Biological Substance, Category B and Exempt Human or Animal Specimen Shipping

BIOLOGICAL SUBSTANCE, CATEGORY B

UN 3373
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**Introduction**

Anyone packaging, handling, completing shipping documentation, shipping or transporting hazardous materials must be informed of the general requirements of handling hazardous materials as well as function specific training for the specific task(s) performed; this is accomplished through required training before performing any tasks associated with shipping hazardous materials and every two years thereafter. This guide reviews packaging requirements, markings and labels, and documentation and record keeping required for Biological Substances, Category B as well as exempt Human and animal specimens. Dry Ice information is also provided. The majority of the emergency response and safe handling information is provided through the appropriate safety training offered by Environmental Health and Safety (EHS), for example Bloodborne Pathogens training provides emergency response and safe handling information for human specimens, and Laboratory Chemical Safety Training provides the same information for handling chemicals.

*This guide is not a training document and is for use by trained individuals only. Training is available online at* [http://www.yale.edu/ehs/hazmatship.htm](http://www.yale.edu/ehs/hazmatship.htm)

Before sending any hazardous material (biological, chemical, or radioactive) a “Research Materials Shipping Request” form must be submitted online to EHS. If you have any question please contact EHS at 785-3550 or via email to ehshazmat@yale.edu.

### Section 1: Classification of Biological Materials

**Infectious Substances** are materials that are known to or reasonably expected to contain a pathogen. Current regulations apply a ranking scheme to infectious substances based on the probability of causing harm to a person or animal. The ranking scheme is as follows:

<table>
<thead>
<tr>
<th>Category &amp; UN #</th>
<th>Potential for Harm</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>B UN 3373</td>
<td>Moderate</td>
<td>Biological substances, such as diagnostic or clinical specimens from humans or animals that are known to harbor a pathogen or have a high probability of containing a pathogen. Biological substances containing or having a high probability of containing a Risk Group 4/BSL-4 agent or a Select Agent MUST be shipped as an Infectious Substance, Category A.</td>
</tr>
<tr>
<td>Exempt Human or Animal Specimen No UN#</td>
<td>Low</td>
<td>Biological substances that are not known to harbor a pathogen or have lower probability of containing a pathogen. Most of the general human and animal specimens in research and diagnostic facilities will fall in this category</td>
</tr>
</tbody>
</table>

**Biological Substance, Category B** – an infectious substance that is not in a form generally capable of causing permanent disability of life-threatening or fatal disease in otherwise healthy humans or animals when exposure to it occurs. Category B Infectious Substances are assigned the identification number UN 3373.

**Example:** You have been asked to ship serum specimens from a research protocol that is involved in determining the prevalence of HIV and other bloodborne pathogens among IV drug users. To date, preliminary data show that roughly 45% of those sampled are positive for one of the 3 major bloodborne pathogens (HIV, HBV, or HCV).

**Ship as: Biological Substance, Category B**

**Technical shipping name:** UN 3373, Biological Substance, Category B

Rationale: You either know that these items are infected or have a very high probability of containing a human pathogen. However, as the samples are of clinical/diagnostic origin, they are not cultured or amplified. Therefore you may ship as a biological substance.
**Exempt Human or Animal Specimen** – human or animal sample (including, but not limited to, secreta, excreta, blood and its components, tissue and tissue fluids, and body parts) being transported for routine testing not related to the diagnosis of an infectious disease, such as for drug/alcohol testing, cholesterol testing, blood glucose level testing, prostate specific antibody testing, testing to monitor kidney or liver function, or pregnancy testing, or for tests for diagnosis of non-infectious diseases, such as cancer biopsies, and for which there is low probability the sample is infectious.

**Example:** You are conducting a research project investigating the role of elevated cholesterol in heart disease. You are required to ship samples collected in the field here in CT to a testing lab in Indiana for analysis. You will be collecting 10 ml of blood from each test subject.

**Ship as:** Exempt Human Specimen

**Technical shipping name:** Exempt Human Specimen

Rationale: You are not shipping known infectious materials and although the material is of human origin, you also don’t have any reason to regard these as having a higher than normal probability of containing an infectious agent. The only way this classification would change is if your study had background pathogen test results on the patient. If you knew that a particular patient had HIV, HBV or some other pathogen, you would be required to ship this as an infectious substance, either Category B or Category A as appropriate.

Proper packaging and training are required before shipping exempt human or animal specimens.

For additional assistance classifying your material please see the flow chart on the next page.
Classification Flow Chart

Material to be shipped (Substance for Classification)

Have any pathogens been neutralized/inactivated?
Is it known **not** to contain infectious substances?
Are all microorganisms present non-pathogenic for humans and/or animals?
Is it a dried blood spot/fecal occult blood test?
Is it an environmental sample, e.g. food or water that is not considered to pose a significant health risk?
Is it for transplant or transfusion?

No

Does it meet the definition of a Infectious Substance, Category A?
Is it a cultured or amplified human pathogen?

Yes to any

Is it a patient specimen for which there is only a minimal likelihood that pathogens are present?

No

UN 2814 Infectious substance, affecting humans; or UN 2900 infectious substance, affecting animals

Training Required

Infectious Substance, Category A Training

Yes

UN 373 Biological substance, category B

UN 373 Biological substance, category B

Training Required

Category B and Exempt Human or Animal Specimen Training

Note: Requirement may also be fulfilled by taking the Infectious Substance, Category A Training

Subject to “Exempt Human Specimen” or “Exempt Animal Specimen” provisions

Not subject to the provisions of the DGR* unless meeting the criteria of another class or division of the DGR, i.e. dry ice.

* DGR = Dangerous goods regulations issued by the US Department of Transportation (DOT) and/or the International Air Transport Association (IATA)

This training does not fulfill the requirements to ship Infectious Substance, Category A material
Section 2: Packaging Requirements for Regulated Biological Materials

Biological Substance, Category B

The figure below shows the generalized "triple" (leakproof primary receptacle, leakproof secondary packaging, and durable outer packaging) packaging required for shipping a Biological Substance, Category B. The entire package must be capable of passing a series of 4’ drop tests as specified by U.S. DOT and IATA; documentation is required. Approved packaging is available in the Stockrooms or from the vendors listed in Appendix A. This packaging requires the "UN3373" label on the outside of the package.

Packaging and Labeling for a Biological Substance, Category B at ambient temperature.
Specifications of Biological Substance, Category B packaging includes:

- Leak proof primary container for liquids, siftproof for solids
- For liquids, absorbent material placed between the primary receptacle and secondary packaging (enough absorbent to contain the entire contents of the primary receptacles)
- Cushioning in between primary receptacles.
- For air shipments:
  - Liquids: primary receptacles may not exceed 1 L and each package may not exceed 4 L
  - Solids: primary receptacles can not exceed the outer packaging limit of 4 Kg.
- For shipments of liquid by air, the primary or secondary container must be capable of withstanding a pressure of 95 kPa (13.8 psi) and temperatures between (-40 F to 130 F). Please note that plastic bags can be used as secondary containers for liquids, but they must be of sufficient strength to pass the 95 kPa pressure test.
- Secondary packaging secured in rigid outer packaging (at least 4 inches in width).
- A list of contents in between the secondary and outer rigid shipping container.
- The packaging must be capable of passing the drop tests specified by the DOT/IATA from a height of 4 feet, without leaking its contents.
- The name and phone number of a “Responsible Person” must be placed on the outer container. This is the phone number of a person who can be reached during normal business hours (8:30 AM – 5:00 PM) to answer questions about the package.
- The UN 3373 Biological Substance, Category B Label (which labels the package and includes the technical name for the shipment). Refer to Section 3 (Markings and Labels) for a description of the UN 3373 label.
- Orientation arrows on either side of the package must be utilized if the net quantity of liquid Category B Biological Substances is > 50 ml.
- If refrigerants such as Dry Ice are utilized, please refer to Section 3 (Markings and Labels) and Section 8 (Refrigerants).

The entire package must be capable of passing a series of 4’ drop tests as specified by U.S. DOT and IATA; documentation is required. Approved packaging is available in the Stockrooms or from the vendors listed in Appendix A.

Specifications of Exempt Human (and Animal) Specimen Packaging

The following criteria are a combination of U.S. DOT, IATA, and the U.S. Postal Service requirements for the shipment and transport of Exempt Human Specimens.

- A leak proof primary container, with sufficient cushioning and absorbent material to surround each primary container that contains liquid. The cushioning will prevent individual containers from damaging each other.
- A leak proof secondary container to house the primary containers with enough absorbent inside this container to absorb the entire liquid contents of the package if all were released. Sealed 50 ml conical plastic tubes, sealed plastic bags and other sealed plastic containers are examples of suitable plastic containers that are probably present within your research or diagnostic clinical laboratory for use with Exempt shipments. The secondary container cannot serve as the outer shipping container for these specimens.
- The universal biohazard symbol must be placed on the outside of the secondary container. An orange biohazard sticker can be affixed to the secondary container, or a bag that is pre-labeled with the universal biohazard symbol.
• The secondary container must fit snugly inside the outer rigid shipping container to prevent excessive movement during shipment, which could damage the primary containers.

• The outer rigid shipping container can be a fiberboard or plastic box. The outside of the container must be labeled with an “EXEMPT HUMAN SPECIMEN” or an “EXEMPT ANIMAL SPECIMEN” label. Please refer to Section 3 (Markings and Labels) for additional information on Exempt Specimens. The Exempt Specimen Labels are required by IATA. DOT does not require the exterior label, but the Exempt Specimen label can be used. The U.S. Postal Service will accept either the Exempt Specimen label or the universal biohazard label. The OSHA Bloodborne Pathogens Standard does require the universal biohazard label on all containers of human blood or other potentially infectious materials, but this label is not required if one of the three shipping labels are affixed (Class 6.2 Infectious Substances label, UN 3373 Category B Biological Substances Label, or the EXEMPT HUMAN SPECIMEN label).

There are no test specifications for the EXEMPT HUMAN (OR ANIMAL) SPECIMEN packaging. This indicates that the shipper can assemble materials to make a packaging that will comply with the requirements outlined above. However, EHS recommends that the complete packaging created for Exempt shipments be able to pass a basic 4 foot drop test performed by the Shipper. For example, if the sealed Exempt Human Specimen package were to be dropped from shoulder height to a solid floor, the primary container would not break or leak.
Section 3: Markings and Labels

All packages of hazardous materials share basic markings, such as the name, address and contact information of the shipper (consignor), recipient (consignee) and the name and phone number of the responsible person. In addition to these mailing markings, hazardous materials packages will be marked with proper shipping name for the hazard. Orientation arrows are required on two opposite vertical sides of packages of Biological Substance, Category B material that contain liquid in excess of 50ml. Arrows must point in the correct upright direction. The orientation arrows are black or red on white background or other suitable contrasting color.

<table>
<thead>
<tr>
<th>Shipping Label</th>
<th>Color(s)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="UN3373" /></td>
<td>Black letters on white</td>
<td>Biological Substance, Category B, UN 3373. For diagnostic and clinical specimens known to contain or that have a high probability of containing a human or animal pathogen.</td>
</tr>
<tr>
<td><img src="image" alt="Dry Ice" /></td>
<td>Black on white</td>
<td>Class 9 label. Use for shipments containing Dry Ice (Carbon Dioxide, Solid), UN 1845, with Net Quantity in kg.</td>
</tr>
<tr>
<td><img src="image" alt="Orientation Arrows" /></td>
<td>Red or black on white or contrasting color</td>
<td>Orientation arrows for packages of Biological Substance, Category B material containing liquids in excess of 50 ml. Placed on 2 opposite sides of the package.</td>
</tr>
</tbody>
</table>

Labels are affixed to any of the surfaces of the package other than the bottom. Labels must be near the proper shipping name and subsidiary labels must be placed next to each other. Example markings and labels for various hazardous materials packages containing biohazards are provided below.

Proper Labeling of an Exempt Human Specimen (or Exempt Animal Specimen) Package > 50 ml on Dry Ice
Proper Labeling of a Biological Substance, Category B (diagnostic/clinical specimen known to harbor, or having a high probability of harboring an infectious agent) Package < 50 ml

Proper Labeling of a Biological Substance, Category B (diagnostic/clinical specimen known to harbor, or having a high probability of harboring, an infectious agent) Package > 50 ml on Dry Ice
Section 4: Refrigerants (Dry Ice and Liquid Nitrogen)

Dry Ice is a hazardous material regulated by both the US Department of Transportation (DOT) and the International Air Transport Association (IATA). Dry Ice is classified as a Class 9, miscellaneous hazard, and is assigned UN 1845.

Three important safety factors to keep in mind when dealing with dry ice are: 1) it is a cryogen and its cold temperatures can cause frostbite and burns upon contact with unprotected skin; 2) it is a simple asphyxiant and can create a suffocation hazard by the displacement of oxygen; and 3) as it sublimates from a solid directly to a gas, the expansion of molecules can create a very pressurized state if placed within a sealed container. To mitigate these risks, please follow the following simple safety guidelines when working with or using dry ice.

- Wear insulated gloves whenever handling dry ice; never handle dry ice with ungloved hands.
- Store dry ice in a well ventilated area (large quantities of dry ice in an unventilated room can create an oxygen deficiency, i.e. hundreds of kg of dry ice in a large ice chest or a large dry ice chest in a small unventilated closet). Please contact EHS at 785-3550 to have the oxygen levels evaluated if you are storing very large quantities of dry ice.
- Never place dry ice inside a sealed transport container (i.e. leak proof secondary container). Dry ice must be placed within an outer shipping container or storage container that will allow venting or release of CO2 gas to avoid pressurization. Sealing dry ice within a leak proof container can result in a bursting or exploding container, which can release its contents and/or create a serious physical hazard.

When shipping dry ice, use a vented container of sufficient strength to hold the amount of dry ice needed to preserve your shipment. The outside of the packages must contain the following labels:

![UN 1845 Label](image)

The net quantity of dry ice within the shipment must also be included on the UN 1845 dry ice label in kg. The maximum allowable net quantity of dry ice allowed per package is 200 kg. This is also the maximum quantity of dry ice allowed in the cargo hold of the aircraft.

A Shippers Declaration form is not required for the shipment of dry ice. However, if dry ice is shipped with a hazard requiring a shippers declaration form, it shall be included on the form as a subsidiary hazard following the major hazards.

If transporting Dry Ice by air, include the following information on the air waybill under the “Nature and Quantity of Dangerous Goods” section:

- Proper shipping name (Dry Ice or Carbon Dioxide, solid)
- UN 1845
- The number of packages; and
- The net quantity of dry ice in each package (with the net weight of dry ice marked on the exterior of the package).
As dry ice sublimes, use containers that have stabilization slots for secondary containers to prevent them from moving during the shipment. You may also secure your samples within the outer box by making stabilizers out of cardboard or Styrofoam to help keep your samples from moving after the dry ice sublimes.

Sample FedEx Airbill. Highlighted area properly documents 1 box containing 6 kg of dry ice.

Sample Airborne Express Airbill. Highlighted area shows format required for 1 box containing 5 kg of dry ice.
LIQUID NITROGEN

Liquid nitrogen is also a cryogen that presents significant risk of frost bite and burns. Extensive tissue damage can result from exposure to liquid nitrogen. It is also a simple asphyxiant, which could create a suffocation risk if enough material were spilled or released in a poorly ventilated or confined area by displacing oxygen. At low oxygen concentrations, unconsciousness and death may occur in seconds without warning.

- Always wear a face shield over safety glasses, lab coat, and insulated gloves designed for handling liquid nitrogen.
- Wear long sleeved shirts, trousers without cuffs, and sensible solid cover shoes when handling liquid nitrogen.
- Never store or pour liquid nitrogen in a poorly ventilated or confined space.
- Never allow any unprotected part of the body to come in contact with un-insulated equipment or pipes that contain liquid nitrogen or other cryogenic liquids.
- It is normal for liquid nitrogen containers to periodically vent product to release pressure. Never plug, remove, or tamper with any pressure relief devices.
- If unprotected skin is ever in contact with liquid nitrogen, immediately soak the affected area in warm water (but not greater than 105 degrees F) and immediately summon emergency assistance.

The U.S. DOT and IATA both regulate liquid nitrogen as a hazardous material. Shipment and transport of liquid nitrogen require the use of a Shipper’s Declaration form.

Please Note: The Biological Substance, Category B and Exempt Human and Animal Specimens training does not complete the training requirements for completing the Shipper’s Declaration. EHS therefore requires the use of a dry shipper for those individuals trained to that level. EHS strongly recommends the use of Dry Shippers in all cases.

Dry Nitrogen Shippers:

Please note that “dry” nitrogen shippers, which maintain the temperature of liquid nitrogen after being charged with liquid nitrogen then emptied before shipment, do not qualify as hazardous materials and are not subject to the shipping regulations if they don’t contain hazardous materials. Researchers are encouraged to pursue the use of dry shippers to reduce their regulatory burden where possible. The liquid nitrogen must be fully absorbed within the container in a porous material, the container must not allow the build-up of pressure, and won’t allow the release of liquid nitrogen in any orientation. If a dry-nitrogen shipper is purchased, follow the manufacturer’s written instructions for its use and double check that there is no free liquid nitrogen inside the container prior to shipment.
Section 5: Materials of Trade Exemption

Category B Infectious Substances and Exempt Human/Animal Specimens transported from one Yale “owned” location to another Yale “owned” location may be transported under a Material of Trade Exemption if:

- Transport is by a private motor carrier in direct support of a principle business that is other than transportation by motor vehicle [i.e. research]
- A combination packaging is used as outlined in this training
- If one or more inner packagings are used, the inner packagings may not contain more than 0.5 Kg (1.1 lbs) or 0.5 L (17 ounces) and the outer package must contain not more than 4 Kg (8.8 Lbs) or 4 L (1 gallon)
- If a single inner packaging is used it may not contain more than 16 Kg (35.2 Lbs) or 16 L (4.2 gallons) in a single outer packaging
- The driver must be informed of the presence of hazardous material and must be informed of the requirements of the Materials of Trade exemption
Appendix 1: Vendors for Shipping Packaging and Labels

This list is not all-inclusive; there are other vendors for UN approved and diagnostic packaging. Shipping labels and declaration forms can also be purchased through any of these vendors. Please be sure to order the appropriate packaging if shipping on dry ice.

<table>
<thead>
<tr>
<th>Vendor Name</th>
<th>Address</th>
<th>Phone Numbers</th>
<th>Fax Numbers</th>
<th>Website Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air Sea Atlanta</td>
<td>1234 Logan Circle</td>
<td>Ph: 404-351-8600</td>
<td>Fax: 404-364-4005</td>
<td><a href="http://www.airseaatlanta.com">http://www.airseaatlanta.com</a></td>
</tr>
<tr>
<td>Air Sea Containers, Inc.</td>
<td>2749 NW 82nd Avenue</td>
<td>Ph: 888-272-9883</td>
<td>Fax: 305-599-1668</td>
<td><a href="http://www.airseacontainers.com">http://www.airseacontainers.com</a></td>
</tr>
<tr>
<td>All-Pak, Inc.</td>
<td>Corporate One West</td>
<td>Ph: 1-800-245-2283</td>
<td>Fax: 412-257-3001</td>
<td><a href="http://www.all-pak.com">http://www.all-pak.com</a></td>
</tr>
<tr>
<td>Air Sea Containers, Inc.</td>
<td>2749 NW 82nd Avenue</td>
<td>Ph: 888-272-9883</td>
<td>Fax: 305-599-1668</td>
<td><a href="http://www.airseacontainers.com">http://www.airseacontainers.com</a></td>
</tr>
<tr>
<td>DG Supplies, Inc.</td>
<td>4 Corporate Drive</td>
<td>Ph: 1-800-347.7879</td>
<td>Fax: 609.860.0096</td>
<td><a href="http://www.dgsupplies.com">http://www.dgsupplies.com</a></td>
</tr>
<tr>
<td>Inmark, Inc.</td>
<td>675 Hartman Road - Suite 100</td>
<td>Ph: 770-373-3300</td>
<td>Fax: 770-373-3301</td>
<td><a href="http://www.inmarkine.com">http://www.inmarkine.com</a></td>
</tr>
</tbody>
</table>

Note: Some of the suppliers listed above also provide shipping labels and primary receptacle containers as separate products. Contact the specific vendor to see if they offer the desired products.

Some Suppliers of Dangerous Goods Forms, Documents and Labels

<table>
<thead>
<tr>
<th>Vendor Name</th>
<th>Address</th>
<th>Phone Numbers</th>
<th>Fax Numbers</th>
<th>Website Address</th>
</tr>
</thead>
</table>
IATA Dry Ice Acceptance Checklist

2009

ACCEPTANCE CHECKLIST FOR DRY ICE (Carbon Dioxide, solid)
(For use when a Shipper’s Declaration for Dangerous Goods is not required)

A checklist is required for all shipments of dangerous goods (9.1.4) to enable proper acceptance checks to be made. The following example checklist is provided to assist shippers and carriers with the acceptance of dry ice when packaged on its own or with non-dangerous goods.

Is the following information correct for each entry? YES NO N/A

The Air Waybill contains the following information in the “Nature and Quantity of Goods” box

1. The UN Number “1845”, preceded by the prefix “UN” .................................................................
2. The words “Carbon dioxide, solid” or “Dry ice” ............................................................................
3. The Class number “9” ......................................................................................................................
4. The number of packages of dry ice ...............................................................................................  
5. The net quantity of dry ice in kilograms .......................................................................................  

Note: The packing group “III” and packing instruction “904” are optional.

Quantity

6. The quantity of dry ice per package is 200 kg or less......................................................................

Packages and Overpacks

7. The number of packages containing dry ice delivered as shown on the Air Waybill .......................
8. Packages are free from damage and in a proper condition for carriage ..........................................
9. The packaging conforms with Packing Instruction 904 and the package is vented to permit the release of gas ...................................................................................................................

Markings (Only use this section when accepting individual packages containing dry ice)

10. The words “Carbon dioxide, solid” or “Dry ice” ............................................................................
11. The UN number “1845” preceded by prefix “UN” ........................................................................
12. Full name and address of the shipper and consignee ....................................................................
13. The net quantity of dry ice within each package .............................................................................

Labels

14. Class 9 label affixed ........................................................................................................................
15. Irrelevant marks and labels removed .............................................................................................

Checked by: _______________________________  
Place: ___________________  Signature: ____________________
Date: ________________  Time: __________________________

*IF ANY BOX IS CHECKED “NO”, DO NOT SEND THE SHIPMENT. CORRECT ISSUE.