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ADVISORY COMMITTEE ON DANGEROUS PATHOGENS

Biological Agents: Managing the Risks in Laboratories and Healthcare Premises

Appendix 1.2 Transport of Infectious Substances – Revision

Issue

1) Appendix 1.2 of the '*Biological Agents: Managing the Risk in Laboratories and Healthcare Premises*' (MTR) guidance published in 2005, was written to anticipate changes in impending transport legislation (ADR 2005). The appendix has been revised to take account of changes in the legislation.

Background

2) The issue of transport of infectious substances is pertinent to many laboratories & healthcare premises. For this reason, a dedicated appendix was drafted for the MTR guidance. When drafted, the appendix predicted changes in transport legislation.

3) The international transport legislation is updated every two years hence several rounds of changes have resulted in Appendix 1.2 incurring a number of inaccuracies and omissions. Appendix 1.2 is also referenced by other guidance documents (e.g. 'TSE agents: Safe Working and the Prevention of Infection'). It is therefore timely to provide an updated Appendix 1.2.

4) Colleagues in the Department for Transport's Dangerous Goods Division have kindly incorporated the necessary legislative changes to Appendix 1.2 and an updated version is attached. For comparison the original version of appendix 1.2 can be viewed or downloaded from: **http://www.hse.gov.uk/biosafety/biologagents.pdf**

5) The Department of Transport also produce guidance on the transport of infectious substances, which is regularly updated and available for download from their website.
www.dft.gov.uk/pgr/freight/dgt1/guidance/guidancenonclass7/guidanceontransportofinfecti3186

Action

- Members are asked to consider the updated version of Appendix 1.2 of the MTR guidance and indicate if they are content with the revisions;

- Members may wish to consider whether given the regular changes to the transport legislation, if a more concise generic appendix, which cross-references the Department for Transport guidance for specific details of transport packaging and labelling requirements, is more appropriate at the next revision.

Annex 1

Biological agents: Managing the risks in laboratories and healthcare premises

Appendix 1.2: Transport of Infectious Substances (revised January 2008)

1 The GB regulations covering the carriage of dangerous goods by road and rail are derived from European Directives (ADR (road) and RID (rail)), which in turn implement international modal agreements governing the transport of dangerous goods. The GB regulations directly reference ADR in relation to the classification, packaging and labelling of all classes of dangerous goods, including infectious substances, and are updated every two years.

2 The requirements for air transport of dangerous goods, both within Great Britain and overseas, are contained in the International Civil Aviation Organisation (ICAO) Technical Instructions for the Safe Transport of Dangerous Goods by Air. They are essentially similar to those for road and rail as they mirror the same international modal agreements, but there are some minor differences (highlighted in the following text).

3 Biological agents, or materials that contain or may contain them, are allocated to UN Division 6.2 - infectious substances. Division 6.2 includes biological products, cultures, genetically modified micro-organisms (GMMs) and genetically modified organisms (GMOs) and medical/clinical waste.

Definitions (from ADR)

Infectious substances

4 Infectious substances are substances that are known or are reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, rickettsia, parasites, fungi) and other agents such as prions which can cause disease in humans or animals.

Biological products

5 Biological products are those products derived from living organisms which are manufactured and distributed in accordance with the requirements of appropriate national authorities (in the UK: the Department of Health and the Medicines and Healthcare Regulatory Authority), which may have special licensing requirements, and are used either for prevention, treatment, or diagnosis of disease in humans or animals, or for related development, experimental or investigational purposes related thereto. They include (but are not limited to) finished or unfinished products such as vaccines.

Cultures

6 Cultures (laboratory stocks) are the result of processes by which pathogens are intentionally propagated in order to generate high concentrations, consequently

increase the risk of infection should exposure occur. This definition does not include human or animal specimens.

Genetically modified micro-organisms and organisms

7 Genetically modified micro-organisms (GMMs) and genetically modified organisms (GMOs) are those in which genetic material has been purposely altered through genetic engineering in a way that does not occur naturally.

Medical or clinical wastes

8 Medical or clinical wastes are wastes that are derived from medical treatment of humans or animals or biological research.

Transport of infectious material

9 There are 4 steps involved in the safe transport of infectious material. These are:

Classification;
Packaging;
Labelling; and
Transporting.

Classification

10 Infectious substances are divided into the following categories:

Category A: an infectious substance which is carried in a form that, when exposure to it occurs, is capable of causing permanent disability, life threatening or fatal disease in otherwise healthy humans or animals. See Table A2 for indicative list. This includes all agents classified as HG4 in the Approved List of biological agents,[24] many HG3 agents and two HG2 agents (*Clostridium botulinum* and poliovirus). Those that can cause disease in humans or animals are assigned to UN 2814. Those that affect animals only are assigned to UN 2900 (additional requirements are in place for animal pathogens in the UK – see the DEFRA website[72] for further details). Exposure occurs when an infectious substance is released outside of the protective packaging, resulting in physical contact with humans or animals.

Category B: any infectious substance that does not meet the criteria for inclusion in Category A. These are assigned to UN 3373. Many cultures of HG3 pathogens will be assigned to UN2814 or 2900 as appropriate.

11 Samples of materials such as blood, tissue, excreta, secreta etc collected from humans or animals are considered, as a minimum, Category B infectious

substances. For example, samples from otherwise healthy individuals or where there is no reason to suspect that they are suffering from a severe infectious disease. However, if there is evidence to suggest otherwise, e.g. on the basis of known medical history, local endemic conditions or professional judgement concerning the circumstances of the source material, then such material should be assigned to Category A.

12 GMMs or GMOs that do not meet the definition of an infectious substance but are capable of altering animals, plants or microbiological substances in a way not normally the result of natural reproduction are assigned to Class 9 (UN 3245).

13 Clinical or medical waste that contains Category B infectious substances (with the exception of cultures) or that only has a low probability of containing infectious substances is assigned to UN 3291.

14 The following substances are not subject to the provisions of the regulations:

non-pathogenic micro-organisms (for either humans or animals);
blood and blood components for transfusion or transplant and tissues or organs for use in transplants;
samples (non-human/animal derived) where there is only a low probability of infectious substances being present, e.g. food screening samples, environmental samples (water, soil etc) or else material (including material derived from human or animal sources) that has been treated to inactivate any infectious substances;
biological products that have been manufactured and packaged in accordance with MHRA/DH requirements, and are carried for the purposes of final packaging and distribution;
decontaminated clinical or medical waste;
live animals that have been intentionally infected or are known to be infectious (see Information box A2); and
GMMs or GMOs when authorised for use by the competent authorities of the governments of the countries of origin, transit and destination.

Information box A2

The regulations covering the transport of live animals, whether they are infectious or not, are the responsibility of the Home Office and DEFRA. These are:

- the Animals Scientific Procedures Act 1986;[73]
- the Animal By-Products Order;[74] and
- the Welfare in Animals Transport Order 1997.[75]

COSHH[1] also applies, and a risk assessment that includes emergency procedures, eg dealing with the escape of an infectious animal, will be required.

Packaging

15 Category A infectious substances (either UN 2814 or 2900) should be packed using Packaging Instruction 620 (PI620) (see Table A3). This packaging must meet UN performance requirements as shown by design type testing. These are known as UN-type approved packaging for Class 6.2 substances and they are certified and marked accordingly. Packaging for Category B infectious substances, packed using PI650, are not required to meet UN performance requirements provided they are capable of passing a 1.2 m drop test.

16 If air transport is to be used, the ICAO PI602 should be followed. The two instructions are essentially the same, but there are quantity limits imposed on material sent by air (see Information box A3).

17 Substances assigned to UN 3373 should be packaged in accordance with PI650 (see Table A3). If you consign UN 3373 by air, ICAO PI 650 applies. This has some differences with PI 650 for land transport see Department for Transport Guidance document 'Transport of Infectious Substances, A guidance document produced by the Department for Transport, the Civil Aviation Authority and the Maritime and Coastguard Agency'
http://www.dft.gov.uk/pgr/freight/dgt1/publications/otherpublications/

Information box A3

PI602: For passenger aircraft, there is a 50 ml/50 g limit (maximum net quantity per package; for cargo craft, there is a 4 litre/4 kg limit (maximum net quantity per package),
PI650: 4 litre/4 kg limit, with a limit of 1 litre in primary receptacle for liquids. Primary receptacles containing solids must not exceed the outer packaging mass limit.

18 If you send infectious substances packaged and labelled in accordance with PI650, no other requirements of the legislation apply.

Labelling

19 Packages containing infectious substances should be marked with:

- the proper shipping name, e.g. 'Infectious substance, affecting humans'. (It is no longer necessary to show the technical name, i.e. the name of the microorganism, on the package but the proper shipping name should be supplemented with the technical name in the accompanying transport documentation);
- with the appropriate UN number (e.g. for 'Infectious substances, affecting humans' this would be UN 2814); and
- the appropriate warning label. The danger sign for infectious substances is shown in Figure 4.

Figure 4 Danger sign for infectious substances

(DN: Insert symbol here)

20 For frozen specimens being transported in an overpack, any certificated markings and labels must be visible through the overpack or repeated on the overpack itself. The packaging should also be marked to indicate any subsidiary hazards.

Transport

21 Although the regulatory requirements only apply to transport of infectious material off site, on-site transport still needs to be carried out in a safe manner. Further detail on this can be found in *Safe working and the prevention of infection in clinical laboratories and similar facilities.*[14]

22 Transport between different parts of private premises, where those parts are within the immediate vicinity of each other, does not generally fall within the scope of the regulations, even if they are separated by a road.

23 You should always discuss your transport requirements with your chosen Carrier. In particular, you may need to provide some of the information that will be used on the accompanying documentation. You will need to establish whether any of the intended transport will be by air, even within the UK, to ensure that the correct packaging is used and that quantity limits are not exceeded. The detail of the documentation that may be required is not given here. You should consult your carrier about this information, as it may vary depending on the carrier and/or the final destination.

24 In general, samples that are sent using UN 3373 can normally be sent via the postal service. Packaging will need to comply with the ICAO standards, as a proportion of the post in the UK will travel by air at some point in its journey.

Importation of biological agents

25 There is no requirement under health and safety law to obtain a licence to import biological agents into the UK, other than the requirement under COSHH[1] to notify the movement of HG4 agents (this would cover movement from, for example, the airport to the receiving laboratory). There is a requirement to notify first use of HG2-HG4 agents at a particular premises (see paragraph 153), but this relates to use of the agents in the laboratory, not the consignment of those agents. This only applies to human pathogens, importation of animal pathogens (some of which may be zoonotic agents) is covered in separate legislation (see Appendix 1.3). For GMMs being exported outside of Europe, there are additional requirements imposed by the Cartagna Protocol *i.e.* provision of details on the

properties of the GMMs, basic risk assessment and the steps to take in the event of spillage.

26 You will also need to notify the Home Office in advance if the agent you are importing is covered under the Anti-terrorism, Crime and Security Act 2001[25] (see Appendix 1.3).

Table A2 Indicative list of Category A infectious substances

UN Number and Name	Micro-organism
UN 2814 Infectious substances affecting humans	Bacillus anthracis (cultures only) Brucella abortus (cultures only) Brucella melitensis (cultures only) Brucella suis (cultures only) Burkholderia mallei – Pseudomonas mallei – Glanders (cultures only) Burkholderia pseudomallei – Pseudomonas pseudomallei (cultures only) Chlamydia psittaci – avian strains (cultures only) Clostridium botulinum (cultures only) Coccidioides immitis (cultures only) Coxiella burnetii (cultures only) Crimean-Congo hemorrhagic fever virus Dengue virus (cultures only) Eastern equine encephalitis virus (cultures only) Escherichia coli, verotoxigenic (cultures only)[a] Ebola virus Flexal virus Francisella tularensis (cultures only) Guanarito virus Hantaan virus Hantaviruses causing hantavirus pulmonary syndrome Hendra virus Hepatitis B virus (cultures only) Herpes B virus (cultures only) Human immunodeficiency virus (cultures only) Highly pathogenic avian influenza virus (cultures only) Japanese Encephalitis virus (cultures only) Junin virus Kyasanur Forest disease virus Lassa virus Machupo virus Marburg virus Monkeypox virus Mycobacterium tuberculosis (cultures only)[a] Nipah virus Omsk hemorrhagic fever virus Poliovirus (cultures only) Rabies virus (cultures only)

	Rickettsia prowazekii (cultures only) Rickettsia rickettsii (cultures only) Rift Valley fever virus (cultures only) Russian spring-summer encephalitis virus (cultures only) Sabia virus Shigella dysenteriae type 1 (cultures only)[a] Tick-borne encephalitis virus (cultures only) Variola virus Venezuelan equine encephalitis virus(cultures only) West Nile virus (cultures only) Yellow fever virus (cultures only) Yersinia pestis (cultures only)
UN 2900 Infectious substances affecting animals only	African swine fever virus (cultures only) Avian paramyxovirus Type 1 – Velogenic Newcastle disease virus (cultures only) Classical swine fever virus (cultures only) Foot and mouth disease virus (cultures only) Lumpy skin disease virus (cultures only) *Mycoplasma mycoides* – Contagious bovine pleuropneumonia (cultures only) Peste des petits ruminants virus (cultures only) Rinderpest virus (cultures only) Sheep-pox virus (cultures only) Goatpox virus (cultures only) Swine vesicular disease virus (cultures only) Vesicular stomatitis virus (cultures only)

[a] When cultures intended for diagnostic or clinical purposes are to be transported by land, they may be classified as infectious substances of Category B. These cultures should not be sent via Royal Mail, but through approved courier. However, they should always be regarded as Category A if they are to be transported by air.

Table A3: Packaging Instruction 620

PACKING INSTRUCTION PI620
This instruction applies to UN 2814 and UN 2900.
The following packagings are authorised provided the special packing provisions are met (see below). Packaging should be UN-type approved and consist of: (a) Inner packagings comprising: (i) leakproof primary receptacle(s); (ii) a leakproof secondary packaging; (iii) other than for solid infectious substances, an absorbent

material in sufficient quantity to absorb the entire contents placed between the primary receptacle(s) and the secondary packaging; if multiple fragile primary receptacles are placed in a single secondary packaging, they shall be either individually wrapped or separated so as to prevent contact between them.

(b) A rigid outer packaging of adequate strength for its capacity, mass and intended use. The smallest external dimension shall be not less than 100 mm.

Additional requirements:

1 Inner packagings containing infectious substances shall not be consolidated with inner packagings containing unrelated types of goods. Complete packages may be overpacked, such an overpack may contain dry ice.

2 Other than for exceptional consignments, e.g. whole organs which require special packaging, the following additional requirements shall apply:

(a) Substances consigned at ambient temperatures or at a higher temperature. Primary receptacles shall be of glass, metal or plastics. Positive means of ensuring a leakproof seal shall be provided, e.g. a heat seal, a skirted stopper or a metal crimp seal. If screw caps are used, they shall be secured by positive means, e.g. tape, paraffin sealing tape or manufactured locking closure.

(b) Substances consigned refrigerated or frozen. Ice, dry ice or other refrigerant shall be placed around the secondary packaging(s) or alternatively in an overpack with one or more complete packages marked in accordance with regulatory requirements. Interior supports shall be provided to secure secondary packaging(s) or packages in position after the ice or dry ice has dissipated. If ice is used, the outer packaging or overpack shall be leakproof. If dry ice is used, the outer packaging or overpack shall permit the release of carbon dioxide gas. The primary receptacle and the secondary packaging shall maintain their integrity at the temperature of the refrigerant used.

(c) Substances consigned in liquid nitrogen. Plastic primary receptacles capable of withstanding very low temperature shall be used. The secondary packaging shall also be capable of withstanding very low temperatures, and in most cases will need to be fitted over the primary receptacle individually. Provisions for the consignment of liquid nitrogen shall also be fulfilled. The primary receptacle and the secondary packaging shall maintain their integrity at the temperature of the liquid nitrogen.
(d) Lyophilized substances may also be transported in primary receptacles that are flame-sealed glass ampoules or rubber-stoppered glass vials fitted with metal seals.

3 Whatever the intended temperature of the consignment, the primary receptacle

or the secondary packaging shall be capable of withstanding without leakage an internal pressure producing a pressure differential of not less than 95 kPa and temperatures in the range -40 ºC to +55 ºC.

Note: The information given in Table A3 is based on the United Nations' Model Regulations on the Transport of Dangerous Goods.[76]

Table A3: Packaging Instruction 620

Special packing provisions for infectious substances (Division 6.2)
Consignors of infectious substances shall ensure that packages are prepared in such a manner that they arrive at their destination in good condition and present no hazard to persons or animals during carriage.Liquids shall be filled into packagings, including IBCs, which have an appropriate resistance to the internal pressure that may develop under normal conditions of carriage. For UN 2814 and 2900, an itemised list of contents shall be enclosed between the secondary packaging and the outer packaging. When the infectious substances to be transported are unknown, but suspected of meeting the criteria for inclusion in Category A and assignment to UN 2814 or UN 2900, the words "suspected Category A infectious substance" shall be shown, in parentheses, following the proper shipping name on the document inside the outer packaging. Before an empty packaging is returned to the consignor, or sent elsewhere, it shall be thoroughly disinfected or sterilized and any label or marking indicating that it had contained an infectious substance shall be removed or obliterated.

Note: The information given in Table A3 is based on the United Nations Model Regulations on the Transport of Dangerous Goods [76]

Table A4 Packaging Instruction 650

PACKAGING INSTRUCTION PI650
This packing instruction applies to UN 3373.
1 The packaging shall be of good quality, strong enough to withstand the shocks and loadings normally encountered during carriage, including trans-shipment between vehicles and containers and between vehicles or containers and warehouses as well as any removal from a pallet or overpack for subsequent manual or mechanical handling. Packagings shall be constructed and closed to prevent any loss of contents that might be caused under normal conditions of carriage by vibration or by changes in temperature, humidity or pressure.

2 The packaging shall consist of three components:
(a) a primary receptacle;
(b) a secondary packaging; and
(c) an outer packaging.

of which either the secondary or outer packaging shall be rigid.

3 Primary receptacles shall be packed in secondary packagings 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 shall be secured in outer packagings with suitable cushioning material. Any leakage of the contents shall not compromise the integrity of the cushioning material or of the outer packaging.

4.For carriage, the mark illustrated below shall be displayed on the external surface of the outer packaging on a background of a contrasting colour and shall be clearly visible and legible. The mark shall be in the form of a square set at an angle of 45° (diamond-shaped) with minimum dimensions of 50 mm by 50 mm; the width of the line shall be at least 2 mm and the letters and numbers shall beat least 6 mm high. The proper shipping name "BIOLOGICAL SUBSTANCE, CATEGORY B" in letters at least 6 mm high shall be marked on the outer packaging adjacent to the diamond-shaped mark.

5 At least one surface of the outer packaging shall have a minimum dimension of 100mm x 100mm

6 The completed package shall be capable of successfully passing the drop test set out in the regulations except that the height of the drop test shall not be less than 1.2 m. Following the appropriate drop sequence, there shall be no leakage from the primary receptacle(s) which shall remain protected by absorbent material, when required, in the secondary packaging.

Figure 5 Packaging marking
(DN: Symbol to be inserted)

7 For liquid substances:

(a) The primary receptacle(s) shall be leakproof.
(b) The secondary packaging shall be leakproof.
(c) If multiple fragile primary receptacles are placed in a single secondary packaging, they shall be either individually wrapped or separated to prevent contact between them.
(d) Absorbent material shall be placed between the primary receptacle(s) and the secondary packaging. The absorbent material shall be in quantity sufficient to absorb the entire contents of the primary receptacle(s)

so that any release of the liquid substances will not compromise the integrity of the cushioning material or of the outer packaging.
(e) The primary receptacle or the secondary packaging shall be capable of withstanding, without leakage, an internal pressure of 95 kPa (0.95 bar).

8 For solid substances:

(a) The primary receptacle(s) shall be siftproof.
(b) The secondary packaging shall be siftproof.
(c) If multiple fragile primary receptacles are placed in a single secondary packaging, they shall be either individually wrapped or separated to prevent contact between them.
(d) if there is any doubt as to whether or not residual liquid may be present in the primary receptacle during carriage then a packaging suitable for liquids, including absorbent materials shall be used.

9 Refrigerated or 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 shall be met. When used, ice or dry ice shall be placed outside the secondary packagings or in the outside packaging or an overpack. Interior supports shall 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 or overpack shall be leakproof. If carbon dioxide, solid (dry ice) is used, the packaging shall be designed and constructed to permit the release of carbon dioxide gas to prevent a build-up pressure that could rupture the packagings and shall be marked “Carbon dioxide, solid” or “Dry ice”.

(b) The primary receptacle and the secondary packaging shall maintain their integrity at the temperature of the refrigerant used as well as the temperatures and the pressures that could result if refrigeration were lost.

10 When packages are placed in an over pack, the package markings required by this packing instruction shall be clearly visible or reproduced on the outside of the overpack.
11 Infectious substances assigned to UN 3373 and are packed and packages which are marked in accordance with this packing instruction are not subject to any other requirement in these Regulations.

12 Clear instructions on filling and closing such packages shall 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.

13 Other dangerous goods shall not be packed in the same packaging as

Class 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 of ADR need be met. 14 If any substance has leaked or has been spilt in a vehicle or container, it may not be reused until after it has been thoroughly cleaned, and, if necessary disinfected or decontaminated. Any other goods or articles carried in the same vehicle or container shall be examined for possible contamination. UN 3373

Note: The information given in Table A4 is based on the United Nations' Model Regulations on the Transport of Dangerous Goods.[76]

Figure 6 Transport of infectious substances: an overview