
Transplantation of Fresh Haemopoietic Progenitor Cells

1. PURPOSE

This procedure describes the process for infusion of fresh Haemopoietic Progenitor Cells (HPC). This applies to the infusion of both related (allogeneic and syngeneic) and allogeneic matched unrelated donor (MUD) HPC derived from either Peripheral Blood (HPC-A) or Bone Marrow (HPC-M) harvest.

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 the **Transplant Physician or delegate** to ensure;

- there is confirmation of donor HPC harvest details.
- that a completed Request for Stem Cell Processing CT-F-089 has been received by the Cell Therapy Flow Cytometry Laboratory.
- that a Pathology Request form has been completed for the **donor** HPC Processing.
- that a Pathology Request form has been completed for the **recipient** to be cross matched with the **donor** HPC product (applicable to ABO identical or minor mismatch)
- that the HPC infusion order is completed on the patients' Complex IV Orders and Fluid Balance Chart MR55C, clearly indicating if the transplant is from a related donor or MUD and if the product is ABO compatible or incompatible (minor / major mismatch).
- that pre-medication (as required) has been ordered on patients' Medicine Chart.
- that intravenous hydration (as required) orders have been completed on the patients' Complex IV Orders and Fluid Balance Chart MR55C.
- that the Ward RMO is present for the beginning of the infusion and available on the ward for the first hour of the infusion if a minor ABO incompatibility. If ABO major incompatibility, RMO or Registrar must be available on the ward for the duration of infusion.

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

- confirm with the Cell Therapy Flow Cytometry Laboratory the infusion time, product type, total volume and blood group.
- confirm with the Transplant Physician or delegate that the HPC infusion, pre medication and hydration orders have been completed.
- administer pre-medication and hydration as ordered on the patients' Charts.
- 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, affixed and attached HPC product identifiers, infusion form MR/207, the blood transfusion record MR/201 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 staff** to;

- inform the requesting Transplant Physician if there is a discrepancy between the fresh product and recorded donor blood group.
- inform the requesting Transplant Physician of **ANY** unexpected parameters concerning the HPC product and confirm any additional or amendments to initial processing requirements; noting critical limits of final HPC product are:
 - total volume >20ml/kg,
 - incompatible RBC of > 0.5ml/kg and
 - CD34 of <2x10⁶/kg or >5x10⁶/kg with the recipient.
- liaise with ward staff to provide the product as requested.
- prepare, deliver and verify product ready for **IMMEDIATE** transplantation according to standard operating procedures.

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

4. DEFINITIONS

CFC – Colony Forming Cells.

CVC – Central Venous Catheter.

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

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

HSCT – Haemopoietic Stem Cell Transplant

NCC – Nucleated Cell Count

RBC – Red Blood Cell

RMO – Resident Medical Officer

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5. EQUIPMENT AND SUPPLIES

- Emergency Trolley in vicinity of the room
- Oxygen and suction equipment at bedside
- Emergency drugs available (Adrenaline)
- Pulse Oximeter
- Blood Pressure Monitor
- Normal Saline 1000mls. Baxter Cat. No:AHB 1324
- Saline Line.
- Sterile Medication set. Baxter Cat. No:
- In-Line Blood Filter Set. Braun Cat. No: V2950 (delivered by Laboratory Scientist with HPC product)
- 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 responsible for the infusion confirms with the Laboratory (**XT 5832**) the anticipated transplant time.

6.1.2 Confirm with Blood Bank (**XT 5829**) that there is a valid **recipient** specimen suitable for cross matching with the donor HPC product or antibody screen as required. If a valid specimen is not in Blood Bank, organise a Pathology Request form and accompanying specimen to be sent to Blood Bank.

6.1.3 The Transplant Physician or delegate must complete orders for infusion of donor HPC and hydration orders on the patients' IV order and Fluid Balance Chart and pre-medication on the patients' Medicine Chart as required;

- Infusion Rate of HPC – Commence slow 10-20ml/hr, for 15minutes, observe. If observations are stable, increase to desired rate, over next hour.
- If infusion rate is high/volume >10ml/Kg – Chart Frusemide 0.5ml/Kg.
- Pre Medication Order –Hydrocortisone 25-100mg IV(2hours prior to infusion)antihistamine-Promethazine(Phenergan) O/IV and Paracetamol (1/2-1hour prior to infusion)

(Premedication is required for major ABO mismatch HPC product)

- IV Hydration Order – 0.9% NaCl (Normal Saline) 125ml/m²/hr (commence 4hours prior to infusion of **major ABO mismatch HPC product**).

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6.1.3 The Transplant Physician or delegate must ensure that a Pathology Request for donor HPC processing and testing is completed and sent to the Cell Therapy Flow Cytometry Laboratory. Request, as applicable;

- HPC Processing (red blood cell / plasma depletion, as applicable)
- Nucleated Cell Count
- CD34 enumeration
- Lymphocyte subsets
- Blood group
- Cell Viability
- DNA extraction and storage
- Clonogenic assay (CFC)
- Product Sterility

6.2 Day of Infusion (Transplant Day 0)

NOTE

| | |
|--|---|
| ABO identical / compatible HPC product | Premedication IS NOT required. |
| Minor ABO mismatch HPC product | Premedication IS NOT required |
| Major ABO mismatch HPC product | Premedication and prehydration IS required |

- HPC product should be infused at a rate proportionate with the patient's weight and circulatory state.

6.2.1 Clinical ward staff responsible for the infusion;

- confirms with the Laboratory transplant time. The Laboratory will continue to update the recipients nurse about the HPC product availability.
- confirms with the Transplant Physician or delegate that the HPC infusion order, and where applicable the pre-medication and hydration orders are completed.

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

6.2.3 If the HPC product is a **major ABO mismatch** with the recipient;

- commence prehydration 4hours prior to HPC product infusion.
- commence premedication 2-4hours prior to HPC product infusion.

6.2.4 Prepare patient central venous catheter (CVC) for infusion of HPC product (close to infusion time) or in the case of **major ABO incompatibility**; for prehydration and premedication (**4hours prior to infusion**). Obtain blood return to confirm patency of CVC. Flush the large lumen with 10mls of normal saline and attach normal saline bag with line. Small lumen may be heparin-locked or maintained with normal saline.

6.2.5 If the HPC product is a **major ABO mismatch**, commence hydration as charted at a rate of 125ml/m²/hr **4hours** prior to transplantation, ensuring a urine output of 2ml/kg/hr. Hydration should continue for **12-24hours post** HPC infusion, depending on the presence of haemoglobinuria as assessed by the Transplant Physician.

6.2.6 If the HPC product is a **major ABO mismatch**, administer pre-medication order as charted **2hours** prior to transplantation. (**NOTE** generally Hydrocortisone 25-100mg IV)

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6.2.7 If the HSC product is a **major ABO mismatch**, administer antihistamine as per order $\frac{1}{2}$ to **1hour** prior to transplantation. (**NOTE** generally Promethazine (Phenergan) and Paracetamol)

6.2.8 Just prior to delivery of the HPC product by the Laboratory Scientist, attach pulse oximeter and Dynamap. Document baseline observations (Temperature, Pulse, Respiration, Blood Pressure, SaO₂) on patients' Observation Chart. Ensure that Adrenaline, Oxygen and emergency trolley are available during the HPC infusion.

6.3 Infusion (Transplant)

NOTE: HPC product **MUST NOT** be irradiated.

HPC product **MUST NOT** be administered via a needle.

HPC product **MUST NOT** be administered via a Leucocyte Filter.

HPC product **MUST BE** administered **IMMEDIATELY**.

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

The Ward RMO **MUST** be present with the patient during the first **10minutes** and available on the ward for the **1st hour** of the infusion.

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

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

6.3.2 Two clinical ward staff will identify the patient identity by verifying the patients' ID wristband with the HPC Product, the blood transfusion record MR/201 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 affixed product label Recipient ID (Name, UR and DOB), the attached product Blood Bank tag, the blood transfusion record MR/201 and the infusion record MR/207. Are they identical?
- HPC product check. Verify the **HPC affixed product label** (Medipath#, Donor ID) with the attached Blood Bank tag, the blood transfusion record MR/201 and the Infusion record, MR/207. Do they match?
- HPC product check. Verify 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. CT-F-089 is checked with the Laboratory Scientist.

NOTE: THERE MAY BE MORE THAN ONE BAG OF HPC PRODUCT FOR INFUSION

- ABO compatibility check. Verify the blood group (ABO and RhD) on the attached Blood Bank tag with the Blood Transfusion record, MR/201. Do they match? Does this concur with the infusion and pre-medication order?

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- Complete documentation as indicated. 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.

6.3.3 Record HPC product details in the patients' medical record and complete Infusion date and time on the MR/207.

6.3.4 Once all the checks are verified, connect the HPC product bag to the line via an in-line blood filter IV set, supplied by the Laboratory Scientist.

6.3.5 Commence HPC product infusion slowly (i.e.: 10-20ml/hr) commensurate with the recipient weight, for 15minutes.

6.4.6 Monitor vital signs (Temperature, Pulse, Respiration, Blood Pressure, SaO₂), **every 5minutes**, if stable after the 15minutes of slow infusion, increase the rate at 10 minute intervals to the desired infusion rate over the next 1/2hour, as specified by attending the Ward RMO.

6.5.7 Monitor vital signs (Temperature, Pulse, Respiration, Blood Pressure, SaO₂), continuously during the HPC product infusion;

- every 5minutes for first 15minutes, then,
- every 15minutes for next 45minutes, then,
- every 30minutes for the remainder of the HPC product infusion.

6.5.8 Slow the infusion rate if patient's Blood Pressure falls or tachycardia develops, inform Ward RMO or Transplant Physician as appropriate.

NOTE: THE HPC PRODUCT MUST NOT BE TAKEN DOWN AND DISCARDED

6.5.9 The nurse **MUST** be at the bedside during the entire infusion if there is a major ABO mismatch, or the first hour of the infusion.

6.5.10 Assess and document for immediate adverse reactions;

- Fever
- Chills
- Hypotension/Hypertension
- Pain (IV site, chest or back)
- Acute respiratory distress/stridor/wheeze/dyspnoea
- Rash
- Fluid overload (careful fluid balance)

6.6.10 In the event of an adverse reaction, inform the Ward RMO and/or the Transplant Physician.

6.6.11 Record time of completion of the infusion on the Infusion Record MR/207. Ensure that **ALL** bags of the HPC product are transplanted as charted.

6.6.12 Discard empty HPC product bag(s) in Biohazard Waste Receptacle.

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6.7 Post Infusion

6.7.1 Continue monitoring vital signs (Temperature, Pulse, Respiration, Blood Pressure, SaO₂) every 1hour for 4hours, then as routine.

6.7.2 Test each void of urine for haemoglobinuria (haemolysis of incompatible red blood cells). Document and assess development and resolution of haemoglobinuria. Report to Transplant Physician as appropriate.

6.7.3 Continue hydration as charted. Encourage frequent voiding, document urine output (1-2ml/kg/hr) for 12hours and **report** oliguria with UOP <2/ml/kg/hr to the Transplant Physician.

7. END POINT

Haemodynamically stable patient following infusion of HPC product.

Documentation summary;

- Pathology Request for crossmatch of the recipient with the donor HPC product.
- Pathology Request for processing and testing of donor HPC product.
- HPC product infusion record MR/207.
- Premedication and all 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 recorded on 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

HPC Product Infusion Record MR/207.

Request for Stem Cell Processing, CT-F-089.

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.