## Changes in this version

*Added to 3.2, no solid organ enquiries, added bullet point 5.4, new 1.6.4, 1.6.6. Re-wrote 1.68. Deleted Tissues COP. 1.10.1 expanded*

# Policy

This policy describes the minimum criteria which should be met to access a BBMR donor. It is for the information of Transplant Centres and Registries who access the BBMR. It is also published on the NHSBT/BBMR website for information (https://hospital.blood.co.uk/patient-services/stem-cells/british-bone-marrow-registry/).

The British Bone Marrow Registry (BBMR) is a division of NHS Blood and Transplant (NHSBT) and a member of the World Marrow Donor Association (WMDA). BBMR has been a WMDA qualified registry since 2010 and achieved full accreditation in 2016. Currently, next generation sequencing (NGS) is used for allelic resolution HLA typing of all new BBMR donors and Cord Blood donations; for HLA-A, B, C, DRB1, and DQB1. Maternal typing is achieved by Luminex SSOP typing for HLA-A, B and DRB1. A small part of the cord blood inventory is NIMA typed additionally. Registry donation samples will always be infectious disease tested according to prevailing WMDA accreditation standard, with the addition of routine Hepatitis E nucleic acid testing and testing for SARS-COV-2. Malarial, T. cruzi and/or West Nile virus testing will be performed as per previous relevant donor residential or travel history.

BBMR is one the UK partners that together form the 'Anthony Nolan and NHS Stem Cell Registry' (in collaboration with the Welsh Bone Marrow Donor Registry – WBMDR, & DKMS UK).

On receipt of a search request from a ***UK based*** Transplant Centre, Anthony Nolan will act as a UK hub and search the Anthony Nolan and other aligned registries for each UK Patient. Anthony Nolan will also search the Anthony Nolan Cord Blood Bank and the WMDA and Netcord-FACT accredited NHS Cord Blood Bank for each UK patient unless otherwise instructed by the Transplant Centre. Anthony Nolan will perform a mismatch search if requested. For more information on the Anthony Nolan and NHS Stem Cell Registry please see the Operations and Service User Guide. See section 3.8 of this guide for repeat search guidance for UK based Transplant Centres.

BBMR provides details about prospective unrelated donors and cord blood units to blood stem cell registries, accredited Transplant and Collection Centres with the understanding that they will adhere to the following access criteria.

***International Establishments*** (Non-UK based Unrelated Hematopoietic Progenitor Cell Donor Registries or Transplant Centres meeting the criteria specified in 1.1 below) may request a Search directly to BBMR electronically (bbmr@nhsbt.nhs.uk) or by fax (+44 117 912 5732) and specify whether it requires Peripheral Blood Stem Cell (PBSC) or bone marrow derived stem cells, or a Cord Blood Unit(s). International requests submitted directly to BBMR will result in only the BBMR register and / or the WMDA and Netcord-FACT accredited NHS Cord Blood Bank inventory being searched.

Users authorised by their affiliated International Establishment may request a direct Search of the BBMR register and NHS Cord Blood Bank inventory using the European Marrow Donor Information System (EMDIS). EMDIS repeats searches every night for live searches, and once a week for all active searches. There are no other limitations on search requests from International Establishments. Products will only be provided to transplant centres willing to sign the BBMR's code of practice declaration (G9024), as doing so satisfies a UK regulatory obligation to obtain an 'end user' agreement.

Search requests may be in any format as long as it contains the following:

- Patient's name
- Patient's gender
- Patient's date of birth
- Patient's ethnicity (if available)
- Patient's weight (if available)
- Patient's ABO (if available)
- Patient's CMV status (if available)
- Invoice Address
- Diagnosis and current status of Patient
- HLA typing of Patient (see section 1.7)
- Registry reference
- Any Patient Identifiers

The WMDA publishes template forms (including for search) which can be found here.

Transplant centres must complete the following request forms or acceptable equivalent:

- 'Formal Recruitment of a Stem Cell Donor'.
- 'Prescription for Marrow Collection'.
- 'Prescription for Stimulated Peripheral Blood Stem Cell Collection'.
- 'Prescription for Peripheral Blood Lymphocyte Collection', if or as appropriate.

All donation requests are subject to approval by the BBMR Medical Director or designee.

Please note: Password protected attachments via incoming email to BBMR will cause automated security software to filter the whole communication into a junk folder, and requests sent this way may be inadvertently missed and not acted upon. Good pseudonymisation practice of email and attachment content can still be GDPR compliant without the need for password protection of attachments, and so requesters are asked to refrain where possible, from password protecting file attachments when sending emails to the BBMR. Section 8.1 of this policy applies

It is the policy of the BBMR for volunteer donors to be harvested at a Human Tissue Authority (HTA) licensed procurement/collection centre appointed by the BBMR in the UK and the product supplied to the Transplant Centre. The BBMR has published separately a list of services that it offers and the respective charges. BBMR does not accept requests or enquiries regarding the provision of solid organ donations from its donor panel.

## 1. Protocol for BBMR HPC Donor Provision

### 1.1. Transplant Centre

**1.1.1.** Unless represented by a WMDA accredited registry, the transplant centre must be eligible or registered for accreditation with appropriate bodies i.e., FACT-JACIE and / or registered with the appropriate national or international transplant outcome organisation for allogeneic transplantation e.g., European Group for Blood and Marrow Transplantation (EBMT), Centre for International Blood & Marrow Transplant Research (CIBMTR) and, or National Marrow Donor Program (NMDP).

**1.1.2.** The transplant centre should meet the applicable FACT-JACIE Clinical Program Standards as specified for where there is more than one clinical site or for a combined paediatric and adult programme. Normally the transplant centre should have been active in allogeneic HPC transplantation for 2 years and perform the number of new allogeneic HPC transplants per year thereafter, as stipulated in the prevailing version of the International Standards for Cellular Therapy Product Collection, Processing and Administration as published by FACT-JACIE

**1.1.3.** Patient diagnoses accepted by the BBMR for allogeneic HSCT should meet prevailing clinical practice. For example, in Europe the EBMT diagnosis classification of diseases as 'standard of care' and 'clinical option' are recognised as appropriate for HSCT (see EBMT published special report **here**). Diseases classified as developmental must be part of an ethically approved research protocol. Diseases classified as generally not recommended would require the approval of the BBMR's external expert advisory panel.

### 1.2. Patient & Donor Consent

**1.2.1.** The Transplant Centre is required to obtain informed consent from the patient for the initiation of the unrelated donor search and for any prospective transplant using a BBMR donor. This must include consent for minimum essential data of the patient to be supplied to the BBMR to facilitate the search process and at final donation request.

**1.2.2.** The Transplant Centre must obtain consent using maintained policies and procedures including obtaining patient agreement for the transfer of data to the national or international transplant outcome organisation or BBMR when performing outcome analysis.

**1.2.3.** The BBMR and the Transplant Centre will manage all data exchanged in accordance with the UK Data Protection Act (2018) and the General Data Protection Regulation (GDPR) - Regulation (EU) 2016/679)

**1.2.4.** BBMR will assure consent of the donor will be obtained in accordance with the requirements of the Human Tissue Act 2004, the Human Tissue (Quality and safety for Human Application) Regulations 2007, current HTA Directions, and as is set out in the current HTA's Code of Practice for consent. Consent will also be obtained in accordance with the prevailing World Marrow Donor Association Standards for Unrelated Hematopoietic Progenitor Cell Donor Registries. Please refer to 1.4 below also.

**1.2.5.** BBMR will undertake the collection at a centre licensed for Procurement by the Human Tissue Authority, the UK competent authority. Collection Centres will be JACIE accredited or working towards such accreditation.

**1.2.6.** The BBMR will undertake the procurement on the preferred dates given by the Transplant centre but that this is subject to agreement by the collection centre, the donor and the determination of their fitness to donate.

**1.2.7.** The Transplant Centre must ensure the patient is informed that any donation of a HPC product using a BBMR donor will be made anonymously. The BBMR policy on contact between recipient and donor post donation is stated in 2 below.

**1.2.8.** BBMR will ensure that the adult stem cell donor is a volunteer and has the right to withdraw their consent to donate at any time, but that the consequences of withdrawing after the commencement of patient conditioning will be fully explained.

**1.2.9.** The patient should also be made aware by the Transplant Centre that the BBMR will obtain consent from its adult stem cell donor for the specific HPC donation requested. The volunteer donor's consent is not a commitment to provide a subsequent donation for the patient, should it be required.

### 1.3. Donation Type

The BBMR will accept requests for 'First' and 'Subsequent' Donations from its donors. A First donation is defined as the first HPC donation by a finally selected donor for a patient. A Subsequent donation is defined as a second or subsequent HPC donation from the same donor for the same patient.

**1.3.1.** Patient acceptance criteria are as follows:

- All current indications generally accepted for stem cell transplantation from unrelated donors as indicated by the EBMT e.g., standard of care and clinical option.
- NMDP indicators.

**1.3.2.** Requests to access donors for procedures not indicated in 1.3.1 e.g., developmental, must be accompanied by an IRB or other ethically approved research protocol. Donors requested for procedures generally not recommended will be referred to the BBMR's external advisory panel.

**1.3.3.** To request a First donation, the Transplant Centre must supply minimum essential data on the patient. BBMR does not require a specific form for First Donation however the means to

request **must** include the same information listed at the bottom of page 1. The WMDA publishes template forms (including donation request forms) which can be found **here**.

**1.3.4.** Subsequent donations for the same patient must be approved by the BBMR Medical Director or designee. See Subsequent Donation Request, refer to 2 below.

### 1.4. The Source of Adult Stem Cells

The Transplant Centre may state their preference for the source of stem cells: from the peripheral blood or bone marrow.

**1.4.1.** Stem cells and donor leucocyte materials are distributed to transplant centres by BBMR purely as a therapeutic graft source for haematopoietic transplantation or treatment (the permitted purpose), solely for the individually named patient recipient as requested on the received product prescription. No portion of primary product or peripheral blood samples are to be used therapeutically, transfused / infused, or otherwise transplanted into any other individual. BBMR may agree however to a portion of the primary graft or other donor derived material provision to transplant centres or their affiliated manufacturing facilities as per section 10 of this policy, in relation to the creation of advanced therapies.

**1.4.2.** The transplant centre receiving BBMR issued material shall not sell, gift, transfer or otherwise supply provided materials to any third party, unless agreed and in accordance with section 10 of this policy.

**1.4.3.** The transplant centre accepts the known risks of stem cell transplantation and confirms that they will / have counselled the patient accordingly e.g., for risk if mucositis, infection, Nausea and vomiting, bleeding and need for blood transfusions, graft versus host disease, graft failure etc.

**1.4.4.** The finally selected donor will have both collection procedures explained and asked to indicate their preference. The BBMR Office will communicate their decision to the requesting centre. The preference of the transplant centre will be indicated to the donor as appropriate. The donor will have the final choice. The exception to this is described in 1.4.6 below.

**1.4.5.** For PBSC, donors' peripheral veins will be used except where a central venous catheter is authorised. Donors who opt for PBSC will have a peripheral venous assessment to determine their suitability to undertake an apheresis procedure and, or the insertion of a central or long line. Donors will also be counselled to consider the risk of a conventional bone marrow collection because in exceptional circumstances, a back-up bone marrow harvest may be necessary.

**1.4.6.** Donors who have a pre-existing back problem or contra-indications for GA for example, may only be suitable for PBSC. Where this is the case the BBMR will inform the Transplant Centre because in the event of a failure to mobilise under G-CSF a back-up bone marrow harvest will not be available. The Transplant Centre must confirm their willingness to proceed with the donation where such limitations apply.

**1.4.7.** Where a conventional bone marrow or PBSC donation only has been requested but, at counselling, the donor will only consider the other method of donation, the Transplant Centre will be advised and agreement to proceed to donation obtained. Bone Marrow is always filtered at collection. BBMR do not currently provide transfer bags with any of its products. If Transplant Centres do receive transfer bags as part of a product shipment; such bags are **not** certified or validated for centrifugation, storage, or cryopreservation.

**1.4.8.** As per WMDA S(P)EAR Committee recommendation; Transplant centres should be aware that transfer bags are generally unsuitable for centrifugation. Before any processing steps are undertaken, it is recommended that stem cell products be transferred to a bag which is validated by the manufacturer and any appropriate regulatory agency for the purpose intended. WMDA further recommends that transplant centres and processing stem cell laboratories check the specifications of all bags to ensure consistency with any intended use, including but not limited to manipulation (e.g., centrifugation), storage, and infusion.

**1.4.9.** For bone marrow collections, unless otherwise instructed, standard anticoagulant will be ACDA 10% and Heparin 10IU/ml.

### 1.5. Cord Blood as a Source of Stem Cells

**1.5.1.** Cord blood is banked from mothers who have met the Cord Blood Bank donor selection criteria, including microbiological screening tests for markers of transmissible diseases.

**1.5.2.** Cord blood is banked for the BBMR at the NHSBT Filton, Bristol site licensed by the Human Tissue Authority. The NHS Cord Blood Bank is also Netcord-FACT and WMDA accredited.

**1.5.3.** Extended HLA typing by the Cord Blood Bank can be requested and will be performed by the BBMR H&I laboratory, Colindale, London. Colindale and all NHSBT H&I laboratories are European Federation of Immunogenetics (EFI) and United Kingdom Accreditation Service (UKAS; ISO 15189) accredited.

**1.5.4.** Other complimentary information on the unit that may facilitate selection will also be supplied or can be requested separately.

**1.5.5.** The Cord Blood Bank will supply information at the time of initial request on how the cord blood unit can be reserved for the patient and also shipment.

**1.5.6.** For Cord Blood Unit (CBU) selection the BBMR recommends consideration of both cell dose and HLA matching in the selection of the CBU. HLA matching of CBUs should follow the current recognised standard of Low/Intermediate resolution typing at HLA-A and –B and allele level for HLA-DRB1.

**1.5.7.** Cord blood unit selection may allow mismatching at one or more loci with consideration of the TNC of the unit, based upon local experience or outcome studies performed e.g., Eurocord registry.

**1.5.8.** When selecting a mismatched CBU it is recommended that an HLA antibody screening on the patient is performed.

### 1.6. Prescription for Stem Cell Harvest

**1.6.1.** The TC must supply a prescription appropriate for the method of collection at the time of making a request. BBMR will accept WMDA forms or similar as long as they contain the same minimum set of information listed on page 1 & 2. The WMDA publishes template forms (including prescription forms) which can be found **here**.

**1.6.2.** Where a conventional bone marrow donation is offered the maximum volume that can be aspirated is 1500ml or 20ml/kg donor weight, whichever is the lesser.

**1.6.3.** For a PBSC collection, the requested CD34+ cell dose should not exceed 5 x 10^6/kg (unless an acceptable rationale is provided). BBMR will undertake a maximum of two apheresis collection procedures. For a Peripheral Blood Lymphocytes (PBL) collection the BBMR will

undertake a maximum of one apheresis collection. The apheresis procedure will process a whole blood volume of 12 – 15 litres per collection.

**1.6.4.** For PBSC donations, BBMR will book two apheresis donation slots. At the first apheresis, we will process the donor's total blood volume 2.5 times. For example, in the case of a male donor who weighs 81kg and is 1.8m tall, will have an estimated total blood volume of 5.32 litres (per Nadler's equation) – this will result in the apheresis procedure processing 13.3 litres of blood.

**1.6.5.** If a target cell dose *range* is provided on a prescription; BBMR will consider achieving or exceeding the lowest value during collection, as meeting requirement.

**1.6.6.** Where the TC would be willing to accept a lower CD34+ dose to enable collection at the end of the first apheresis collection, this should be communicated to BBMR.

**1.6.7.** For a PBSC collection BBMR donors will be administered a short course of G-CSF of 10µl/kg/day for 4 or 5 days.

**1.6.8.** If BBMR achieve <90% of target or fail to achieve specified minimum CD34 yield, BBMR will automatically proceed to a second apheresis collection the following day. The donor will be administered G-CSF at the Collection Centre once the CD34 counts are available, so it is therefore not practical for BBMR to consult with the TC to see if a particular yield is acceptable.

**1.6.9.** If after Collection Day 1 a second apheresis collection is indicated the Collection Centre physician will proceed if the donor can tolerate this and blood tests are acceptable.

**1.6.10.** Requests where the volume or cell dose required does not accord with the donor and patient weight will be referred to the Medical Director, or designee for review.

**1.6.11.** Collection centre indicating / verifying a target cell yield is feasible offers no guarantee the target will be met. It is recommended minimum acceptable target yields are provided rather than aspirational ideal targets so that requests are not declined unnecessarily, especially when there is a large discrepancy in weight between the patient and donor.

### 1.7. Patient HLA Typing and Search

**1.7.1.** It is recommended that HLA typing should be performed using DNA methods.

**1.7.2.** It is recommended that the level of HLA typing at the time of search is as high a resolution as possible, but the minimum standard is medium/low resolution HLA-A-B-C-DRB1 with -DQB1, -DPB1, -DRB3/4/5 as optional.

**1.7.3.** It is recommended that the selection of an unrelated donor for HPC donation be made using high-resolution typing results for HLA-A, -B, -C, -DRB1.

**1.7.4.** It is highly recommended that CMV antibody status and blood grouping information are supplied.

### 1.8. HLA Matching and Final Adult Donor Selection

There are numerous studies which have evaluated the role of HLA matching on patient outcomes. Although the results from these studies are not all identical there are numerous similarities which allow certain recommendations to be made.

**1.8.1.** DNA-based typing methods must be used.

**1.8.2.** The final typing of the donor and the patient should be tested within a reasonable timeframe of one another, should be performed in the same laboratory (i.e., the transplant centre designated laboratory), and must include at a minimum HLA-A, -B, -C, -DRB1 DNA based typing at high resolution

**1.8.3.** An NHS CBB cord blood unit at a minimum of HLA-A, -B, -DRB1 DNA based typing must be performed prior to shipment for a specific patient in a way that at least one typing result (previous or extended typing) for each locus is at high resolution. The transplant centre tissue typing laboratory can request a cord blood continuous segment or pilot vial to achieve this.

**1.8.4.** The 'optimal donor' is one matched at high resolution for HLA-A, -B, -C, -DRB1.

**1.8.5.** If such an adult stem cell donor is unavailable a donor with a single allele or antigen mismatch (7/8) should be sought. Recommendations cannot currently be made regarding whether mismatching at one of these 4 loci is 'better' than another. Individual Transplant Centres may preferentially select a mismatch at one locus over another, based on local experience or outcome studies.

**1.8.6.** The use of a less well-matched donor (6/8) is not absolutely contra-indicated; however, the risks and benefits of using such a donor need to be weighed against the outcome from other alternative treatments available to the individual patient. Registries may require additional patient information in such cases or may request confirmation that other treatments have been considered (e.g., use of umbilical cord blood or haploidentical donors).

**1.8.7.** Typing for other HLA loci (HLA-DQB1, -DPB1) may be routine practice in some Transplant Centres or may be requested by it for certain patients. This may be covered by Service Level Agreements or may be considered in individual cases.

### 1.9. Reservation of Adult Stem Cell Donors for a Patient and Frequency of Donation

**1.9.1.** Once Confirmatory or Extended Typing is requested, BBMR will apply a deferral to the donor record with an expiry date of 91 days. This deferral code will exclude the donor from being searched for any other patient. The reservation can be extended beyond this time for a further 91 days by Transplant Centre request to the BBMR office within 90 days of deferral. Any further requests for reservation beyond 182 days (e.g., If the donation/shipping date is not scheduled or is delayed) will be escalated to the BBMR Operations and Planning Manager / the BBMR Medical Director, as required and may be grated in exceptional circumstances.

**1.9.2.** Reservation period after HPC donation: BBMR donors will be reserved for 24 months after donation of HPC for the same patient. After this time and it is ascertained that the primary recipient does not need a second donation of HPC or PBL then the donor may be released to potentially donate for another patient.

**1.9.3.** Reservation period after PBL donation:

| Interval Between HPC Donation and PBL Donation | Period That Donor is Reserved for Primary Recipient |
|---|---|
| Less than 12 months | 2 years from HPC donation |
| 12 – 24 months | 1 year from PBL donation |
| More than 24 months | 1 year from PBL donation |

**1.9.4.** Maximum number of donations - HPCs: BBMR donors may donate HPC to 2 different patients and up to twice per patient i.e., a maximum of 4 times in total.

**1.9.5.** Maximum number of donations – PBL: Requests for donation of unstimulated PBL are dealt with on a case-by-case basis. Requests for second or subsequent unstimulated PBL donations are reviewed by the medical director (or designee) with no fixed cap on the number of donations.

**1.9.6.** Interval between donations ([1]or designee):

| Type of Donation | Minimum Interval | Requests for Shorter Interval |
|---|---|---|
| HPC followed by HPC | 4 weeks | Review by medical director[1] |
| HPC followed by PBL | 4 weeks | Review by medical director[1] |
| PBL followed by PBL | 4 weeks | Review by medical director[1] |

**1.9.7.** A minimum of 4 weeks should elapse between the first and subsequent donation of an HPC product. Second donations after shorter intervals requested in exceptional circumstances will be reviewed by the medical director[1] on an individual case basis.

### 1.10. Donor as Research Subjects or as Participants in 'Research Support Activity'

**1.10.1.** No portion of product or donor samples shall be sold, gifted, transferred, or otherwise supplied to any third parties unless explicitly approved by BBMR.

**1.10.2.** The Senior Management Team and BBMR Medical Director must approve all study requests to access donors who will be part of a clinical trial or if components of the donation or collection procedure are intended to address research questions under an ethically approved protocol.

**1.10.3.** A donor will not be considered as a research subject or be participating in research support activity by virtue of a stem cell donation and, or provision of other therapeutic products for a patient on a research protocol. Only if the collection is altered in some way or information about the donor or additional donor material will be collected that is not part of a standard HPC collection.

**1.10.4.** Requests may be referred by the BBMR Medical Director for expert adjudication within the BBMR, UK registry Joint Medical Affairs Committee, (JMAC), or its Expert Advisory Group, prior to approval.

**1.10.5.** Informed consent of the donor must be obtained if donor blood or other biological material or information is stored and or used for the purpose of an ethically approved research project or associated with research support activity.

**1.10.6.** A donor who declines to participate in a research protocol for a patient can still be asked to donate HPC for the patient outside of the research protocol, if the Transplant Centre agrees.

## 2. Subsequent Donation Requests

**2.1.** All requests to re-access a BBMR donor for the same patient are approved by the BBMR Medical Director or designee.

**2.2.** Transplant centres must complete appropriate WMDA forms for Subsequent donations (see 'Formal Request for a 2nd Transplant' templates **here**, or similar and include the data listed in 2.3 below).

**2.3.** The patient must consent for the Transplant Centre to provide the following data information in addition to that described in paragraphs 1.2.1and the information requirements listed at the bottom of page 1, this will include:

- Reason for second donation and back-up stem cell product availability.
- Details of the First or previous donation.

- Graft data.
- Patient's current condition.
- Current laboratory data.
- Proposed Subsequent donation type.
- Assessment of patient survival and possibility of successful outcome.

**2.4.** Subsequent donation requests may be referred by the BBMR Medical Director for expert adjudication prior to approval. BBMR aim to provide a decision within 72 hours of receipt of the request.

## 3. Fresh Product Transport

**3.1.** Fresh HPC products requested by **UK based** Transplant Centres through the Anthony Nolan and NHS Stem Cell Registry will be transported according to the **Service User Guide**

**3.2.** International Registries / Transplant Centres are to collaborate with BBMR for the transportation of PBSC, bone marrow or Lymphocytes from BBMR UK Collection Centres to the appropriate overseas hospital, using the International Establishment's own volunteer or commercial courier. It is requested that International Establishment's accept responsibility to ensure all couriers are adequately trained and audit the transporters compliance with agreed service levels, WMDA and national standards. Additionally, it is requested that International Registries / Transplant Centres take care choosing appropriate return flight times accounting for courier travel between BBMR collection centre stem cell laboratories and airports, as typically products will not be ready for onward pick up until after 4pm local time on the day of collection. The World Marrow Donor Association promulgates standards that cover product transport requirements ("World Marrow Donor Association International Standards for Unrelated Hematopoietic Stem Cell Donor Registries," Section 8). In addition, the WMDA recommendation entitled 'Transport Guidelines' also provide additional recommendations for transport of fresh products.

**3.3.** The utilised container/package must be secure and ensure that the cells are maintained in the specified conditions. All containers and packages need to be qualified as fit for purpose.

**3.4.** Procedures and critical conditions for transportation and shipping of collected hematopoietic stem cells must be defined (e.g., temperature and time limit) and qualified. Critical transport conditions, must be defined to maintain the required cell properties

**3.5.** The NHS CBB cord blood bank uses defined and qualified procedures and dry shippers.

## 4. Cryopreservation Requests

**4.1.** This section applies to International Establishments only as UK centres follow the Anthony Nolan and NHS Stem Cell Registry **Service User Guide** (Cryopreservation section).

**4.2.** The International Establishment must not store or cryopreserve collected haematopoietic stem cells for more than 48 hours without the prior written agreement of the BBMR medical director or their deputy, unless this is storage or cryopreservation of excess material from the collection or international guidelines prevail, recommending routine cryopreservation on product receipt e.g., during the COVID pandemic that started in 2020. The International Establishment must notify BBMR in writing when the cryopreserved Cell Product is either infused or discarded. Excess material post transfusion may be cryopreserved for therapeutic purposes or discarded according to standard protocols without applying to BBMR. BBMR will consider requests to cryopreserve product at the collection centre, on a case-by-case basis.

**4.3.** BBMR donor lymphocyte collections and starting material for advanced cellular therapies are labelled with an ISBT 128 label. Transplant Centre may cryopreserve Lymphocytes without the prior approval of BBMR provided that the first aliquot is infused within 14 days of the Lymphocytes being donated, and this date of infusion is stated in the Cell Processing Report referred to in section 4.2 above. If the Transplant Centre desires to cryopreserve the Lymphocytes for longer than 14 days before administering the first dose it must notify BBMR and must also notify BBMR in writing when the cryopreserved product is either infused or discarded.

## 5. Patient / Donor Confidentiality and Contact Policy

**5.1.** HPC donations are made completely anonymously to comply with WMDA standard.

**5.2.** Access to donor and recipient files must be limited only to staff whose job function requires access to donor or patient information. The BBMR and third parties contracted by it will manage all data exchanged in accordance with the UK Data Protection Act (2018) and the General Data Protection Regulation (GDPR) - Regulation (EU) 2016/679). BBMR staff receive mandatory information governance training. Breaches of confidentiality will be managed under NHSBT Quality Management procedures.

**5.3.** The BBMR with the Transplant Centre must always ensure the complete anonymity of the donor and recipient. In cases where our donor is accessed via your national registry it is likely there will be two registry policies governing donor patient contact. In these cases, whichever policy elements are the most stringent will apply. For example, if your national registry has a policy that allows direct donor / patient contact after 3 years, this length of time will need to be adhered to as it is more stringent than the BBMR's policy of allowing contact after 2 years.

**5.4.** When 2 years have elapsed from the time of donation and when the following conditions are met it is acceptable for the donor and patient to be given each other's details and be allowed direct contact and to meet, should they so wish.

- The donor has indicated in writing their agreement and desire to meet the recipient of their stem cells or other cellular therapy product.
- The donor has indicated in writing their agreement and desire to meet the recipient of their stem cells or other cellular therapy product plus the recipient has also indicated in writing their agreement and desire to meet the donor of their stem cells or other cellular therapy product.
- It is considered extremely unlikely that a further donation of stem cells or other cellular therapy product will be required from the donor for that specific recipient and when the patient is physically and mentally well. It is usually the case in such circumstances that the donor and their recipient have been exchanging anonymously cards and, or letters for some time and it should be obvious to the BBMR Medical Director or designee that they are mutually agreeable to such a meeting.
- There is no known recipient need for an organ donation or chance the BBMR donor may be asked to consider providing such a donation (International registries should refrain from allowing the patient they represent direct contact with BBMR donors in such cases),

## 6. Service Costs

The Transplant Centre will be advised of the service cost as published by BBMR before each financial year beginning in April, or more than 30 days before amendment.

## 7. Patient Follow - Up Data

**7.1.** The BBMR will request follow up information on patients for whom it provides an HPC product. The information is collected for quality assurance purposes. The information may be requested directly or electronically in collaboration with the Worldwide Network for Blood and Marrow Transplantation (WBMT) and, or its constituent members.

**7.2.** The BBMR reserves the right to request follow up information on the stem cell or therapeutic apheresis product at 100 days' post donation.

**7.3.** The follow-up form supplied can be completed or the Transplant Centre can alternatively provide a copy of the EBMT registry MED-A form.

**7.4.** NHSBT reserves the right to request and receive outcome data where starting material is provided.

## 8. Quality Management and Legal Compliance

**8.1.** BBMR is committed to a system of total quality management, which will ensure that its services fully meet the requirements of clinicians, patients and donors and conform to relevant national and international standards. The main principal guidelines covering the activities of BBMR services are current versions of:

- Guidelines for the Blood Transfusion Services in the United Kingdom. Current Edition
- Prevailing Department of Health. Guidance on the Microbiological Safety of Human Organs, Tissues and Cells used in Transplantation. Advisory committee on the microbiological safety of blood and tissues for transplantation.
- Prevailing International Standards for Cellular Therapy Product Collection, Processing and Administration. FACT-JACIE
- Human Tissue Authority Codes of Practice
- Prevailing HTA Directions and the Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatments
- International Standards for Unrelated Hematopoietic Stem Cell Donor Registries, World Marrow Donor Association. Current Edition
- BBMR Policy for Research and Ethics (POL130)
- NHS Cord Blood Bank Regulatory Requirements (POL95)
- General Data Protection Regulation (GDPR - Regulation (EU) 2016/679)
- UK Data Protection Act 2018

The General Data Protection Regulation 2016/679 is a regulation in EU law on data protection and privacy for all individuals within the European Union and the European Economic Area. GDPR was implemented in the UK through the Data Protection Act 2018. GDPR also addresses the export of personal data outside the EU and EEA areas and so is applicable to the data you hold on our donor even though it is pseudonymised. Specifically, your TC will have records e.g., a search report that contains the BBMR donor's personal identifiable data such as gender, date of birth and HLA type etc. Regarding GDPR (and BBMR donor data the Transplant Centre holds). Your Transplant Centre agrees to:

- Ensure that people accessing / processing the donor data are subject to a duty of confidence.
- Agree to take appropriate measures to ensure the security of this data and any further processing that occurs.
- Only engage a sub-processing of BBMR donor data with the prior consent of BBMR and only under a written contract
- To assist BBMR in providing subject access and allowing donors to exercise their rights under the GDPR.
- Assist BBMR in meeting its GDPR obligations in relation to the security of processing, the notification of personal data breaches and data protection impact assessments.
- Delete or return all personal data to BBMR in the highly unlikely event it is requested.

- Allow audits and inspections; providing BBMR with whatever information it needs to ensure that they both BBMR and your TC are meeting our Article 28 obligations,
- Inform BBMR immediately if your TC is asked to do something infringing the GDPR or other data protection law of the EU or a member state.

## 9. Traceability, Serious Adverse Events and Reactions

**9.1.** International Establishments/Transplant Centres are asked to report product related adverse events or reactions (relating to supplied main product or starting material) to BBMR (via email bbmr@nhsbt.nhs.uk) within 24 hours of detection (UK establishments are to kindly follow the Anthony Nolan and NHS Stem Cell Registry **Operations & Service User Guide -** SEAR section). BBMR will report all donor or product related adverse events to the Human Tissue Authority and, or the World Marrow Donor Association Serious Events and Adverse Effects Registry and Serious Product Events and Adverse Effects Registry schemes.

**9.2.** Therefore, International Establishments/Transplant Centres further agrees to:

- Report any relevant information to the BBMR, in order to facilitate traceability and onward reporting to the UK national regulator, to ensure quality and safety control
- Maintain procedures to ensure retention of copies of all records of products supplied and to notify the BBMR within 24 hours of any serious adverse events or serious adverse reaction observed during or after clinical application of product and any serious adverse event which may be linked to the quality and safety of supplied products. Reporting will be via completion of the 'G9307 - HPC and TC Products Infusion Adverse Incident Report' form, within 24 hours
- Record in your patient's notes clearly indicating when (date and time) your patient has been transplanted or infused with BBMR supplied products
- To return fully completed copies of all forms that require completion supplied accompanying the product

## 10. Provision of Starting Material for Advanced Therapy (Investigational) Medicinal Products

N.B. This section is only applicable to Transplant Centres who are seeking approval to request donor material (e.g., Use of a portion of the original graft or provision of extra peripheral blood samples from BBMR donors that you wish to participate in 'Research Support Activity'), to be shipped to a cellular / gene manufacturing site, as part of a clinical trial.

**10.1.** Starting material is shipped on the understanding that the transplant centre and / or its affiliated cellular / gene therapy manufacturing facility(s) that will receive donated material warrant that:

- Critical transport conditions required to maintain the properties of the cell targets within the starting material for manipulation are defined and documented
- BBMR has / will be informed or instructed so that an expiry date / time of the starting material can be calculated
- The starting material will only be used to manufacture advanced medicinal products for the patient(s) identified during the routine registry, or direct request process
- All the affiliated cellular / gene therapy manufacturing facility(s) to receive and utilise any BBMR provided starting material, are made known in documents submitted to the BBMR
- No starting material shall be sold, gifted, transferred, or otherwise supplied to any third parties except those listed within the study protocol / documentation, as approved by BBMR
- All the affiliated cellular / gene therapy manufacturing facility(s) to receive and utilise any BBMR provided starting material work to the required standard and are fully approved / certified / licenced and / or accredited to the relevant national competent authority standard (e.g., GMP, FDA in the US)
- The study / clinical trial has been appropriately ethically approved as required by national standards

- Product manufacturing will only be as described in the (BBMR approved) study protocol or as per authorised amendments to the study protocol
- Any starting material that is unused for whatever reason, will be ethically discarded and not stored