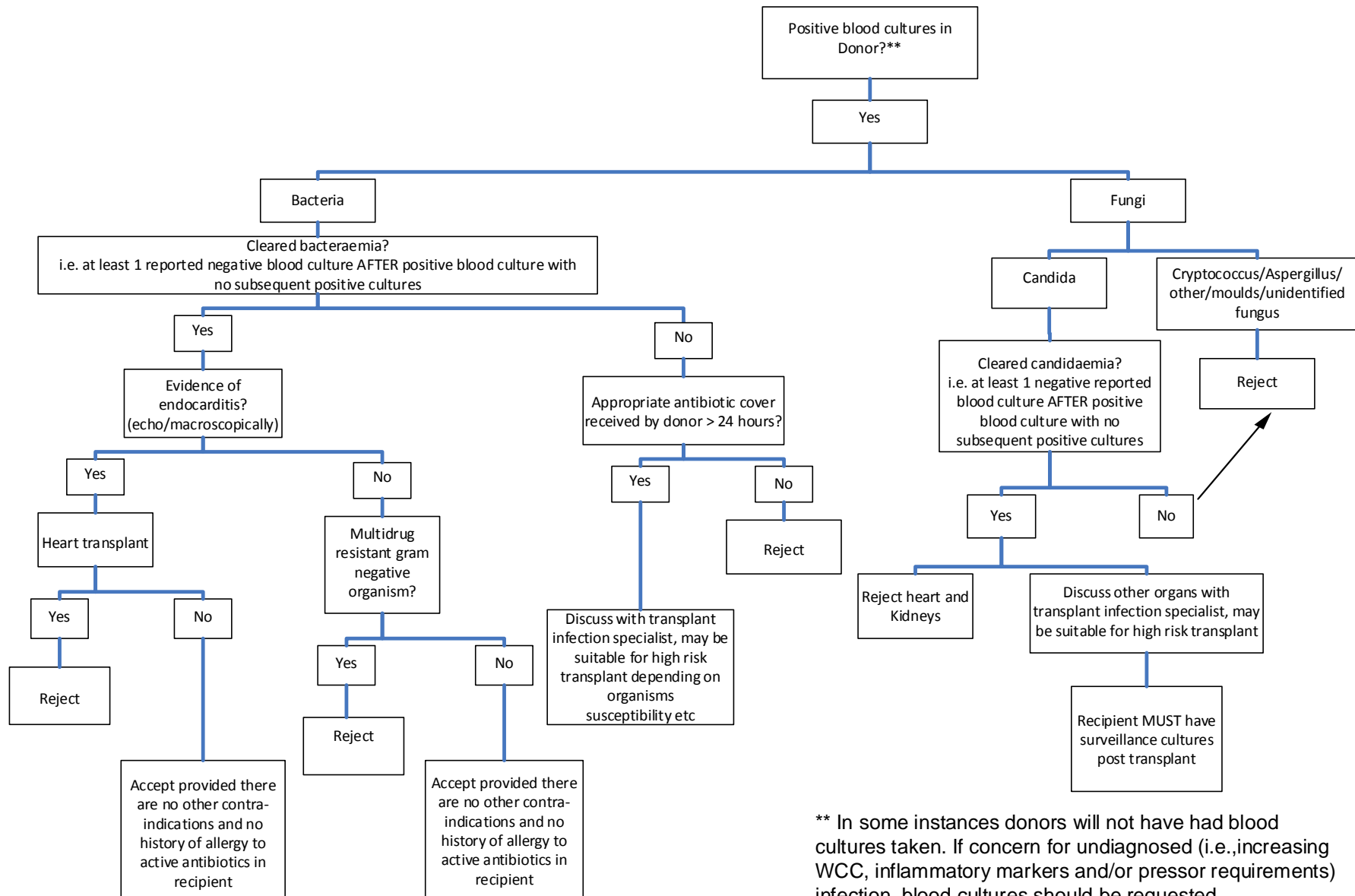
14.2 Lower Respiratory Tract Infection

- 14.2.1 Acute infection is a relative contraindication to lung transplantation. Individual assessment is required.
- 14.2.2 Bacterial infection (not TB), if localised to lung, is not an absolute contraindication but advice regarding bacteraemia and drug resistant bacteria pertain for both solid organ and tissue donation.

14.3 Blood Stream Infection

- 14.3.1 Where an organ donor has had a positive blood culture in the 5 days preceding the donation but there is no visible damage or local infection in the organ at retrieval, donation of an organ may be acceptable with appropriate recipient prophylaxis. See the decision tree in Figure 2.
- 14.3.2 Tissues should not be retrieved from a donor who has been found to be bacteraemic until after clinical recovery. If a risk assessment of the organism(s) isolated has been undertaken and is unlikely to represent a hazard to the recipient, tissues may be retrieved. Specialist microbiological advice must be sought.
- 14.3.3 Bacteraemia is not considered a contraindication for corneal donation provided the corneas are stored by organ culture at 28°C-37°C where there is a greater opportunity to detect bacterial contamination and where the antibiotics in the organ culture medium are more effective than under hypothermic storage conditions.
- 14.3.4 Gamma irradiation offers a method for tissue sterilisation for those tissues able to withstand this process.

Figure 2 : Decision making in potential organ donors with possible blood stream infection

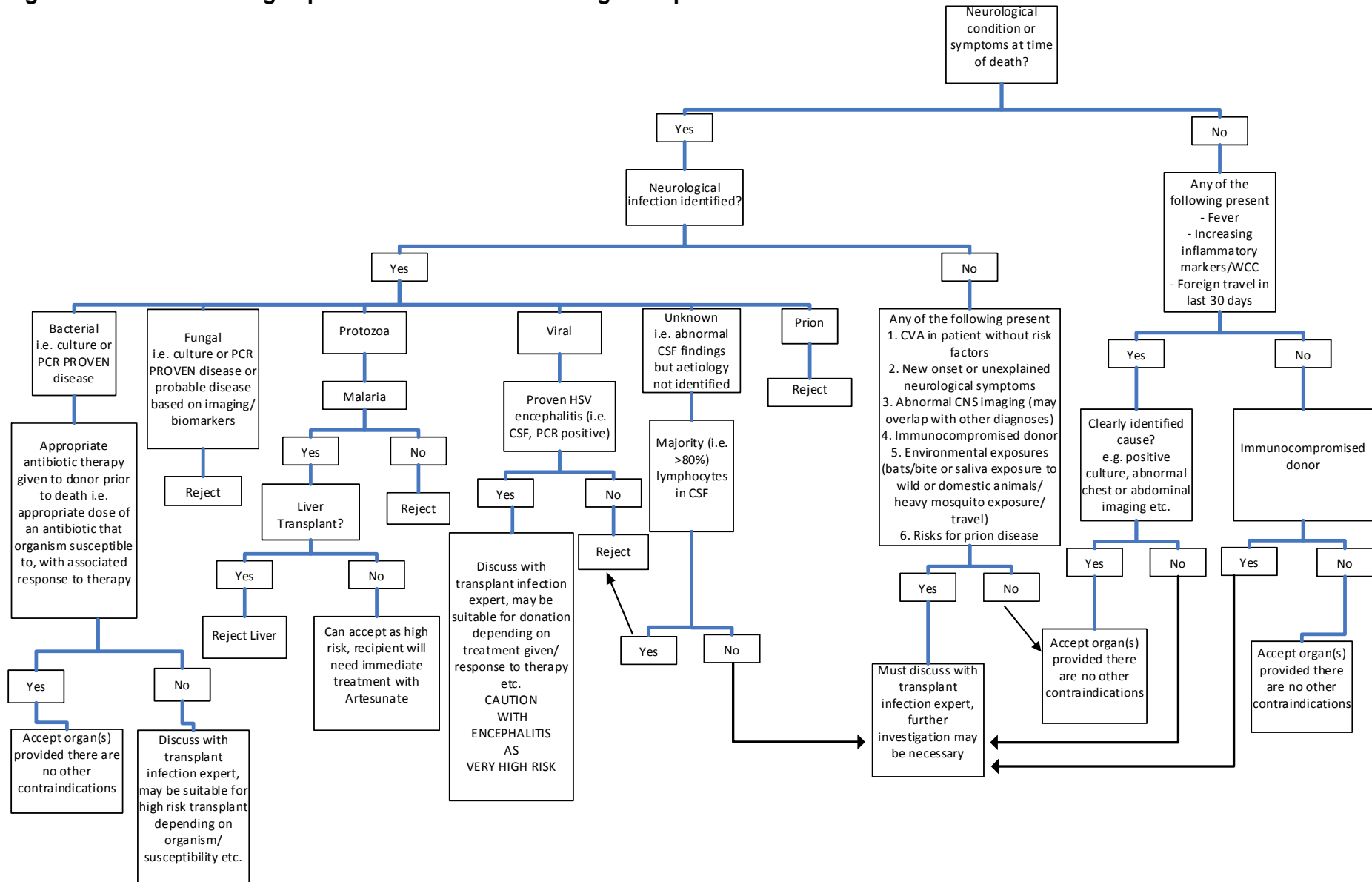


** In some instances donors will not have had blood cultures taken. If concern for undiagnosed (i.e., increasing WCC, inflammatory markers and/or pressor requirements) infection, blood cultures should be requested

14.4 Meningo-encephalitis

- 14.4.1 The following decision tree (Figure 3) details the approach to the donor where CNS infection exists or should be considered to exist.
- 14.4.2 If bacterial meningitis has been confirmed, and there is no visible damage or local infection in the organ or tissues required at retrieval, the donation of the organs, tissues and cells are acceptable provided appropriate treatment has been administered to the donor.
- 14.4.3 Appropriate antibiotic prophylaxis covering any organism isolated from the donor should be considered for identifiable recipients, especially in the case of organs.
- 14.4.4 Material from cases of death from meningo-encephalitis where no organism is cultured should not be used for donation, except in the circumstance that the following conditions are met;
 - 14.4.4.1 The infection is thought due to a bacterium by clinicians caring for the patient.
 - 14.4.4.2 Microbiological cultures are negative because they were taken after antibiotics had been started.
 - 14.4.4.3 Appropriate and adequate antibiotic treatment has been given to the recipient.
 - 14.4.4.4 Expert microbiological advice has been obtained.
- 14.4.5 A travel history should be obtained. Donation is contraindicated if there is any possibility of acquisition of a neurotropic infection from abroad due to the potential for rabies virus, West Nile virus or other geographically restricted neurotropic infections.
- 14.4.6 A history of close occupational or other animal contact should be explored because of the risk of zoonotic infection.
- 14.4.7 Herpes simplex virus (HSV) or varicella zoster virus (VZV) CNS infection is diagnosed as a manifestation of systemic viral infection (as seen in neonates and the immunosuppressed), donation of organs, tissues and cells is contraindicated as the viruses may be disseminated widely with associated viraemia.
- 14.4.8 HSV encephalitis without evidence of systemic infection can be treated with antiviral therapy and the likelihood of disseminated infection in the donor is small, even without antiviral therapy. In this situation antiviral prophylaxis should be considered for the organ recipient.
- 14.4.9 Organs can be considered for donation if local HSV/VZV infection has been treated with adequate antiviral therapy for >7 days; if treated <7 days, the recipient should receive antiviral prophylaxis. Serological status of the recipient may also inform a risk and benefit analysis.
- 14.4.10 Eyes must not be donated if the donor has active or a past history of HSV or VZV keratitis.

Figure 3: Decision making in potential donors with meningoencephalitis



14.5 Myocarditis

- 14.5.1 May be due to a number of causes including infections.
- 14.5.2 There is the potential for transmission of infection where myocarditis is due to a pathogen. However, there is limited available data regarding risk of transmission.
- 14.5.3 Careful consideration of benefits from transplant is required.
- 14.5.4 In organ transplantation.
 - 14.5.4.1 Myocarditis in the donor is an absolute contra-indication to cardiac transplantation.
 - 14.5.4.2 Current myocarditis in the donor is a relative contra-indication for other allografts
- 14.5.5 Current myocarditis is an absolute contraindication to tissue donation unless the transplant is life preserving.
- 14.5.6 Specialist microbiological advice must be sought.

15 Exceptional use of organs and tissues from donors potentially or known to be infected

Derogation of exclusion criteria for donors who carry an infection risk

- 15.1 We acknowledge the overwhelming clinical need for, and shortage of, organs suitable for transplantation in the UK. The unnecessary loss of potential organs needs to be avoided at all times and has been addressed in part by the guidelines for testing described above.
- 15.2 We accept that there may be clinical need for transplantation of such urgency that it may be appropriate to consider the use of organs and tissues for life-preserving purposes from donors who would not otherwise be considered eligible to donate, due to a known or perceived infection risk. Potential organs from such donors should be offered to the transplant community. Fully informed consent to such a procedure is required from the recipient of such transplantation and all measures for risk reduction, including onward transmission, must be taken. Transplants of this nature are likely to be infrequent. Intensive immediate post-transplant monitoring and long-term follow-up of the infection status of recipients should be set in place and the long-term outcome of the recipient recorded centrally by the transplant community.

Matching infection status of donor and recipient

- 15.3 Usually any reactivity in one or more of the mandatory marker assays used for screening donors renders the donor ineligible and the potential donations unsuitable for use without any leave to alter this decision. This is exemplified by the protocols surrounding the practice of blood transfusion and the exclusion of "risk donors". In principle the same applies to any donor of tissues and organs although, as we discuss below, in truly life-preserving situations, relaxation or even derogation of this exclusion may be possible, in particular in situations of discordant serological results in the donor.
- 15.4 Where a donor sample is repeatedly reactive in one assay and is un-reactive in one or more assays of similar sensitivity, the likelihood of subsequent confirmatory testing indicating this initial reactivity to be specific is very low. If testing

laboratories have evidence based and validated SOPs which indicate such discordant reactivity is likely to be non-specific, only then can consideration be given to disregarding the discrepant repeat reactivity in terms of allowing donation.

- 15.5 The risk of transmission of a pathogen may be reduced or eliminated through the use of an organ from a donor who is known to be infected, or at risk of infection, with a pathogen into a recipient infected with the same pathogen (infection match).
- 15.6 Similarly previous infection or immunisation may decrease or remove the risk of infection following the use of a transplant from a donor who is known to be infected, or who is potentially infected. This approach involves matching of the immune status of the recipient to the infection status of the donor. For example a recipient shown to be immune to hepatitis B, naturally or by immunisation, is unlikely to suffer re-infection should the transplant be taken from an HBV-infected donor. In this type of matching it is essential that the immune status of the recipient be known with absolute certainty.
- 15.7 Matching the status will also include an assessment of the likelihood of transmitting viral phenotypes which may pose an additional hazard to the already-infected recipient including viruses of increased pathogenicity, drug resistant variants, immune escape variants and a number of co-infections such as hepatitis delta virus and herpes virus 8. Specialist microbiological/virological support should be sought at the earliest possible stage to ensure that appropriate testing has been undertaken in the correct manner and within the available time to inform the risk assessment and to confirm the recipient's status.

Balancing risk and benefit

- 15.8 In general, derogation of the exclusion of infected donors should only be considered when the donation is truly considered to be life-preserving. In this situation the transplant clinician should, with the informed consent of the potential recipient, balance the risk of infection against the risk of dying whilst waiting for another graft.
- 15.9 Heart, lung and liver transplants will almost always fit within this definition, generally because the clinical situation of the recipient requiring these organs is likely to be one of incipient death. Other solid organs and some specialised tissues such as haematological stem cells may for individual recipients also fulfil this definition. Other tissues are unlikely to do so but exceptions may occur.
- 15.10 Where, however, short-term or intermediate support measures can be employed to avoid the immediate need for transplantation, and where there is a reasonable expectation of future availability of an appropriate organ, the balancing of risk and benefit may favour delaying the transplantation of a higher infection risk donation.

Risk mitigation

- 15.11 Specialist advice should be sought in order to aid decision making by the transplant surgeon and to inform discussions with the intended recipient in order to allow for informed consent. The nature of the specialist advice will depend on the infection risk but may include information on the following
 - 15.11.1 Risk of transmitting the infection

- 15.11.2 Possible prophylactic measure reducing the risk of transmission of infection
 - 15.11.3 Monitoring for the recipient following transplant in order to determine whether the infection has been transmitted
 - 15.11.4 The risk of disease arising from the transmitted infection
 - 15.11.5 Potential treatment options for the infection or the consequences of the infection
 - 15.11.6 Outcomes related to the specific infection in the transplant setting
- 15.12 Prophylaxis for close contacts may include active immunisation, antimicrobial drugs and advice over the routes of transmission in order to reduce the risks of secondary transmission.
- 15.13 In the immediate post transplant period comprehensive surveillance for infection of the recipient will be required with interventions planned should they become necessary in the face of active infection.

The offering, collection and use of organ donations carrying infection risks

- 15.14 Guidelines on the suitability for donation are issued by the Organ Donation and Transplantation directorate of NHSBT. However, where a potential donor is found by laboratory screening to be infected, or possibly be infected, with a pathogen, the Specialist Nurse-OD should still consider offering life-preserving organs to the transplant community.
- 15.15 The decision to use such organs or tissues ultimately lies with the transplant surgeon and team and must only be taken with the express permission and informed consent of the recipient. If consent cannot be obtained from the individual undergoing transplant then transplantation may be undertaken within the legal frameworks existing at that time, but it would be expected that the potential recipient's next of kin would be involved in the discussions informing the decision making process.
- 15.16 Discussions, decisions and consent must be recorded.
- 15.17 Expert microbiological advice should be sought and any recommendations recorded in the patient's notes.
- 15.18 The retrieval team should be made aware of the potential hazards of organ retrieval where the donor is known to be infected, and appropriate control of infection procedures and risk reduction measures should be undertaken during organ retrieval. This may include appropriate personal protective equipment as required. Expert microbiological and infection control advice should be sought.
- 15.19 Any pre-transplant manipulation of the donation, either at the time of retrieval or at the time of transplantation must also be carried out observing the appropriate containment and risk reduction procedures relevant to the infection risk. They should include appropriate site terminal decontamination.
- 15.20 Organs for transplantation taken from infected or potentially infected donors must be appropriately labelled for transplantation as normal but in addition, where third-party contact with the donation could lead to a risk of infection, the external packaging should clearly be marked with "infection risk" and carry the appropriate

UN hazard labelling. Internal labelling must clearly state the nature of the infection risk.

16 Adverse incidents relating to transplantation

- 16.1 Individuals involved in the transplantation of organs, tissues and cells should remain vigilant for the possibility of transmission of infection from donors. The identification of the possibility of transmission of a pathogen may occur at any point in the donation and transplant process. Once an actual or potential risk is identified there is a legal obligation to report that risk to the appropriate supervisory organisation.
- 16.2 In view of the time pressures implicit in organ transplantation, and the possibility of a multi-organ donor also being a tissue donor, laboratory testing of tissues may identify an infection risk to recipients of organs that have already been transplanted. It is also possible that an adverse incident arising from an organ transplant may identify an infectious risk not known at the time tissues were retrieved. There are cases of transmission of disease that could have been prevented had an adverse event in an organ recipient been linked appropriately to involved tissues from the same donor.
- 16.3 Where an infection in a transplant recipient indicates potential transmission from the donor, it is the duty of the clinician looking after the transplant recipient to ensure that this information is communicated to the relevant supervisory organisation in order that this information is disseminated to clinicians caring for the recipients of other organs / cells and tissues from the same donor. In the setting of solid organ transplantation it is mandatory to inform the Duty Office at the Directorate for Organ Donation and Transplantation, NHSBT. They will assist in ensuring that all relevant clinicians and Tissue Establishments are informed as well as co-ordinate central quality control processes and microbiological advice. Any involved Tissue Establishment must in addition undertake a risk assessment of tissues from the donor held in their inventory or, where these have been issued to clinicians, contact the clinicians and, if the tissues have not already been transplanted, undertake a tissue recall. Where a donor-derived infection is detected in a tissue recipient, or there is concern about the potential transmission of donor-derived infection, the Tissue Establishment must inform all other Tissue Establishments where tissues or cells from the same donor have been processed in order to initiate, where necessary, a tissue recall, and, where the tissue donor also donated organs, the ODT Duty Office must be informed in order to assist in informing all relevant clinicians.
- 16.4 Where a potential for transmission exists, appropriate follow-up of all recipients must be undertaken:
- 16.4.1 It is essential that confirmatory testing, be undertaken on the donor sample to confirm specificity of the serological reactivity and the likelihood of transmission;
 - 16.4.2 A risk assessment should be undertaken to assess the susceptibility of the recipient to infection and to disease;
 - 16.4.3 Advice should be sought and appropriate monitoring and or post-exposure prophylaxis administered to recipients.
 - 16.4.4 Prophylaxis should also be considered for close contacts of the recipient where secondary transmission is possible;

- 16.5 It is good medical practice to make an appropriate referral for assessment of an infected living donor and close contacts of an infected donor, living or deceased.

17 Adverse Incident Reporting

- 17.1 It is a mandatory requirement to report Serious Adverse Events (SAEs) and Serious Adverse Reactions (SARs) to the relevant Competent Authority (Table 16). For organs, the HTA has delegated the responsibility for managing the adverse event reporting system to NHSBT. The Designated Individual has responsibility to ensure that any and all SAEs and SARs are reported.
- 17.2 For organ donation and transplantation the EUODD defines a
- 17.2.1 Serious Adverse Event (SAE) 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’. 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.
 - 17.2.2 Serious Adverse Reactions (SAR) 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’. 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.
- 17.3 The HTA has published [guidance](#) regarding the reporting of Serious Adverse Event And Reactions (SAEARs) in organ donation and transplantation⁸.
- 17.4 For tissues and cells the EUTCD defines a:
- 17.4.1 Serious Adverse Event as any untoward occurrence associated with the procurement, testing, processing, storage and distribution of tissues and cells that might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients or which might result in, or prolong, hospitalisation or morbidity
 - 17.4.2 Serious Adverse Reaction as an unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs, hospitalisation or morbidity
- 17.5 The HTA has produced [guidance](#) regarding the reporting of SAEARs regarding tissues and cells⁹.

⁸<https://www.hta.gov.uk/sites/default/files/Guidance%20for%20reporting%20SAEARs%20for%20or%20gans%20intended%20for%20transplantation%20FINAL.pdf>

17.6 The HFEA has published guidance regarding reporting SAEARs regarding gametes and embryos for human applications in note 27 of the [HFEA Code of Practice](#)

⁹ <https://www.hta.gov.uk/policies/human-application-adverse-event-and-reaction-saeas-reporting>

Table 16: Reporting of SAEs and SARs

	Responsible organisation	Link
Organs	NHSBT	https://safe.nhsbt.nhs.uk/IncidentSubmission/Pages/IncidentSubmissionForm.aspx
Tissues, cells and stem cells	HTA	https://www.hta.gov.uk/policies/serious-adverse-event-or-reaction-saears
Gametes and embryos	HFEA	Email form to incident.reporting@hfea.gov.uk

17.7 In the case of tissue donors, many donations increasingly cross national boundaries. The EU mandated requirement to inform Competent Authorities of adverse reactions will allow other Competent Authorities (UK or otherwise) to be informed.

17.8 For Adverse Incidents related to gametes and embryos, relevant guidance is given in note 27 of the [HFEA Code of Practice](#).

18 Links to other resources

Reference	Link
Advisory Committee on Dangerous Pathogens TSE Working Group guidance	https://www.gov.uk/government/groups/advisory-committee-on-dangerous-pathogens
Advisory Committee on the Safety of Blood, Tissues and Organs	https://www.gov.uk/government/groups/advisory-committee-on-the-safety-of-blood-tissues-and-organs
Cellular Therapy Standards – FACT (Foundation for the Accreditation of Cellular Therapy)	http://factwebsite.org/ctstandards/
Directive 2004/23/EC Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:en:PDF
Directive 2006/17/EC Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:038:0040:0052:EN:PDF
Directive 2006/86/EC Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:294:0032:0050:EN:PDF
Directive 2010/53/EU Standards of quality and safety of human organs intended for transplantation	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:207:0014:0029:EN:PDF
European Union Standards and Training in the Inspection of Tissue Establishments working group	http://www.notifylibrary.org/content/european-union-standards-and-training-inspection-tissue-establishments-project-eustite
Guidance notes on the processing, storage and issue of bone marrow and blood stem cells – Department of Health 1997	http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Healthserviceguidelines/DH_4018321

Reference	Link
Guidelines for the Blood Transfusion Services in the UK	http://www.transfusionguidelines.org.uk/index.aspx?Publication=RB
HTM 07-01 – Safe management of healthcare waste – Department of Health	https://www.gov.uk/government/publications/guidance-on-the-safe-management-of-healthcare-waste
Human Fertilisation and Embryology Act 1990 2008 amendment	http://www.legislation.gov.uk/ukpga/1990/37/contents http://www.legislation.gov.uk/ukpga/2008/22/contents/enacted
Human Fertilisation and Embryology Authority (HFEA)	www.hfea.gov.uk
Human Fertilisation and Embryology (Quality and Safety) Regulations 2007	http://www.legislation.gov.uk/uksi/2007/1522/contents/made
HFEA Code of Practice	http://www.hfea.gov.uk/code.html
HFEA Directions	http://www.hfea.gov.uk/188.html
Human Tissue Act 2004	http://www.legislation.gov.uk/ukpga/2004/30/contents
Human Tissue (Scotland) Act 2006	http://www.legislation.gov.uk/asp/2006/4/contents
Human Tissue Authority (HTA)	www.hta.gov.uk
Human Tissue (Quality and Safety for Human Application) Regulations 2007	http://www.legislation.gov.uk/uksi/2007/1523/contents/made
HTA Codes of Practice	http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/codesofpractice.cfm
HTA Directions	http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/htalegaldirections.cfm
JACIE	http://www.jacie.org/
SHOT	http://www.shotuk.org/home/
SABRE	https://aic.mhra.gov.uk/mda/sabresystem.nsf/Login?Open https://www.gov.uk/guidance/blood-authorisations-and-safety-reporting

World Marrow Donor Association	https://www.wmda.info
Reference	Link
World Marrow Donor Association International Standards for Unrelated Hematopoietic Stem Cell Donor Registries	http://www.worldmarrow.org/fileadmin/WorkingGroups_Subcommittees/Accreditation/Documents/standards_history/WMDA_Standards-version_November_2008_01.pdf
Haematopoietic stem cell donor registries: World Marrow Donor Association recommendations for evaluation of donor health. <i>Bone Marrow Transplantation</i> (2008), 1–6	http://www.worldmarrow.org/fileadmin/Education/Publications/bmt200876a.pdf
UK Stem Cell Tool Kit	http://www.sc-toolkit.ac.uk/home.cfm
NHS Blood and Transplant Organ Donation and Transplant	http://www.odt.nhs.uk
British Transplant Society	http://www.bts.org.uk/BTS/Guidelines_Standards/BTS/Guidelines_Standards/Current_Guidelines.aspx?hkey=94dd25f6-8a90-444a-9563-d3a0c01553e6
Council of Europe Organs, Tissues and Cells – Technical Guides	https://www.edqm.eu/en/organ-tissues-cells-transplantation-guides-1607.html

19 Abbreviations

ACDP	Advisory Committee on Dangerous Pathogens
Anti-HBc	Hepatitis B core antibody
Anti-HBs	Hepatitis B surface antibody
ATMP	Advanced therapeutic medicinal products
CMV	Cytomegalovirus
CNS	Central Nervous System
CJD	Creutzfeldt-Jakob Disease
DBD	Donation after brain death (previously heart beating donor)
DCD	Donation after circulatory death (previously non heart-beating donors)
DNA	Deoxyribonucleic acid
EBMT	European Society for Blood and Marrow Transplantation
EBV	Epstein Barr virus
EDTA	Ethylene diaminetetracetic acid
EU	European Union
EUSTITE	European Union Standards and Training in the Inspection of Tissue Establishments Working Group
EUTCD	European Union Tissue and Cells Directives
FACT	Foundation for the Accreditation of Cellular Therapy
GP	General Practitioner
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
hESCs	Human embryonic stem cells
HFEA	Human Fertilisation and Embryology Authority
HIV	Human immunodeficiency virus
HSPC	Haematopoietic stem and progenitor cells
HSV	Herpes simplex virus
HTA	Human Tissue Authority
HTLV	Human T cell Lymphotropic virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
iPS	Induced pluripotent stem cells
ISCT	International Society for Cellular Therapy
IU	International Units
IVF	In-vitro fertilisation

JACIE	Joint Accreditation Committee ISCT-EBMT
JPAC	Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
MHRA	Medicines and Healthcare products Regulatory Agency
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
MSM	Men who have sex with men
NAT	Nucleic acid testing
NHS	National Health Service
NHSBT	NHS Blood and Transplant
ODT	Organ Donation and Transplantation Directorate of NHSBT
PA1	NHS Blood and Transplant Patient Assessment form
PCR	Polymerase Chain Reaction
PrP	Prion related protein
RNA	Ribonucleic acid
SABRE	Serious Adverse Blood Reactions and Events
SaBTO	Advisory Committee on Safety of Blood Tissues and Organs
SAEARs	Serious Adverse Events and Reactions (HTA)
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction(s)
SHOT	Serious Hazards of Transfusion
SOP	Standard Operating Procedure
TC	Therapeutic cells
TSE	Transmissible Spongiform Encephalopathy
UK	United Kingdom
UN	United Nations
vCJD	Variant CJD
VZV	Varicella zoster virus
WMDA	World Marrow Donor Association

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