POLICY POL129/4

Minimum Criteria to Access a BBMR Donor

This Policy replaces	**Copy Number**
POL129/3	
	Effective **23/01/18**

Summary of Significant Changes

Accreditation status and GDPR ref. included. 1.6.3 cell dose cap added. New section 4. Added to section 8

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.

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. NIMA typing is also performed to optimise CBU characterisation.

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).

On receipt of a search request from a ***UK based*** Transplant Centre, Anthony Nolan will search the Anthony Nolan and NHS Stem Cell Register for each UK Patient. Anthony Nolan will also search the Netcord-FACT accredited 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 Service User Guide. See section 4.9 and 4.10 of this guide for repeat search guidance for UK based Transplant Centres.

BBMR provides details about prospective unrelated bone marrow 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) and also has EMDIS-Cord connections with some registries. 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.

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.

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

It is the policy of the BBMR for volunteer donors to be harvested at a Human Tissue Authority (HTA) licensed procurement 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.

1. Protocol for BBMR HSC 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 programmes. Normally the transplant centre should have been active in allogeneic HSC transplantation for 2 years and perform the number of new allogeneic HSC 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. This is as specified at the bottom of page 1, except where a Subsequent donation is planned, refer to 2 below.

1.2.2. The Transplant Centre must obtain consent from the patient 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 (1998) and the General Data Protection Regulation (GDPR) - Regulation (EU) 2016/679)

1.2.4. The Transplant Centre will establish and maintain policies and procedures to obtain patient consent.

1.2.5. 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.

1.2.6. BBMR will undertake the collection at a centre licensed for Procurement by the Human Tissue Authority, the UK competent authority under the EU Directive on Tissues and Cells (EUCTD). Collection Centres will be JACIE accredited or working towards such accreditation.

1.2.7. 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.

1.2.8. The patient must be informed that any donation of a HSC 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.

1.2.9. 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.

1.2.10. The patient should also be aware that the BBMR will obtain consent from its adult stem cell donor for the specific HSC 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 HSC donation by a finally selected donor for a patient. A Subsequent donation is defined as a second or subsequent HSC 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. 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 1.4.4 below.

1.4.2. 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.

1.4.3. 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.

1.4.4. Where a conventional bone marrow or PBSC donation only has been requested the donor will not be offered the alternative collection modality. At counselling, if the donor will only consider one method of donation and it is not the Transplant Centre preference the Transplant Centre will be advised and agreement to proceed to donation obtained.

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 Clinical Pathology Accreditation (UK) Ltd (CPA) or 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. 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 a PBSC collection BBMR donors will be administered a short course of G-CSF of 10µl/kg/day for 4 or 5 days.

1.6.5. Where a PBSC collection is offered and if after Collection Day 1 a CD34+ cell count of ≥90% of the agreed target cell count is obtained a second apheresis collection will not be undertaken. Exceptions to this policy will require the approval of the BBMR Medical Director with the Collection Centre physician.

1.6.6. 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.

1.6.7. 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.

1.7. 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 HSC donation be made using high-resolution typing results for HLA-A, -B, -C, -DRB1.

1.7.4. The final typing of the donor and the patient should be performed in the same laboratory (i.e. the transplant centre laboratory), using the same techniques, and tested within a reasonable timeframe of one another. This may not, however, apply in all cases such as when umbilical cord blood is used as the stem cell source, or where a centralised laboratory is utilised.

1.7.5. 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. Typing for HLA-A, -B, -C, -DRB1 loci should be performed to high resolution i.e. alleles are determined at least where this is currently possible with current methods.

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

1.8.4. 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.

1.8.5. 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).

1.8.6. 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. BBMR donors will be reserved for 24 months (after donation) for the same patient. After this time, and it is ascertained that the primary recipient does not need a second HSC donation or PBLC then the donor may be released to potentially donate for another patient.

1.9.3. BBMR donors may donate HSC on a total of 4 occasions.

1.9.4. If a donor has donated HSC 3 times to the same patient, they are not permitted to donate again to a different patient.

1.9.5. A minimum of 4 weeks should elapse between the first and subsequent donation of an HSC product.

1.9.6. A BBMR donor may donate un-stimulated PBL for the primary recipient routinely twice. Subsequent requests for a PBL donation will be at the discretion of the Medical Director. The minimum interval between PBL donations should be 3 months.

1.10. Donor as Research Subjects

1.10.1. The Senior Management Team and BBMR Medical Director must approve all 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.

1.10.2. A donor will not be considered as a research subject 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 HSC collection.

1.10.3. Requests may be referred by the BBMR Medical Director for expert adjudication within the BBMR or its Expert Advisory Group, prior to approval.

1.10.4. 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.

1.10.5. A donor who declines to participate in a research protocol for a patient can still be asked to donate HSC 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;
- 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 HSC 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. 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 product.

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. 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.

4.3. BBMR donor lymphocyte collections are labelled with the Single European Code (SEC). 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 and Donor Confidentiality

5.1. HSC 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 (1998) and the General Data Protection Regulation (GDPR) - Regulation (EU) 2016/679). BBMR staff receives mandatory information governance training. Breaches of confidentiality will be managed under NHSBT Quality Management procedures.

5.3. Post-donation the recipient and donor by mutual consent may exchange an anonymised ‘thank you’ or ‘best wishes’ card or brief note through the BBMR Office and the Transplant Centre. If either party indicates at counselling that they do not wish to receive any form of communication or information their wishes must be respected.

5.4. When 2 years have elapsed from the time of donation and the following considerations 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.

5.5. The donor has indicated in writing their agreement and desire to meet the recipient of their stem cells or other cellular therapy product.

5.6. The recipient has also indicated in writing their agreement and desire to meet the donor of their stem cells or other cellular therapy product.

5.7. 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.

6. Service Costs

The Transplant Centre will be advised of the service cost as published by BBMR before each financial year beginning in April.

7. Patient Follow - Up Data

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

7.2. The BBMR will 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.

8. Quality Management

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:

- Department of Health. A Code of Practice for Tissue Banks.
- Guidelines for the Blood Transfusion Services in the United Kingdom. Current Edition
- 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.
- International Standards for Cellular Therapy Product Collection, Processing and Administration. FACT-JACIE
- EU Directive on Tissues and Cells (2004/23/EC)
- Human Tissue Authority Codes of Practice
- HTA Directions 003/2010 and the Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatments
- Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Products, Food and Drug Administration
- International Standards for Unrelated Hematopoietic Stem Cell Donor Registries, World Marrow Donor Association. Current Edition
- BBMR Policy for Research and Ethics (POL130)
- Central Venous Catheter Insertion and PBSC Donor Care (MPD159)
- NHS Cord Blood Bank Regulatory Requirements (POL95)
- General Data Protection Regulation (GDPR - Regulation (EU) 2016/679)

8.2. International Establishments/Transplant Centres are asked to report product related adverse events or reactions 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 **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.