

Interstate Shipment of Etiologic Agents

Background and References

For information on the transportation of etiologic agents (infectious substances) and related materials, such as specimens for testing, please refer to regulations issued in the Department of Transportation (DOT) final rule “Hazardous Materials: Infectious Substances; Harmonization with the United Nations Recommendations” (49 CFR Parts 171–178; June 2, 2006). The rule revises the definition of an infectious substance from Risk Groups 1–4 to a two-category system adopted by the World Health Organization, wherein Category A is for high-risk substances and Category B is for all other substances. The result is a set of standards that are easier to use and impose a high level of safety appropriate to the degree of risk and conditions of transport. The rule also revises packaging, exceptions, and other shipping requirements for infectious substances to make them more consistent with requirements in international standards.

For more information, please contact the DOT Hazardous Materials Information Center at 1-800-467-4922 from 9:00 a.m.–5:00 p.m. Eastern time, Monday–Friday, except federal holidays. For information on specific regulations, refer to: <http://www.dot.gov/regulations.html>.

A DOT brochure on transporting infectious substances is available at: http://hazmat.dot.gov/training/Transporting_Infectious_Substances_Safely.pdf.

For information on international air transport (International Air Transport Association), please see <http://www.iata.org>. Specific information on dangerous goods cargo is at: http://www.iata.org/whatwedo/cargo/dangerous_goods/index.htm.

For information on the U.S. Department of Agriculture (USDA) Select Agent programs, please refer to: http://www.aphis.usda.gov/programs/ag_selectagent/index.html.

The Shipper’s Declaration—Manual Completion worksheet can be found at: http://www.iata.org/NR/rdonlyres/5A231396-76AD-47D7-BD93-B9501B6D25BA/0/DGD_ColumnFormat_F.pdf.

Packaging and Shipping of Biomedical Material

The regulations that describe requirements for the proper packaging and shipping of biomedical material are contained in the following parts of the DOT final rule “Hazardous Materials: Infectious Substances; Harmonization with the United Nations Recommendations” (49 CFR)

- Part 171 General Information, Regulations, and Definition
- Part 172 Hazardous Materials [HM] Table, Special Provisions, HM Communications, Emergency Response Information, and Training Requirements
- Part 173 Shippers—General Requirements for Shipments and Packaging

- Part 174 Carriage by Rail
- Part 175 Carriage by Aircraft
- Part 176 Carriage by Vessel
- Part 177 Carriage by Public Highway
- Part 178 Specifications for Packagings

It is the intent of the regulation that biomedical material, which may contain etiologic agents, will be packaged and shipped in such a way as to ensure an acceptable level of safety and facilitate domestic and international transportation. Following is a list of applicable definitions and instructions extracted from the regulations.

Definitions (49 CFR 173.134)

Biomedical materials that are known to contain, or could contain, etiologic agents belong to Class 6, Division 6.2, and are categorized into two groups: **Biological Substance, Category A and Biological Substance, Category B**. Category A infectious substances pose a higher degree of risk than Category B infectious substances.

A **Category A** infectious substance is one that is transported in a form capable of causing permanent disability or life-threatening or fatal disease to otherwise healthy humans or animals when exposure to it occurs. An exposure occurs when an infectious substance is released outside of its protective packaging, resulting in physical contact with humans or animals. Examples are the Ebola, Junin and Nipah viruses. These substances are assigned the identification number of UN 2814, UN 2900, as appropriate.

A **Category B** infectious substance is one that does not meet the criteria for inclusion in Category A. A Category B infectious substance is not in a form generally capable of causing permanent disability or life-threatening or fatal disease to humans or animals when exposure to it occurs. Specimens previously termed “diagnostic” and “clinical” belong to Category B substances. These substances are assigned the identification number UN 3373.

Biological product: a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, ... applicable to the prevention, treatment, or cure of a disease or condition of human beings or animals.

Culture: an infectious substance containing a pathogen that is intentionally propagated. Culture does not include a human or animal “patient specimen” as defined below.

Etiologic agent: (See “Infectious substance”)

Hazardous material: a substance or material that the Secretary of Transportation has determined is capable of posing an unreasonable risk to health, safety, and property when transported in commerce, and has designated as hazardous under section 5103 of Federal hazardous materials transportation law (49 U.S.C. 5103). The term includes

hazardous substances, hazardous wastes, marine pollutants, elevated temperature materials, materials designated as hazardous in the Hazardous Materials Table (see 49 CFR 172.101), and materials that meet the defining criteria for hazard classes and divisions in part 173 of subchapter C of this chapter.

Infectious substance (etiologic agent): a material known or reasonably expected to contain a pathogen. A pathogen is a microorganism (including bacteria, viruses, rickettsiae, parasites, fungi) or other agent, such as a proteinaceous infectious particle (prion), that can cause disease in humans or animals. An infectious substance must be assigned a UN identification number, as appropriate to either category A or category B.

Patient specimen: human or animal material collected directly from humans or animals and transported for research, diagnosis, investigational activities, or disease treatment or prevention. Patient specimen includes excreta, secretions, blood and its components, tissue and tissue swabs, body parts, and specimens in transport media (e.g., transwabs, culture media, and blood culture bottles).

Packaging of Etiologic Agents, Biological Products, and Diagnostic Specimens (49 CFR 173.196 and 173.199)

Packaging for hazardous materials is required to be tested and to meet the package performance criteria established by the shipping regulations: the packaging must be able to contain the contents of the package under extreme circumstances, and the contents cannot escape into the environment, possibly injuring people or equipment such as aircraft. Packaging that passes the rigorous package performance testing requirements is considered to be UN Certified for that specific hazard. Additionally, a Test Report is required to be available to the users of the packaging. UN Certified 6.2 Infectious Substances Packaging, as marked, has been tested by a competent testing authority and meets the specifications as stated in the shipping regulations for infectious substances.

Category A Infectious Substances

A Category A infectious substance must be packaged in a triple packaging consisting of 1) a primary receptacle, 2) a secondary packaging, and 3) a rigid outer packaging.

- Primary receptacles must be watertight. The primary receptacle or secondary packaging used for infectious substances must be capable of withstanding, without leakage, an internal pressure producing a pressure differential of not less than 95 kPa (0.95 bar, 14 psi). The primary receptacle or secondary packaging must be capable of withstanding without leakage temperatures in the range of -40°C to +55°C (-40°F to +131°F).
- Secondary packaging must be watertight. If multiple fragile primary receptacles are placed in a single secondary packaging, they must be either wrapped individually or separated to prevent contact between them. The primary receptacle or secondary packaging used for infectious

substances must be capable of withstanding, without leakage, an internal pressure producing a pressure differential of not less than 95 kPa (0.95 bar, 14 psi). The primary receptacle or secondary packaging must be capable of withstanding without leakage temperatures in the range of -40°C to +55°C (-40°F to +131°F).

- A rigid outer packaging must be of adequate strength for its capacity, mass and intended use. The outer packaging must measure not less than 100 mm (3.9 inches) at its smallest overall external dimension.

For a **liquid infectious substance**, an absorbent material should be placed between the primary receptacle and the secondary packaging. The absorbent material must be sufficient to absorb the entire contents of all primary receptacles. An itemized list of contents should be enclosed between the secondary packaging and the outer packaging.

A “Shipper’s Declaration of Goods” (DGD) is required for each shipment of Category A substances.

Category A infectious substances packaging must meet the test standards in accordance with 49 CFR 178.609.

Category A infectious substances must be packaged according to the following requirements, depending on the physical state and other characteristics of the material.

Infectious substances shipped at ambient temperatures or higher:

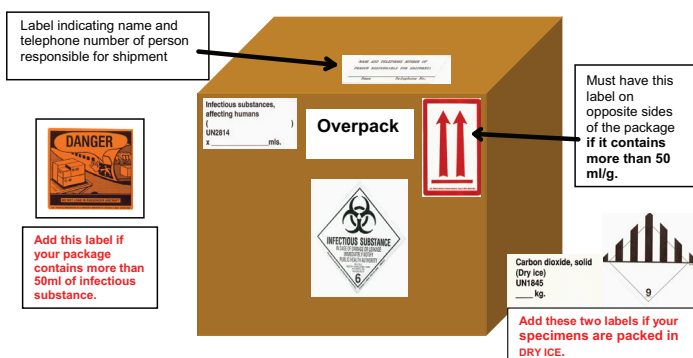
- Primary receptacles must be made of glass, metal, or plastic.
- Positive means of ensuring a leakproof seal must be provided, such as heat seal, skirted stopper, or metal crimp seal. If screw caps are used, they must be secured by positive means, such as with adhesive tape, paraffin sealing tape, or manufactured locking closure.
- Lyophilized substances may also be transported in primary receptacles that are flame-sealed with glass ampoules or rubber-stoppered glass vials fitted with metal seals.

Infectious substances shipped refrigerated or frozen (ice, pre-frozen packs dry ice):

- Ice, dry ice, or other refrigerant must be placed around the secondary packaging or in an overpack with one or more complete packages marked in accordance with § 178.503 of this subchapter.
- Interior supports must be provided to secure the secondary packaging in the original position after the ice or dry ice has dissipated. If ice is used, the outer packaging or overpack must be leakproof.
- If dry ice is used, the outer packaging or overpack must permit the release of carbon dioxide gas.
- The primary receptacle and the secondary packaging must maintain their integrity at the temperature of the refrigerant used, as well as the temperatures and pressures of transport by aircraft to which they could be subjected if refrigeration were lost.

Infectious substances shipped in liquid nitrogen:

- The primary receptacle and the secondary packaging must maintain their integrity at the temperature of the liquid nitrogen as well as the temperatures and pressures of transport by aircraft to which they could be subjected if refrigeration were lost.
- Refrigerated liquid nitrogen packagings must be metal vacuum insulated vessels or flasks vented to the atmosphere to prevent any increase in pressure within the packaging. The use of safety relief valves, check valves, frangible discs, or similar devices in the vent lines is prohibited.
- Fill and discharge openings must be protected against the entry of foreign materials that might cause an increase in the internal pressure.
- The packaging must be designed to prevent the release of any refrigerated liquid nitrogen irrespective of the packaging orientation.



UN Certified 6.2 Substances packaging; outer package labeling for Category A substances

Live animals may not be used to transport infectious substances unless such substances cannot be sent by any other means. An animal containing or contaminated with an infectious substance must be transported under terms and conditions approved by the Associate Administrator for Hazardous Materials Safety.

Category B Infectious Substances

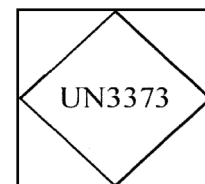
A Category B infectious substance must be packaged in a triple packaging consisting of 1) a primary receptacle, 2) a secondary packaging, and 3) a rigid outer packaging.

- Primary receptacles must be packed in secondary packaging in such a way that, under normal conditions of transport, they cannot break, be punctured, or leak their contents into the secondary packaging.
- Secondary packagings must be secured in rigid outer packagings with suitable cushioning material such that any leakage of the contents will not impair the protective properties of the cushioning material or the outer packaging.
- The completed packaging must be designed, constructed, maintained, filled, its contents limited, and closed so that under conditions normally encountered in transportation, including removal from a pallet or overpack for subsequent

handling, there will be no release of hazardous material into the environment.

Package effectiveness must not be substantially reduced for minimum and maximum temperatures, changes in humidity and pressure, and shocks, loadings and vibrations normally encountered during transportation. The packaging must be capable of successfully passing the drop tests [49 CFR 178.609(d) and (h)] at a drop height of at least 1.2 meters (3.9 feet).

This mark must be displayed on the outer packaging on a background of contrasting color. The width of the line must be at least 2 mm (0.08 inches), and the letters and numbers must be at least 6 mm (0.24 inches) high. The size of the mark must be such that no side of the diamond is less than 50 mm (1.97 inches) in length.



The proper shipping name "Biological substances, Category B" must be marked on the outer packaging adjacent to the diamond-shaped mark in letters that are at least 6 mm (0.24 inches) high.

When packages are placed in an overpack, the package markings must be either clearly visible or reproduced on the outside of the overpack. The name and telephone number of a person who is either knowledgeable about the material being shipped and has comprehensive emergency response and incident mitigation information for the material, or has immediate access to a person who possesses such knowledge and information, must be included on a written document (such as an air waybill or bill of lading) or on the outer packaging.

For transportation by aircraft, each package, overpack, pallet, or unit load device containing a Category B infectious substance must be inspected for leakage when it is unloaded from the aircraft. If evidence of leakage is found, the cargo compartment in which the package, overpack, pallet, or unit load device was transported must be disinfected. Disinfection may be by any means that will make the material released ineffective at transmitting disease.

A packaging containing inner packagings of Category B infectious substances may not contain other hazardous materials except refrigerants, such as dry ice or liquid nitrogen; anticoagulants used to stabilize blood or plasma; or small quantities of Class 3, Class 8, Class 9, or other materials in Packing Groups II and III used to stabilize or prevent degradation of the sample, provided the quantity of such materials does not exceed 30 mL (1 ounce) or 30 g (1 ounce) in each inner packaging.

Clear instructions on filling and closing a packaging used to transport a Category B infectious substance must be provided by the packaging manufacturer and subsequent distributors to the consignor or person who prepares the package to enable the package to be correctly prepared for transport. A copy or electronic image of these instructions must be retained by the manufacturer and subsequent distributors for at least 1 year

from the date of issuance, and be made available for inspection by a federal or state government representative upon request. Packagings must be filled and closed in accordance with the information provided by the packaging manufacturer or subsequent distributor.

Each person who offers or transports a Category B infectious substance under the provisions of this regulation must know about the requirements of same.

Liquid Category B infectious substances must be packaged in conformance with the following provisions:

- The primary receptacle must be leakproof.
- Absorbent material must be placed between the primary receptacle and secondary packaging. If several fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them. The absorbent material must be of sufficient quantity to absorb the entire contents of the primary receptacles and not compromise the integrity of the cushioning material or the outer packaging.
- The secondary packaging must be leakproof.
- For shipments by aircraft, the primary receptacle or the secondary packaging must be capable of withstanding without leakage an internal pressure producing a pressure differential of not less than 95 kPa (0.95 bar, 14 psi).
- For shipments by aircraft, the maximum quantity contained in each primary receptacle, including any material used to stabilize or prevent degradation of the sample, may not exceed 1 L (34 ounces), and the maximum quantity contained in each outer packaging, including any material used to stabilize or prevent degradation of the samples, may not exceed 4 L (1 gallon). The outer packaging limitation does not include ice, dry ice, or liquid nitrogen when used to maintain the integrity of the material.

Solid Category B infectious substances must be packaged in a triple packaging, consisting of 1) a primary receptacle, 2) secondary packaging, 3) and outer packaging, conforming to the following provisions:

- The primary receptacle must be siftproof.
- If several fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them.
- The secondary packaging must be siftproof.
- If residual liquid might be present in the primary receptacle during transportation, the material must be transported in accordance with requirements in paragraph (b) of 49 CFR 173.196. A solid material that may become liquid during transportation must be transported as described in “Liquid Category B substances” above.
- For shipment by aircraft, the outer packaging may not contain more than 4 kg (8.8 pounds), including any material used to stabilize or prevent degradation of the samples. (Exception: packages containing body parts, organs, or whole bodies) The outer packaging limitation does not

include ice, dry ice, or liquid nitrogen when used to maintain the integrity of the material.

Refrigerated or frozen specimens (ice, dry ice, and liquid nitrogen):

- Ice or dry ice must be placed outside the secondary packaging or in an overpack. Interior supports must be provided to secure the secondary packagings in the original position after the ice or dry ice has dissipated.
- If ice is used, the outside packaging must be leakproof or must have a leakproof liner.
- If dry ice is used, the outside packaging must permit the release of carbon dioxide gas.
- The primary receptacle and secondary packaging must maintain their integrity at the temperature of the refrigerant used, as well as the temperatures and pressures of airport transport they would be subjected to if refrigeration were lost; sufficient absorbent material must be provided to absorb all liquid, including melted ice.
- The package should be marked “Carbon Dioxide, solid” or “Dry Ice” and should have an indication that the material being refrigerated is used for diagnostic treatment purposes (e.g., frozen medical specimens).