

## **DANGEROUS GOODS PANEL (DGP)**

### **NINETEENTH MEETING**

**Montreal, 27 October to 7 November 2003**

#### **Agenda Item 2 Development of recommendations for amendments to the Technical : Instructions for incorporation in the 2005/2006 edition**

### **INFECTIOUS SUBSTANCES REQUIREMENTS**

(Presented by R. Richard)

#### **1. INTRODUCTION**

During WG02 and WG03, the Working Group as a Whole considered the infectious substance requirements in the 13th revised edition of the UN Model Regulations for incorporation in the 2005-2006 TI. A number of concerns raised by various members regarding the new requirements were documented in Flimsy 18. Since the working group meeting, many of these issues have been discussed in a number of meetings between regulators and the regulated communities.

The intention of this paper is to comment on a number of the issues raised and to provide recommendations and proposals for addressing them in the 2005-2006 TI. The comments in this paper are based on the text that the Secretariat provided in DGP-WG/03-WP/6.

#### **(a) Quantity Limits for P650 Packagings**

The outer packaging quantity limits of 4 liters/4 kilograms should be maintained in P650. The text in special provision A81 should be incorporated directly in P650. A81 authorizes an inner packaging quantity limit of 1 liter for liquids. It is proposed that the Panel maintain the 1 L limit for liquids and eliminate the inner packaging quantity limit for solids since solids pose a less significant risk in transport. The quantity limit exceptions for bodies, body parts or whole organs should be maintained.

It is proposed that the quantity limits be added in sections (6) and (7) as follows:  
In section (6)

c amend paragraph (a) by adding the words “**and must not contain more than 1 liter.**”

c add a new paragraph (f) as follows:

- (f) the outer package must not contain more than 4 liters. This quantity excludes ice, dry ice or liquid nitrogen when used to keep specimens cold.

In section (7) add a new paragraph (d) as follows:

- (d) except for packages containing body parts, organs or whole bodies, the outer package must not contain more than 4 kg. This quantity excludes ice, dry ice or liquid nitrogen when used to keep specimens cold.

A81 should be deleted.

Currently A81 indicates that “The quantity limits shown in columns 10 and 12 do not apply to body parts, organs or whole bodies known to contain or suspected of containing infectious substances. These materials must be packed in accordance with Packing Instruction 602 so as to present no hazard to persons or animals during transport.” However, P602/620 does not provide specific requirements for packaging body parts, organs or whole bodies. P602/620 states that “other than exceptional consignments, e.g. whole organs which require special packaging...” - the packing instruction does not prescribe requirements for the special packaging. Packaging requirements for body parts, organs or whole bodies should be considered further by the UN TDG Sub-Committee and the Panel in their future work programs.

The Panel should consider including a competent authority approval provision for authorizing quantities larger than those indicated in sections (6) and (7) on a case by case basis.

## **(b) Marking**

During WG03 it was suggested that the size of the diamond-shaped mark should be indicated and that the proper shipping name for UN3373 should be marked on the packaging adjacent to the diamond-shaped mark to enhance communication that a Category B infectious substance is present. Since there will not be a transport document required for these substances, the diamond-shaped mark will be the only means of hazard communication. The PSN will be a useful addition to the package mark. The TI currently requires that the words "DIAGNOSTIC SPECIMEN" be marked on packages. Shippers, operators, handlers and emergency response personnel are familiar with the meaning of these words.

The DGP should consider mandating a size for the diamond shaped package mark of 50mm x 50 mm as opposed to a minimum size. The current Division 6.2 label is the only hazard label that can be 50mm x 50mm as stated in ICAO TI Part 5; 3.4.1.1 a). The proposed minimum marking size would be consistent with the smallest dimension allowed for the Division 6.2 label for Category A substances. Establishing a minimum size will ensure that the Category B mark is visible. It is proposed that subsection (4) of P650 be revised as follows:

- (4) For transport, the mark illustrated below must be displayed on the external surface of the outer packaging on a background of a contrasting color and must be clearly visible and legible. The mark must be in the form of a square set at an angle of 45° (diamond-shaped) with each side having a length of 50 mm and the letters and numbers inside the mark at least 6 mm high. The proper shipping name “Diagnostic Specimen” or “Clinical Specimen” in

letters at least 6mm high must be marked on the outer package adjacent to the diamond-shaped mark.

The first sentence of subsection (4) would remain the same. The sentence “The width of the line must be at least 2 mm; the letters and numbers must be at least 6 mm high.” would be deleted and replaced with the bold/italicized text. Paragraph 5;2.4.8 would no longer be necessary and should be deleted.

### **Orientation markings**

Currently orientation arrows are required on packages containing Division 6.2 infectious substances except when the primary receptacle has a volume of less than 50 ml (see 4; 1.1.3). The proposed P650 packing instruction does not require orientation arrows. Packaging designs for infectious substances have evolved whereby it may not be necessary for primary receptacles to be placed upright in the secondary and outer packaging. Package orientation markings should not be required for P650 packagings and further consideration should be given to whether they are necessary for P620 packagings.

### **(c) Documentation**

A transport document should not be required, however, an alternative document such as an airway bill, shipping label or alternative written document should be required. The airway bill or alternative document should include the following information: The proper shipping name, UN number, name, address and telephone number of the shipper and number of packages. The PSN should not be required to be supplemented with the technical name. At this time we have not finalized our position on whether a NOTOC should be required.

### **(d) Training**

P650 should be amended to clarify that persons who offer or transport Category B infectious substances must be able to determine whether the infectious substance being placed in the packaging meet the criteria for Category A or Category B and should be thoroughly knowledgeable of the P650 requirements.

The following revision to section (10) is proposed:

- (10) Clear instructions on filling, closing be provided by packaging manufacturers and subsequent distributors to the consignor or to the person who prepares the package (e.g., patient) to enable the package to be correctly prepared for transport. **The person who prepares and offers the package for transport must be able to determine whether the infectious substances are classified in Category A or Category B.**

### **(e) Rigid Outer Packaging**

P650 does not require the outer packaging to be rigid. Non-rigid outer packagings will not afford the same level of protection from crushing or puncture of the inner receptacles as a rigid outer packaging. It is proposed that the outer packaging should be rigid.

Paragraph (2)(c) should be amended as follows:

- (c) a rigid outer packaging of adequate strength for its capacity, mass and intended use.

The proposed text would be consistent with the text in P620.

**(f) Overpack**

It is proposed that P650 be amended to include a requirement to address overpack marking. It is noted that DGP/19-WP/6 proposes an Overpack marking (see page 6, paragraph (c)) but the text should more appropriately be placed in P650. The following text is proposed:

- (11) When packages are placed in an overpack, the package markings [it may be more user friendly to restate the exact marking requirements] required by this packing instruction must either be clearly visible or be reproduced on the outside of the overpack.

**(g) Special marking requirement for dry ice**

Section 2.4.7 requires that the net mass of dry ice be marked on the packaging. Since P650 is intended to be a "stand alone" document this requirement needs to be stated in P650.

It is proposed that paragraph (8)(a) be amended as follows:

- (8) Frozen specimens: Ice, Dry ice and liquid nitrogen
- (a) When dry ice or liquid nitrogen is used to keep specimens cold, all applicable requirements of these Regulations **must** be met. When used, ice or dry ice **must** be placed outside the secondary packagings or in the outside packaging or an overpack. If ice is used, the outside packaging or overpack **must** be leakproof. If Carbon dioxide, solid (dry ice) is used, the packaging **must** be designed and constructed to permit the release of carbon dioxide gas to prevent a build-up of pressure that could rupture the packagings and must be marked with the words "Carbon dioxide, solid" or "Dry ice" **and with the net mass of the solid carbon dioxide (dry ice).**

**(h) Other dangerous goods packed with infectious substances**

During WG03 the issue of how to address the presence of small quantities of other dangerous goods packed with infectious substances was discussed. It is expected that all of the applicable requirements of the TI for those dangerous goods would be met. However, in view of the minimal risk posed by quantities less than 30 ml of Classes 3, 8 and 9 dangerous goods that are commonly shipped with infectious substances, the Panel should consider including an exception for these small quantities. 30 ml was selected because this is the quantity that applies for these dangerous goods according to the excepted quantity provisions.

It is proposed to add a new section (12) as follows:

- (12) Other dangerous goods must not be packed in the same packaging as Division 6.2 infectious substances unless they are necessary for maintaining the viability, stabilizing or preventing degradation or neutralizing the hazards of the infectious substances. A quantity of 30 ml or less of dangerous goods included in Classes 3, 8 or 9 may be packed in each primary receptacle containing infectious substances. When these small quantities of dangerous goods are packed with infectious substances in accordance with this packing instruction no other requirements in these Instructions need be met.

This provision should also be included in P620.

**(i) Minimum outer packaging dimensions**

It is proposed that the minimum packaging dimensions in P620 also be applied to P650. Minimum packaging dimensions are necessary to ensure safe handling in sorting facilities and from damage during loading. It is proposed that the following sentence be added at the end of section (5):

At least one side of the outer packaging must have a minimum dimension of 100 mm x 100 mm.

**(j) Improved guidance for residual liquid or liquids absorbed in solid materials:**

During WG03 it was stated that P650 should be amended to establish clear requirements for determining when a liquid or solid packaging should be used in the case of liquids absorbed in solid materials. It is proposed that a new paragraph (d) be added to section (7) as follows:

- (d) If there is any doubt as to whether or not residual liquid may be present during transport then a packaging suitable for liquids, including absorbent materials, must be used.

**(k) Amendments to clarify 2.6.3.2.4 and 2.6.3.2.5 and the definition of cultures as discussed during WG03 -**

Amendments to improve the clarity of these sections should be referred to the UN Transport of Dangerous Goods Sub-Committee.

**(l) Incident reporting**

It is proposed that P650 be amended to require incident reporting (see proposed amendment to section (9) below).

**(m) Proposed revisions to section (9)**

It is proposed to amend section (9) of P650 as follows:

- (9) Infectious substances assigned to UN 3373 which are packed and marked in accordance with this packing instruction are not subject to any other requirement in these Instructions **except for the following:**
  - (i) **an airway bill or similar written document (such as a consignment note) must be provided and must include the proper shipping name, the UN number, the name, address and telephone number of the shipper and the number of packages;**
  - (ii) **classification must be in accordance with 6.3.2; and**
  - (iii) **the incident reporting requirements in 7;4.4 must be met.**

**(n) Consequential amendments**

Currently 5;4.2 of the TI addresses the use of live animals for the transport of infectious substances. This provision should more appropriately be included in Part 2 of the TI. The 13th revised edition of the UN Model Regulations includes a similar provision in 2.6.3.2.6. Paragraph 2; 6.3.2.6 in DGP19-WP/3 (see page 15) already addresses this requirement. It should be noted that the text in paragraph 2; 6.3.2.6 of DGP19-WP/3 needs to be aligned with the latest UN text which reads as follows:

“A live animal which has been intentionally infected and is known or suspected to contain an infectious substance may only be transported under terms and conditions approved by the competent authority.”

However, the Panel should consider maintaining the current provision that states “Unless an infectious substances can not be consigned by any other means”. If the Panel decides to maintain this condition then the text should read:

**A live animal which has been intentionally infected and is known or suspected to contain an infectious substance must not be transported by air unless the infectious substance contained can not be consigned by any other means. Infected animals may only be transported under terms and conditions approved by the competent authority.**

**(o) Exception for dry blood spots**

Dried blood spot specimens are clinical specimens collected by carefully applying a few drops of blood, freshly drawn by finger stick with a lancet from adults, or by heel stick with a lancet from infants, onto specially manufactured absorbent specimen collection (filter) paper. The blood is allowed to thoroughly saturate the paper and is air dried for a minimum of 3 hours. Caked or clotted specimens are not acceptable and are therefore not shipped. The specimen collection technique and the specifications for specimen matrix and shipment have been published as a national standard by the National Committee for Clinical Laboratory Standards. These specimens pose extremely minimal risk of infection and should be afforded exceptions from the requirements of the TI if properly prepared and packaged. Dried blood spot specimens are routinely collected for numerous biochemical tests. The presence of an infectious agent in such specimens would be

rare and incidental. Millions of these specimens are currently shipped as not subject to the regulations. During the CDC meeting held in Washington it became apparent that operators have varying interpretations with respect to whether dried blood spots are subject to transport regulations.

Dried blood spot specimens are mailed to laboratories where the specimens are subject to various analytical procedures. One of the most important uses of this specimen collection technique is in screening for congenital and inherited metabolic disorders among the more than 4.2 million infants born annually in the United States. Efficient collection, shipment, and analysis of dried blood spot specimens on filter paper comprise the foundation of this important public health service. Other important applications include DNA (genetic) analyses, forensic studies, immunologic studies, and nutritional evaluations of infants, children, and adults.

Additional information concerning the risk posed by dried blood spots is provided in Annex 1 to this paper.

### **Proposal**

This matter will be brought to the attention of the UN TDG Sub-Committee for consideration but it is believed that dried blood spots are excepted from the requirements of the TI consistent with 2; 6.3.2.5 which states "Substances for which there is a low probability that infectious substances are present, or where the concentration is at a level naturally encountered, are not subject to these Regulations. Examples are: foodstuffs, water samples, living persons and substances which have been treated so that the pathogens have been neutralized or deactivated."

A simple way of addressing dried blood spots would be to add them as an example in the above paragraph.

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## APPENDIX A

### GUIDELINES FOR THE SHIPMENT OF DRIED BLOOD SPOT SPECIMENS

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Centers for Disease Control and Prevention  
Office of Health and Safety | Biosafety Branch  
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#### Guidelines for the Shipment of Dried Blood Spot Specimens

Dried blood spot specimens are clinical specimens collected by carefully applying a few drops of blood, freshly drawn by finger stick with a lancet from adults, or by heel stick with a lancet from infants, onto specially manufactured absorbent specimen collection (filter) paper. The blood is allowed to thoroughly saturate the paper and is air dried for a minimum of 3 hours. Caked or clotted specimens are not acceptable and are therefore not shipped. The specimen collection technique and the specifications for specimen matrix and shipment have been published as a national standard by the National Committee for Clinical Laboratory Standards (1).

Specimen collection materials ("collection kits") for newborn screening may include a sturdy paper overlay that covers the absorbent filter paper containing the dried specimen. These are then enclosed and sealed in a high-quality bond envelope. The paper overlay and the sealed bond envelope provide a double-layer barrier that protects casual handlers (i.e., shipping handlers and other nonlaboratory, non-technical personnel) from accidental exposure to the dried blood specimens and protects the specimens from exposure to the environment during shipping.

The dried blood spot specimens must NOT be packaged in airtight, leak-proof plastic bags (1) because the lack of air exchange in the inner environment of a sealed plastic bag causes heat buildup and moisture accumulation that can damage the dried blood spot test substances (2-5). In addition, various chemicals that can adversely affect the test substances in the dried blood spots could leach from these plastics and thus cause incorrect analytical test results. The inclusion of desiccant packs (1) will aid in prevention of moisture accumulation, but shipping conditions are uncontrolled and desiccant has a limited effectiveness.

Dried blood spot specimens are mailed to laboratories where the specimens are subject to various analytical procedures. One of the most important uses of this specimen collection technique is in screening for congenital and inherited metabolic disorders among the more than 4.2 million infants born annually in the United States. Efficient collection, shipment, and analysis of dried blood spot specimens on filter paper comprise the foundation of this important public health service. Other important applications include DNA (genetic) analyses, forensic studies, immunologic studies, and nutritional evaluations of infants, children, and adults.

### **Regulations Applicable to Packaging and Shipping**

The U.S. Department of Health and Human Services regulation 42: Code of Federal Regulations (CFR) Part 72 - "Interstate Shipment of Etiologic Agents" (6) - specifically addresses the packaging and shipment of etiologic agents.

"Occupational Exposure to Bloodborne Pathogens: Final Rule" (7) generally addresses the shipping, transporting and labelling of containers of blood and body fluids. However, 42 CFR Part 72 specifically addresses, in detail, the shipment of biological products, clinical specimens, and etiologic agents. The 42 CFR 72 regulation is the reference source upon which other related guidelines are based.

### **Applicability of 42 CFR Part 72 to "Dried Blood Spot" Specimens**

Paragraph 72.2 on page 48626 states that "No person may knowingly transport or cause to be transported in interstate traffic, directly or indirectly, any material including, but not limited to, diagnostic specimens and biological products which such person reasonably believes may contain an etiologic agent unless such material is packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation."

If no evidence exists that a specific diagnostic specimen (including a dried blood spot), biological product, or other material contains an infectious agent, then there is no need to package the specimen or place a biohazard label on the specimen in compliance with 42 CFR Part 72. The packaging and shipping of these materials must comply with the requirements in 42 CFR Part 72 only if there is evidence that a diagnostic specimen or other material contains an etiologic agent. The package must bear the specified biohazard label to meet the requirements of this regulation.

Note that regulation 42 CFR Part 72 applies only to liquid or semisolid materials--including diagnostic specimens and biological products. Because blood spot specimens are absorbed into filter paper and dried, the packaging requirements of the blood spots as described in paragraph 72.3 on page 48626 do not apply, regardless of the source material. Therefore, all dried blood spot specimens contained on filter paper collection kits may be packaged for shipment in quality-bond paper envelopes, which meets the requirement of "packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation."

However, if a dried blood spot specimen is reasonably believed to contain an etiologic agent (that is, if there is clear, underlying evidence that one or more etiologic agents are present), the packaging envelope should also bear a biohazard label to meet the requirements of this regulation. (This label may be supplemented with

appropriate identifiers pertaining to newborn screening program specimens: e.g., "Dried biological materials [nonliquid] on absorbent paper--low biohazard risk.")

### **How the Proposed Amendment to 42 Part 72 could apply to Dried Blood Spot Specimens**

Readers should be aware of the proposed amendment to 42 CFR Part 72, which was published in the Federal Register, March 2, 1990 (8). Final approval and release of this amendment is pending. If this amendment is approved, all human material would require a "clinical specimen" label whether or not such materials contain etiologic agents (e.g., "Dried biological materials [nonliquid] on absorbent paper").

The regulation would also require that the specimen be packaged in a primary container that "shall be packaged in an outer shipping container using shock resistant material to withstand conditions incident to ordinary handling in transit." Under this proposed amended regulation, dried blood spot specimens could still be packaged in the manner described in this paper, because the filter paper collection kit containing the dried blood spots is the primary container, and the high-quality bond envelope is the outer container.

### **Risk Evaluation**

Dried blood spot specimens are routinely collected for numerous biochemical tests. The presence of an infectious agent in such specimens would be rare and incidental.

If a blood specimen that is absorbed and dried into the filter paper matrix did contain human immunodeficiency virus (HIV), the viral agent would be destroyed as the specimen was dried prior to shipping. When present, HIV is normally of low concentrations in circulating blood (2-3 logs per mL), and at least one log of infectivity titer is lost after several hours at ambient temperature in the dried state (9-11). Hepatitis B virus (HBV), on the other hand, may survive for an extended period of time in dried blood (12). However, when in the dried state, HBV is not readily transmissible. A person could not be exposed to HBV from a dried blood spot unless a suitable liquid, such as water, penetrated the sealed envelope, flowed inside to the absorbent paper, mixed with dried blood to suspend the virus, escaped in sufficient quantity to the external environment, and came in contact with a package handler. Opportunities for infection with HIV or HBV require direct entry into the blood stream through an open cut or penetration.

Thus for a package handler to be infected with HIV or HBV from a dried blood spot in a sealed envelope, a rare combination of circumstances would have to occur: the blood specimen would have to contain viable HIV or HBV; the virus would have to be present in blood in sufficient quantity to cause an infection; the virus would have to survive for extended periods of time in the dried blood spot; liquid would have to penetrate the sealed envelope; the virus would have to escape to the outside environment; and the virus would have to directly enter the bloodstream of a package handler by penetration or through an open wound. In other words, a shipping handler or other casual package handler could be exposed to infectious agents that may occasionally be present in dried blood spot specimens only under the most unusual circumstances -- circumstances that extend beyond those "conditions incident to ordinary handling in transportation."

### **Summary**

Dried blood spot specimens can be shipped or transported by mail or other carrier with no reasonable expectations of occupational exposure to blood or other potentially infectious material. "Universal precautions"

are to be followed in collecting and preparing these specimens for shipment. Standard filter paper collection kits should be enclosed and sealed in high quality paper mailers -- ideally, extra-strong, tear-proof, air-permeable, and waterresistant envelopes. These steps provide reasonable safety from occupational exposure and maintain optimal specimen integrity.

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