
Transplantation of Cryopreserved Haemopoietic Progenitor Cells

1. PURPOSE

This procedure describes the process for infusion of thawed cryopreserved Haemopoietic Progenitor Cells (HPC). This applies to the infusion of both autologous and allogeneic HPC derived from either Peripheral Blood (HPC-A), Bone Marrow (HPC-M) or Umbilical Cord Blood (HPC-CB) collections.

2. SCOPE

This procedure applies to all trained staff who are involved with the care and treatment of patients within the Haemopoietic Stem Cell Transplant (HSCT) Programme of the Children's Cancer Centre (CCC) at the Royal Children's Hospital (RCH).

3. RESPONSIBILITY

It is the responsibility of **Transplant Physician or delegate** to ensure;

- that there is **WRITTEN** confirmation of HPC availability from the Cell Therapy Flow Cytometry Laboratory **BEFORE** commencing patient conditioning (as denoted on CT-F-089 Request for Stem Cell Processing).
- that a Pathology request has been completed for the Cell Therapy Flow Cytometry Laboratory requesting preparation and testing of the designated product.
- that additional / alternative instructions have been communicated to the Laboratory and Ward where total HPC infusion volume **exceeds limits >10ml/kg and /or DMSO>1.0ml/kg within 24hr period of infusion.**
- that the HPC infusion order is completed on patients' Complex IV Orders and Fluid Balance Chart MR55C.
- and clearly indicates if the product is autologous or allogeneic.
- that pre-medication has been ordered on patients' Medicine Chart.
- that intravenous hydration orders have been ordered on patients' Complex IV Orders and Fluid Balance Chart MR55C.
- that the Ward RMO is available on the ward for the duration of the infusion.

It is the responsibility of **trained medical staff and / or Div 1 Nurse** who will infuse the product to;

- liaise with the Cell Therapy Flow Cytometry Laboratory prior (Day -1) to the day of infusion to organise a mutually convenient time.
- confirm with the Transplant Physician or delegate that the HPC infusion, pre-medication and hydration orders have been completed.
- confirm with the Cell Therapy Flow Cytometry Laboratory the infusion time, product type, total volume and whether the HPC product will be in bag or syringe.
- administer pre-medication and hydration as ordered on the patients' Medicine Chart.
- visually check the HPC product, confirming appropriate labelling and integrity of the product.
- perform checks of the intended recipient from an in place identification wristband, HPC product identifiers CT-F-044, Cell Therapy and Flow Cytometry infusion form MR/207 and the Request for Stem Cell Processing form, CT-F-089.
- Ensure correct and safe administration of HPC product in accordance with this procedure.
- Report **ANY** adverse reaction during or following infusion **IMMEDIATELY** to the Ward RMO and or Transplant Physician as appropriate.

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It is the responsibility of **trained Cell Therapy Flow Cytometry Laboratory Scientists** to;

- notify the requesting Transplant Physician if total HPC infusion volume **exceeds limits >10ml/kg and /or DMSO>1.0ml/kg within 24hr period of infusion.**
- liaise with ward staff to provide product as requested.
- prepare, deliver and verify product ready for **IMMEDIATE** transplantation according to procedures.

It is the responsibility of the **Quality Manager (QM) or equivalent** to ensure implementation, maintenance and compliance with this procedure.

4. DEFINITIONS

CVC – Central Venous Catheter

CD34 – Antigen found on Haemopoietic Progenitor Cells. Surrogate marker for Haemopoietic Stem Cell,

DMSO – Dimethylsulphoxide cryoprotectant used in the cryopreservation of Haemopoietic Cells

HPC – Haemopoietic Progenitor Cell which can be derived from Peripheral Blood, Bone Marrow or Umbilical Cord Blood and / or placental blood.

HPC-A – Haemopoietic Progenitor Cells-Apheresis. Peripheral blood collected by apheresis as a source of haemopoietic progenitor cells. Mobilised unless otherwise stated.

HPC-CB – Haemopoietic Progenitor Cells-Cord Blood. Umbilical cord and/or placental blood collected as a source of haemopoietic progenitor cells.

HPC-M – Haemopoietic Progenitor Cells-Marrow. Bone Marrow collected as a source of haemopoietic progenitor cells.

HSCT – Haemopoietic Stem Cell Transplant

RMO – Resident Medical Officer

UCB – Umbilical Cord Blood

5. EQUIPMENT AND SUPPLIES

- Emergency Trolley in vicinity of room
- Oxygen and suction equipment at bedside
- Emergency drugs available (Adrenaline)
- Pulse Oximeter
- Dynamap
- Normal Saline for bag infusion 1000mls Baxter Cat No: AHB 1324
- Normal Saline for syringe infusion (10-20ml) Pfizer Cat No:61045033
- Saline line.
- Sterile Medication set Baxter Cat:

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- Sterile dressing pack.
- Betadine® Antiseptic. MCD Operations Pty. Ltd. Cat No:411183/14 **OR**
- Chlorhexidine in alcohol 70%. David Craig. Galenicals. Cat No:72138/1
- Sterile gloves. Ansell Nutex Dermashield (or equivalent)
- Alcohol wipes. Kendall Webcoll. Cat No:6818-2
- Heparin for CVC care. Pfizer Cat No:61024014 (note or equivalent as approved by RCH Drug Usage Committee)

Documentation of Orders

- Pre Medication order – Medicine Chart MR690/A
- IV Hydration order – Complex IV Orders and Fluid Balance Chart MR55C
- Order for Transplantation of HPC – Complex IV Orders and Fluid Balance Chart MR55C

6. PROCEDURE

6.1 Day prior to Infusion (Transplant Day-1)

6.1.1 Clinical ward staff must organise a mutually convenient time with Cell Therapy Flow Cytometry Laboratory (XT 5832) for the thawing of the cryopreserved HPC product for infusion.

6.1.2 The Transplant Physician or delegate must complete orders for infusion of cryopreseved HPC and pre-medication on the patients' IV order and Fluid Balance Chart and Medicine Chart MR690/A.

- Pre Medication Order –Hydrocortisone 25-100mg IV (2hours prior to infusion) and antihistamine-Promethazine(Phenergan) O/IV and Paracetamol (1hour prior to infusion)
- IV Hydration Order – 0.9% NaCl (Normal Saline) 125ml/m²/hr (commence 2hours prior to infusion of **Umbilical Cord Blood (HPC-CB) or Bone Marrow (HPC-M)**).

6.1.3 The Transplant Physician or delegate must ensure that a Pathology Request for thawing and testing of the HPC product has been completed and sent to the Cell Therapy Flow Cytometry Laboratory. Request;

- Thaw
- Nucleated Cell Count
- Cell viability
- CD34 enumeration
- Clonogenic assay (CFC)
- Product Sterility

6.2 Morning of Infusion

6.2.1 Clinical ward staff responsible for the infusion, confirms with the Laboratory transplant time, product volume and whether the HPC will be administered via a syringe or transfusion bag. (**NOTE** the majority of products will be in transfusion bags)

6.3 2-4hours Prior to Infusion

6.3.1 The infusion nurse will explain the Transplant procedure to the patient according to the age and development level and to the parent / caregiver.

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6.3.2 If using a double lumen catheter, infuse through the large lumen. Obtain blood return to confirm patency of the central venous catheter (CVC). If lumen is blocked, notify Laboratory to delay thaw, obtain order for heparin flush ie 5IU/ml (dilute heparin in 0.9% NaCl).

6.3.3 If product is to be administered from a bag, flush the large (red) lumen with 10mls of normal saline and attach normal saline bag with line. Small lumen may be heparin-locked or maintained with normal saline.

6.3.4 Administer first part of pre-medication order, as per the patients' Medicine Chart. (**NOTE** generally Hydrocortisone 25-100mg IV)

6.3.5 If the HPC product is derived from **Umbilical Cord Blood (HPC-CB)** or **Bone Marrow (HPC-M)** commence IV hydration fluids (normal saline) running at 125ml/m² /hr **2 hours** prior to transplantation. This is to ensure good urine flow and clearance of any residual incompatible red blood cells and free haemoglobin following infusion of the HPC product.

6.4 1hour Prior to Infusion

6.4.1 Administer remainder of pre-med order as per patients' Medicine Chart. (**NOTE** generally antihistamine-Promethazine (Phenergan) O/IV and Paracetamol)

6.5 10minutes Prior to Infusion

6.5.1 If the HPC product is supplied in a bag, saline line should be in place. If product is to be administered from a syringe, equipment required includes sterile dressing pack, sterile gloves, sterile towel, 10 or 20ml syringe and normal saline for flushing the CVC line.

6.5.2 Attach the pulse Oximeter and Dynamap. Document baseline observations (Temperature, Pulse, Respiration, Blood Pressure, SaO₂) on patients' Observation Chart MR 77. Ensure that Adrenaline, Oxygen and emergency trolley are available.

NO OTHER FLUIDS/MEDICATIONS OTHER THAN 0.9% NaCl ARE TO BE INFUSED DURING HPC PRODUCT INFUSION

6.6 Infusion (Transplant)

NOTE: Thawed HPC Product **MUST NOT** be administered via a needle.

Thawed HPC Product **MUST NOT** be administered via a Leucocyte Filter.

Thawed HPC Product **MUST BE** administered **IMMEDIATELY**.

The person infusing the product **MUST** wear gloves.

6.6.1 It is essential that **TWO** clinical ward staff are with the patient and ready to commence the infusion **IMMEDIATELY** once the thawed HPC product arrives on the ward with the Laboratory Scientist.

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6.6.2 Ensure that the Ward RMO is available on the ward for the duration of infusion.

6.6.3 Two clinical ward staff will VERIFY the patient identity by crosschecking the identifiers on the patients' ID wristband with those on the HPC Product and the Stem Cell Infusion Record, MR/207.

- Check the patients' ID wristband for correct name, DOB and UR.
- Patient identification check. Verify the patients' ID wristband against the HPC product label Recipient ID (name and UR) and infusion record, MR/207. Are they identical?
- HPC product check. Verify HPC affixed product label (Medipath#, Donor ID) with the Infusion record, MR/207. Do they match?
- HPC product check. Check the HPC affixed product label (date, time, product, volume (bag number)) with the Infusion record MR/207 **AND** the laboratory infusion record, CT-F-089. The laboratory infusion form is checked with the Laboratory Scientist. Sign all records where indicated.

NOTE: The Infusion Record section on the original Request for Stem Cell Processing, CT-F-089, **MUST** be completed. This form is filed by the Cell Therapy Flow Cytometry Laboratory staff.

6.6.4 Record HPC product details on the Complex IV Orders and Fluid Balance Chart and complete Infusion date and time on the Infusion Record.

6.6.5 Once all the checks are verified, connect HPC product bag to the line or directly to CVC if the HPC product is in a syringe.

6.6.6 Administer 1-5mls of the total volume and observe patient for 5minutes.

6.6.7 During this observation time, restart IV fluids or flush line (if cells supplied in a syringe) with normal saline to prevent blockage.

6.6.8 Record vital signs (Temperature, Pulse, Respiration, Blood Pressure, SaO₂), if stable after 5minutes, continue with infusion. Recommended infusion times are;

- 10minutes if HPC product is in a syringe.
- 15-60minutes if HPC product is in a bag.

NOTE: Infusion rate depends on HPC product volume and patient's weight, check infusion order for specific requirements as ordered by the Transplant Physician or delegate.

6.6.9 Monitor vital signs (Temperature, Pulse, Respiration, Blood Pressure, SaO₂) every 10minutes during infusion.

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6.6.10 Assess for immediate adverse reactions and record on HPC infusion record;

- Nausea / vomiting
- Arrhythmia (bradycardia / tachycardia / ectopics)
- Hypertension / hypotension
- Haemoglobinuria
- Flushing
- Allergic reaction / anaphylaxis (stridor / cough / vomit / rash / hypotension)
- Tachypnoea, dyspnoea, ↓O₂ saturation
- "Bad", yuk taste in the mouth
- Feeling restless, agitated

Notify Ward RMO and inform Transplant Physician or delegate of any adverse reaction as appropriate.

6.6.11 Record time of completion of HPC product infusion on Infusion Record.

6.7 Post Infusion

6.7.1 Continue monitoring vital signs every 15minutes for 1hour, then 30minutes for 2hours, then hourly for 4hours following HPC transplant.

6.7.2 Discard empty HPC product bags /syringes in Biohazard Waste Receptacle.

6.7.3 Continue IV hydration fluids as charted.

6.7.4 Test first void of urine for haemoglobin. Haemoglobinuria is related to haemolysed red blood cells which were in the HPC product.

6.7.5 Continue hydration as charted. Document development and resolution of Haemoglobinuria. Encourage frequent voiding and report oliguria with UOP <2ml/kg/hr to Transplant Physician or delegate.

6.8 Discharge (for patients not admitted to CCC Ward)

6.8.1 Patients who are haemodynamically stable, **NOT** hypertensive and **DO NOT** have haemoglobinuria may be discharged 4/24 post HPC infusion, as assessed by the Transplant Physician or delegate.

6.8.2 Heparin lock CVC prior to discharge according to standard procedure.

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7. ENDPOINT

Haemodynamically stable patient following infusion of thawed cryopreserved HPC product.

Documentation summary;

- Pathology Request for thawing and testing of the HPC product has been completed and sent to the Cell Therapy Flow Cytometry Laboratory.
- HPC product infusion order on patients' Chart.
- Premedication and other medications given during HPC product infusion recorded in patients' Medicine Chart.
- Hydration orders on the patients' IV Orders and Fluid Balance Chart.
- Patient/family teaching and level of understanding recorded in patients' progress notes.
- Baseline assessment, vital signs, tolerance of procedure and any interventions during and post infusion of HPC product recorded on patients' Observation Chart.
- HPC product details in patients' Medicine Chart.
- HPC product checking and infusion commencement and completion details on the patients' Infusion Record.
- Completion of Infusion Record section on the original Request for Stem Cell Processing, CT-F-089. This form is filed by the Cell Therapy Flow Cytometry Laboratory staff.

8. ATTACHMENTS

NIL

9. REFERENCES

1. International Standards for Cellular Therapy Product Collection, Processing and Administration. FACT-JACIE. Fourth Edition. October 2008.
2. Blood Transfusion Policy. Royal Children's Hospital Policies and Procedures Manual. Policy Number: RCH0395. 2006.
3. Occurrence and Severity of Adverse Events after Autologous Hemopoietic Progenitor Cell Infusion are Related to the Amount of Granulocytes in the Apheresis Product. Calmels B. et al. Transfusion 2007;47:1268-1275.