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Safe Passage: Navigating Regulations and Best Practices in Packaging and Transporting Biological Samples

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The transportation of biological materials, including infectious substances, is governed by regularly updated regulations at international, regional, or national levels. These rules are based on the Recommendations for the Transport of Dangerous Goods established by the UN Subcommittee of Experts. They cover various transportation modes such as air, rail, road, sea, and international mail (Gray and Snyder, 2006).

It is essential for all personnel involved in packaging, labeling, and shipping biological materials to have the necessary training, certification, competence, and understanding of applicable regulations. Biological materials are transported by experienced logistics service providers knowledgeable in shipping and transportation procedures to ensure efficient and dependable delivery.

The sender (also known as the shipper or consignor) bears the responsibility of furnishing the necessary documentation, such as certifications and permits, mandated by the national authorities of the exporting, transshipment, and importing countries. Additionally, it is incumbent upon the sender to ensure that the shipment adheres to all relevant regulations.

The Sender

Before shipping biological materials, the sender must:

1. Identify, classify, pack (including temperature control), ensure quantity limits, mark, and label the package.
2. Ensure accurate documentation for all biological materials slated for transport.
3. Complete and generate a Shipper's Declaration for Dangerous Goods (DGD) when necessary.
4. Verify that biological materials are permissible for transport.

Additionally, the sender is responsible for:

- ❖ Preparing essential documentation, including permits, dispatch, and shipping documents, as needed.
- ❖ Notifying the recipient well in advance of transportation arrangements and the expected arrival time.
- ❖ Providing the airway bill (AWB), the standard shipping document for air freight, which may be completed by the air carrier or freight forwarder.
- ❖ Making advance arrangements with the recipient, including investigating the need for import/export permits.
- ❖ Coordinating with the carrier to ensure:
- ➢ Acceptance of the shipment for appropriate transport.
- ➢ Undertaking the most direct routing, as appropriate (Snyder, 2002).

The Carrier/ Courier

The carrier must take the following steps

- Ensure appropriate routing, opting for the shortest or most secure route.
- Exercise precautions during transshipment, ensuring careful handling, expedited processing, and ongoing monitoring of substances in transit for safety and security reasons.

For air transport, the carrier is obligated by regulations to use an acceptance checklist, verifying compliance with:

- Marking and labeling requirements.
- Documentation requirements.

The carrier is also responsible for:

- Guiding the sender and assisting with necessary shipping documents, including instructions for completion and proper packaging.
- Aiding the sender in organizing the most suitable routing, confirming the routing, and, if feasible, offering ways to track the shipment.
- Maintaining and archiving documentation for both shipment and transport (Snyder, 2002).

The Recipient

The recipient is tasked with

- Acquiring the essential authorization(s) from national authorities for the material's importation.
- Supplying the sender with the necessary import permit(s), authorization letters, or other documents mandated by national authorities.
- Coordinating the most prompt and effective collection upon arrival.
- Acknowledging receipt to the sender (Snyder, 2002).

Classification and Categorization

When transporting biological materials, the sender must determine if the material qualifies as dangerous goods, also referred to as hazardous materials or HAZMAT. These substances have the potential to cause harm to humans, animals, the environment, or property, leading to their regulation by United Nations (UN) guidelines.

Dangerous goods are assigned a UN number and proper shipping name based on their classification. Transport regulations prescribe a packing instruction linked to the UN number and proper shipping name, guaranteeing that these goods are packaged to minimize hazards during transportation (Osei and Smith, 2022).

Table 1. Summary of classification, categorization, and packaging of infectious substances

Dangerous goods classifications	Categorization	Proper shipping name	UN number	Packaging instruction/ packaging requirements
Class 6, Division 6.2	Category A	Infectious substances, affecting humans	UN 2814	P620
		Infectious substances, affecting animals	UN 2900	
Class 6, Division 6.2	Category B	Biological substance, Category B	UN 3373	P650

Class 6, Division 6.2	Exempt human/animal specimens	Exempt human/animal specimens	N/A	Triple packaging
not subject to dangerous goods regulations	Biological materials not subject to dangerous goods regulations	N/A	N/A	N/A
Class 9	GMMOs and GMOs that are not classified as Category A or B infectious substances	Genetically modified microorganisms; Genetically modified organisms	UN 3245	P904 (ICAO/IATA PI 959), IBC99

If there is a likelihood that microorganisms within the biological materials can pose harm to humans or animals, they must be categorized as either Category A or B. The proper shipping name should be accompanied by the technical name (scientific name of the pathogen) within parentheses on the transport document, excluding the outer packaging.

In instances where the identity of the infectious substances for transport is unknown but is suspected to meet the criteria for Category A inclusion, the term "suspected category A infectious substance" must be indicated within parentheses following the proper shipping name on the transport document.

1. Category A: Category A substances are infectious materials that, when exposed to, can cause severe diseases or permanent disability in healthy humans or animals. They are assigned UN numbers 2814 or 2900 based on factors like medical history, signs, and local disease conditions.

Some organisms, like Bacillus anthracis, are Category A only in culture form. Medical waste with Category A substances is assigned UN 2814 or 2900, while solid medical waste from human or veterinary treatment may be designated UN 3549. Liquid waste or bio-research waste should not be assigned UN 3549 (Denys et.al., 2004).

2. Category B: Biological materials with pathogens not meeting the criteria for Category A (non-life-threatening to humans or animals) are categorized as Category B (UN 3373). Specimens with a high likelihood of pathogenic organisms, intended for disease diagnosis (e.g., confirmatory diagnosis, differential diagnosis), can be assigned to Category B. Medical or clinical waste with Category B infectious substances is designated UN 3291.

3. Exempt specimens: Animal specimens with minimal likelihood of containing pathogens can be transported as Exempt Specimens. This includes specimens from veterinary surveillance studies, export controls of healthy animals (e.g., certification of freedom from classical swine fever), or determination of immune status (post-vaccination). Exempt Specimens are not subject to dangerous goods regulations if transported in leak-proof packaging appropriately marked (Denys et.al., 2004).

4. Biological materials not subject to dangerous goods regulations: Biological materials exempt from dangerous goods regulations include those without infectious substances, containing non-pathogenic microorganisms, or where pathogens have been neutralized or inactivated. Additionally, environmental specimens posing no significant risk of infection, and dried blood spots collected on absorbent material, are exempt. These exemptions are contingent on factors like the medical history of animals, signs, source circumstances, and local disease conditions, unless they meet criteria for another class (such as Class 9).

5. Contaminated items: These listed below are also included in infectious substances in the international regulations on transport of dangerous goods.

Table 2. Summary of classification, categorization, and packaging of contaminated items with infectious substances

Dangerous goods classifications	Categorization	Proper shipping name	UN number	Packaging instruction/ packaging requirements
Class 6, Division 6.2	Category A	Medical* devices or equipment contaminated with or containing infectious substances in Category A	UN2814, UN2900 as appropriate	Must be marked "Used Medical Device" or "Used Medical Equipment"
Class 6, Division 6.2	Exemption when the condition is met	Medical* devices, medical equipment	N/A	IATA Dangerous Goods Regulations (DGR)
Class 6, Division 6.2	Category A	Medical* waste, Category A, affecting humans, solid; Medical waste, Category A, affecting animals only, solid	UN 3549	P622, LP622
Class 6, Division 6.2	Category A	Clinical waste, Unspecified, n.o.s.(not otherwise specified); (Bio) medical waste, n.o.s.; Regulated medical waste, n.o.s.	UN3291	P621 (PI622), IBC620, LP621

*Including Veterinary use.

Packaging

Principles: All biological materials must adhere to local, national, and international regulations during packaging and transportation to minimize risks to personnel, the environment, and vulnerable animal populations. Inadequate packaging may lead to delays or prevent critical laboratory analyses. Specimens should be packaged to maintain integrity, prevent leakage, and avoid cross-contamination. Transport requirements typically involve triple packaging: a primary receptacle, secondary packaging, and outer packaging, with at least one layer being rigid (Osei and Smith, 2022).

A primary receptacle: The primary receptacle, whether for liquids (leak-proof) or solids (sift-proof), should contain the specimen and be placed within the secondary packaging along with adequate absorbent material to manage any potential leaks. While glass is not prohibited, non-breakable materials are preferred. Primary receptacles should not include sharps, especially when using soft secondary or outer containers. Screw cap vials should be secured with tape, and flip-top vials should be avoided.

Secondary packaging: The secondary packaging, which should be durable and leak-proof, surrounds and safeguards the primary receptacle(s). This can be achieved with materials such

as sealed plastic bags, plastic containers, or screw-cap cans. Both the primary receptacle and secondary packaging must withstand internal pressures of 95 kPa without leakage, within a temperature range of -40°C to +55°C (-40°F to +130°F).

Outer packaging: Secondary packaging is placed in outer shipping packaging (e.g. sturdy insulated fiber board box) with suitable cushioning material. Outer packaging protects the contents from outside influences, such as physical damage, while in transit (Osei and Smith, 2022).

Category A: Category A samples are highly hazardous, requiring specialized packaging that adheres to strict regulations. This involves triple packaging and compliance with United Nations class 6.2 specifications, specifically Packing Instruction P620. Rigorous testing, including a 9-meter drop test, puncture test, pressure test, and stacking test, ensures compliance and safety. Packages are labeled to indicate contents, hazards, and packaging standards

Marking and labeling are as follows

i) The delivery address (consignee) and sender's details (the shipper), as well as 24/7 emergency contact details including named persons with telephone numbers to guarantee safe delivery.

ii) The proper shipping name and the UN number.

Proper shipping name	UN number
INFECTIOUS SUBSTANCE, AFFECTING HUMANS	UN2814
INFECTIOUS SUBSTANCE, AFFECTING ANIMALS only	UN2900

iii) The Infectious Substance label

iv) UN specification marking for P620 packaging (printed on the box).

v) Orientation label, Cargo only label, if required (depending on the Net Weight [Kg] of the infectious substance in a P620 box) (Denys *et.al.*, 2004)

For air transport:

1. The primary or secondary packaging must endure internal pressures of 95 kPa and temperatures from -40°C to +55°C without leakage.
2. Liquid infectious substances must not exceed 50 ml per P620 box for passenger aircraft cargo and 4 liters for cargo-only aircraft.
3. Solid infectious substances must not surpass 50 g per P620 box for passenger aircraft cargo and 4 kg for cargo-only aircraft, excluding animal parts, organs, and whole carcasses.
4. Triple packaging is mandatory using suitable systems.
5. The entire package must pass tests and adhere to Packing Instruction P620 (adapted from Denys et al., 2004).

Category B: Category B substances require packaging compliant with packing instruction P650. Government approval of the box is not necessary; thus UN specification marking is unnecessary.

Marking guidelines include:

- Packages must prominently display the delivery address and sender's details for accurate and timely delivery.
- Proper shipping name "BIOLOGICAL SUBSTANCE, CATEGORY B" must be labeled in letters at least 6 mm high, accompanied by the UN3373 mark in a diamond symbol, which must be visible on the outer packaging.

For air transport:

1. Primary or secondary packaging must withstand internal pressures of 95 kPa and temperatures from -40°C to +55°C without leakage.
2. Liquids must be contained in primary receptacles not exceeding 1 litre, and the outer packaging must not exceed 4 litres.
3. Solids must not exceed 4 kg in the outer packaging, excluding animal parts, organs, and whole carcasses (Denys et al., 2004).

Exempt specimens: Biological materials with minimal pathogen likelihood are exempt from regulations if packaged to prevent leakage and marked appropriately as "Exempt animal specimens." The triple packaging system remains mandatory.

Biological materials not subject to Dangerous Goods Regulations: Refers to materials without infectious substances, exempt from dangerous goods regulations (e.g., class 6.2) and packaging requirements, unless fitting other class criteria (e.g., class 9). Note: Some countries may have specific regulations for nucleic acid shipment.

Overpack: "Overpack" combines packages into one unit for a single shipper and destination. Required marks and labels, excluding UN specification marking on P620, must be repeated on the outermost overpack layer. All infectious substances, including Categories A and B, must be marked "overpack."

Cold chain transportation: Refrigerants stabilize specimens during transport. Ice, ice packs, or dry ice outside the secondary receptacle are permissible. Wet ice needs a leak-proof container. Dry ice can't be inside receptacles due to explosion risk; a specially designed insulated packaging, marked accordingly, is required. Secondary receptacles must be secured within the outer package, adhering to original orientation post-refrigerant dissipation. Liquid nitrogen usage follows relevant dangerous goods regulations (Division 2.2, UN 1977) (Kiepper et al., 2009; Lin et al., 2020).

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