GLOBAL HEALTH SECURITY

Transport of Infectious Substances

Background to the amendments adopted in the 13th revision of the United Nations Model Regulations guiding the transport of infectious substances

2004

WORLD HEALTH ORGANIZATION

Department of Communicable Disease Surveillance and Response

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Acknowledgement

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PART I

Background

Foreword

Recommendations on the Transport of Dangerous Goods

The Recommendations on the Transport of Dangerous Goods (*1*) are developed by the United Nations Economic and Social Council's Committee of Experts on the Transport of Dangerous Goods in light of the requirement to facilitate transport whilst ensuring the safety of people, property and the environment. They are addressed to governments and international organizations concerned with the regulation of the transport of dangerous goods.

The recommendations concerning the transport of dangerous goods are presented in the form of Model Regulations on the Transport of Dangerous Goods. The Model Regulations aim at presenting a basic scheme of provisions that will allow uniform development of national and international regulations governing the various modes of transport; yet they remain flexible enough to accommodate any special requirements that might have to be met. It is expected that governments, intergovernmental organizations and other international organizations, when revising or developing regulations for which they are responsible, will conform to the principles laid down in these Model Regulations, thus contributing to worldwide harmonization in this field.

The scope of the Model Regulations should ensure their value for all who are directly or indirectly concerned with the transport of dangerous goods. Among other aspects, the Model Regulations cover principles of classification and definition of classes, listing of the principal dangerous goods, general packing requirements, testing procedures, marking, labelling or placarding, and transport documents. There are, in addition, special requirements related to particular classes of goods. With this system of classification, listing, packing, marking, labelling, placarding and documentation in general use, carriers, consignors and inspecting authorities will benefit from simplified transport, handling and control and from a reduction in time-consuming formalities. In general, their task will be facilitated and obstacles to the international transport of such goods reduced accordingly.

The Model Regulations are addressed to all modes of transport. Where less stringent requirements can be applied to only one mode, the fact is generally not indicated. For air transport more stringent requirements may occasionally apply.

Classifications for substances in the Model Regulations are made on the basis of consideration of data submitted to the Committee by governments, intergovernmental organizations, and other international organizations.

Whenever dangerous goods are offered for transport certain measures should be taken to ensure that the potential risks of the dangerous goods offered are adequately communicated to all who may come in contact with the goods in the course of transport. This is accomplished through special marking and labelling of packages to indicate the hazards of a consignment and through the inclusion of relevant information in the transport documents and by placarding transport units.

The competent authority should ensure compliance with the regulations.

This document, Transport of Infectious Substances, focuses on the recommendations described in the 13th edition of the Model Regulations on the Transport of Dangerous Goods for the transport of infectious substances.

The development of the 13th edition of the United Nations Model Regulations

The biennium 2001-2002 introduced major revisions to Division 6.2 – Infectious substances of the Model Regulations.

To provide a scientific basis to assist the Committee of Experts on the Transport of Dangerous Goods (UNCETDG) in the development of improved recommendations pertaining to the transport of infectious substances, the World Health Organization (WHO) called a meeting of experts in October 2001. Participants included representatives of the scientific and medical communities (including infectious disease and biosafety experts), of the United Nations Environmental Programme's Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal, and of the Convention on Biological Diversity/Cartagena Protocol on Biosafety, the Universal Postal Union, and representatives of the Expert Committee UNCETDG.

This group considered a number of factors in developing guidance on the transport of biological materials, devoting particular consideration to the intrinsic hazards of microorganisms and the risks they pose as infectious substances in transport. The outcome was a consensus document which identified those infectious substances that should be transported subject to the full realm of transport regulations (e.g., shipping papers, labels, P620 packaging, and training) and those infectious substances for which P650 packaging should be authorized.

This work was presented at the UNCETDG meeting in December 2001, and subsequently incorporated into a document which provided the basis for deliberations of a working group meeting in March 2002 of members of UNCETDG, WHO and other groups having consultative status with UNCETDG. From this meeting a revised document was subsequently submitted to UNCETDG in July 2002 and the proposed revisions for the transport of infectious substances were adopted with only minor changes. The adoption was confirmed in December 2002, for the 13th revised edition of the Model Regulations.

In the 12th revised edition of the UN Model Regulations of 2001, infectious substances, diagnostic specimens, biological products, genetically modified microorganisms, genetically modified organisms, and wastes, were classified according to WHO Risk Groups.

In the 13th edition of the UN Model Regulations of 2003, infectious substances, cultures, biological products, genetically modified microorganisms, genetically modified organisms, and wastes, are classified according to new transport categories A and B.

The following explains the reasons behind the changes.

Introduction

In the interest of global public health, of progress in scientific research, and of the development of new drugs and treatments to combat diseases, human and animal specimens need to be transported safely, timely, and efficiently from the place where they are collected to the place where they will be analyzed. Regardless of the presumed infection status of the patient, specimens of human and animal origin should be packaged and transported in such a way as to protect those engaged in transportation from the risk of infection. Risks of infection of personnel involved in transport may not be fully eliminated. However, they can undoubtedly be kept to a minimum.

The goal of the amendments to "Division 6.2 – Infectious substances" in the 13th edition of the United Nations Model Regulations for Transport of Dangerous Goods is to facilitate the safe transportation of infectious substances for the benefit of individual patients and for global public health while protecting those engaged in such transportation and the general public from the risk of infection.

The importance of safe and rapid transport of infectious substances was illustrated in early 2003 by the Severe Acute Respiratory Syndrome (SARS) epidemic when, through the worldwide collaboration of scientists based on efficient sharing of samples for analysis and data for interpretation, unprecedented strides in the rapid identification and containment of this disease were achieved.

An understanding of the hazards (potential to cause harm) of microorganisms and the potential risks (probability that harm will occur) during their transport is critical to safeguard those who handle such substances in transport. Often the perceived risk is greater than the actual risk, resulting in delays which may have significant consequences for public health.

The 13th edition of the Model Regulations is based on expert scientific evaluation of the risks in transportation posed by biological materials.

The key changes from previous editions include the move from the concept of risk groups to that of categories of infectious substances based on risk principles, risk assessment, and the clarification and simplification of the packaging requirements for infectious substances in each of the defined categories. Thus the revised Model Regulations define suitable packaging affording a level of safety appropriate to the degree of risk.

The changes incorporated in the 13th edition of the United Nations Model Regulations are the result of long and thoughtful consultations among regulators, the transport industry, medical professionals, scientists, and others. It is anticipated that this effort to produce clearer requirements will lead to higher levels of compliance which will in turn enhance safety in the transport of infectious substances.

Aim of this document

This document provides background to the amendments adopted in the 13th revision of the Model Regulations and seeks to:

1. Clarify risks associated with the transport of infectious substances;
2. Outline the process for modifying Model Regulations;
3. Explain the rationale for changes to the Model Regulations and

4. Provide the United Nations revised text for the transport of infectious substances included in the 13th edition of the Model Regulations.

Rationale for changes in the United Nations Model Regulations

The key changes in the 13th revision of the Model Regulations include:

1. The move from the concept of risk groups to that of categories of infectious substances based on scientific assessment of their risks to humans and animals;
2. Clarification of instructions for packaging infectious substances and clinical specimens.

The move from risk groups to categories of infectious substances

The use of risk groups in transport

The concept of risk groups was introduced into the Model Regulations in 1995. However, the classification of microorganisms into risk groups, originally developed by WHO (*2*), is based on the risks that they pose in the laboratory environment and does not appropriately reflect the risks of infection during transport.

> *In contrast to transport workers, laboratory workers carry out extensive manipulations with microorganisms which place them at higher risk of infection (through accidental exposures caused by splashes, cuts, scratches). Moreover, certain laboratory procedures (e.g., vortexing, mixing, centrifuging) can generate aerosols which place the workers performing those operations at increased risk of infection. These conditions do not usually occur in transport. Spills or leakage of substances alone do not generate aerosols. The generation of aerosols requires energy to be applied to liquid substances using some type of equipment or device, and therefore, the potential for microorganisms to become airborne during transport is extremely remote. Thus overall, microorganisms in transport do not pose the same level of risk as they do in laboratory situations*.

Furthermore, the Model Regulations did not specify which microorganisms fell into which risk groups and since there are differences in classification of organisms between countries, and lack of any classification system in many countries, inconsistencies arose especially in international transport.

However, the most severe consequence of the inappropriate use of risk groups in transport were the over-regulations that the risk group system brought about.

> *Transport requirements derived from previous editions of the Model Regulations were often found to be unclear and open to subjective interpretation; some were overly restrictive and unnecessarily cumbersome, while others were surprisingly lax. This led to an increased level of noncompliance which in turn resulted in a greater potential risk of exposure for transport workers and the public. In addition, the use of risk groups in*

transport caused many infectious substances to be transported according to full dangerous goods regulation even though the hazards they represent, and the risks they pose in transport, could have been more appropriately managed in a less stringent manner, following the performance of a transport-specific risk assessment.

Clarification of instructions for packaging infectious substances and clinical (diagnostic) specimens

The WHO meeting of experts performed a transport-risk assessment based on two principles:

1. Standard Precautions, originally developed for the hospital setting, are designed to reduce the risk of transmission of microorganisms from both recognized and unrecognized sources of infection by providing barrier protections. Standard Precautions apply to blood, all body fluids, secretions, excretions (except sweat), non-intact skin, and mucous membranes. As a consequence, health care providers are encouraged to wear protective clothing, including gloves, gowns, and masks, to protect themselves, the patients or materials, and the environment from infections. For transport purposes, the barrier protection is represented by the package.

2. The Chain of Infection explains the factors that should be taken into consideration when assessing the risk of infection by any given pathogen. These include:
    1. Stability of the agent in the environment
    2. The likely outcome of exposure to the agent
    3. Pathogenicity of the agent and infectious dose
    4. Natural and unnatural routes of infection
    5. Preventive and/or treatment measures.

Transmission of infection and risks in transport of infectious substances

This section provides background to the scientific rationale behind some of the changes in the Model Regulations and illustrates how practices and procedures can be put in place to minimize the risk of infection during transport. Key stages in the chain of infection are described and presented in Figure 1, in order to assist in the understanding of the transmission of infection and the potential risks to workers involved in the transport of infectious substances.

Risk assessment in relation to transport of infectious substances

1. Damage to package

In order for a pathogen to be released, the packaging must either be damaged with sufficient force that the contents of the primary container are released outside the secondary container, the outer packaging, and, if present, the overpacking materials. In addition, there would also have to be a failure of the required absorbent material in the packaging to completely contain the liquid contents.

2. Pathogens released

In order to establish infection, pathogens must be released in sufficient numbers and in a suitable form to harm a susceptible host. The form and purity of the substance directly affects the pathogen's ability to establish infection in the host. In addition, environmental conditions can influence the viability of microorganisms and their ability to cause infections. Conditions such as dehydration, heat (>70°C for most bacteria and viruses), freezing, and exposure to UV light can adversely affect viability.

3. Exposure incident

An incident must occur that provides the opportunity for a pathogen to come into physical contact with a susceptible host.

4. Entry to host

Pathogens must be introduced into a host before infection can be initiated. Although there are several routes of entry available, most pathogens are specific to a particular route of entry. In the event of an exposure incident, some routes of entry are very unlikely (Table 1).

Aerosols and droplets

To generate an aerosol, force must be applied to a liquid. In laboratories, this is done with nebulizers, sonicators, homogenizers, and other similar high-energy equipment. In the transport situation, that "force" is lacking; normal ventilation does not provide sufficient force. Spillage or leakage from packages does not generate any appreciable aerosols either.

People can be very effective aerosol generators. Coughing, sneezing, and even talking generate aerosols; one sneeze can release 2×10^6 viable particles. If that person has tuberculosis, then someone close to him or her (within 1.5 m) can inhale the particles and could become infected. However, infection of the lungs occurs only when aerosolized particles of less than 5 microns in size are inhaled, fail to be trapped by the defence mechanisms in the upper respiratory tract, and manage to reach the lungs.

A thermal explosion of a package containing infectious substances could conceivably generate an aerosol. However, explosions are too powerful for microorganisms to survive and retain their infectivity.

Viruses which cause common colds, influenza, or SARS, are most effectively spread from person to person by aerosols or droplets. Droplets are usually larger than 10 microns in size and are ejected by a person sneezing or coughing. If they land on a person's face or onto an object which someone touches before touching their eyes or mouth, viable organisms in these droplets can be transmitted and cause infection. The organisms are not inhaled deep into the lungs but penetrate through the mucous membranes of the upper respiratory tract. While this mechanism of spread is a potential risk from passenger to passenger in transport, it is highly unlikely that a package can generate viable aerosols or droplets and eject them. Thus aerosol or droplet spread is not considered a significant risk in transport.

Concern is often expressed about the risk of breathing infectious substances following an exposure incident. It is important to recognize that only those pathogens which have the capacity to attach to and invade into the respiratory tract present a risk; others will be removed by the host's efficient natural defence mechanisms. Consequently, respiratory transmission is not generally considered a significant risk in transport of infectious substances.

Bloodborne agents, such as hepatitis B virus (HBV) and human immunodeficiency virus (HIV) can efficiently enter a new host by injection or through broken skin in contact with infected blood or body fluids, and by sexual intercourse (genital tract). Transport exposures are more likely to occur when individuals clean up materials which have leaked without adopting appropriate safety precautions.

Table 1. Routes by which microorganisms can enter an exposed host

Route of entry	Comments
Skin	Intact skin is an effective barrier to almost all microorganisms; wounds, abrasions, or burns are more common sites of entry and infection. Biting arthropods (insects) penetrate the skin during feeding and may introduce microorganisms and parasites. Penetration of skin by infected needles also provides a route for infection.
Conjunctiva (eye)	The conjunctiva is kept clean by the flushing action of tears aided by wiping action of eyelids; the few microbes which successfully enter via the conjunctiva have specific attachment mechanisms.
Oropharynx	Microorganisms entering by the nose or mouth may be inhaled and reach the respiratory tract, swallowed, and enter the gastrointestinal tract, or adhere to the pharynx and invade from this site.
Respiratory tract	Efficient cleansing mechanisms deal with the particles and microorganisms inhaled from the environment; under conditions of light exercise, 95% of 10-micron particles and 80% of 5-micron particles which are inhaled are trapped in the nose and never reach the lower parts of the respiratory tract. Some microorganisms have developed specific mechanisms to avoid being removed by ciliary action in the throat and swallowed.
Gastrointestinal tract	To gain entry microorganisms must be swallowed, survive destruction by stomach acid, bile and enzymes, and attach to the intestinal mucosa.
Genitourinary tract	Some microorganisms are sexually transmitted

5. Infectious dose

The dose or number of microorganisms required to initiate an infection depends on the virulence of the pathogen and the route of entry. Based on available data (*3*), some examples of infectious doses are shown in Table 2.

Table 2. Infection doses for some pathogens

Pathogen	Infectious doses and routes of entry
Vibrio cholerae (to cause cholera)	10^8 organisms by ingestion
Hepatitis B virus	10 virus particles by injection
Influenza A2 virus	800 virus particles by nasopharyngeal inoculation
West Nile fever virus	1 virus particle by intramuscular inoculation

However, it is important to note that most of these data are collected under experimental conditions. Clearly, the higher the concentration of microorganisms in a given volume, as is the case in cultures as opposed to clinical specimens, the higher the risk of there being sufficient organisms to cause an infection.

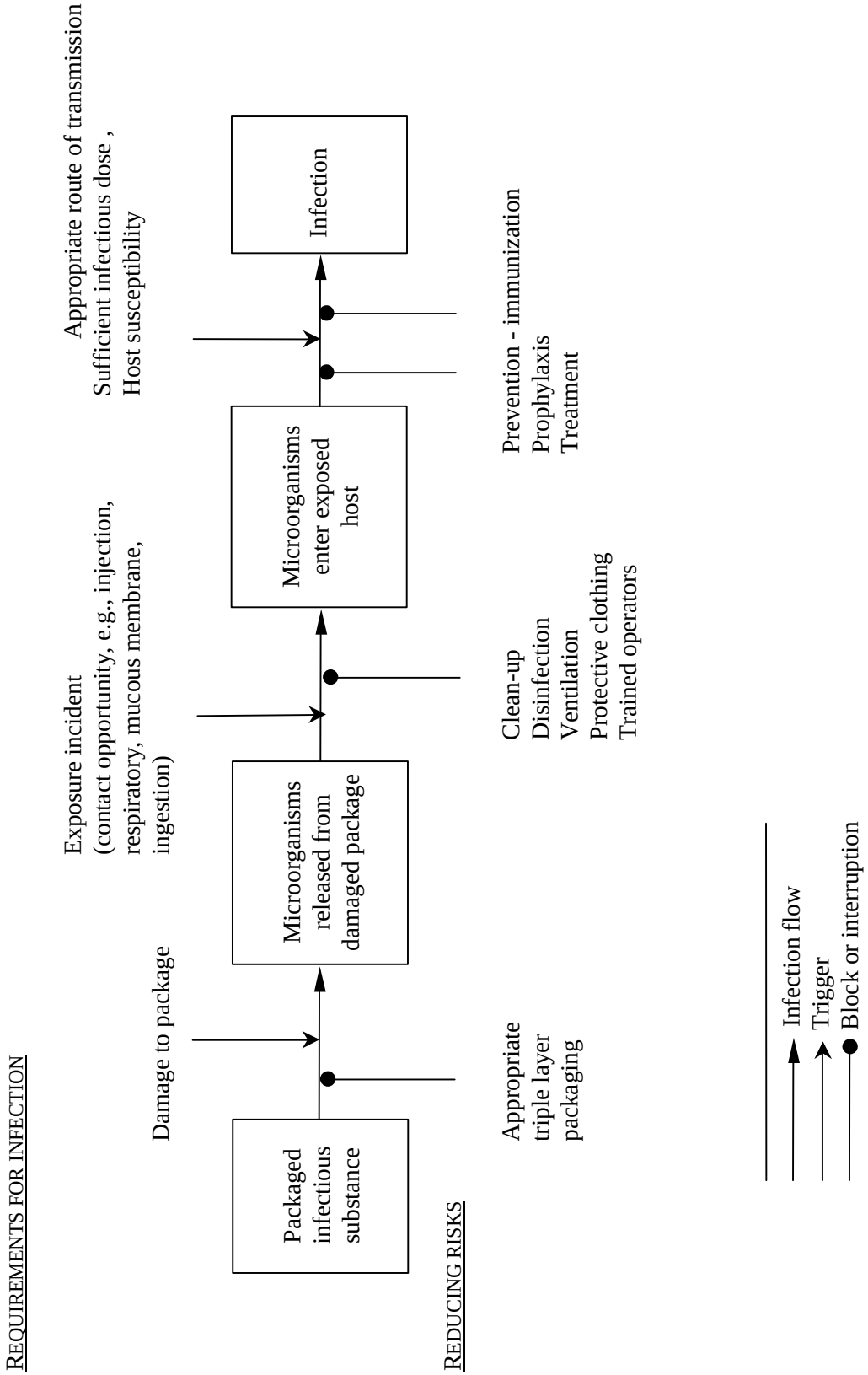
6. Host susceptibility

Gaining entry to a host is not enough to cause an infection. Not only must a sufficient number of microorganisms invade (infectious dose; see above) but they must also withstand the host's defence mechanisms. The human body has a number of natural defence mechanisms to protect itself from daily microbial onslaught (e.g., enzymes in tears and saliva, mucus in the oropharynx and respiratory tract, cilia lining the trachea, stomach acids, and phagocytes in blood and tissues). In addition, immunity can be acquired from previous infections or successful vaccinations that serve to protect the exposed person from specific infections.

7. Infection

Only when an exposure incident involves pathogens in sufficient quantity and virulence, which gain access to an individual's body through an appropriate route of entry and survive that person's immune defences, can infection occur and disease may develop. If any of these conditions fails to be achieved, or if the chain of infection is broken, infection will not occur.

Figure 1. The chain of infection



Hazards and risks

As outlined above, one of the characteristics of pathogens is that they present hazards (qualities with potential to cause harm to humans and animals). Depending on the nature of the pathogen and of the human or animal host, this harm ranges from mild to severe infection.

Hazards are intrinsic to microorganisms

Risks can be reduced

Perceived risks

An understanding of the hazards of microorganisms and the potential risks during their transport is critical to enable the rapid and safe transport of infectious substances for public health investigations and to safeguard those who handle such substances in transport. Often the perceived risk is greater than the actual risk resulting in, for example, packages stopped at airports, refused by carriers, etc. A delay in transport or a refusal to transport specimens may have life-threatening consequences for a patient, delay implementation of appropriate measures to address disease outbreaks, and hinder research necessary to develop treatments or slow the spread of disease.

Reducing risks

As indicated in Figure 1, the risks to those engaged in the transport of infectious substances can be reduced at key points in the chain of infection by:

Appropriate packaging

The key to efficient control and minimization of risk lies in the choice of the most appropriate package. Appropriate packaging provides the necessary and sufficient barriers to prevent leakage of the material to the outside. Triple packaging comprises

1. Leakproof **primary packagings** which are packed in **secondary packagings** in such a way that they cannot break, be punctured or leak their contents into the secondary packaging,
2. Leakproof secondary packagings secured in strong **outer packagings**
3. Suitable cushioning material and **absorbent materials** placed between the primary receptacle(s) and the secondary packaging in a quantity sufficient to absorb the entire contents of the primary receptacle(s) so that any release of liquid substances will not compromise the integrity of the cushioning material or of the outer packaging.

The use of triple packaging has over the years provided effective containment of infectious substances.

Clean-up

The appropriate response in the event of exposure to any infectious substance (including one of unknown nature) is to wash or disinfect the affected area as soon as possible, regardless of the

agent. Even if an infectious substance comes in contact with non-intact skin, washing of the affected area with soap and water can reduce the risk of infection. Where access to soap and water is not readily available, antiseptic hand wipes, or antiseptic solutions can be used instead. The following procedure for clean-up can be used for spills of all infectious substances.

Spill clean-up procedure

Procedure to be followed for cleaning up spillage of infectious substances or blood:

1. Wear gloves and protecting clothing, including face and eye protection
2. Cover the spill with cloth or paper towels to contain it
3. Pour an appropriate disinfectant over the paper towel and the immediately surrounding area (generally, 5% bleach solutions are appropriate but for spills on aircraft, quaternary ammonium disinfectants should be used)
4. After 30 minutes, clear away the materials. If there is broken glass or other sharps are involved, use a dustpan or a piece of stiff cardboard to collect the materials and deposit it into a puncture-resistant container for disposal
5. Clean and disinfect the area of the spillage (repeat steps 2-4)
6. Dispose of contaminated materials into a waste bag

Categories of infectious substances based on scientific assessment of risk

The new Model Regulations have moved away from the concept of risk groups and have placed infectious substances into two categories based on a detailed, case-by-case, risk assessment of microorganisms known to be pathogens.

The new transport categories are defined as:

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 to humans or animals

Category B - an infectious substance which does not meet the criteria for inclusion in category A

Infectious substances included in category A are shown in the list on Part II of this document under Key text of 13th edition of the United Nations Model Regulations 2.6.3.2.2.1.

It is important to recognize that the move from risk groups to categories has not been a simple transformation of risk group 4 microorganisms to category A and all others to category B. Indeed, Category A includes microorganisms which are classified differently (i.e., in risk groups 2, 3, and 4) in different countries and regions (for examples, see box below). Instead, the categorization is the result of the consideration of scientific data concerning the risks of transmission and infection posed during transport of each species of microorganism. The outlined revisions should therefore not be considered as a relaxation or lowering of existing shipping standards, but as a readjustment of shipping parameters according to an appropriate risk assessment.

From risk groups (RG) to Category A – some examples

Flexal virus	RG3 in Europe and
Hantaan virus	RG3 in Canada and Europe
Monkeypox virus	RG3 in Europe, RG4 in Canada
Omsk haemorrhagic fever virus	RG4 in north America, RG3 in Europe

All these are now included in Category A infectious substances

Clarification of instructions for packaging infectious substances and clinical (diagnostic) specimens

Packaging which does not comply with the regulations has an increased likelihood of damage or leakage in transport. The WHO Meeting of Experts in 2001, together with the UNCETDG group, agreed that two package performance levels would be adequate to contain the hazards posed by the full range of known pathogens. Based on the risk assessment (see previous section on Risk assessment in relation to infectious substances), infectious substances containing pathogens for which particular precautions are warranted were placed in category A (see Part II of this document under Key text of 13th edition of the United Nations Model Regulations, 2.6.3.2.2.1a). These must be consigned in P620 packaging. Category B agents are considered to be of less risk because they are not easily transmissible and basic precautions and hygienic practices will serve to prevent exposure and infection in the event of an incident. Category B agents should be consigned in P650 packaging.

Clinical (diagnostic) specimens should be shipped in P650 packaging as a minimum standard. However, cultures (laboratory stocks), even of infectious substances which fall into category B, must be shipped in P620 packages. This is because cultures generally contain higher concentrations of microorganisms in a given volume compared to clinical specimens and consequently have a greater probability of releasing an infectious dose as a result of an exposure incident.

Volumes

The two packing instructions described in the revised 13th edition of the Model Regulations (see Annexes 1 and 2) are refinements and re-evaluations of the performance of previous packing instructions. The differences between P650 and P620 packaging are shown in Table 3. It was considered to be unnecessary to impose inner receptacle or package quantity limits on the substances permitted for transport under the provisions of P650. Providing the specified amount of absorbent material is included in the package, as required by P650, removal of the

inner receptacle (500ml or 500g) and package quantity limitations (4l or 4kg) should not increase risks in transport and there should be no release of liquid substances from the package in case of incident.

Table 3 . A comparison of P650 and P620 packaging

Feature	P650	P620
Primary container	Present	Present
Secondary container	Present	Present
Outer container	Present	Present
Absorbent material for entire contents	Present	Present
United Nations design type testing* (performance requirements)	Should be capable of passing	Must be tested
1.2 m drop test	Must pass	Not required
9 m drop test	Not required	Must pass
Puncture test	Not required	Must pass
Water immersion test	Not required	Must pass
Test reports	Should be available	Must be available
UN approval mark	Not required	Required
Minimum dimensions	Not defined	Defined
Volume and weight restrictions	Not defined	Defined
Packaging size restrictions	Not defined	Defined

*P650 packages are not required to meet UN performance requirements provided they pass a 1.2 m drop test.

The packing instruction P650 is self-contained. That is, no other requirements of the regulations apply provided the requirements of P650 are met.

Incident reporting

No reports of infections resulting from transport-related exposures have been documented. However, there have been reports of the spread of respiratory infections (e.g., tuberculosis) associated with airline travel. Indeed, these were attributed to direct person-to-person contact and not to packaging problems or shipping incidents.

Statistical data collected by a group of central laboratories show that compliant packaging, P650 and P620, accomplishes the goal of assuring that infectious substances are transported

without leakage and loss of materials: 106 broken vials from 4.92 million shipped primary containers per year (21.5 ppm) to any of the worldwide regional offices of the above mentioned central laboratories provides performance records for the efficacy of the recommended packing instructions. Moreover, the same statistical data show that leakages were all contained by the absorbent material, and no damage to secondary containers or outer packages were reported.

References

1. United Nations. *Recommendations on the Transport of Dangerous Goods - Model Regulations, Thirteenth revised edition. 2003*, http://www.unece.org/trans/danger/publi/unrec/rev13/13files_e.html.

2. World Health Organization. *Laboratory Biosafety Manual, 2nd (revised) edition. 2003*, http://www.who.int/csr/resources/publications/biosafety/Labbiosafety.pdf.

3. Collins CH, Kennedy DA. *Laboratory-acquired infections, 4th*. Oxford, Butterworth-Heinemann, 1999.

Part II

United Nations Model Regulations

Key text of 13th edition of the United Nations Model Regulations with explanatory comments

The comprehensive revision of the Model Regulations starts with the definitions of those terms that are used repeatedly within the United Nations text associated with Division 6.2, Infectious Substances. Extracts from the text are set out and explained below. (The United Nations text is italicised).(*1*)

2.6.3 Division 6.2 - Infectious substances

2.6.3.1 Definitions

For the purposes of these Regulations:

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

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

2.6.3.1.3 Cultures (laboratory stocks) are the result of a process by which pathogens are amplified or propagated in order to generate high concentrations, thereby increasing the risk of infection when exposure to them occurs. This definition refers to cultures prepared for the intentional generation of pathogens and does not include cultures intended for diagnostic and clinical purposes.

2.6.3.1.4 Genetically modified micro-organisms and organisms are micro-organisms and organisms in which genetic material has been purposely altered through genetic engineering in a way that does not occur naturally.

2.6.3.1.5 Medical or clinical wastes are wastes derived from the medical treatment of animals or humans or from bio-research.

2.6.3.2 Classification of infectious substances

2.6.3.2.1 Infectious substances shall be classified in Division 6.2 and assigned to UN 2814, UN 2900 or UN 3373, as appropriate.

2.6.3.2.2 Infectious substances are divided into the following categories:

2.6.3.2.2.1 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 to humans or animals. Indicative examples of substances that meet these criteria are given in the table in this paragraph.

NOTE : *An exposure occurs when an infectious substance is released outside of the protective packaging, resulting in physical contact with humans or animals.*

(a) Infectious substances meeting these criteria which cause disease in humans or both in humans and animals shall be assigned to UN 2814. Infectious substances which cause disease only in animals shall be assigned to UN 2900.

(b) Assignment to UN 2814 or UN 2900 shall be based on the known medical history and symptoms of the source human or animal, endemic local conditions, or professional judgement concerning individual circumstances of the source human or animal.

In the case of outbreaks of disease of unknown etiology, individuals should consult with their national competent authorities and/or WHO to determine whether the specimens should be consigned as UN 2814, UN 2900 or UN 3373. Depending on the situation, appropriate ad hoc guidelines may be generated and posted on the world wide web (as was the case for the Severe Acute Respiratory Syndrome (SARS) in early 2003).

NOTE 1*: The proper shipping name for UN 2814 is INFECTIOUS SUBSTANCE, AFFECTING HUMANS. The proper shipping name for UN 2900 is INFECTIOUS SUBSTANCE, AFFECTING ANIMALS only.*

Infectious substances assigned to Category A and present in the form described in the table below must be transported in P620 packaging with full dangerous goods documentation.

NOTE 2**:** *The following table is not exhaustive. Infectious substances, including new or emerging pathogens, which do not appear in the table but which meet the same criteria shall be assigned to Category A. In addition, if there is doubt as to whether or not a substance meets the criteria it shall be included in Category A.*

NOTE 3: *In the following table, the micro-organisms written in italics are bacteria, mycoplasmas, rickettsia or fungi.*

INDICATIVE EXAMPLES OF INFECTIOUS SUBSTANCES INCLUDED IN CATEGORY A IN ANY FORM UNLESS OTHERWISE INDICATED (2.6.3.2.2.1 (a))	
UN NUMBER AND PROPER SHIPPING 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)
	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)
	Nipah virus
	Omsk hemorrhagic fever virus
	Poliovirus (cultures only)
	Rabies virus
	Rickettsia prowazekii (cultures only)
	Rickettsia rickettsii (cultures only)
	Rift Valley fever virus
	Russian spring-summer encephalitis virus (cultures only)
	Sabia virus
	Shigella dysenteriae type 1 (cultures only)
	Tick-borne encephalitis virus (cultures only)

INDICATIVE EXAMPLES OF INFECTIOUS SUBSTANCES INCLUDED IN CATEGORY A IN ANY FORM UNLESS OTHERWISE INDICATED (2.6.3.2.2.1 (a))	
UN NUMBER AND PROPER SHIPPING NAME	MICRO-ORGANISM
	Variola virus
	Venezuelan equine encephalitis virus
	West Nile virus (cultures only)
	Yellow fever virus (cultures only)
	Yersinia pestis (cultures only)
UN 2900 Infectious substances affecting animals only	African horse sickness virus
	African swine fever virus
	Avian paramyxovirus Type 1 - Newcastle disease virus
	Bluetongue virus
	Classical swine fever virus
	Foot and mouth disease virus
	Lumpy skin disease virus
	Mycoplasma mycoides - Contagious bovine pleuropneumonia
	Peste des petits ruminants virus
	Rinderpest virus
	Sheep-pox virus
	Goatpox virus
	Swine vesicular disease virus
	Vesicular stomatitis virus

2.6.3.2.2.2 Category B: An infectious substance which does not meet the criteria for inclusion in Category A. Infectious substances in Category B shall be assigned to UN 3373 except that cultures, as defined in 2.6.3.1.3, shall be assigned to UN 2814 or UN 2900 as appropriate.

NOTE: *The proper shipping name of UN 3373 is "DIAGNOSTIC SPECIMENS" or "CLINICAL SPECIMENS."*

Infectious substances assigned to Category B must be transported in P650 packaging as a minimum standard. They may be transported in P620 packaging. Cultures of Category B substances must be shipped in P620 packaging (as required for Category A) because the increased number of organisms in cultures pose an increased risk of infection in the event of an exposure incident.

Exemptions from the Model Regulations

As in the past editions of the Model Regulations, there are some exemptions to the rules. These exemptions are outlined below. Despite the thorough revisions of the previous sections on infectious substances, this part concerning the exemptions from the Model Regulations may still be unclear and give rise to a series of questions. The Committee UNCETDG is aware of these problems and is planning to clarify this section within the current 2003-2004 biennium. The revisions will be published in the 14th edition of the UN Model Regulations. Pending the new revisions, some explanatory text to the current 13th edition of the Model Regulations is given below.

2.6.3.2.3 Substances which do not contain infectious substances or substances which are unlikely to cause disease in humans or animals are not subject to these Regulations unless they meet the criteria for inclusion in another class.

Microorganisms that are non-pathogenic for humans or animals are not subject to these regulations.

2.6.3.2.4 Blood or blood components which have been collected for the purposes of transfusion or for the preparation of blood products to be used for transfusion or transplantation and any tissues or organs intended for use in transplantation are not subject to these Regulations.

People offering blood for use in transfusions undergo a verbal screening test that allows to estimate/evaluate the probability for pathogens to be present in their blood as minimal. This verbal screening test is sufficient for blood samples, tissues, or organs cleared for transfusion or transplantation, to be exempted from these Model Regulations.

2.6.3.2.5 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.

This text refers to environmental isolates from uninfected areas, or food samples, or other human or animal-sourced substances in a form that any pathogens have been neutralized or inactivated such that they no longer pose a health risk. Samples collected from healthy-looking living persons are considered infectious substances of category B to be shipped in P650.

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

2.6.3.3 Biological products

2.6.3.3.1 For the purposes of these Regulations, biological products are divided into the following groups:

(a) those which are manufactured and packaged in accordance with the requirements of appropriate national authorities and transported for the purposes of final packaging or distribution, and use for personal health care by medical professionals or individuals. Substances in this group are not subject to these Regulations.

(b) those which do not fall under paragraph (a) and are known or reasonably believed to contain infectious substances and which meet the criteria for inclusion in Category A or Category B. Substances in this group shall be assigned to UN 2814, UN 2900 or UN 3373, as appropriate.

***NOTE**: Some licensed biological products may present a biohazard only in certain parts of the world. In that case, competent authorities may require these biological products to be in compliance with local requirements for infectious substances or may impose other restrictions.*

2.6.3.4 Genetically modified micro-organisms and organisms

2.6.3.4.1 Genetically modified micro-organisms not meeting the definition of infectious substance shall be classified according to Chapter 2.9.

2.6.3.5 Medical or clinical wastes

2.6.3.5.1 Medical or clinical wastes containing Category A infectious substances or containing Category B infectious substances in cultures shall be assigned to UN 2814 or UN 2900 as appropriate. Medical or clinical wastes containing infectious substances in Category B, other than cultures, shall be assigned to UN 3291.

2.6.3.5.2 Medical or clinical wastes which are reasonably believed to have a low probability of containing infectious substances shall be assigned to UN 3291.

***NOTE**: The proper shipping name for UN 3291 is "CLINICAL WASTE, UNSPECIFIED, N.O.S." or "(BIO) MEDICAL WASTE, N.O.S". or "REGULATED MEDICAL WASTE, N.O.S.".*

2.6.3.5.3 Decontaminated medical or clinical wastes which previously contained infectious substances are not subject to these Regulations unless they meet the criteria for inclusion in another class.

Special provisions

***318** For the purposes of documentation, the proper shipping name shall be supplemented with the technical name (see 3.1.2.8). Technical names need not be shown on the package. 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 transport document, but not on the outer packagings.*

Special provision 318 applies to UN 2814 and UN 2900.

***319** This entry applies to human or animal material including, but not limited to, excreta, secreta, blood and its components, tissue and tissue fluids, and body parts being transported for purposes such as research, diagnosis, investigational activities, disease treatment or prevention. Substances packed and marked in accordance with packing instruction P650 are not subject to any other requirements in these Regulations.*

Special provision 319 applies to UN 3373.

Annex 1

Packing instruction P620

P620	**PACKING INSTRUCTION**	**P620**

This instruction applies to UN Nos. 2814 and 2900.

The following packagings are authorized provided the special packing provisions of **4.1.8** are met:

Packagings meeting the requirements of Chapter 6.3 and approved accordingly consisting of:

(a) Inner packagings comprising:

(i) watertight primary receptacle(s);

(ii) a watertight 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 in accordance with the provisions of 1.2.1 and 5.1.2: 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 6.3.1.1. 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. Plastics 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.

Annex 2

Packing instruction P650

P650	PACKING INSTRUCTION	P650

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 transport, including transhipment between transport units and between transport units 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 transport 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.

(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 transport, 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 width of the line shall be at least 2 mm; the letters and numbers shall be at least 6 mm high.

(5) The completed package shall be capable of successfully passing the drop test in 6.3.2.5 as specified in 6.3.2.3 and 6.3.2.4 of the Model Regulations except that the height of the drop test shall not be less than 1.2m.

(6) 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).

(7) 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.

(8) 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.

(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 Regulations.

(10) 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.