Infusion of Hematopoietic Stem Cells (HPC)

Prepared by Alicia Cianflone
Clinical Nurse Consultant
Autologous Bone Marrow Transplantation and Apheresis
Objectives

- General Principles
- Responsibilities
- Preparation
- Cryopreserved HPC
- Infusion Techniques
- Nursing Care
- Adverse Reactions
General Principles

- Inpatient or Outpatient setting
- Follows conditioning treatment
- Fresh HPC
- Cryopreserved HPC
Responsibilities

- Medical Officer
- Bone Marrow Transplant Clinical Nurse Consultant (BMT CNC)
- Registered Nurse
- Bone Marrow Transplant Scientist
- Training and Competency of Stem Cell Infusion
- Blood Safe e-learning
Preparation

- Planning
Preparation

- Patient Assessment
- Patient Education and Consent
Preparation

- Venous Access
- Intravenous Line
Preparation

- Prescriptions
- Emergency Preparedness
Cryopreserved HPC
Dimethly Sulphoxide (DMSO)

- Water absorbing compound
- Stabilises the movement of water across the cell membrane during cryopreservation
- Each bag of HPC will contain about 10% DMSO
- Serum half-life of 20hrs
- Excreted by kidneys
DMSO

- Maximum dose 1mg/kg/day
- Multiple bags to infuse - consider infusion over multiple days
Thawing
## Product Storage & Transport Form

### Sending Facility
- **Name**: Vicki Antoniades, Senior Scientist
- **Department**: Sydney Cellular Therapies Laboratory
- **Hospital**: Level 2, ICPMR, Westmead Hospital
- **Address**: Cnr Hawkesbury and Darcy Rd, Westmead, NSW 2145 Australia
- **Mobile**: +61 422 007 200
- **Phone**: +61 2 88906212
- **Fax**: +61 2 8890 5303
- **Email**: vwlhs.wmibmtlab@health.nsw.gov.au

### Receiving Facility
- **Name**: BMT Coordinators: Alicia Cianfrone
- **Department**: Nepean Cancer Care Centre, Nepean Hospital,
- **Hospital**: Cnr Great Western Hwy and Somerset St, Kingswood, NSW 2747
- **Phone**: 02 4734 1494
- **Pager**: 02 4734 3500 pager 17587
- **Fax**: 02 4734 2230

### Planned Transport Arrangements
- **Courier**: RLC
- **Pick-up date**: Monday
- **Approx. arrival date**: Tuesday
- **Time (24 hr)**: Time
- **Person notified at receiving facility**: Alicia Cianfrone
- **Phone**: 
- **Email**: 
- **Faxed**: 
- **Date**: 23/03/18

### Packing
- **Name**: [Name]
- **DOB**: [DOB]
- **MRN**: [MRN]
- **Donor**: [Yes/No]
- **Recipient**: [Yes/No]
- **Product ID (if allocated)**: [ID]
- **Collection date(s)**: [Date]
- **For apheresis products**: Blood volume processed (mL)
- **Apheresis machine / program (optional)**: [Machine]
- **No. product bags (inc plasma)**: [No.]
- **No. blood samples**: [No.]
- **Signature**: [Signature]
- **Collected and label checked by**: [Name]
- **Labelling checked by**: [Name]
- **Dry shipper ID**: [ID]
- **Validated at ≤-150°C for**: [Days]
- **Temperature (°C) on packing**: [Temperature]
- **Data logger or thermometer ID**: [ID]
- **Code for lock**: [Code]
- **Date packed by (signature)**: [Date]
- **Time (24 hr)**: [Time]

### Receipt
- **Date received**: 12/4/18
- **Time (24 hr)**: 12:15 hrs
- **Locked**: [Yes/No]
- **Damaged**: [Yes/No]
- **Tiltwatch**: [Yes/No]
- **Temperature (°C)**: On arrival: -19°C Min: -19°C Max: -19°C
- **Product(s) received**: [Yes/No]
- **Correct number of products**: [Yes/No]
- **Correctly labelled**: [Yes/No]
- **Accepted**: [Yes/No]

### Product Storage
- **Fridge ID**: [ID]
- **Date & time in**: [Date]
- **Signature**: [Signature]
- **Date & time removed**: [Date]
- **Signature**: [Signature]

### Completed form sent to:
- [RE-BMT-F3 Version 6]
- [Dated]: 19/02/2018
Thawing Process
### Product Infusion Form

**Facility:** Nepean

**Diagnosis:**
- Weight (kg): [ ]
- Recipient Blood Group: [ ]
- Donor MRN or ID: [ ]
- ABO mismatch: [ ]
- Donor Blood Group: [ ]
- RBC mL/kg: [ ]

**Laboratory to complete this section**
- Eligible: [ ]
- Ineligible (warning labels checked): [ ]
- Incomplete (warning labels checked): [ ]
- Product Type: [ ]
  - HPC, Apheresis
  - HPC, Marrow
  - 2 x HPC, Cord Blood
  - Other
- Manipulation: [ ]
  - Cryopreserved
- Plasma reduced: [ ]
- Buffy coat enriched: [ ]
- CD34 enriched: [ ]
- CD34 depleted: [ ]
- RBC depleted: [ ]
- Diluted: [ ]
- Washed: [ ]

**Product Check**
- Product distribution checking: [ ]
- Against infusion notification: [ ]

**Signature:**
- Date: [ ]
- Time: [ ]

**Infusion record**
- Infusion number: [ ]

**Product ID / Bag ID**
- Collection date: [ ]
- Volume (mL): [ ]
- TNC x 10^6/kg: [ ]
- CD34 x 10^6/kg: [ ]
- CD3 x 10^6/kg: [ ]

**Premedication(s)**
- None: [ ]
- Given as prescribed: [ ]
- HPC prescribed on filled order sheet: [ ]
- Blood Filter (Not leukodepletion): [ ]

**Blood Filter**
- Lot Number: [ ]
- Expiry: [ ]

**Infusion date**
- Date: [ ]

**Thaw**
- Start time: [ ]
- Finish time: [ ]

**Infusion**
- Start time: [ ]
- Finish time: [ ]

**ID check 1**
- Name: [ ]

**ID check 2 and infusion**
- Name: [ ]

**Infusion route**
- Gravity: [ ]
- Syringe push: [ ]
- Pump Rate: [ ]
- Water bath temp (°C): [ ]

**Solutions added**
- Batch number/expiration: [ ]

**Signature:**
- [ ]
Potential Issues

• Bag Expansion
• Bag rupture
• Unable to infuse cells within 20 minutes
Infusion of HPC

- Ensure everyone involved is ready
- PPE
- Clean, no touch technique
Cross checking of HPC cells

- Cross check label of HPC cells with:
  - Patient ID
  - Production infusion form
  - HPC notification
  - Second person involved with the HPC infusion

- Cross check blood component details
  - Type of product
  - Blood group of patient and HPC Cells
  - HPC ID number

- Time Out
# Checklist for sending frozen HPC to Off-Site BMT Hospitals

<table>
<thead>
<tr>
<th>Task</th>
<th>Task Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm infusion date with the BMT CMC Coordinator</td>
<td>✓</td>
</tr>
<tr>
<td>Completed notification of the Cryopreserved Product Infusion form (TX-BMT-F3)</td>
<td>✓</td>
</tr>
<tr>
<td>Product Infusion Form (TX-BMT-F1)</td>
<td></td>
</tr>
<tr>
<td>Product Distribution Checklist (PR-BMT-F3)</td>
<td>✓</td>
</tr>
<tr>
<td>Product Storage and Transport Form (RE-BMT-F3)</td>
<td></td>
</tr>
<tr>
<td>Final BMT report</td>
<td>✓</td>
</tr>
<tr>
<td>Circular of Information booklet (EX-BMT-X3)</td>
<td></td>
</tr>
<tr>
<td>Cassettes and foam/towels are used during transport to comfort support the bags.</td>
<td></td>
</tr>
<tr>
<td>Shipper locked with padlock and chain</td>
<td></td>
</tr>
<tr>
<td>Check label # on lid to dry shipper is the same # to the dry shipper container</td>
<td></td>
</tr>
<tr>
<td>Set temp and alarm logger (Tinytag)</td>
<td></td>
</tr>
<tr>
<td>Record dry shipper TEMPERATURE and NUMBER before it leaves Westmead BMT Laboratory</td>
<td>✓</td>
</tr>
<tr>
<td>Record colour of <strong>Tilt watch</strong> tag before dry shipper leaves WMH BMT Laboratory</td>
<td>✓</td>
</tr>
<tr>
<td>Record colour of <strong>Shock watch</strong> tag before dry shipper leaves WMH BMT Laboratory</td>
<td>✓</td>
</tr>
<tr>
<td>ALL COURIERS should have with them a copy of the ‘Local courier information’ (RE-BMT-F59)</td>
<td>✓</td>
</tr>
<tr>
<td>Is external signage clear and present? Keep upright- do not x-ray, human cells for a transplant (RE-BMT-F9)</td>
<td>✓</td>
</tr>
<tr>
<td>Are old address stickers removed from the outer mushroom protective case?</td>
<td>✓</td>
</tr>
<tr>
<td>Record in BMT diary frozen transport log book including dry shipper number, courier name signature and mobile</td>
<td></td>
</tr>
<tr>
<td>WOLLONGONG ONLY: Record in the Specimen Reception Log book for the Hospital couriers to come by the BMT lab to collect dry shippers with cells.</td>
<td></td>
</tr>
</tbody>
</table>

Completed by: ☑️  Date: 11/4/18

---

# Product Distribution Checklist

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Acceptable parameters</th>
<th>Initials/ date</th>
<th>Initiates 2/ Date (optional)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processing records</td>
<td>Complete &amp; reviewed</td>
<td>Yes</td>
<td>No*</td>
<td></td>
</tr>
<tr>
<td>Frozen storage</td>
<td>Frozen storage ≤5yrs ✓</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Storage temp &amp; duration</td>
<td>Family products: 35°C-45°C ✓</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Donor ID</td>
<td>IDM ≤90 days before collection</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Microbial screen</td>
<td>No growths (or pending if within 7 days of collection)</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Patient weight check (corticosteroids)</td>
<td>Weight change &gt;5% ✓</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Cell dose</td>
<td>TNC, CD34 and/or CD3 content meets Physician’s request</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>OFI</td>
<td>No OFIs</td>
<td>Yes</td>
<td>No*</td>
<td></td>
</tr>
<tr>
<td>Product Check</td>
<td>Clean, undamaged, normal colour &amp; appearance, access port available</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Label Check</td>
<td>Intact, legible, complete, meets Q5-BMT-S9 Product Labelling</td>
<td>Yes</td>
<td>No*</td>
<td></td>
</tr>
</tbody>
</table>

*If the criteria are not met do the result(s) have the potential to affect the product clinically?*

☐ No - Laboratory Director or designee Signature: [Signature] Date: 12/4/2018

☐ Yes - Exceptional Release - I understand that this product does not comply with the above release criteria. The Transplant Physician, Dr [Name] and/or on-call BMT Physician, Dr [Name] has been notified, there is documented “Urgent Medical Need” for the product use and release is approved.

☐ The patient has consented for the infusion of a non-comforming product (TX-BMT-F18)

☐ Do not release this product.

Laboratory Medical Director or designee: [Signature] Date: [Date]

# Infusion Products

- **Infusion vol (mL)**: [Volume] 
- **Pt wt (kg)**: [Patient weight]
- **If > 10 mL/kg, Tx Physician was informed that DMSO dose is > 1 mL/kg**

# Cryo Products

- **Trolley / Water bath cleaned by**: [Cleaned by]
- **Cryostorage records updated by**: [Updated by]
- **L10 fill**: [Fill date]
- **L10 removal**: [Removal date]
Infusion Technique

- Cells **must** be infused within 20 minutes
- Re-establish patency prior to commencing
- Visually inspect the cell bag
- Administer as fast as patient can tolerate
- Flush HPC bag
- Document of start and finish time on product infusion record
  - Sign completion of product infusion record
**Product Infusion Form**

**Diagnosis:**

**Weight (kg):**

**Recipient Blood Group:**

**Donor MRN or ID:**

**ABO mismatch:**

- [ ] Non-match
- [ ] Minor
- [ ] Major
- [ ] RBC

**Donor Blood Group:**

**HKA**

**Laboratory to complete this section**

- **Donor eligibility:**
  - [ ] Eligible
  - [ ] Ineligible (warning labels checked)
  - [ ] Incompatible (warning labels checked)

- **Product Type:**
  - [ ] HPC, Apheresis
  - [ ] HPC, Marrow
  - [ ] 2 x HPC, Cord Blood
  - [ ] HPC, Cord Blood
  - [ ] T Cells, Apheresis
  - [ ] Other

- **Manipulation:**
  - [ ] not modified
  - [ ] Cryopreserved
  - [ ] Plasma reduced
  - [ ] Buffy coat enriched

- **Product Check:**
  - [ ] Product distribution checklist complete

- **Signature:**
  - [ ] Labelling integrity
  - [ ] Against infusion notification

- **Bags checked:**
  - [ ] Bags listed below placed in Esky/Shipper

**Infusion record**

- **Infusion number:**

**Product ID / Bag ID:**

**Collection date:**

**Volume (mL):**

- [ ] 70
- [ ] 70

**TNC x 10^6/kg:**

- [ ] 2.0
- [ ] 2.0

**CD34 x 10^6/kg:**

- [ ] 8.55
- [ ] 8.55

**CD3 x 10^5/kg:**

**Premedication(s):**

- [ ] Given as prescribed
- [ ] None prescribed
- [ ] HPC prescribed on blood product order

**Blood Filter (Not leucodepletion):**

- [ ] None
- [ ] 170 um blood filter

**Lot Number:**

**Expiry:**

**Infusion date:**

**Thaw**

- **Start time:**
  - [ ] 13:45
- [ ] 13:58

- **Finish time:**
  - [ ] 13:45
- [ ] 13:58

**Infusion start time:**

- [ ] 13:45
- [ ] 13:58

**Infusion finish time:**

- [ ] 13:45
- [ ] 13:58

**ID check 1 (thaw-cryo product):**

- [ ] Name: TMP

**ID check 2 and infusion:**

- [ ] Name: A. CIANFIRE

**Infusion route:**

- [ ] Gravity
- [ ] Syringe push
- [ ] Pump Rate

**Solutions added:**

**Active:** 11/12/2017

**TX-BMT-F1 Version 10**

**Refer to PR-BMT-S9 Product Distribution**
Potential Issues

- No Flow
  - Kinks
  - Check position of the spike

- Flow becoming sluggish or stops completely
  - Gentle Massage around the spike or the filter
  - Jiggling/gentle massage in middle of bag intermittently
  - Raise IV pole (gravity infusion)
  - Flush line with small amount of normal saline
  - Consider changing filter/line prior to infusing next HPC bag (if multiple bags required)
Potential Issues

- Infusion likely to take longer than 20 minutes
  - Consider syringing remaining cells
  - Add 10% of HPC product volume ACDA to the infusion bag
    - 10-15 minutes added viability

- Report Issues
  - Senior BMT staff on your team
  - BMT laboratory staff
  - Submit an OFI (opportunity for improvement)
Nursing Care

- 2 RNs (ideally) to be present at all times during infusion
- Assist with cross-checks
- Continuous monitoring of patient
- Continuous monitoring of HPC infusion (infusionist)
- Vital signs
  - As per Standard of Practice in your centre
  - As often as patient requires
  - Post completion of infusion
- Documentation
## Product Infusion Form

**POST Infusion Adverse Reaction** – CNC or MO to complete – refer to Circular of Information

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>☑ No</th>
<th>☐ Mild (Report &gt; 24 hours)</th>
<th>☐ Moderate</th>
<th>☑ Severe</th>
</tr>
</thead>
</table>

* Moderate/Severe requires review by the BMT Program Director & OFI. Report Immediately

☐ Haemolytic  ☐ Allergic / Anaphylactic  ☐ Acute respiratory distress  ☐ Febrile ________°C

☐ DMSO toxicity requiring MO review (nausea, vomiting, hyper/hypotension)

☐ Other

Details (reaction, OFI number etc)

---

Section completed by: [Signature]  
Date: 3/1/17

BMT Program Director:  
(Review of adverse reaction) ☐ N/A  
Signature: [Signature]  
Date: [Date]

Affix labels – Collection centre/ Processing Laboratory / Engraftment label

### Processing Laboratory:

BMT Laboratory  
Westmead Hospital,  
Westmead, NSW 2145, AUSTRALIA  
Phone: +61 2 88906212  
Fax: +61 2 88905303  
e: W3LHD WMHBMTLAB@health.nsw.gov.au
Managing Reactions

- Mild
  - Slow the Infusion
  - Monitor patient for worsening
  - Notify MO immediately

- Moderate-Severe
  - Stop Infusion
  - Notify MO immediately
  - Administer medication/fluids prescribed
  - Consider steps to increase viability of HPC cells/clumping
  - As soon as symptoms resolve- continue infusion
CIRCULAR OF INFORMATION FOR THE USE OF CELLULAR THERAPY PRODUCTS

This circular was prepared jointly by the AABB, America’s Blood Centers, the American Association of Tissue Banks, the American Red Cross, the American Society for Apheresis, the American Society for Blood and Marrow Transplantation, the College of American Pathologists, the Cord Blood Association, the Foundation for the Accreditation of Cellular Therapy, ICCBBA, the International Society for Cellular Therapy, the Joint Accreditation Committee of ISCT and EBMT, the National Marrow Donor Program, and Neicord. Federal law prohibits dispensing the cellular therapy products described in this circular without a prescription.
# Adverse Reactions - Cryopreserved HPC

<table>
<thead>
<tr>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweet cream corn odour</td>
<td>Dyspnoea</td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td>Nausea and emesis</td>
<td>Brady/Tachycardia</td>
<td>Neural toxicity</td>
</tr>
<tr>
<td>Gastro intestinal upset, cramps</td>
<td>Chest tightness</td>
<td>Cardiac Arrhythmia and Arrest</td>
</tr>
<tr>
<td>Chills/ Flushing</td>
<td>Pyrexia</td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td>Rigors</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>Fluid overload</td>
<td></td>
</tr>
<tr>
<td>Cough / Itchy throat</td>
<td>Hyper/hypotension</td>
<td></td>
</tr>
</tbody>
</table>

*Adapted from (reference 10.3) St George / Sutherland Hospitals and Health Services Haematopoietic Progenitor Cell (HPC(A) Reinfusion Clinical Business Rule.*

At any time these reactions may develop and become severe if not treated promptly and appropriately.

RE-BMT-XXX Version:1 Cryopreserved HPC Infusion Competency Package (Autologous)
Adverse Reactions

- Acute Haemolytic Reactions
  - Chills
  - Fever
  - Headache
  - Burning sensation along the vein
  - Abdominal Bleeding
  - Lower back pain
  - Facial Flushing
  - Chest pain
  - Rapid or laboured respirations
  - Tachycardia
  - Shock
  - Haemoglobinuria
    - Positive coombs test (DAT)
    - Elevation of lactate dehydrogenase (LDH) or bilirubin
Adverse Reactions

- Febrile Non-Haemolytic Reactions
  - Temperature increase of greater than 1 degrees shortly after commencement of infusion or up to 2 hours post infusion (without another source of pyretic stimulus)
  - Chills

- Transfusion–Related Acute Lung Injury (TRALI)
  - Acute respiratory distress (within 6hrs of administration)
  - Hypoxemia
  - Bilateral pulmonary infiltrates on frontal chest x-ray
Allergic/Anaphylactic Reactions

- Uticaria (hives)
- Pruritus (itching)
- Bronchospasm/Laryngospasm
- Hypotension
- Severe Dyspnoea
- Facial, glottal and/or laryngeal oedema
- Facial burning/flushing
- Abdominal Pain
- Nausea
- Vomiting
- Diaphoresis
- Diarrhoea
- Dizziness
Adverse Reactions

- Alloimmunization

- Delayed Haemolytic Reactions
  - Unexplained fever
  - Unexplained decreased haemoglobin/haematocrit
  - Mild jaundice
  - Development of a positive DAT
  - Elevation of LDH or bilirubin
  - Hemoglobinuria and hemoglobinuria (rare)
  - Acute intravascular haemolysis (rare)
Adverse Reactions

- Graft vs Host Disease
- Septic Reaction
  - Onset of high fever (>2 degree rise in temperature)
    - During
    - Immediately after HPC infusion
  - Fever with chills
  - Severe hypotension
  - Dry, flushed skin
  - Pain in abdomen/extremities
  - Vomiting
  - Bloody diarrhoea
Adverse Reactions

- Fat Emboli
  - Dyspnoea
  - Hypoxia
  - Tightness of the chest
  - Coughing
  - Petechiae
  - Confusion

- Transmission of Infectious Disease
Adverse Reactions

- Circulatory overload
  - Dyspnoea
  - Peripheral Oedema
  - Rapid increase of blood pressure

- Hypothermia
  - Risk of cardiac arrhythmia or cardiac arrest

- Non-immunologic Haemolysis
  - Signs & symptoms same as for haemolytic reactions
Useful Resources

GUIDELINES FOR THE ADMINISTRATION OF BLOOD PRODUCTS

REQUIREMENTS FOR PROCEDURES RELATED TO THE COLLECTION, PROCESSING, STORAGE AND ISSUE OF HUMAN HAEMOPOIETIC PROGENITOR CELLS
(Fifth Edition 2015)