

## Shipping

Most frozen biospecimens will be shipped by the biobank to you on dry ice to maintain their frozen status. This section will outline how to ship biospecimens on dry ice correctly and what you can expect when receiving biospecimens on dry ice.

### **Introduction:**

Dry ice is the solid phase of carbon dioxide (CO<sub>2</sub>). CO<sub>2</sub> solidifies at - 78.5°C. To maintain frozen temperatures (-70° C) during shipping, dry ice pellets can be used. Dry ice is not classified as a dangerous substance by the Department of Transportation (DOT) for ground transportation. However, when shipped by air or water, it is regulated as a dangerous good and therefore specific packaging and labelling requirements apply (ISBER Best Practices 2018). The instructions below are relevant to shipping by air.

### **Types of Biospecimens:**

Exempt human specimens are those for which there is "minimal likelihood there are pathogens present". Patient material shipped from a tumour biobank usually falls under the Exempt human or animal category and does not need special identification (UN number) or strict packaging requirements. See definitions for Exempt human specimens and infectious substances in Appendix A. Visit the IATA web site ([www.iata.org](http://www.iata.org)) for further details. If your samples are potentially infectious these instructions do not apply.

### **Packaging, Labelling & Required Documentation:**

Consult [www.iata.org](http://www.iata.org) to confirm appropriate labelling, packaging and documentation required.

### **Overview of Requirements:**

If you are sending exempt human biospecimens on dry ice you will need:

1. To ensure your staff have undergone Transportation of Dangerous Goods Training. Dry ice is classified as a dangerous substance when shipped by air. All shippers of dangerous goods (including dry ice only packages) are required by law to have applicable training. This document serves only as a guideline and does not constitute training. Training may be provided by your institution. Training is also provided by some courier companies such as World Courier.
2. A supply of dry ice. If you don't have any dry ice in your institution you may:
  - a. Order dry ice
  - b. Use a courier that will supply dry ice for shipment (e.g. World Courier)
3. A Courier. If you don't have a regular courier, see Appendix B on things to consider when selecting a courier.
  - a. For international shipments, consider choosing a courier that will (1) act as a Customs Broker (to avoid delays in Customs) and (2) replenish dry ice during the shipment to ensure samples will remain at temperature if unexpected delays occur.
4. Packaging and labelling materials.
5. To research required **documentation** requirements. If the correct documentation is not sent with the shipment, the package may be significantly delayed and/or returned. For international shipments in particular research specific documentation required by the country you are sending the specimens to.

6. Other. Optional: You may wish to use a temperature-recording device that can verify the temperature of the material being shipped throughout the transport cycle.

**The 1-2 weeks before the shipment is to go out:**

1. Retrieve the samples to be shipped. Keep frozen (in -80°C freezer or on dry ice until packaged).
  - a. Verify that samples match researcher's request.
  - b. Start to complete the Shipping Manifest (Appendix C).
2. Calculate the amount of dry ice required.
  - a. Confirm how long it will take the package to arrive at the destination (call your courier if you're unsure).
  - b. Use sufficient dry ice to ensure that the sample will remain frozen even if delayed in transit for 24 hours in cases of national shipments and 72 hours for international shipments. International shipments may be delayed at customs so additional delays should be expected. Be aware that some couriers do not 'top up' dry ice during shipments (e.g. Fed Ex) and some couriers will 'top up' dry ice (e.g. World Courier).
  - c. In general, shipments should contain 2.27-4.54 kg (5-10 pounds) of dry ice per 24 hours.
3. Ensure you have sufficient dry ice for the shipment.
4. Ensure the packaging material is large enough to fit the required amount of dry ice as well as your samples.
5. Shipments involving a large number of specimens should be divided into multiple, smaller shipments.
6. Ensure you have the correct packaging material (See Appendix D). You will need:
  - a. A leak-proof primary container (e.g. tissue or blood should be in cryovials and the cryovials should be placed in a cryovial box; frozen sections on slides should be placed in slide shippers).
  - b. A leak-proof secondary container (e.g. a biohazard bag).
  - c. Absorbent material between the primary and secondary containers (e.g. *absorbent material in sufficient quantity to absorb the entire contents so that, during transport, any release or leak of a liquid substance will not reach the outer packaging.*)
  - a. Outer packaging (a box): insulated bio-shipment box, which consists of an inner styrofoam box placed inside an outer cardboard box.
    - a. Select a cooler that is specifically made for use with dry ice; it will have the necessary ventilation. Adequate ventilation is needed because the CO<sub>2</sub> emitted by dry ice as it sublimates can cause packaging to expand, and possibly burst.
    - b. Courier label with the individual site's address in the "Sender" area and the central storage facility's address in the recipient area. Ask the courier to send you a label to fill out in advance (ask the courier to send extra labels to use for the next shipment).
    - c. Labels (See Appendix F)
      - i. Class 9 (dry ice) including amount of dry ice in kg. The net weight of the dry ice in the package must be marked on the outside of the package in addition to the other required marks and labels (e.g., Dry Ice, UN 1845, Class 9 Miscellaneous label).
      - ii. Exempt Human Specimens (See Appendix A for definition. If your samples are Category A or B, further labelling and packaging requirements apply. See the IATA website ([www.iata.org](http://www.iata.org)) for details).
      - iii. 'Keep Upright' labels (so couriers will not place the package on the side or upside down).

- iv. Specify to whose attention the shipment is being delivered on the courier address label to prevent the shipment from arriving and being held in the receiving department for too long.
7. Decide the day of pick up. Consider:
  - a. Schedule pick-up for early in the week (Monday or Tuesday) to prevent delivery on the weekend if delays occur.
  - b. Be aware of public holidays at the destination.
  - c. Do not ship just before a holiday long weekend as delays in transit may occur.
  - d. Confirm that someone will be present to receive the package and properly store the samples.
8. Contact shipper/courier:
  - a. Tell the courier:
    - i. The type of sample (e.g. exempt human specimens)
    - ii. Number and amount of sample
    - iii. How much dry ice you will be using
    - iv. Size of container
    - v. Where your package is going (e.g. it is important if the package is being sent to another country because the required documentation will differ)
    - vi. Day, time and location of pick up
    - vii. Whether or not you will require any packaging material/dry ice
      1. NOTE: If you are requesting the courier to supply the dry ice and/or packaging material, sufficient notice is required. If you are supplying your own dry ice and packaging, a day notice is usually sufficient to call the courier to arrange the pick-up day/time.
  - b. Ask the courier what documentation will be required (see list of 'Required Documentation')
    - i. Ask the courier to send you the Waybill and (if international shipment) the Commercial Invoice in advance so you can complete the information in advance and make the required number of copies
  - c. For international shipments consider asking:
    - i. if the courier will act as a Customs Broker and if so, what (if any) paperwork is required to establish the courier as the Customs Broker
    - ii. if the courier is capable of replenishing refrigerant in the event of a delay

#### **The day before the shipment is to go out:**

1. Verify that there is an adequate stock of dry ice available.
2. Ensure the packaging material is ready.
3. Get documentation ready (See Required Documentation below).
4. Contact shipper/courier to schedule package pick-up (if not done previously).
5. Verify that all shipping information, contacts and required documents are accurate and complete.
6. Document sample retrieval in biobank database and complete shipping manifest according to established procedure. Verify that samples match researcher's request.

#### **The day of the shipment:**

1. Package samples as is appropriate.
2. If you are sending samples in cryovials:
  - a. Primary container: Package cryovials to prevent contact with each other by placing them in a cryovial box (e.g. 81 slot box) or wrapping them individually with absorbent material.
  - b. Line a biohazard bag with absorbent material.
  - c. Secondary container: Place the cryovial box in the biohazard bag and seal tightly.
3. If you are sending frozen slides:
  - a. Primary container: Place the slides in a slide shipper.
  - b. Wrap the slide shipper with bubble wrap.
  - c. Line a biohazard bag with absorbent material.
  - d. Secondary container: Place the wrapped slide shipper in the biohazard bag and seal tightly. Ensure that the slides are not directly in contact with the dry ice.
4. Place enough dry ice in the cooler to completely cover the bottom.
5. Place the biohazard bags containing the samples in the cooler with dry ice.
6. Put the remaining dry ice around and on top of the biohazard bags. Minimize the volume of air to which the dry ice is exposed in order to slow the rate of sublimation and prevent movement. If there is any air space after you fill your package with dry ice, fill it with packing material (e.g. Styrofoam or wadded paper) to reduce the volume of air space.
7. Place the lid on the cooler. Do not seal tight. Dry ice must NEVER be placed into a tightly sealed container (explosion hazard); the packaging must allow the release of CO<sub>2</sub>.
8. Place the cooler in the outer box.
9. Fill out the shipping manifest and place it in a separately sealed leak-proof plastic bag inside the box. For international shipments, also include a copy of any other documentation such as the Commercial Invoice (see Required Documentation, # 4).
10. Securely tape the outer box but do not completely seal it to allow for CO<sub>2</sub> ventilation. If re-using a shipping box check the bottom on the box for proper closure also.
11. Affix the labels on the outside of the box (e.g. Class 9 label designating dry ice, Exempt human Specimen label and direction labels, address labels).
12. Fill out the courier label completely, with the sender and recipient's full name and address, and affix it to the outside of the box.

#### **Required Documentation**

1. Complete the Shipping Manifest (See example in Appendix C).
  - a. Make a copy for your records and send a copy with the shipment. Also email an electronic copy to the receiver.
2. Complete the IATA checklist for dry ice (See Appendix E).
  - a. Make 3 copies (retain one for your records and give 2 to the courier).  
<http://www.iata.org/whatwedo/cargo/dgr/Documents/acceptance-checklist-dry-ice-en.pdf>
3. Complete shippers Waybill (obtain from courier) and affix to the outside of the box.
4. Commercial Invoice (for international shipments – obtain from courier).
  - a. A Commercial Invoice is required for international shipping. Information provided on other international shipping documents, including the air waybill number or shipping label, must correspond with the Commercial Invoice. The courier should provide you with a Commercial Invoice (please ask that they send you one in advance).

- b. Make multiple copies (e.g. 8 copies, keep 1 for your records) and have them ready when the courier arrives to pick up the package. Put one copy inside the package with the Shipping Manifest.
5. Identify all requirements for shipping to a designated country prior to the initiation of the shipment. For international shipments, research any new regulations that may have been adopted or special permits that are needed for that destination. Use of a customs broker can be helpful or even critical. Certain couriers can provide this service which can be essential for transport to/from a foreign country. One or more of the following additional documents may apply to an international shipment:
  - a. Commercial Invoice (as described above)
  - b. Shipper's Export/Customs Declaration (see Appendix G)
  - c. Export Permit or Authorization and/or
  - d. Import Permit or Authorization
6. Special permits or other requirements may be unique to certain countries and regions. Some countries have regulations related to ethical issues which prohibit the import/export of certain types of human specimens or have specific requirements concerning the import/export of such specimens. If collecting non-human biological samples that are endangered or protected, special permits such as the Convention on International Trade in Endangered Species of Wild Fauna and Flora permit, as well as additional paperwork may be required.
7. A shipper's declaration of dangerous goods is not required unless the dry ice is used as a refrigerant for other dangerous goods  
<http://www.ercweb.com/resources/viewreg.aspx?id=6779>.

**After the shipment is picked up:**

1. Contact (call or e-mail) consignee to provide them with Waybill number and inform them that package has been shipped. Give them an estimated delivery time so that they can anticipate arrival of the sample. Remind them to fax back the Shipping Manifest to confirm receipt of all samples and to record any issues.
2. Track delivery (using the online tracking capability of the courier) to monitor shipment and expedite sample if delayed by Customs or regulatory agencies.

## Appendix A:

### Definitions:

Patient specimen: material collected directly from human or animals for diagnostic, treatment, prevention, investigational or research purposes. Patient specimens have to be categorized as Category A, Category B or Exempt Specimens.

Category A substance is "an infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, or life-threatening or fatal disease to otherwise healthy humans or animals".

Category B substance is "an infectious substance which does not meet the criteria for inclusion in Category A". Typical clinical or patient specimens being shipped for routine culturing or other testing for a non-Category A infectious microorganism or suspected of containing a non-Category A infectious microorganism are examples of Category B substances.

Exempt human or animal specimens: those for which there is "minimal likelihood there are pathogens present".

Patient specimens for which there is minimal likelihood that pathogens are present are not subject to the DGR if the specimen is transported in Packaging for Exempt Patient Specimens (**see below for the Packaging requirements for Exempt Patient Specimens**).

*In determining whether a patient specimen has a minimal likelihood that pathogens are present, an element of professional judgment is required to determine if a substance is exempt under this paragraph. That judgment should be based on the known medical history, symptoms and individual circumstances of the source, human or animal, and endemic local conditions. Examples of specimens which may be transported under this paragraph include the blood or urine tests to monitor cholesterol levels, blood glucose levels, hormone levels, or prostate specific antigens (PSA); tests required to monitor organ function such as heart, liver or kidney function for humans or animals with non-infectious diseases, or therapeutic drug monitoring; tests conducted for insurance or employment purposes and are intended presence of drugs or alcohol; pregnancy tests; biopsies to detect cancer; and antibody detection in humans or animals in the absence of any concern for infection (e.g. evaluation of vaccine induced immunity, diagnosis of autoimmune disease, etc.).*

<http://www.iata.org/whatwedo/cargo/dgr/Pages/download.aspx>

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