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INTRODUCTION

The WMDA is a worldwide network of organisations that provide hematopoietic progenitor cells (HPC) from voluntary unrelated donors to those in need of hematopoietic stem cell transplantation. Over 49% of the HPC collected from unrelated donors are transported across international borders. The fresh products collected from adult volunteer donors are transported by a trained courier. The cord blood products which are cryopreserved are shipped with a dry shipper and are not included in these guidelines.

1. COURIERS

The courier has sole responsibility for the safe and timely transport of HPC from the collection centre to the transplant centre. Selection and assignment of courier responsibility is a collaborative process between the national registry, transplant centre and collection facility.

Typically, either the supplying registry or the receiving registry will take responsibility for the courier and be designated as the courier registry. If there is no Hub, the transplant centre may serve this role. It is the responsibility of the courier registry to ensure that the courier is properly trained. The courier registry is deemed to have provided the courier if they are either directly using a courier from within their organisation or have arranged for collection and delivery of the product by a third party (e.g. a specialised courier company).

The transfer of all HPC products should be transferred to and from the courier in a clinical setting.

1.1 Courier requisites

Couriers must be trained and equipped to fulfil the responsibilities as described below. The transplant centre/receiving registry is responsible for providing any extra/special transport specifications. To be selected as a courier, the person must:

- not be related to the donor or patient;
- be an experienced independent international traveller;
- have no other obligations until after the HPC have been delivered;
- be trained in all policies and procedures required for the transportation of HPC;
- must have adequate command of the English language or the language(s) used in the countries and airports to be visited for international transport;
- have a mobile phone with international roaming;
- have access to a credit card with a reasonable limit.

It is preferable that the courier has experience in transporting HPC within their country of residence prior to acting as an international courier.

1.2 Commercial courier companies

If a commercial courier company is used, there needs to be a direct committed relationship between the transport company and the registry making the arrangement. The commercial courier company must understand that their 'normal' business/ transport procedures will not apply to the

transportation of HPC products, and the company must be able to customise the service they provide to meet these needs, unless they are specialized in transporting human tissues and cells.
The commercial courier company must be able to provide trained couriers that meet the registry's guidelines. The commercial courier company must have an established quality management system that ensures that the company consistently meets all the requirements of these guidelines and the registry's standards for transport. At a minimum, the quality system must address courier selection, courier training and incident management. While commercial courier companies may be given the authority to conduct their own training, it remains the responsibility of the Registry making the arrangement to ensure that the courier is properly trained. Commercial courier companies should plan for backup couriers, transport traceability, and 24/7 availability of the first point of contact.

1.3 Courier responsibilities

The courier is responsible for ensuring that the HPC is transported safely from the collection to the transplant centre in the shortest possible time and at the temperature requested by the transplant centre. Some registries reserve the right, however, to recommend that non-cryopreserved HPC(A) are transported between +2 and +8° C[2].
The courier must:

- remain in possession of the HPC product at all times;
- carry documentation relating to transportation of the HPC product (for example registry source documentation with IDs, product type and transportation temperature);
- verify accuracy of information on HPC labels and accompanying blood tubes with accompanying documentation, received by transplant centre or receiving registry;
- place the product bags and samples properly in the cooler (see section 4);
- make every possible effort to ensure that the HPC does not pass-through X-ray screening at security checkpoints;
- follow the export-, transit-, import-, customs- and flight security regulations of the involved countries and partners;
- deliver the HPC directly to the designated person at the transplant centre or processing laboratory;
- inform the nominated "First Point of Contact" (either the registry or transplant centre) of possible delays or incidents – see section 7;
- not consume nor be under the influence of alcohol or sedative drugs while transporting the HPC;
- always maintain patient and donor confidentiality (see 1.7).

If transport of the HPC would be jeopardised by refusal to allow X-ray screening of the HPC, the courier should try to contact before X-ray a responsible person either at the sending registry or transplant centre or receiving registry, if possible. In such cases, the courier should permit the HPC cells to pass through the X-ray screening device in a single instance. Note that the effect of cumulative X-ray screening on HPC product viability has not been determined[3].

1.4 Equipment

All couriers should carry the following equipment:

- an isothermal transport box or a rigid puncture proof thermally insulated cooler for transport of non-cryopreserved HPC. There should be a validation for the transport device in place (see WMDA recommendation on validation);
- coolant packs or isothermal temperature shells;
- packaging material to protect glass tubes;
- programmed data loggers or thermometers with an exterior temperature display if required by the registry or transplant centre;
- disposable gloves for assistance with inspection of HPCs;
- labels for transport container;
- labels required by the sending and/or receiving registry.

1.5 Documentation

Product documentation must be provided by the transplant or collection centres or sending registry and is the responsibility of transport organiser/registries according to local policy. Commercial courier companies and transport organisers are responsible for ensuring appropriate personal documentation is on-hand.

Product documentation may consist of:

- clearance documents for all countries as required;
- verification of prescription for HPC collection;
- donor infectious disease marker testing (most recent results and within 30 days of collection);
- import/export permits for HPC as required by local authorities;
- letters to airport security at departure, transit and arrival airports or train stations as required;
- HPC product accompanying documentation (provided at collection centre);
- name, address and 24-hour phone number of contact at the collection facility/donor registry;
- name, address and 24-hour phone number of contact at the transplant centre/courier registry;
- results of preliminary testing (cell counts as appropriate for product release);
- required customs import or export permits;
- quarantine requirements;
- circular of Information or equivalent;
- additional documents not listed.

Personal documentation may consist of:

- passport valid for 6 months following trip completion;
- travel authorization;
- airline ticket or electronic ticket information;
- public transport ticket (or instructions on how to purchase these tickets);
- hard copy of the travel route in the case of travel by motor vehicle;
- information on reservation of accommodation;
- travel insurance if required;
- letters of introduction from transplant centre and/ or registry;
- foreign currency as needed;
- mobile phone with international roaming.

1.6 Luggage

The HPC product must **never** be placed inside checked luggage or inside the courier's personal cabin baggage. It is recommended that the HPC product be placed under the seat in front of you. Most airlines, especially on international sectors, strictly enforce the limit on the number, size and weight of items that may be carried as cabin baggage including the cooler used for transportation of HPC. Therefore, couriers should be aware that although carriage of personal items as cabin baggage is recommended, many international airlines will require couriers to check in their personal luggage. The courier should only take as much personal luggage that he/she can travel on cabin baggage exclusively. When not used for the transportation of HPC, unfrozen coolant packs may need to be checked in.

1.7 Confidentiality

The courier must accept the policies and procedures of the relevant national registries and/or the transplant and collection centre regarding courier, recipient and donor interaction. Couriers will not disclose to the recipient's family or staff of the transplant centre or collection centre, details that could result in identification or location of the donor or recipient. The courier must ensure that labels on the outer transport container do not compromise donor/ recipient confidentiality. Couriers must not accept gifts, letters, or other materials for delivery to the donor or the recipient.

1.8 Insurance

Couriers may be covered by travel insurance for international destinations in accordance with their registry or commercial courier company policies. It is recommended that the courier's institution considers product liability insurance.

2. TRANSPORT ARRANGEMENTS

2.1 Flight arrangements

The following must be taken in to account when arranging courier flights:

- flights must be booked in advance and should occur as soon as possible after the product is released to minimize risk by initiating transport;
- flights should be booked with minimum stopovers when HPC products are in-hand;
- the courier must be aware of alternative modes of transport and have appropriate contingencies in place if substantial delays to airline schedules arise due to inclement weather or other incidents.
- backup flights should be arranged if permitted by the airline; if not permitted backup flights should be arranged with another airlines.
- notification of airline and security staff at airports, by the registry organising the shipment, is required at some airports and generally recommended for any departure, arrival and transit airport;
- the courier must contact the collection centre at least one day prior to the scheduled collection or follow specific instructions provided by the collection centre regarding contact;
- all changes in original transport arrangements must be communicated immediately to the transplant centre and requesting registry;
- the collection centre and registry must be provided with the itinerary and contact numbers of the courier prior to departure of the courier.

2.2 Motor vehicle transport arrangements (excluded taxi, ride share services and public transport)

When the transplant centre, in consultation with the registry decides that the most efficient method of transport of the HPC is by car the following issues must be considered to ensure that the transport of the HPC will not be delayed should the car breakdown, be involved in an accident, or held up by other road conditions or unrelated events.

- two couriers should accompany the HPC so that one courier may stay with the car whilst the other accompanies the HPC by other means of transport;
- both couriers must have no other commitments that may interfere with timely delivery;
- both couriers must have a valid driver's licence;
- an up-to-date GPS car navigation system should be available;
- a hard copy of the travel route must be available;
- the couriers must maintain contact with the cell product at all times, do not place in trunk;
- the couriers must be aware of alternative modes of transport in case substantial delays arise in consultation with the requesting registry;
- all changes to original transport arrangements must be communicated immediately to the transplant centre and receiving registry;
- the couriers are responsible for their driving behaviour. Traffic fines are to be paid by the courier, not by the transplant centre;
- insurance must be arranged.

3. LABELLING

Labelling should adhere to IATA (International Air Transport Authority) and national regulations concerning the safe handling and transport of biological material at all times (www.iata.org).

3.1 Labelling of HPC product and blood samples

Labelling of the HPC and accompanying blood samples should comply with any regional, state or national regulatory/legal requirements or manufacturing license requirements of the collection centre and/or transplant centre and with current FACT/JACIE standards.
Labels must be legible and printed using waterproof ink labels.

Labels may contain as example the following information:

- unique numeric or alphanumeric product code; (preferably an international product code like ISBT128)
- donor identification code;
- recipient identification code;
- type/ proper name of product, as defined as a globally unique product code like ISBT128;
- ABO group and Rh type of donor;
- collection date, time and time zone at end of collection;
- product volume / cell count;
- bag number and total number of bags (Courier is responsible to verify this information);
- mandatory statements if applicable in accordance with Appendix I (FACT/JACIE standards)[4]

3.2 Labelling of transport container

The outside of the cooler should be labelled with the appropriate wording (with regard to local regulations), for example:

MEDICAL SPECIMEN – HANDLE WITH CARE
DO NOT X-RAY
WARNING: Contains human tissue for transplantation
Do not place near heat
Do not freeze
Do not delay delivery

When transporting the cooler without HPC, the label should be covered by the courier and allowed to pass through all security checkpoints including X-ray machines if required. Address labels for the transplant centre including institution, address, contact details and phone numbers should be affixed to the cooler in accordance with current FACT-JACIE International Standards for Haematopoietic Cellular Therapy Product Collection, Processing, and Administration[4] or other local regulations but ensuring donor/ recipient confidentiality during transportation.

4. PACKING HPC FOR TRANSPORTATION

4.1 Containers

- packaging and shipping containers should be validated to hold at the required temperature in excess of the anticipated transit time, under the expected range of external temperatures;
- if required by the registry or transplant centre, temperature data loggers should be used to record the temperature of the HPC during transportation (if required by the registry or transplant centre, thermometers with a protected probe and exterior temperature display may be used);
- the courier should be familiar with using instructions for the container and data logger;
- individual donor registries can formulate policies on behalf of transplant centres and procedures will vary, however the following items in 4.2 and 4.3 should be considered.

4.2 Isothermal Transport Box

- place the HPC with a data logger or temperature probe (if required) inside the temperature shell (frames and extenders) that has been preconditioned at +4°C and secure top;
- place the temperature shell with other preconditioned temperature shells inside the isothermal stem cell box;
- pack in accordance with manufacturer packing instructions;
- the courier must be familiar with the duration limits and general handling instructions of the transport container.

4.3 Cooler and Coolant Packs

- **It is highly recommended to use transport boxes that provide sufficient cooling capabilities >72 hours to avoid the need to reconditioning coolant packs;**
- if required, place the data logger in the container;
- arrange bags, pre-chilled or pre-frozen coolant packs and any insulating material as specified by transplant centre for adequate temperature control over the estimated transit time into the cooler;
- bags of HPC must be thermally insulated from frozen coolant packs to avoid spot freezing;
- rock the cooler gently at specified intervals if requested;
- the temperature of the HPC should be maintained at greater than +2°C.
- **NEVER place dry ice in the cooler with non-cryopreserved HPC. The presence of dry ice may result in the bags containing the HPC becoming brittle and subject to fracture. Furthermore, the HPC may never be exposed to temperatures that causes freezing in the absence of cryoprotectant.**

4.4 Additional product samples

- Additional peripheral blood or bone marrow samples should be placed inside smaller transport containers or plastic bags prior to placing in cooler or isothermal transport box with the HPC; In accordance with IATA requirements (packing instruction P650).

4.5 Transportation of HPC, Marrow

- The collection centre should ensure that the collection media has been validated according to local protocols to provide sufficient anticoagulation and viability of bone marrow during the estimated transit time.
- Bone marrow collected for adults and large paediatric recipients should be divided into at least two blood collection/ transfer packs.
- If the scheduled departure time is late in the day, transplant coordinators, or the courier company on their behalf, may request the collection centre via the relevant registry to store the cells at +4°C for collection by the courier at a time suitable for flight connections.
- Collection centres should wherever possible, depending on availability of equipment, provide HPC in bags:
    - validated for the use of transport HPC;
    - without spikes or access sites inserted;
    - with lines heat sealed rather than clipped and of sufficient length to allow the use of a sterile connecting device to access the bag if required; and
    - with at least one port available for use at the transplant centre.

4.6 Transportation of HPC, Apheresis; TC, Apheresis and MNC, Apheresis

- Although this may vary according to local protocols, anticoagulant will be added to apheresis products during collection on the cell separator and as programmed by the apheresis machine.
- For long distance transportation and/ or overnight storage of HPC(A), the final concentration of nucleated cells in the collection is important for viability. To minimize the loss of viability, the concentration of nucleated cells should be reduced by the addition of autologous plasma in the processing laboratory. Apheresis products are usually transported in the collection pack of the cell separator kit (i.e. 1 bag per apheresis collection).
- The majority of HPC collections by apheresis require a single day of collection, so the courier should anticipate leaving after the first scheduled day of collection depending upon flight availability. If a second collection is required, the first collection should be stored at +4°C without agitation in a blood product refrigerator at the collection centre.
- If the scheduled departure time is late in the day, transplant coordinators, or the courier company on their behalf, may request the collection centre via the relevant registry to store the cells at +4°C for collection by the courier at a time suitable for flight connections.
- Collection centres should wherever possible, depending on availability of equipment, provide HPC in bags:
    - Validated bags for the use of transport HPC
    - without spikes or access sites inserted;
    - with lines heat sealed rather than clipped and of sufficient length to allow the use of a sterile connecting device to access the bag if required; and
    - with at least one port available for use at the transplant centre.

5. COURIER TASKS DURING ASSIGNMENT

5.1 Arrival at the city of collection centre

On arrival at the city where the collection centre is located, the courier must contact the designated person in order to:

- confirm arrival, contact and travel details;
- deliver isothermal shells or the cooler and coolant packs (if required);
- if necessary place coolant packs or cooling panels inside a labelled bag in a freezer at the hotel;
- confirm the time and location for collection of the HPC;
- confirm transportation from the collection centre to the airport or train station.

5.2 On the day of collection

On the day of collection, the courier must:

- arrive at collection centre at arranged time and location;
- contact designated contact person;
- carry personal identification (e.g., passport) and the documentation required for the transport of HPC;
- crosscheck with the collection centre representative, the type, number and labelling of bags containing HPC (if required),
- the cell count and the addition of anticoagulant against the request for HPC (if required);
- pack HPC and additional samples into the cooler according to instructions provided by the transplant centre;
- collect and confirm donor and recipient identifiers on all accompanying paperwork;
- declare the HPC on all customs/ immigration and quarantine forms for inspection as required;
- supervise any visual inspection of the HPC.

5.3 Arrival at city of transplant centre

On arrival at the city where the transplant centre is located, the courier must:

- travel immediately to the transplant centre or processing laboratory according to instructions;
- contact the designated staff member at the transplant centre or processing laboratory for hand over (or as stated on the delivery instructions);
- record the time of delivery and temperature of the HPC upon arrival;
- cross check the HPC and sample tubes against the details provided by the collection centre and the request for HPC;
- visually inspect the bags and the HPC for anomalies such as visible clumping;
- record any events or incidents during transport;
- sign for delivery of the HPC to the transplant centre using the appropriate forms;

- alert transplant centre staff regarding documents requiring completion and return to the collection centre post-delivery and/ or post-transplant;
- report incidents or adverse events to the "first point of contact" described below.

6. Courier incident management

6.1 Introduction

The transportation of HPC by a courier is a critical step in transplantation using voluntary unrelated donors. Any incidents or deviations in transport can have a significant impact on patient outcome; this is particularly important for long distance transport. An incident is defined as an unplanned event that occurs during the transportation of HPC that results in, or has the potential for, injury to the recipient or damage, delay or other loss to the HPC.

6.2 Active management

- The 'first point of contact' must be clearly communicated to, and understood by, the courier in advance of travel;
- A courier must notify their 'first point of contact' as soon as they are aware of any incident or potential incident, although the requirement for notification should not delay resolution of the incident;
- Either the supplying or receiving registry or the transplant centre will be the nominated 'first point of contact'. Additional nominated organisations may need to be copied in on all correspondence;
- The courier company acting on behalf of these organisations may be nominated as ‘first point of contact’;
- The organisation providing the courier should perform a risk analysis to identify any potential incidents or deviations that might occur during the transportation of HPC. An incident management plan should be developed that outlines the procedures required to avoid or mitigate these risks, and to resolve any incidents if they occur.

6.3 Analysis and Corrective Action

- Any organisation involved in transport of HPC must conduct a thorough review of all incidents using appropriate methodologies, such as root cause analysis (this includes commercial courier companies and registries) to identify the underlying causes of the incident and any systemic problems;
- The review of each incident should outline both the corrective actions taken either immediately or after the event to remedy the incident and preventive actions taken to prevent recurrence of the incident;
- All corrective and preventive actions must be followed-up to ensure that changes have been effective and lead to process improvement;
- a SPEAR shall be submitted to WMDA when a reportable incident occurs.

REFERENCES

[1] WMDA Global Trends Report 2020
[2] Antonenas, V. Fresh PBSC harvests, but not BM, show temperature-related loss of CD34 viability during storage and transport. Cytotherapy (2006) Vol 8, No 2, 158-165
[3]Petzer et al. (2002) Breaking the rules? X–ray examination of haematopoietic stem cell grafts at international airports. Blood 99: 4632-4633
[4]FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing and Administration.

ADDITIONAL REFERENCES

Goldman JM (1994) 'A Special Report: Bone Marrow Transplants Using Volunteer Donors - Recommendations and Requirements for a Standardised Practice Throughout the World – 1994' Update Blood 84: 2833 – 2839
Cleaver SA, Warren P., Kern M. et al., (1997) 'World Marrow Donor Association (WMDA) Special Report: Donor Workup and Transport of Bone Marrow' (Website: www.wmda.info)
Code of Federal Government Regulations, Title 21-Food and Drugs, Part 1271 Human Cells, Tissues and Cellular and Tissue Based Products (USA)
Circular of Information for the Use of Cellular Therapy Products (AABB)

WEBSITES Referred to in the preparation of these guidelines

World Marrow Donor Association - www.wmda.info
American Association of Blood Banks – www.aabb.org
International Society for Cellular Therapy – www.celltherapysociety.org
National Marrow Donor Program – www.marrow.org or www.network.nmdp.org/
Australian Bone Marrow Donor Registry - www.abmdr.org.au
Japanese Marrow Donor Program - www.jmdp.or.jp
Anthony Nolan Trust – www.anthonynolan.com
ZKRD – www.zkrd.de
IATA – www.iata.org