26

Safe Dispatch and Transport of Biological Material

Vera Weihs and Christine Rohde

Summary

The correct transport of biological material is one of the major aspects of biolegislation. The awareness of this fact has only quite slowly come into being. The demands on the export, packaging, and shipping of biological material are manifold and the number of possible mistakes is endless. On the other hand, to be in conformity with all regulations is easy under the premises that a person with a sound knowledge of all the relevant regulations feels responsible for the shipment. This chapter describes which laws, regulations, and restrictions have to be respected before a biological substance can be released (*see* **Note 1**). Before a living microorganism is offered for dispatch, whether it is a transborder supply or supply within a country, it has to be made sure that the organism does not fall into wrong hands so that dispatch might be illegitimate. According to the International Air Transport Association Dangerous Goods Regulations (IATA DGR) ***(1)***, the sender of infectious substances has to be a trained person, as infectious substances are classified as dangerous goods in Class 6, Division 6.2. The regulations for shipping biological substances by postal mail are laid down by the Universal Postal Union (UPU). The transport of hazardous biological material—performed in compliance with these regulations—can be regarded as safe by using triple-packaging UN combination systems.

Key Words: Dispatch; transport; IATA Dangerous Goods Regulations; infectious substances; export; import; Universal Postal Union (UPU); WHO Risk Groups; EEC Dual Use Directive; triple packaging; Shipper's Declaration; EN 829; genetically modified organisms; diagnostic specimens.

1. Export and Import of Biological Material and Dispatch Within a State

As a general rule, biological material—at least pathogens or otherwise hazardous biological material—should never be sent to private persons. Only adequately trained staff in sufficiently equipped laboratories should receive microorganisms in order to guarantee safe handling and proper use. **Table 1** demonstrates which issues have to be clarified before any dispatch of biological material.

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Table 1
Issues to Be Clarified Before the Dispatch of Biological Material

Risk group	Destination	Notice	Action/proof	Kind of dispatch
1	Intranational	National laws like:		
		Genetic Engineering Act	Permission/registration/ authorization	Mail
		Plant Protection Act		
		Infectious Diseases of Animals Act		
	Foreign country	Within the EU: Plant Protection Act		Mail/air mail
		Air mail might not be admitted		Air freight
		Act on the Control of War Weapons	Only for civil use	
		Total embargo?	**No dispatch**	
2	Intranational	National laws like:		
		Infectious Diseases Act	Permission/registration/ authorization/registered laboratory	Private carriers by road
		Infectious Diseases of Animals Act		
		Plant Protection Act		
		Genetic Engineering Act		
		Act on the Control of War Weapons	Only for civil use	
	Foreign country	EEC Regulation for the Control of Exports of Dual-Use Goods	Authorization	Private carriers by road or air freight
		Act on the Control of War Weapons	Only for civil use	
		Import or quarantine restrictions		
		Import permit permission		
		EU: Plant Protection Act		
	Non-OECD country	Embargo? →→→→	**No dispatch**	
		Act dealing with foreign trade →→→→	**No dispatch**	
3 and 4	See Risk Group 2	See Risk Group 2	See Risk Group 2	Private carrier

Table 2
Useful Websites

Biological safety	Export restrictions	Transport
http://www.who.int/en/	http://www.un.org/News/ossg/sanction.htm	http://www.unece.org/trans/danger/danger.htm
http://www.biodiv.org	http://binas.unido.org/binas	http://www.iata.org/index.htm
http://biosafety.ihe.be/Menu/BiosEur1.html	http://www.biodiv.org	http://www.icao.int
	http://biosafety.ihe.be/Menu/BiosEur1.html	http://www.upu.int
	http://www.opbw.org	
	http://www.dfat.gov.au/isecurity/pd/pd_4_96/pd9.html	

1.1. Export

The export of microorganisms is usually governed by national law. However, there is international or regional (e.g., in Europe) harmonization on the lists of microorganisms affected (*see* **Table 2**). The Biological and Toxin Weapons Convention (BTWC) states that the prohibition of the development, production, and stockpiling of chemical and biological weapons as well as their elimination will facilitate the achievement of general and complete disarmament under strict and effective international control (*see* **Table 2**). With few exemptions, organisms classified in Risk Group 1 (no or very low individual and community risk according to WHO definition) ***(2)*** are admitted for export without restrictions. Respective lists allocating organisms to the Risk Groups can, for example, be found in EEC Directive 2000/54/EC on the protection of workers from risks related to exposure to biological agents at work ***(3)***. However, a total embargo would exclude even such organisms from export. Sanctions by the United Nations (*see* **Table 2**) might be in place and have to be observed.

More general restrictions are imposed by those laws and directives controlling the export of goods with a possible dual use, which means they could be used for civil or military purposes. A regulative example is EEC Council Directive 3381/94/EEC setting up a Community regime for the control of exports of goods with dual use ***(4)***. Organisms categorized as potential biological weapons include the causative agents of anthrax (*Bacillus anthracis,* Risk Group 3), pestilence (*Yersinia pestis,* Risk Group 3), or toxin-producing strains of organisms like *Aspergillus fumigatus, Clostridium botulinum,* and

Staphylococcus aureus (all Risk Group 2). Other examples are certain plant (crop) pathogenic species and all those genetically modified microorganisms that meet the definition of the respective paragraph in the EU list of dual-use goods ***(4)***.

1.2. Import

The import of biological material might be subject to the quarantine regulations of a given recipient country. These restrictions often depend on the special ecological or climatic situation of a certain country: It is free of a certain pathogen and it might be expected that an introduced microorganism could spread excessively. The United States only permit entry of animal cell cultures after a certain period of quarantine in connection with an import permit. Any individual case of import of microorganisms to Australia, Canada, and New Zealand requires an import permit. The European Community Commission Directive 97/3/EC ***(5)*** restricts the import of organisms harmful to plants and plant products and their spread within the Community. In Germany, comparable restrictions concerning, for example, *Synchytrium endobioticum,* the causative agent of potato cancer, or *Erwinia amylovora,* causing fire blight in fruit trees, are imposed according to the German Plant Protection Act ***(6)***. Similarly, the German Infectious Diseases of Animals Imports Enactment ***(7)*** restricts the import of *Chlamydia psittaci,* causing psittacosis, or *Zymonema farcinimosus,* responsible for lymphatic vessel inflammation of one-hoofed animals. In other countries, similar laws exist.

1.3. Dispatch Within a State

Handling of certain kinds of biological material might be restricted to certain persons or registered laboratories having the required permissions or registrations. Pathogens or otherwise hazardous biological material should only be delivered after having verified that the recipient has the respective permissions to handle the material: (1) to handle human pathogens, (2) to handle animal pathogens, (3) to handle plant pathogens, and (4) to handle genetically modified organisms. It should be noted that also the intranational dispatch of certain agents listed as potential dual-use material might be regulated: A signed end-user certificate is possibly required. The best sources of information are the respective national export offices.

2. Transport

Living, potentially or definitely pathogenic biological material is sent all around the world for scientific, industrial, or teaching purposes. During transport, such material might present a menace or danger for those persons involved in the transportation chain who are all not trained with respect to working with

biological substances (e.g., postal employees, secretaries, and others who could be exposed if an accident occurs). To prevent or to reduce the possibility of an inadvertent release of microorganisms, national and international laws and regulations for the transport and the packaging of the material exist (*see* **Table 2**).

2.1. Packaging of Biological Material

The principle of the safe packaging of biological material relies on the system of triple packaging. The system specifically designed for transport of infectious substances (Class 6, Division 6.2) serves as the only protection for people, animals, and the environment. Also, nonhazardous biological substances (allocated to WHO Risk Group 1) that are consequently not regulated by dangerous goods transport regulations should, of course, reach their destination in a vital and undamaged status, as fast as possible.

The system of triple packaging is as follows. The packaging must consist of (1) a watertight primary receptacle, (2) a watertight secondary packaging, and (3) an outer packaging. Absorbent material has to be placed between the primary and the secondary packaging. Several primary receptacles should be wrapped individually. There should be sufficient absorbent material present (e.g., cotton wool) to absorb the entire liquid if a leakage occurs. The outer packaging bears all the labels and documentation: (1) label the package containing infectious materials as "Infectious Substance" by using the correct label (*see* **Fig. 1**) and (2) label shipments containing noninfectious material as "Perishable Biological Substances" (*see* **Fig. 2**). Labels are commercially available or are already printed on ready-to-use packaging.

Figures 3 and **4** depict the schematic construction of the triple-packaging principle. UN certified combination packagings ***(8)*** as well as EN 829 systems ***(9)*** are commercially available and have to meet the respective specific performance tests. In comparison to EN 829 packaging, the UN combination packaging has a much higher strength and stability.

2.2. Transport by Mail

National postal services are merged in the Universal Postal Union (UPU). In the Letter Post Compendium ***(10)***, guidelines are laid down for the postal transport and packaging of perishable biological substances and infectious material. It is differentiated between noninfectious organisms (Risk Group 1) and infectious organisms (Risk Groups 2, 3, and 4).

Generally, the exchange of biological substances by mail is restricted to countries whose postal administrations agree to accept biological material. The national postal services of several countries do not allow shipment (receipt or dispatch) of perishable biological substances by mail, either by surface or air ***(11)***. Almost all postal administrations prohibit infectious substances like all

Fig. 1. Label for infectious substances.

Fig. 2. Label for noninfectious biological substances.

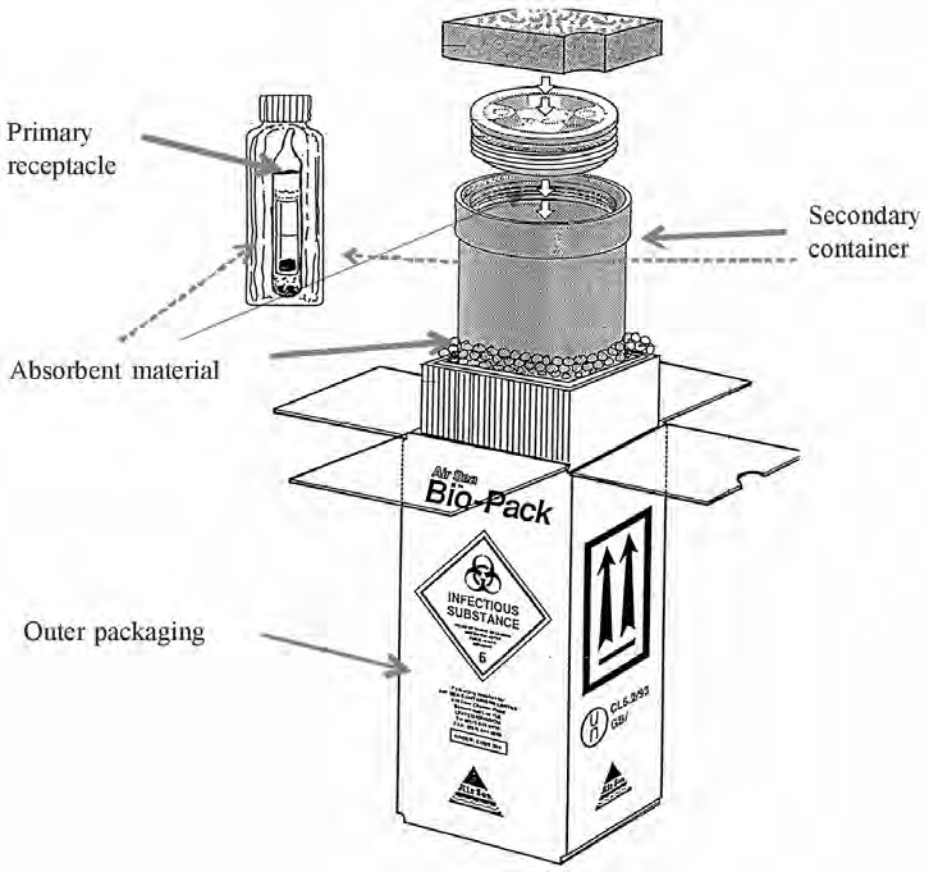


Fig. 3. Triple packaging for infectious substances according to UN Packing Instruction 620(IATA P1602).

other kinds of dangerous goods in the mail. Consequently, all postal administrations involved (senders, consignees, and all transit countries) would have to permit such a transport. As this is almost never possible, the only alternative of sending the material by freight and private courier has to be chosen. The national postal authorities or postal offices concerned give advice whether transport by mail is admitted (*see* **Table 2**). The following requirements have to be fulfilled in addition to those described in **Subheading 2.1:** (1) Indicate which organisms are shipped (e.g., on a delivery slip) between the outer and secondary container. (2) Label as "Lettre" to speed up transport and delivery (please note that any biological material must not be sent by postal parcel service).

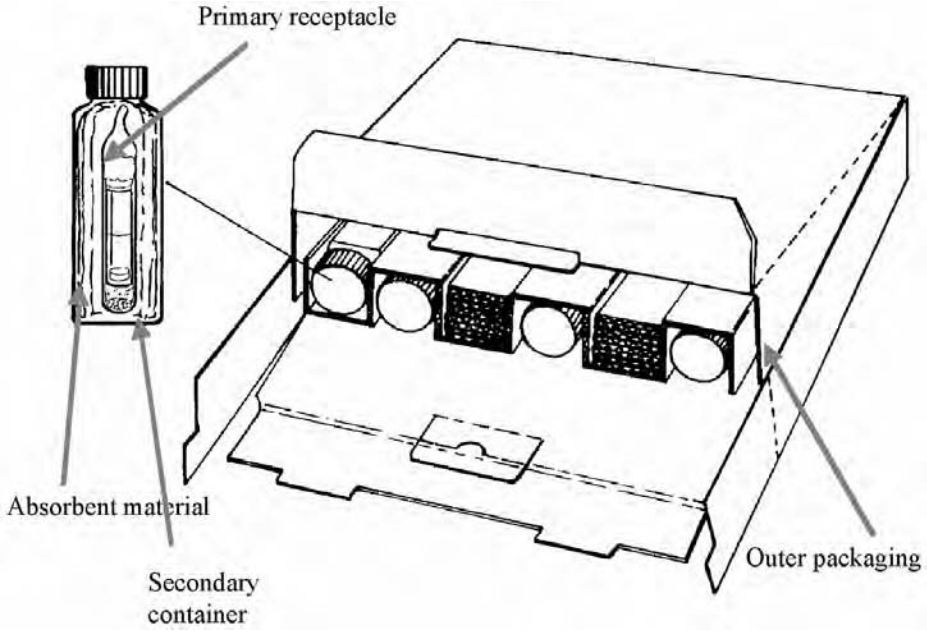
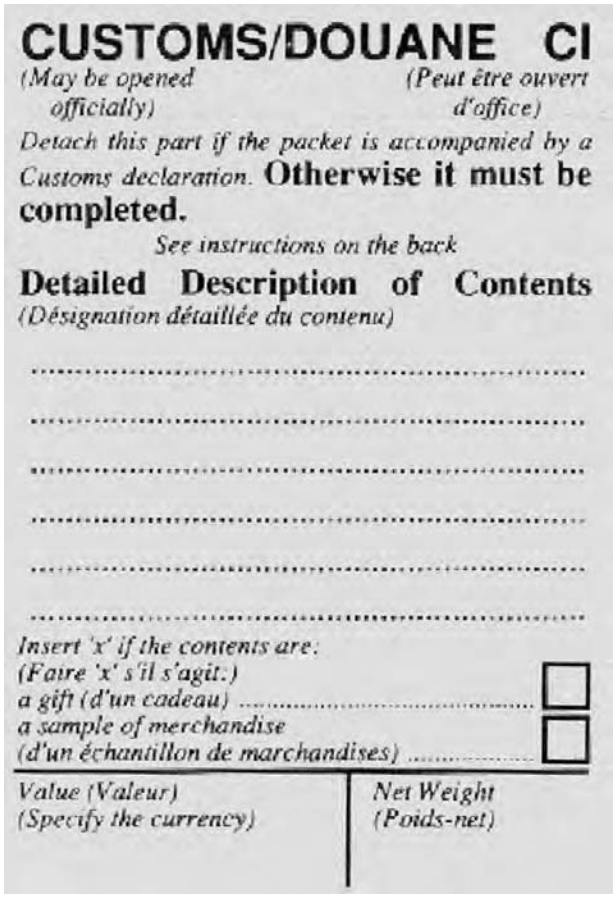


Fig. 4. Packaging according to standard EN 829 for noninfectious biological substances.

(3) Shipments of biological material into foreign countries might be subject to customs inspection. They must carry the green customs declaration C1 (*see* **Fig. 5**). Indicate number and type of material (e.g., 3 bacterial cultures, 2 plasmid preparations). The note "No commercial value" must be attached in case of free exchange between laboratories or any other supply free of charge. (4) If infectious substances are shipped by air mail (if permitted at all!), the IATA Dangerous Goods Regulations (DGR) ***(1)*** have to be followed and the Shipper's Declaration for Dangerous Goods must be filled in (*see* **Subheading 2.3.**).

2.3. Transport as Freight

If shipments containing biological material are not accepted in (air) mail, shipping by using private carrier service and (air) freight has to be chosen. The carrier will decide on the fastest mode of transport (road, rail, air, waterways) and will assist in filling in the necessary documents. The United Nations Committee of Experts for the Transport of Dangerous Goods established a system for the classification of all kinds of dangerous substances, called "Orange Book" ***(8)***, with the aim of ensuring safe shipping for all modes of transport. The nine different classes include explosives, gases, flammable liquids, flam-


CUSTOMS/DOUANE CI

(May be opened officially) *(Peut être ouvert d'office)*

Detach this part if the packet is accompanied by a Customs declaration. **Otherwise it must be completed.**

See instructions on the back

Detailed Description of Contents

(Désignation détaillée du contenu)

.....

.....

.....

.....

.....

.....

Insert 'x' if the contents are:
(Faire 'x' s'il s'agit:)
a gift (d'un cadeau) .....
a sample of merchandise
(d'un échantillon de marchandises) .....

Value (Valeur) *(Specify the currency)*	*Net Weight* *(Poids-net)*

Fig. 5. Label needed for customs clearance.

mable solids, oxidizing substances and organic peroxides, toxic and infectious substances, radioactive material, corrosives, and miscellaneous dangerous goods. The UN number, proper shipping name, Class, hazard label, packing group (not relevant for biological substances), and Packing Instruction (*see* **Table 3**) are important for shipping procedures. Infectious substances are classified in Class 6, Division 6.2. The UN numbers for infectious substances affecting humans and those affecting animals are UN 2814 and UN 2900, respectively. All consignments containing infectious substances (dangerous goods) are to be accompanied by the transport emergency card (available from courier services) and must be packed in UN-certified packagings.

For transport of infectious substances on the road or by rail the ADR (Accord Européen relatif au transport international des marchandises dangereuses par routes) ***(12)*** and COTIF/RID (regulations concerning the international carriage of dangerous goods by rail) ***(13)***, respectively, apply in Europe. Rules for the international traffic of dangerous goods by inland waterways (ADN) ***(14)*** have been developed and the carriage of dangerous goods by sea is internationally regulated by the International Maritime Dangerous Goods Code (IMDG) ***(15)***.

The International Civil Aviation Organization (ICAO) established guidelines for the transport of dangerous goods by air, implemented by the International Air Transport Association (IATA) (*see* **Table 3**). The regulations governing the transport by air are the most stringent but also the most clear. Air transport is playing a major role today, at least in case of international exchange of biological material. In this context, the IATA Infectious Substances and Diagnostic Specimens Shipping Guidelines ***(16)*** are especially concerned with the shipping of infectious biological material, whereas the transport of noninfectious biological material is not included. When sending infectious substances by air, a Shipper's Declaration for Dangerous Goods has to be filled in (in English). The Shipper's Declaration is a legal document and has to be signed by a trained person; general or job-specific training of a person involved in packing and shipping of dangerous goods is a precondition according to IATA Dangerous Goods Regulations (DGR), and certified training courses have to be attended by shippers of dangerous goods. The shipper is responsible for the correct documentation.

If the packaging contains infectious substances as the only dangerous good, the following labeling is necessary: (1) UN number plus technical (scientific) name of the infectious substance (UN 2814 or UN 2900, respectively); (2) name, address, and telephone number of sender; (3) name, address, and telephone number of recipient; (4) hazard label (*see* **Fig. 1**); (5) packaging orientation label (if it contains liquid material). Advance arrangements prior to dispatch are indispensable: The sender is urgently advised to contact the courier service when preparing a shipment. Also, the consignee has to be informed of the intended dispatch of infectious substances.

If noninfectious, perishable material is not accepted in air mail, it can be shipped by air freight. The Shipper's Declaration for Dangerous Goods is not applicable.

2.4. Transport of Genetically Modified Organisms

Genetically modified microorganisms have been altered through genetic engineering in a way that does not occur naturally. Five groups are differentiated when offered for air transport ***(1)***:

Table 3
Relevant Extract From the IATA Dangerous Goods List

UN No.	Name and description	Class	Hazard label	Packing instruction	Max. net quantity per Package: Passenger aircraft	Max. net quantity per Package: Cargo aircraft
1845	Carbon dioxide, solid (dry ice)[a]	9	Miscellaneous	904	200 kg	200 kg
2814	Infectious substance, affecting humans[a] (solid or liquid)	6.2	Infectious substance	602	50 g or mL	4 kg or L
2900	Infectious substance, affecting animals[a] (solid or liquid)	6.2	Infectious substance	602	50 g or mL	4 kg or L
3245	Genetically modified microorganisms *(acc. 3.6.2.1.2 (c))*	9	Miscellaneous	913	100 g or mL	100 g or mL
3373	Diagnostic specimens		None	650	4 kg or L	4 kg or L

[a] *See* **Note 2.**

1. Organisms being infectious to humans and/or animals. They are to be shipped as infectious substances according to IATA DGR, Class 6, Division 6.2, UN 2814 or UN 2900, following Packing Instruction 602.
2. Animals containing genetically modified microorganisms with infectious potential. They are not to be transported by air. Other modes of transport have to be chosen. Exemptions might be granted by the States concerned.
3. Organisms known or suspected to be dangerous to humans, animals, or the environment. They are not to be transported by air. Other modes of transport have to be chosen. Exemptions might be granted by the States concerned.
4. Organisms capable of altering animals, plants, or microbiological substances in a way that does not occur in nature but which do not meet the definition of an infectious substance. They are allocated to Class 9 (Miscellaneous Dangerous Goods), UN 3245. The applicable Packing Instruction (PI 913) is comparable to PI 602 for infectious material.
5. Genetically modified organisms which are not included under paragraphs 1 to 4. They are not regulated by IATA DGR and will be transported as Articles not Regulated as Dangerous Goods.

2.5 Transport of Diagnostic Specimens

The IATA DGR ***(1)*** define diagnostic specimens as any human or animal material including excreta, secreta, blood and its components, tissue and tissue

fluids transported for diagnostic purposes (except living infected animals). Diagnostic specimens are assigned to UN 3373. (*See* **Note 1**; changes expected for 2005.) Packing Instruction 650 has to be followed. The Shipper's Declaration for Dangerous Goods is not to be used. Samples of diagnostic specimens without infectious substances like blood collected for blood transfusion are not subject to IATA DGR and, therefore, are not to be dispatched as dangerous goods.

3. Conclusion

As it has been shown, numerous steps have to be done before biological material can be shipped in compliance with the law (*see* **Note 1**). Please note that this chapter can only provide an overall picture on the complex topic of dispatch and transport. Special recurrent training courses have to be attended by personnel involved in shipment. By giving deep insight, the training courses also are invaluable fora for discussion and help.

4. Notes

1. Legislation concerning the dispatch and transport of infectious substances underlies constant changes. Organizations involved in shipping regulations can submit variations so that actuality in this chapter cannot be guaranteed. Therefore, it is necessary to keep oneself informed about recent changes before biological material is offered for transport.
2. If dry ice (carbon dioxide, solid) is used as a refrigerant to keep the biological material cold during transport, a special containment has to be used that allows constant release of carbon dioxide gas. There are special combination containments for infectious substances on the market that can keep the low temperature up to 3 d. Dry ice is a dangerous good (Class 9, miscellaneous dangerous goods) and can only be transported by freight. It has to be included in the documentation that accompanies the consignment and the latter has to be labeled accordingly.

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