Highlights of major changes in the 2017 SaBTO Microbiological Safety Transplantation Guidelines

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Executive summary

The Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) last published Guidance on the Microbiological Safety of Human Organs, Tissues and Cells in 2011. That document helped provide for the use of donor organs, tissues and cells, safe from infection, in the vast majority of patients. However, as with all guidance there is a need to review previous recommendations to ensure that they remain fit for purpose. The 2017 Guidance on the SaBTO Transplantation Microbiological Safety Guidelines has provided an update that aims to ensure that the clinical use of human organs, tissues and cells within the United Kingdom continues to be conducted according to legislation and consistent with current knowledge.

Since the 2011 recommendations, there have been major advances in the understanding and management of disease. For example, notable progress has occurred in the treatment of the major blood borne viruses with treatments that provide for effective control of the hepatitis B virus (HBV) and the human immunodeficiency virus (HIV), and direct acting antiviral therapy has become available that provides cure for almost all individuals with the hepatitis C virus (HCV). These advances, and others, require a reconsideration of previous recommendations especially in relation to solid organ transplantation, in which the demand for solid organ transplantation is not matched by the number of donors and patients continue to die waiting for transplants, where there remains a need to ensure that transplantation is safe, but equally a need to ensure that organ donation is not limited by inappropriate assessment and management of actual or potential infection in the donor.

There has also been an identified need to update previous guidance to include recommendations that concern established infectious agents or conditions that had not been previously included, but also to provide for new or emerging human pathogens, such as Ebola Virus and Zika Virus. It is acknowledged that the although it is intended that the 2017 Guidance on the Microbiological Safety of Human Organs, Tissues and Cells is up to date at the time of agreement, SaBTO will need to remain vigilant and provide further new recommendations as future emerging infections appear.

Those involved in drafting the 2017 Microbiological Safety of Human Organs, Tissues and Cells recognise that the need for transplantation is frequently greater than the risk of remaining without the transplant. Therefore, the 2017 Guidance on the Microbiological Safety of Human Organs, Tissues and Cells aims, where possible, to be permissive rather than restrictive in order to maximise the number of organs available for use, emphasising that the risk of transplant transmitted infection be kept to an “acceptable minimum”. The Guidance recognises that what constitutes an “acceptable minimum” is dependent on the clinical situation and the wishes of the intended recipient. It is recognised that consideration of the risk of transmission of infection during transplantation is an essential part of the consent process and must be discussed with the intended recipients.

It is also recognised that the 2017 Microbiological Safety of Human Organs, Tissues and Cells provides recommendations that are appropriate for the state of knowledge that exists at the time of publication and that with the passage of time the guidance contained within will require further change.

The following text highlights areas of change within the 2017 Guidance on the Microbiological Safety of Human Organs, Tissues and Cells and is provided as a guide to all current users. The 2017 Guidance on the Microbiological Safety of Human Organs, Tissues and Cells is an extensive revision of the previous guidance recommended by SaBTO in 2011 and therefore the following does not and cannot replace the need to refer to the main document, rather it illustrates the extent of the revised recommendations thereby demonstrating the need for

individuals to careful read carefully the complete 2017 Guidance on the Microbiological Safety of Human Organs, Tissues and Cells.

1. Introduction

The underlying principle is that the risk of an infection being passed on through the transplantation of human organs, tissues and cells be kept to an acceptable minimum and that 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”.

New is an emphasis that "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."

New is that "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/).

2. Legislation and accountability

Updated to detail current UK legislation and regulatory bodies that are relevant to the transplantation of human organs, tissues and cells.

Clarification of individuals that are accountable for the transplantation of human organs tissues and cells.

3. Overview of the principles underpinning these guidelines

New emphasis "where unusual ..... or extra risks .....of infection are identified with a particular donation, these should be discussed before transplantation with the person who would receive the organ .....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."

New recommendation around the consent process with regard to individuals who lack capacity - “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.”

4. Referral for donation

New emphasis on the fact that 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."

Recommendations regarding cell and tissue based therapies re-drafted and clarified and includes links as appropriate "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)"

5. Donor assessment

This section has been extensively re-written.

Links to relevant on line resources included. For example "Infections may be acquired during travel outside the UK that have the potential for transmission through transplantation. .....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 alsoNational Travel Health Network & Centre website (NaTHNaC, http://travelhealthpro.org.uk/), Health Protection Scotland Fit For Travelwebsite (http://www.fitfortravel.nhs.uk/home.aspx),and the European Centre for Disease Control (ECDC http://ecdc.europa.eu/en/Pages/home.aspx)"

6. Collection of material for donor testing

Clarification of recommendations with summary of Mandatory / Recommended / Not required tests presented in a single table (Table 3).

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-T. pallidum antibody	R	M	M	R
Toxoplasma gondii	Anti-T. gondii 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
Chlamydia trachomatis	n/a	NR	NR	NR	M
Neisseria gonorrhoea	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 invidual 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

Clarification of recommendations for HSPC cord donations.

Addition of recommendations regarding HSPC bone marrow and apheresis donors.

Clarification of recommendations around the testing of non-partner sperm donors.

7. Haemodilution, Transfusion and Donor Testing

Rewritten to improve clarity and recommendations around situations where haemodilution may affect donor microbiological testing.

8. Handling and transportation of samples for testing

No major changes.

9. Laboratory Requirements for the Microbiological Screening of Donors

Updated recommendations around organ donor testing laboratories "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."

Clarification that “The tests used for testing donors of cells, tissues and organs should be CE marked.”

Recommendation that “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 years. 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

New clarity of the need for additional samples and tests to be undertaken where increased risk of infection for organ and tissue donors is present.

Updated recommendations about tissue and gamete retrieval / collection and processing.

11. Microbiological risk of cryopreservation of donations.

No major changes

12. Interpreting donor test results

Section extensively revised, clarified and shortened. New is an estimate of the residual risk for undetected blood born 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

1Anti-HBc antibody + HBsAg

2Anti-HBc antibody + HBsAg + HBV DNA PCR

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

Made explicit is that "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, 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".

Recommendations regarding the responsibility for results from donor testing

"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."

Change in recommendations regarding the counselling of close contacts in situations where microbiological tests identify risks during the donation process.

"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."

The appropriate interpretation and the decision to be made based on specific test results for many individual pathogens has been clarified by tabulating the recommendations for an example see for 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	Donation permitted	Donation permitted. Informs need for post transplant EBV	EBV testing not required.

Test result(s) suggesting possible EBV infection of donor	Organs	Tissues	HSPC, TC and Human embryonic stem cells	Gametes and embryos
	monitoring.		monitoring	

CMV: Tests required reduced and clearer recommendations about management of post transplant risk

EBV: Tests required reduced and clearer recommendations about management of post transplant risk

HBV: Improved clarity about interpretation of tests and management of risk of transmitting infection

HCV: New "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". EUTCD requirements for HCV testing and implications of results included in table 8.

HIV: New ", 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."

HTLV: New “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."

Toxoplasma gondii: Effects of cryopreservation of tissues upon Toxoplasma gondii included.

HEV: Reflects recent guidance “SaBTO has recently published guidance recommending HEV NAT testing for donors of organs, tissues and cells. https://www.gov.uk/government/publications/protecting-patients-from-getting-hepatitis-e-through-transfusion-or-transplantation.

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.

Treponema pallidum (Syphilis): New: “The interpretation of syphilis serology can be difficult, and may require help from an experienced clinician. Serological tests for are not specific for ...(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."

Transmissible Spongiform Encephalopathies (TSEs): New "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. .....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."

13. Infections present at the time of donation

This section of the document relates to organ and tissue donors only

Abscesses: No change

Malaria: New "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 recommendations should be sought to inform a risk assessment.....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.....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

Fungal Infection: New "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 recommendations should be sought for an accurate risk assessment to be made."

Aspergillosis: No change

Unusual bacterial/fungal/protozoal infections: "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)."

Endemic mycoses: New section explores geographic and other risk factors but "There are no uniform recommendations for donor screening for endemic mycoses such as histoplasma, blastomycosis and coccidioidomycosis."

Trypanosoma cruzi (Chagas Disease): New "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.....If donor serology is subsequently shown to be positive, specialist microbiological recommendations should be sought and an appropriate post-transplant management plan instituted."

Strongyloides stercoralis: New section “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 but may not be present. Transmission to immuno-compromised recipients is often associated with significant morbidity and a high mortality rate."

Bacillus anthracis (anthrax): New section "absolute contraindication to donation"

Sexually Transmitted Infections: New section "Not contra-indication to donation of solid organs for transplantation.....A Marker of increased risk of transmissible disease"

Influenza: New "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-notifcations-issued-in-2009"

Tuberculosis: No change

Current Infective Endocarditis: New section “Is not a contraindication to solid organ transplantation;.....If organ does not have features of sepsis. .....If the organism is known.....There has been adequate microbiological treatment. What constitutes adequate microbiological treatment will be dependent on knowledge of the identified organism.

Is a contraindication to tissue donation (cornea donation permitted)....Specialist microbiological recommendations should be sought."

Drug resistant bacteria: Previous section on MRSA removed and new section detailing recommendations around donors with drug resistant bacteria added.

Urinary Tract Infection: New section

Lyme Disease: New section

Dengue Virus: New section

Chikungunya Virus: New section

Zika Virus: New section

West Nile Virus: New Section

Progressive Multifocal Leukoencephalopathy: New Section

Listeria monocytogenes: New section

Mumps, measles and rubella: New section

Middle East Respiratory Syndrome – coronavirus (MERS-CoV): New section

Severe Acute Respiratory Syndrome (SARS): New section

Rabies: New section

Yellow Fever: New section

Viral Haemorrhagic Fevers (VHF): New section

14. Clinical conditions present at the time of death

Hepatitis: New section

Lower Respiratory Tract Infection: New section

Blood Stream Infection: New section including a decision tree to aid assessment

Meningo-encephalitis: New section updating and expanding the previous advice on “Viral meningo-encephalitis”. Recommendations around the donation from individuals with meningoencephalitis clarified.

A decision making tree to aid assessment has been added.

Myocarditis: New section

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

New: “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

New: "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."

16. Adverse incidents relating to transplantation

New: “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"

New: “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."

17. Adverse Incident Reporting

Rewritten to improve clarity around Serious Adverse Events (SAEs) and Serious Adverse Reactions (SARs) and include links to appropriate organisations to report incidents provided.

18. Links to other resources

Updated

19. Abbreviations

Updated