Change Notification for the UK Blood Transfusion Services

Date of Issue: 18 April 2024 **Implementation:** to be determined by each Service

No. 05 – 2024

Red Book Chapter 21 and Annexe 7

This notification includes the following changes:

		BM-DSG Bone Marrow & Peripheral Blood Stem Cell	CB-DSG Cord Blood	GDRI Geographical Disease Risk Index	TD-DSG Tissue – Deceased Donors	TL-DSG Tissue – Live Donors	WB-DSG Whole Blood & Components	Red Book Guidelines for the BTS in the UK
1.	Chapter 21 Tissue banking: tissue retrieval and processing	○	○	○	○	○	○	●
2.	Annexe 7 Requirements for the timing of testing for HPCs	○	○	○	○	○	○	●

Dr Akila Chandrasekar
Chair of Standing Advisory Committee on Tissues & Cellular Therapy Products (SACTCTP)

Dr Stephen Thomas
Professional Director of JPAC

Changes are indicated using the key below. This formatting will not appear in the final entry.

original text	«inserted text»	~~deleted text~~

1. Changes apply to the **Red Book**

Chapter 21: Tissue banking: tissue retrieval and processing

(no changes to sections 21.1 – 21.2)

21.3: Transportation conditions from retrieval site to Tissue Establishment

Transportation systems must be validated to show maintenance of the required storage temperature.

Transport solutions must be validated to preserve the required characteristics of the tissue to be transported.

~~*For viable tissue the grafts should be placed into a transport solution with due regard to its effects on the ability of cells to propagate or metabolise. There must be adequate control of buffering capacity, osmolarity and tissue oxygenation.*~~ External contamination and desiccation must be avoided.

The type, lot, manufacturer and the expiry date of the transport solution and components coming into contact with the tissue, such as the primary container, must be documented.

21.4: Bacteriostasis and disinfection

Storage conditions and expiration periods must be supported by validation. Historical data, experience and documented literature are acceptable as evidence of validation. Any new processing or significant changes to existing processing are subject to pre-authorisation by the HTA.

21.4.1: Tissue without terminal antimicrobial processing

Tissue must be subjected to one of the following treatments, as soon as possible and within 24 hours of retrieval:

- antibiotic disinfection
- an alternative disinfection method
- frozen storage at –20°C or lower.

In the case of tissue taken from heart-beating donors in the operating theatre at the time of organ retrieval, this period may be extended to 48 hours.

21.4.2: Tissue with terminal antimicrobial processing

Tissue with terminal antimicrobial processing must be subjected to one of the treatments detailed in the above section within 24 hours of retrieval with a maximum of 72 hours following death. A summary of the guidance regarding temperature/time relationships contained in these guidelines is given in Tables 21.1 and 21.2.

Table 21.1 Temperature/time relationships for banked tissues from living donors

Retrieved tissue	Must be placed at «a» ~~*an ambient*~~ temperature of «between» 0–10°C within 4 hours of retrieval.«1»
Bacteriostasis	Freezing tissue to ~~*at least*~~ –20°C «or colder» within 24 hours of retrieval can be used as a bacteriostatic treatment. Bone from living donors which is not frozen until 24–48 hours after retrieval must be subjected to terminal antimicrobial processing.
Long-term storage	Bone from living donors may be stored at –20°C or «colder» ~~*lower*~~ for up to 6 months or at –40°C or «colder» ~~*lower*~~ for up to 5 years. Temporary storage of frozen living donor bone between –20°C and –40°C is limited to 6 months in total. Grafts stored at this temperature must then be transferred to –40°C or colder to give an expiry of up to a maximum of 5 years from donation. Amnion preserved in low-concentration (50%) glycerol may be stored «at» ~~*below*~~ –40°C «or colder» for up to 2 years.
Transportation and local storage	Must be transported and stored locally prior to clinical use, at –20°C or «colder» ~~*lower*~~ in order to have the designated expiry (specified above).
«1 As the tissue itself it taken directly from a living individual, setting temperature criteria for the tissue itself during this initial storage and transport is not feasible, therefore only the ambient temperature it must be kept at is specified.»	

Table 21.2 Temperature/time relationships for banked tissues from deceased donors

Retrieval	For eyes, retrieval must be completed within 24 hours after death and the body should preferably be refrigerated For all other tissues, if the body has not been refrigerated, procurement of tissues must be completed within 12 hours after death. If the body has been refrigerated within 6 hours of death procurement should preferably start within 24 hours and must be completed within 48 hours of death.
Retrieved tissue	Must be placed at «a» ~~*an ambient*~~ temperature of «between» 0–10°C within 4 hours of retrieval.«1»
Bacteriostasis	Freezing tissue to «a temperature of» ~~*at least*~~ –20°C «or colder» within 24 hours of retrieval (or up to a maximum of 72 hours of death) can be used as a bacteriostatic treatment.
Long-term storage	**Frozen* ~~*non-viable*~~ tissue may be stored:** 1. At –20°C or «colder» ~~*lower*~~ for up to 6 months. 2. At –40°C or «colder» ~~*lower*~~ for up to 5 years. Temporary storage of frozen musculoskeletal tissue between –20°C and –40°C is limited to 6 months in total. Grafts stored at this temperature must then be transferred to –40°C or colder to give an expiry of up to a maximum of 5 years from donation. **Cryopreserved** ~~*viable*~~ tissue:** At –135°C or «colder» ~~*lower*~~ to claim a 10-year expiry for all grafts to maintain a reasonable inventory of size-matched grafts (e.g. heart valves and menisci). Other cryopreserved tissues should have a 5-year expiry. **Glycerol-preserved tissue:** Skin preserved in high-concentration (>90%) glycerol may be stored at «between» 0–10°C for up to 2 years. **Freeze dried tissue:** Freeze-dried tissue may be stored at ambient temperature for up to 5 years. This includes freeze dried demineralised bone tissue mixed with a glycerol carrier.

	Decellularised Tissue: Decellularised dermis tissue that has been terminally sterilised may be stored at «colder than» ~~below~~ –40°C for up to five years, or at «up to» ~~below~~ +40°C for up to two years.
Transportation and local storage	**Frozen* tissues** must be transported and stored locally prior to clinical use, at «colder than –40°C if they are to retain their original expiry date. If they are stored locally at temperatures colder than» –20°C «or warmer than –40°C, the expiry date must be reduced to a maximum of 6 months or the balance of the original expiry date, whichever is lower.» ~~or lower in order to have the designated expiry (specified above).~~ **Cryopreserved** tissues** may be transported in the vapour phase of liquid nitrogen (–135°C «or colder») or on dry ice (–79°C «or colder»). If tissues are transported on dry ice they should continue to be stored locally at ~~around~~ –80°C «or colder» for a maximum of 6 months.
For the purposes of this guidance, the following definitions apply: * Frozen tissue – «Tissue stored at sub-zero temperatures, with or without cryoprotectant.» ~~tissue frozen and stored under conditions unlikely to be compatible with preservation of cells.~~ ** Cryopreserved tissue – «Tissue preserved and stored at sub-zero temperatures using a cryoprotectant, either by controlled slow freezing or by vitrification.» ~~tissue treated with a cryoprotectant and/or cooled at a controlled rate in order to preserve cells.~~	
«[1] As the tissue itself it taken directly from a living individual, setting temperature criteria for the tissue itself during this initial storage and transport period is not feasible, therefore only the ambient temperature it must be kept at is specified.»	

21.4.3: Positive bacteriology or mycology

It is the responsibility of the designated medical officer or designated microbiologist to develop written policies regarding the selection and conduct of tests for bacterial and fungal contamination and the acceptance criteria for specific tissues.

Where tissues are shown to carry viable bacteria or fungi they may be suitable for clinical use (e.g. skin grafts) depending on microbial types and densities of growth on culture. For other tissues the material may be approved for use provided that a validated antimicrobial processing technique is used.

(no changes to sections 21.5 – 21.6.5)

«21.6.6: Relevant Material and Storage Licences

The Human Tissue Act defines ‘Relevant Material’ as: “material, other than gametes, which consists of or includes human cells.” Tissue Establishments must determine for each type of graft they prepare, and the processing applied, whether or not a graft type is classified as Relevant Material. If so, the Tissue Establishment must hold a Human Tissue Authority storage licence if it holds the tissue for more than 48 hours. Tissue Establishments should inform hospitals if a graft is classified as Relevant Material, and ensure that the hospital has an appropriate storage licence if they intend to hold the graft for more than 48 hours.»

(no further changes to chapter 21)

2. Changes apply to the **Red Book**

Annexe 7: Requirements for the timing of testing for Haematopoietic Progenitor Cells (HPCs): Minimum standards and good practice

Terminology

HPC-A	Peripheral Blood (stem cells, collected by apheresis)
HPC-M	Bone marrow (stem cells, collected from bone marrow)
MNC-A	Mononuclear cells (collected by apheresis, including starting material for advanced therapy medicinal product (ATMP) manufacture and donor lymphocyte infusions (DLIs))
HPC-CB	Umbilical cord blood
Mandatory	The test is either a regulatory requirement or deemed necessary to ensure regulatory requirements relating to the assessment of donor suitability are met to ensure donor and recipient protection
Discretionary	The test must be performed on certain donors/donations if indicated by medical, social or travel history
Recommended	This test is recommended by an advisory committee or a professional body, but is not a regulatory requirement
Optional	«The test is not mandatory and done at the discretion of individual organisations or establishments. This also applies to situations where a mandatory test is repeated at the discretion of individual organisations or establishments» ~~*The test may be done at timepoints outside of the mandatory testing timeline*~~

Table 1 – Allogeneic HPC-A, HPC-M

Test	**Performed on donor, product or both?**	**Test mandatory, discretionary, recommended or optional?**	**Timing of test**	**Notes**
ABO + RhD	Donor	Mandatory	Prior to donation	Using two independently collected samples; different needlesticks
Mandatory infectious markers	Donor	Mandatory	Within 30 days prior to the donation episode	See Table 9.2 «Testing the donor once within the specified timescale is mandatory, repeating the test is optional»
		Optional	At the time of donation or within seven days post donation	
Discretionary Additional infectious markers (e.g. Malaria, WNV, T.cruzi)	Donor	Discretionary	Prior to donation, depending on travel history or residential risk	Align with JPAC Donor Selection Guidelines
CMV	Donor	Recommended	At donor selection, and Within 30 days prior to the donation episode	

Toxoplasma	Donor	Recommended	Within 30 days prior to the donation episode	
«EBV» ~~***Epstein Barr Virus***~~	Donor	Recommended	Within 30 days prior to the donation episode	
Pregnancy test	Donor	Discretionary	Seven days prior to starting donor mobilisation regime «(G-CSF),» and (as applicable) within seven days prior to the initiation of the recipient's preparative regime	Applies to all donors of childbearing potential
Haemoglobinopathies	Donor	Discretionary	At the time of donor assessment	Applies to those donors thought to be at risk of sickle cell disease and compound haemoglobinopathies
Bacteriology testing	Product (processed)	Optional	Pre-processing	
		Mandatory	Post-processing	
	Product (fresh)	Mandatory	Post collection	
FBC	Donor	Mandatory	Immediately before every collection for HPC-A; prior to first donation for HPC-M	

Table 2 – Autologous HPC-A, HPC-M

Test	Performed on donor, product or both?	Test mandatory, discretionary or optional?	Timing of test	Notes
ABO + RhD	Donor	Optional	Prior to donation	Due to autologous nature of product, not essential
Mandatory infectious markers	Donor	Mandatory	Within 30 days prior to the donation episode	April 2023: Sample timing currently under review by HTA. See Table 9.2 «Testing the donor once within the specified timescale is mandatory, repeating the test is optional»
		Optional	At the time of donation or within seven days post donation	
Discretionary Additional infectious markers (e.g. Malaria, WNV, *T.cruzi*)	Donor	Discretionary	Prior to donation, depending on travel history or residential risk	In selected circumstances based on individual risk assessment, testing may be requested/required. Align with JPAC Donor Selection Guidelines.
Pregnancy test	Donor	Discretionary	7 days prior to starting donor mobilisation regime «(G-CSF),» and, as applicable, within 7 days prior to the initiation of the recipient's preparative regime	Applies to all donors of childbearing potential

«CMV»	«Donor»	«Optional»	«Within 30 days prior to the donation episode»	«In selected circumstances based on individual risk assessment, testing may be requested/required if indicated by donor history»
«Toxoplasma»	«Donor»	«Optional»	«Within 30 days prior to the donation episode»	«In selected circumstances based on individual risk assessment, testing may be requested/ required if indicated by donor history»
«EBV»	«Donor»	«Optional»	«Within 30 days prior to the donation episode»	«In selected circumstances based on individual risk assessment, testing may be requested/ required if indicated by donor history»
Haemoglobinopathies	Donor	Discretionary	At the time of donor assessment	Applies to those donors thought to be at risk of sickle cell disease and compound haemoglobinopathies
Bacteriology testing	Product (processed)	Optional	Pre-processing	
		Mandatory	Post-processing	
	Product (fresh)	Mandatory	Post collection	
FBC	Donor	Mandatory	Immediately before every collection for HPC-A; prior to first donation for HPC-M	

Table 3 – Autologous & Allogeneic MNC-A

Test	Performed on donor, product or both?	Test mandatory, discretionary, recommended or optional?	Timing of test	Notes
ABO + RhD	Donor (allogeneic)	Mandatory	Prior to donation	Using two independently collected samples; different needlesticks
	Donor (autologous)	Optional	Prior to donation	Due to autologous nature of product, not essential
Mandatory infectious markers	Donor «(allogeneic and autologous)»	Mandatory	At the time of donation or within seven days post donation[1]	See Table 9.2
Discretionary Additional infectious markers (e.g. Malaria, WNV, *T.cruzi*)	Donor «(allogeneic and autologous)»	Discretionary	Prior to donation, depending on travel history or residential risk	Align with JPAC Donor Selection Guidelines. For autologous donors in selected circumstances based on individual risk assessment, testing may be requested/required.

CMV	Donor «(allogeneic)»	Recommended	At donor selection, and Within 30 days prior to the donation episode	
	«Donor (autologous)»	«Optional»	«Within 30 days prior to the donation episode»	«In selected circumstances based on individual risk assessment, testing may be requested/required if indicated by donor history»
Toxoplasma	Donor «(allogeneic)»	Recommended	Within 30 days prior to the donation episode	
	Donor «(autologous)»	«Optional»	«Within 30 days prior to the donation episode»	«In selected circumstances based on individual risk assessment, testing may be requested/required if indicated by donor history»
«EBV» ~~***Epstein Barr Virus***~~	Donor «(allogeneic)»	Recommended	Within 30 days prior to the donation episode	
	Donor «(autologous)»	«Optional»	«Within 30 days prior to the donation episode»	«In selected circumstances based on individual risk assessment, testing may be requested/required if indicated by donor history»
Pregnancy test	Donor «(allogeneic and autologous)»	Discretionary	«Within 7 days prior to collection»	Applies to all donors of childbearing potential
Haemoglobinopathies	Donor	Discretionary	At the time of donor assessment	Applies to those donors thought to be at risk of sickle cell disease and compound haemoglobinopathies
Bacteriology testing	Product (processed)	Optional	Pre-processing	
		Mandatory	Post-processing	
	Product (fresh)	Mandatory	Post collection	
FBC	Donor	Mandatory	Immediately before every collection	
[1] If MNC are collected at the same time as HPC, the same time specified in Tables 1 and 2 apply				

(no changes to Table 4 – HPC-CB)