



WFCC Information Resource on International Regulations for Packaging & Transport of Genetically Modified Microorganisms

This information resource concentrates on the special requirements for packaging and shipping genetically modified organisms (GMOs). It exclusively deals with genetically modified microorganisms and is a compilation of all aspects regarding GMO shipment.

The main contents of this information resource

- Dangerous goods transport: the international regulatory framework and its hierarchical structure
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- General safety philosophy of dangerous goods transport
- Shipment of GMOs - a specific view
- Dangerous goods classes 6.2 and 9
- Correct classification of GMOs prior to shipment: dangerous goods (dg) or not dg?
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Before shipping or exporting GMOs it is necessary to

1. ensure the recipient has permission to work with GMOs
2. find out whether the GMOs might fall under export restrictions in the sense of “dual-use” regulations (note: biological substances are classical dual-use substances)
3. classify the GMOs properly in accordance with the applicable national and international transport regulations (does a GMO fall under dangerous goods regulations?)
4. ensure the GMOs are packaged safely according to the Packing Instructions in place (PI602, PI650 or PI913, respectively)
5. provide handling & safety information along with the shipment documentation

Dangerous goods transport: the international regulatory framework and its hierarchical structure

The UN Sub-Committee of Experts for the Transport of Dangerous Goods (UNSCETDG) regularly update the Recommendations on the Transport of Dangerous Goods = “UN Model Regulations” = “Orange Book”. Being compulsory for all modes of transport world-wide for all carriers and for all dangerous goods, they are the safety standards for transport by

- road ADR¹, in Europe
- air ICAO TI (Technical Instructions), international
- railway RID in Europe and neighbour states
- waterways IMO² International Maritime Organization

¹ADR: Accord européen relatif au transport international des marchandises dangereuses par route (the European agreement concerning the international carriage of dangerous goods by road), UNECE, 2007.

²IMO regulates international sea transport whereas other waterways (rivers) may have separate (national) regulations in place.

The outstanding role of air transport

Particularly for transport of biological substances and transport over long distances in general, air transport is most often the mode of transport used. Therefore, this information resource focuses on this.

IATA DGR: International Air Transport Association Dangerous Goods Regulations

The regulations are updated annually, being valid from January to December. The DGR are available in several languages and fully implement the ICAO TI (International Civil Aviation Organization, Technical Instructions) plus additional special restrictions and requirements set by the IATA member airlines. Therefore, the IATA DGR regulations are necessarily stricter than the ICAO TI. IATA is the world's airlines association and the DGR provides the most reliable guide for shippers and all other persons involved in dg transport by air. Furthermore, IATA places quite strict but clear standards on packaging and shipping of each individual dg and therefore covers the requirements of other modes of transport, e.g. by road.

General safety philosophy of dangerous goods transport

IATA DGR 2008: "Dangerous goods can be transported safely by air transport provided certain principles are strictly followed..."

A **harmonised system** is provided by the international regulations for operators to accept and transport dangerous goods safely and efficiently.

Training is an essential element in maintaining a safe regulatory regime.

Packaging is the essential component in the safe transport.

While the **harmonised system** is guaranteed by the international framework structure of regulations recurrent **training** and correct **packaging** are factors to be verified by the responsible shipper and other persons in the transportation chain: freight forwarders, operators, ground handling agents, security screeners etc.

Background on **training requirements**: The IATA DGR dedicate a whole chapter (1.5) on training requirements: 1.5.0.2: "Training must be provided or verified upon the employment of personnel identified in the categories specified in Table 1.5.A (Minimum requirements for training curricula, including the shipper)". 1.5.0.3: "Recurrent training must take place within 24 months of previous training to ensure knowledge is current". 1.5.0.4: "A test must be undertaken following dangerous goods training to verify understanding of the regulations...". Note that the shipper is fully responsible for correct classification, packaging, labelling, documentation of a dg shipment, the transportation chain relies on the shipper. UN 3373 shipping is an exemption in that the resp. Packing Instruction is saying that if PI 650 is followed, "no other DGR requirements need be met". This is in contrast to all other dangerous goods having a unique UN number. Some shippers interpret PI 650 in a way that training is not necessary. However, interpretation depends exclusively on the resp. national aviation authority and therefore, at least function-specific training requirement (face-to-face, with exam) can vary from country to country. ICAO strongly supports some kind of training to ensure good knowledge. In order to harmonise training requirements internationally and to design an acceptable scheme for training of UN 3373 shippers, a working group was founded at the WHO Meeting "**Ensuring Efficient Transport of Infectious Substances**", WHO HQ, Geneva, December 2007.

Which hazards might a GMO bear?

- * Infectious potential
- * Potential to modify other living organisms
- * Both criteria
- * None of both criteria

According to these possibilities GMOs are classified as:

Dangerous goods classes 6.2 and 9

Class 6, Division 6.2: all kinds of infectious substances, Category A (UN 2814 and UN 2900) and Category B (UN 3373)

Infectious substances must be classified in Div. 6.2 and assigned to **UN 2814, UN 2900, UN 3291** (clinical waste, not relevant for this information resource) or **UN 3373**, as appropriate (IATA DGR 2007, 3.6.2.2.1). **IATA DGR 3.6.2.2.2.1 Category A:** An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans (UN 2814) or animals (UN 2900). Indicative examples are given in Table 3.6.D. Note: Category A infectious substances are mostly allocated to the Risk Groups 3 or 4 whereas Risk Group 2 microorganisms should normally be classified in Category B (UN 3373). There is no examples list given for Category B. **IATA DGR 3.6.2.2.2.2 Category B:** An infectious substance which does not meet the criteria for inclusion in Category A.

It can be assumed that most biological substances travelling world-wide are allocated to Risk Group 1 (not dg, not regulated by dangerous goods regulations, though postal transport regulations must be followed) or Risk Group 2 (mostly UN 3373). Interestingly, the requirements for packaging quality is comparable in both cases because postal transport also needs a triple containment packaging system offering the minimum strength to withstand mechanical stress during transport. This is achieved with PI 650 packaging!

Class 9: miscellaneous dangerous goods presenting a danger to the environment, not covered by other classes

Packing Instructions PI602, PI650, PI913

In 2005, the UN Model Regulations set in force this new classification system for infectious substances and moved away from the Risk Group allocations, defining the two Categories instead. This offered the desirable possibility to separate the Risk Group 2 microorganisms from the "highly hazardous" microorganisms with the consequence of having deregulated packaging requirements, namely the PI 650 for Category B, UN 3373. Formerly, there was only one Packing Instruction, PI 602, for all infectious substances of Class 6. Div. 6.2.

Note: Category A infectious substances MUST be packed in a PI 602 packaging system. Category B infectious substances, UN 3373, CAN be packed in a PI 602 packaging system, but their minimum packaging requirement is PI 650. Take care that the outer packaging bears the correct labels, UN number and the proper shipping name!

The proper shipping name for UN 3373 is "Biological Substance, category B".

The proper shipping name for UN 2814 is "Infectious substance, affecting humans" (technical name, species name of infectious substance)

The proper shipping name for UN 2900 is " Infectious substance, affecting animals only" (technical name, species name of infectious substance)

Another main difference is that there is **no Shipper's Declaration for Dangerous Goods required for UN 3373 substances**. Of course, they are still dangerous goods, but the requirements have received adequate deregulation.

It is advisable to study the details and differences of PI 650 and PI 602, IATA DGR 2008, pp. 457-459 and p. 433-435, respectively, as there are other differences concerning the quality and strength of the secondary packaging containment and the outer packaging (usually a carton box in both cases) and the sizes as well. See also the ***WFCC Information Resource on International Postal Regulations for Shipping Biological Materials***.

PI 913 was defined for GMO packaging and requires the same packaging quality as PI 602, but the packaging does not have to be tested (by an authorised national body). Note that such packaging that has not passed a test is probably not available! Therefore, a usual PI 602 packaging should/must be used. PI 913 permits a maximum quantity in a primary receptacle of 100 mL or 100 g (IATA DGR 2008, p. 505). PI 602 permits a maximum net quantity per package of 50 mL or 50 g. PI 650 permits a maximum net quantity per package of 4 L and a maximum quantity per primary receptacle of 1 L. As a consequence, these quite high limits of permitted dg net quantities acc. to PI 650 have led to restrictions set by many airlines resulting in that they do not accept PI 650 packagings anymore! This impacts heavily on the shipment of UN 3373 items, the new important UN number for most of the Risk Group 2 organisms. Couriers available for accepting UN 3373 in PI 650 is reduced to an absolute minimum, these are such courier services having their own large fleet (like e.g., Fedex), not depending on offering freight to the big airlines.

Correct classification of GMOs prior to shipment: dangerous goods or not dangerous goods?

Definitions concerning genetically modified microorganisms acc. to IATA DGR 2008:

3.2.6.2.4.1: genetically modified microorganisms not meeting the definition of an infectious substance must be classified according to Subsection 3.9.

3.9.1.2: GMOs are (micro) organisms in which genetic material has been purposely altered through genetic engineering in a way that does not occur naturally.

3.9.2.5.2: GMOs are not subject to these regulations when authorised for use by the appropriate national authorities of the States of origin, transit & destination.

If a GMO is an infectious substance, this fact has priority over the fact that it is a GMO. Therefore, all such infectious GMOs are to be classified and transported as UN 2814, UN 2900 or UN 3373, respectively. The resp. Packing Instructions apply (PI 602 or PI 650). A Shipper's Declaration form has to be filled in in case of UN 2814 and UN 2900. No SD is required in case of UN 3373. If a GMO does NOT meet the definition of being an infectious substance but has the ability to modify other organisms (animals, plants, microorganisms) in a way that does not occur in nature, such a GMO falls under Class 9, Miscellaneous Dangerous Goods, UN 3245. PI 913 applies. A different label must be used and affixed on the outside of the outer packaging: the black-white-striped label of Class 9 (Note: e.g., also carbon dioxide, solid (dry ice), falls under Class 9; it is UN 1845). Shipment of UN 3245 requires a SD form!

All GMOs shipped as UN 2814, UN 2900, UN 3373 or UN 3245 are dangerous goods!

In case of a GMO that does not meet any of these criteria like e.g. a Risk Group 1 host bearing a non-transmissible vector plasmid that is not able to modify other organisms such a GMO is NOT regulated as dangerous goods. It can be transported as done with a Risk Group 1 organism. However, the requirements for shipping such RG 1 organisms must be met. These minimal requirements are assured by following the "triple containment system" including a primary receptacle (it carries the liquid culture or agar slant or ampoule etc.), a secondary containment (plastic screw capped receptacle, water-tight) and an outer (carton) box bearing all documentation and labels. Probably, quite a large number of such GMOs are transported for research and other application purposes.

Differences between postal and courier freight services

UPU, the Universal Postal Union, forbids dg in postal mail. Infectious substances might be an exemption, under the premises that all (!) transit countries on the way of a single shipment do permit this. Please note that this is very rarely the case. See the ***WFCC Information Resource on International Postal Regulations for Shipping Biological Materials***. It is known that many countries do not permit GMOs in postal mail services whereas they permit certain infectious substances (UN 3373). Also note that any (!) biological substance can only be transported in letter mail (registered letters), **not in postal parcels**. It is urgently recommended to be thoroughly conversant with the UPU regulations. Specialised private carriers are in many cases a reliable alternative offering tracking during the complete transit path from sender to destination.

Export restrictions applying to GMOs

Within the European Union, the Dual-use Council Regulation 394/2006 of 27 February 2006 is in force amending and updating Regulation 1334/2000. The export list of "dual-use goods" (part C) describes goods the export of which from the EU is controlled by the relevant national authorities, in most cases the Export Offices, see list position 1C353 for GMOs. The U.S. counterpart to the EU export list is the Commerce Control List. These are two examples of "regional" regulations with outstanding importance; other regions in the world do have comparable regulations.

EU Dual-use export list, 1C353, genetic elements and genetically modified organisms, as follows (extract taken from the legal publication):

- a. Genetically modified organisms or genetic elements that contain nucleic acid sequences associated with pathogenicity of organisms specified in 1C351 a. to c. or 1C352 or 1C354;***
- b. Genetically modified organisms or genetic elements that contain nucleic acid sequences coding for any of the "toxins" specified in 1C351 d. or "sub-units of toxins" thereof.***

Technical Notes:

- 1. Genetic elements include, inter alia, chromosomes, genomes, plasmids, transposons and vectors whether genetically modified or unmodified.***
- 2. Nucleic acid sequences associated with the pathogenicity of any of the micro-organisms specified in 1C351 a. to c. or 1C352 or 1C354 means any sequence specific to the specified micro-organism that:***
 - a. In itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or***
 - b. Is known to enhance the ability of a specified micro-organism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to humans, animals or plant health.***

Note: 1C353 does not apply to nucleic acid sequences associated with the pathogenicity of enterohaemorrhagic *Escherichia coli*, serotype O157 and other verotoxin producing strains, other than those coding for the verotoxin, or for its sub-units.

GMO transport – examples

Which packaging for which GMO?

UN 2814 and UN 2900: PI 602

UN 3373: PI 650

UN 3245: PI 913

Not regulated as dg: PI 650

- 1.) *Mycobacterium africanum* with harmless, non-transmissible but modified vector plasmid: UN 2814, Category A, PI 602, Shipper's Declaration form required
- 2.) *E. coli* EHEC O157:H7 with a modified plasmid that is *tra* and *mob* positive and carries phage mu plus sequences coding for a new substance toxic for animal only: UN 2814, Category A, PI 602 (note that only one UN number can be allocated to any dg; here, the high potential for infectivity against humans has received priority), SD required
- 3.) *Pseudomonas aeruginosa* with a modified vector plasmid that is *tra* and *mob* minus: UN 3373, Category B, PI 650, SD not required
- 4.) *E. coli* K-12 with a modified plasmid that carries cloned transposons of unknown potential to modify other microorganisms: UN 3245, PI 913, SD required
- 5.) *Bacillus cereus* with a modified plasmid the transmissibility of which has to be checked in the recipient's lab: UN 3373, Category B, PI 602 packaging quality recommended, SD not required because of UN no.
- 6.) *Bacillus subtilis* with a harmless, non-transmissible modified plasmid vector: not regulated as dg, can be sent like a Risk Group 1 organism in PI 650, SD not required

Security plans and "high consequence dangerous goods"

IATA DGR 2008, 1.6.3 deals with new security provisions for dg transport: Operators, shippers and others engaged in the transport of high consequence dg should adopt, implement and comply with a security plan that addresses at least the elements specified in 1.6.3.2 (8 issues are mentioned). Category A infectious substances, UN 2814 or UN 2900, are listed under the high consequence dg (1.6.3.3): High consequence dg are those which have the potential for misuse in a terrorist incident and which may, as a result, produce serious consequences such as mass casualties or mass destruction. It has to be admitted that not only many airlines refuse transport of PI 650 packagings containing UN 3373 because of much a too high net quantity limit permitted by PI 650 (see chapter above); road transport is very restrictive now re. transport of Category A substances in PI 602 packagings because of biosecurity plans. In most cases where Category A substances are shipped, special individual transport are required.

Bibliography

IATA DGR 2008: <http://www.iata.org/>

ADR, European Agreement concerning the International Carriage of Dangerous Goods by Road. United Nations Economic Commission for Europe (UNECE), 2007.

Legal notice: Information given in this document has been compiled with great care according to the best knowledge of the author. However, there are many variations in the way airlines regulate and implement rules therefore the author cannot guarantee all is covered here and responsibility for errors or omissions cannot be taken.

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