Cell Management

Purpose
To outline the management pathway for peripheral blood stem cells, bone marrow, donor lymphocytes and cord blood from the point of cell request to cell delivery, engraftment and discard.

To describe the procedures related to administration of these products.

Process

1. Pre Transplant

The BMT Coordinators manage the transplant process with use of an electronic planner.
Transplant slots are allocated following discussion of the patient at the Blood and Marrow Transplant Multi-disciplinary Team (BMT MDT) meeting. The Bone Marrow Transplant & High Dose Therapy schedule, Peripheral Blood Stem Cell Harvest (PBSCH) and Donor Lymphocyte Infusion (DLI) schedules are updated and circulated weekly using nhs.net.
Peripheral Blood Stem Cell Harvest (PBSCH) slots for patients and related donors are booked at the weekly joint NHSBT Therapeutic Apheresis Service (TAS), Stem Cell and Immunotherapy (SCI) and BMT planning meeting, or by email to the SCI team.
Unrelated donors, cord blood donations and related donors needing a bone marrow harvest are requested via the Anthony Nolan (AN) Registry. The BMT Specialist Nurse team is responsible for the coordination of transplant related processes ensuring good communication with the AN, NHSBT and relevant clinical areas.

Notification of intent to collect, test and process including consent
Confirmation of a PBSCH slot for an autologous or related donor is undertaken with NHSBT Therapeutic Apheresis Services (TAS) by completing/sending Request for Collection of Stem Cells or Lymphocytes FRM5110 and Request to Collect and Process Stem Cell and Immunotherapy Products FRM5071
For a related donor bone marrow harvest via Anthony Nolan a Request to Process Stem Cell and Immunotherapy Products form FRM5071 is completed and sent to SCI.
All forms should ideally be completed at least 10 days before the intended harvest date.

Virology screening (IDM’s) for autologous and related stem cell donors is undertaken within 30 days of the harvest and at least 7 days before the intended harvest date.
Autologous patients will be invited to TAS within the 30 day period to have veins assessed and blood samples taken on site.
Related donor samples will be taken on the Churchill site after the medical screening consultation. These samples should be clearly labelled and sent to the Stem Cell and Immunotherapy (SCI) Laboratory, NHSBT, Level 2, JR Site, and sent via the Churchill laboratory transport, to the Blood Transfusion lab. The samples are sent with a completed (2B), FRM1570 Consent for the Testing, Storage and Discard of Stem Cells or Lymphocytes.

For autologous patients the Peripheral Blood Stem Cell Harvest/Final Donor Clearance FRM3721 should be completed and sent within 30 days of the scheduled harvest date via nhs.net mail to NHSBT TAS and NHSBT Consultant, to confirm eligibility for PBSCH. For
Oxford autologous patients this will be completed by the Haematology Consultant in Oxford on the first day of priming or before commencing GCSF injections.

**For related allograft donors** a completed *Peripheral Blood Stem Cell Harvest/Final Donor Clearance FRM3721* will be sent by the clinician or Specialist Nurse following the initial screening visit.

**For both autologous patients and related donors** the criteria will be reviewed and the form signed by an NHSBT Consultant or SpR. This form will then be returned to the BMT Specialist Nurse via nhs.net email to be filed in the autologous patients/related donor and allogeneic recipient medical notes. Any planned deviation from protocol will be clearly documented on this form.

For patients having autologous PBSCH, bloods are to be reviewed as per priming chemotherapy protocol, and any assessment/necessary, replacement plans are to be communicated to NHSBT TAS prior to stem cell harvest.

**For Matched Unrelated Donor (MUD) cells** a NHSBT *Request to Collect and Process Stem Cell and Immunotherapy Products FRM5071* form is forwarded as a request to test or process peripheral blood stem cells, bone marrow or lymphocytes. This form is forwarded at least 10 days in advance. All planned cell harvests and infusions from unrelated donors and related donors being coordinated via the Anthony Nolan related donor service are discussed at the weekly joint NHSBT Stem Cell Services and BMT planning meeting. NHSBT SCI laboratory is copied in to the relevant Anthony Nolan Registry (AN) communication chains. Copies of all forms are filed in the appropriate patient and/or donor notes, ensuring complete confidentiality.

**Harvest Target Doses**

<table>
<thead>
<tr>
<th>Transplant Type</th>
<th>Minimum cell dose x 10⁶/kg</th>
<th>Harvest target Ideal x 10⁶/kg</th>
<th>Ideal cell dose per transplant x 10⁶/kg</th>
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<tbody>
<tr>
<td><strong>Allograft</strong></td>
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<tr>
<td>Autograft</td>
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<tr>
<td>MUD cells: If an excess of cells are collected, the maximum dose of CD34 x 10⁶/kg given should be increased up to 10 x 10⁶/kg ensuring the full range of CD3 doses as per protocol B.2.28 is obtained first. If there are still an excess of cells these should be frozen as a single dose.</td>
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<tr>
<td><strong>Autograft</strong></td>
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</tr>
<tr>
<td>Myeloma (where 2 BMT’s are possible)</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Myeloma (1 BMT)</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Solid Tumour</td>
<td>2</td>
<td>4</td>
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</table>
Request for Issue of Cells
For the issue of cryopreserved cells, usually autologous cells but including cord blood, donor stem cells and donor lymphocytes originating from a registry, NHSBT SCI Final Report of Donation and Processing Request for Issue of Cryopreserved products (pages 2 & 3) is completed and emailed to SCI. On occasions when cells collected before 1st June 2015, NHSBT Form (2F) FRM1599 is used. Upon receipt of the form the SCI laboratory will complete the bottom section and return it to the BMT Nurse Specialist team confirming that cells are available. It is then filed in the patient notes.

2. Prior to transplant conditioning

For sibling allograft and MUD transplants: the date of donor harvest is confirmed and donor clearance obtained prior to the start of conditioning. This is filed in the notes. NHSBT SCI must receive a copy of donor clearance from AN.

For autologous infusions: On admission and prior to commencement of conditioning, confirm cell availability with NHSBT SCI and negotiate timing of cells, reconfirm timing on day -1.

Prescription of cells
Cell prescription is undertaken on the electronic prescribing systems. All cells with conditioning regimes should be prescribed on ARIA. DLI and additional CD34 cells should be prescribed on EPR under the correct EPR encounter.

Prescribers have undertaken medical BMT competencies and are trained in the electronic prescribing system.

Positive microbial cultures
The SCI laboratory is responsible for undertaking microbial testing on all products. Where cells have been identified as having positive microbial cultures, the NHSBT laboratory lead will notify their medical lead and the treating consultant, who will then discuss with the programme director. If the cells are to be used a Deviation from protocol B.1.2 Appendix 1 or 2 must be completed, a copy put in the patient notes and a copy forwarded to the quality manager for logging and discussion at BMT Quality Meeting (BMTQM). When a concession is obtained, the NHSBT paperwork is sent with the cells for filing in the medical notes. The patient will be informed of the positive cultures and informed consent obtained to use the cells.

Where the cells are from a sibling donor, the assessing consultant will notify the donor and referrals made as appropriate.

Where the cells come from a registry, NHSBT staff will notify the registry.

Clinical management of the positive culture will be determined by its nature, and/or advice from the microbiology team and is the responsibility of the treating consultant.

Recipient outcome and analysis is undertaken at the BMTQM, NHSBT Clinical Governance and at the Stem Cell Steering group meetings.

3. Administration of the Cells

Preparation of the patient
Prior to hospitalisation, the patient is given written and verbal information on the process of transplantation and written consent is obtained. Once admitted the ward staff reinforce this information, and consent is reviewed. Information on the day of transplant will include:
explanation of the events of the day, likely side effects, timing of cells, monitoring equipment, visiting, the need for weight and fluid balance, role of NHSBT laboratory staff etc. Full explanations are given to the patient and relatives throughout the treatment.

Detailed patient care is found in nursing care plans N.18, 30, 51, 80. If allogeneic donor cells are cryopreserved, use nursing care plans N.30 and N.18; and in the case of autologous marrow, use nursing care plan N.18. General international information about cell collection and cell management processes can be found in the Circular of information, for the use of Cellular Therapy Products: http://www.aabb.org/resources/bct/Documents/coi_ct1109.pdf

**Clinical measures**
- Intravenous hydration is commenced pre cell infusion as per patient conditioning protocol
- Fluid balance commenced at midnight pre cell infusion. Urine output is monitored
- Daily/bd weight
- Anti-emetics
- Premedication
- Baseline observations: T, P, RR, Bp, O2 Saturations

**Preparation of the environment**
- Prepare a clear uncluttered environment
- Anaphylaxis tray checked and in room
- Ensure additional IV blood giving sets, 0.9% saline, 10ml syringes and ampoules of Sodium Chloride (0.9%) are present
- Ensure a clear sterile dressing is available in the event of damage to the cell bag during infusion
- Working call bell, oxygen and suction
- Monitoring equipment present and working
- Ensure ward coordinator and medical team aware
- Plan location of water bath in room
- Ensure sufficient supply of clean non sterile gloves and aprons, emesis bowls and urinals/bedpans

**Document and incident management for all cells**
It is imperative that the NHSBT *Summary of Products Issued for Transplant* form and the *Infusion Adverse Incident Report FRM1567* form, is completed and filed chronologically in the patient notes and a copy emailed to NHSBT SCI laboratory sci.oxford@nhs.net within 24 hours of cell infusion. NHSBT have responsibility for reporting HTA reportable incidents related to the cell products, to the HTA within 24 hours of an incident being discovered.

If there is an infusion adverse incident an OUH Datix should also be completed.

All clinical incidents related to the cell management process must be reported to the BMT Programme Director.
Working with the NHSBT scientist with cryopreserved products

- Ensure a safe space for the scientist to work in
- Orientate to ward
- Document lot numbers of infusion giving sets and Normal saline bags on *Summary of products issued for transplant* form.
- Ensure a copy of the *Summary of products issued for transplant* form is completed and retained
- Ensure scientist has a clean supply of gloves to change after hands are washed and before each bag is thawed
- NHSBT scientists are responsible for being aware of their own standard operating policies and procedures, and where they can access these documents should they require them
- NHSBT are responsible for the thawing of the cells, checking patient identify with the nurse and up to the point of handing to the nurse for infusion. At this point there is joint responsibility until cells are infused. NHSBT retain reporting responsibility to the HTA within 24 hours of an incident being discovered

Working with the NHSBT scientist with fresh cells

- Document lot numbers of infusion giving sets and Normal saline bags on *Summary of products issued for transplant* form
- Accept hand over of cells, ensuring bags are checked for damage, leaks, clumping before the scientist leaves.
- Ensure you retain and complete a copy of the *Summary of products issued for transplant* form.
- NHSBT scientists may be able to leave a contact number in case of damage to the HSC bag during infusion.
- NHSBT scientists are responsible for being aware of their own standard operating policies and procedures, and where they can access these documents should they require them.

Checking fresh cells or bone marrow

For each bag of cells confirm patient identity using the patient wrist label and 3 verbal identifiers as per OUH Trust policy. Check details against cell bag and on NHSBT *Request to Collect and Process Stem Cell and Immunotherapy Products* form *FRM5071* form which is filed in the notes.

Observe cells for clumping, check bag for damage or leakage.

Checking cryopreserved cells

For each bag of cells confirm patient identity using the patient wrist label and 3 verbal identifiers as per OUH/ Bucks Health Care Trust policy. Check details against cell bag and on NHSBT *Request to Collect and Process Stem Cell and Immunotherapy Products* *FRM5071* form.

Observe cells for clumping, check bag for damage or leakage.

Infusing Haemopoietic Stem Cells (HSC)

- HSC should be administered by nursing staff that have completed or are being assessed for the *Stem Cell Infusion Competency H.29c*
• Ensure that on taking receipt of the HSC that no delay is incurred in proceeding to infusion and that infusion of the cells is a priority. If there has been any unavoidable delay with the infusion ensure the Consultant is informed and an incident form completed
• On receipt of bag of HSC, ensure examination of bag for defects or signs of breakage
• Ensure patient has pre-med 15-30 minutes pre infusion
• Refer to nursing care plans sited above for administration guidance, infusion rates and management of specific products
• Ensure pre-hydration and fluid balance monitoring is commenced as per protocol, if there is an ABO mismatch, infuse additional hydration as directed to reduce renal damage due to red cell lysis
• Observations should be undertaken every 15mins, more frequently as indicated. All changes in condition and signs of adverse reaction, such as chest tightness or changes in observations should be notified to the ward medical team immediately and treated as directed
• Ensure that the infusion process is documented in the patient’s medical notes.
• Under NO circumstances should a leucocyte depleting filter be used, as this will remove viable cells. These sets are no longer in use and should not be available on the ward

Donor Lymphocyte Infusion (DLI)
• DLI should only be infused by nurses who have completed Donor Lymphocyte Infusion competency H.29e
• On receipt of bag of DLI, ensure examination of bag for defects or signs of breakage
• On receipt of DLI ensure all the necessary equipment for administration is available before the NHSBT scientist leaves
• If DLI are not going to be administered immediately put cells in locked treatment room until time of infusion
• DLI should be administered following infusion of DLI care plan N.62 and checked by 2 nurses
• DLI should be infused via a Y blood administration set
• On rare occasions only part of a bag of DLI will be required, in this situation the NHSBT scientist will draw up the required volume of DLI and hand to the nurse to administer as a bolus via a fast running drip. Please note that DLI should not routinely be drawn up and bolused

Management of a damaged bag
This can include: a punctured bag, or where the bag is found to be cracked or broken for frozen cells.
When frozen cells are administered in both Oxford and Buckinghamshire Healthcare Trust the NHSBT scientist will be present and will follow NHSBT procedure as described in NHSBT SOP: Issue and Thaw HPC and T cells, SOP2346/2. ’Transfer the cells to a new 600ml transfer pack via a new port, and use line clips to seal the line with a hand sealer.

Management of leakage of cells from a punctured bag for fresh Allo/MUD HSCs
• The immediate action should be to stop the infusion, apply a sterile clear dressing to the punctured area of the bag, take the bag down and place it with the bunged giving set in a clean blue tray and then seek advice from Stem Cell Services
• When the cells are delivered within working hours the stem cell laboratory should be contacted on 01865 387949, out of hours call 07764 280663
- If this fails the ward sister, junior sisters or BMT Nurse Practitioners should be contacted for advice
- Contact the Haematology consultant on call and inform them
- Then using 2 members of staff prepare a sterile field and transfer the cells to a new 600ml transfer pack via a new port (Stored in a tray in the drawer in the treatment room containing the anaphylaxis tray. A small stock is maintained, provided by the SCI laboratory)
- If this is not possible because of where the damage has occurred, use a new port and 50ml luer lock syringe and 16g-18g needle, gently extract cells and gently insert the cells into the transfer pack
- Infuse the cells only if advised by the consultant. As per NHSBT policy, use of ‘rescued’ cells requires specific written authorisation from the hospital consultant. If this happens out of hours a minimum of verbal authorisation from the Consultant is required to continue with infusion and this should be documented clearly in the medical notes.
- Ensure sound documentation is completed, including the transfer packs set number and expiry and the process of transferring of cells
- Ensure an OUH Datix is completed as well as the NHSBT Adverse Incident Report FRM1567 form and email to sci.oxford@nhs.net.
- Please note, damaged bags should not be ‘taped up’ and use continued as this is a greater infection and contamination risk

**Serious Incident requiring investigation reporting (SIRI)**

Any adverse reactions/incidents associated with the administration of the cells should be reported using the OUH Datix process and the *Adverse Incident Report FRM1567* form to be emailed to sei.oxford@nhs.net. All SIRI should be reported directly to the Programme Director and Clinical Director. Notify consultant in charge. Consider whether this is a matter that should be referred to the HTA and Anthony Nolan if appropriate. SIRI management and reporting to the HTA are covered further in policy H.2.32 and the OUH policy.

4. **Post cells**

**Engraftment**

Day 30 engraftment data are collated by the BMT Data Manager. Engraftment data is forwarded from NHSBT SCI quarterly to the Quality Manager and discussed at the BMTQM. Data is also discussed at the Oxford Cellular Therapies Steering Group annually.

All graft failure is notified to NHSBT.

5. **Long Term Cell storage**

All unused cells, with the exception of post autograft Lymphoma patients and deceased patients, are stored for seven years as recommended by BSBMT. Cells may be stored for longer at Consultant discretion.

6. **Cell discard**

All patients are written to (using standardised documents B.19e, B.19f) at the appropriate interval (detailed below) regarding consent for cell discard or transfer to an alternative Biobank of their choosing. This process is outlined in B.19g *Pathway for Stem cell discard.*

Cell discard for deceased patients is managed on a monthly basis using the NSHBT cell discard form.
Lymphoma patients post autograft, who have additional cells in storage, will be contacted regarding discard, one year following their autograft.

7. **Training of staff**
All staff administering cells will have undertaken and passed a competency assessment, except those in training, whose practice will be supervised.
Staff will be competency assessed and work to the OUH Trust central line management policies and procedures, and IV drug administration policies and procedures.

**Authors**
Mandy Ellis, BMT Coordinator; Sandy Hayes, Quality Manager; Lara Rowley, BMT CNS. Jan 2011

**Documents**
Circular of information, for the use of Cellular Therapy Products: http://www.aabb.org/resources/bct/Documents/coi_ct1109.pdf

**Audit**
The above processes are subject to the OxBMT audit programme

**Circulation**
NSSG Haematology Website

**Review**

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<th>Name</th>
<th>Revision</th>
<th>Date</th>
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<td>Lara Rowley</td>
<td>Addition of Jacie standards to document</td>
<td>June 2012</td>
<td>2.0</td>
<td>June 2014</td>
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<td>Mandy Ellis</td>
<td>Process review and update</td>
<td>June 2013</td>
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<td>Tracy Mitchell-Floyd, Lara Rowley, Mandy Ellis, Sandy Hayes</td>
<td>Process Review, harvest targets and update</td>
<td>Jan 2016</td>
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<td>Mandy Ellis, Sue Moore, Denise Wareham, Lara Rowley, Sandy Hayes.</td>
<td>Ratified at both allogeneic and autologous protocol review meetings.</td>
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<td>Cell discard management</td>
<td>Mar 2016</td>
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<td>January 2018</td>
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<td>Denise Wareham, BMT Coordinator</td>
<td>Virology screening &amp; donor clearance processes. Management of excess cells collected from MUD donors</td>
<td>Nov 2016</td>
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<td>Lara Rowley, BMT Specialist Nurse</td>
<td>Minor amendments including contact details EPR prescribing Clearer document identification</td>
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