Shipping of Infectious Substances and Diagnostic Specimens

SAND No. 2008-0480P
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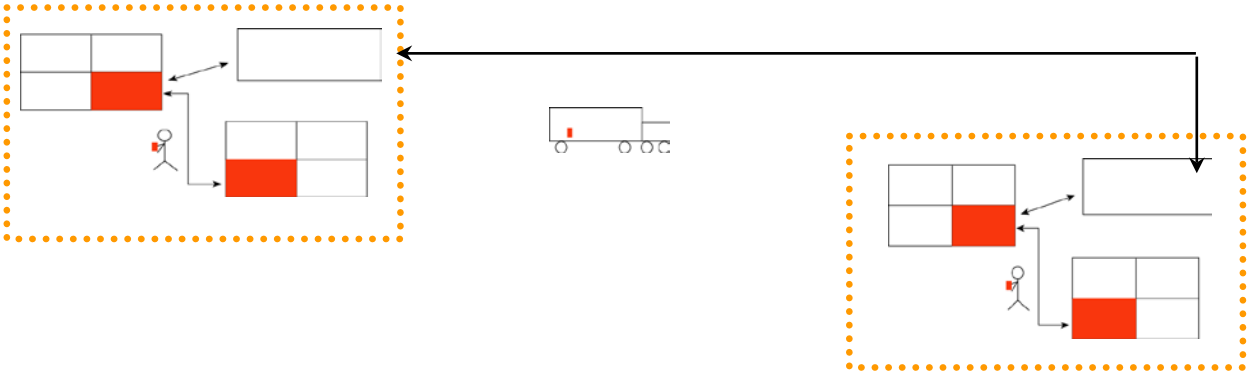
Infectious Substance Transport

- **Transport – movement of biological material outside of a restricted area**
  - Research labs
    - Sample transfers are necessary for study and to further research
  - Public health labs and diagnostic labs
    - Sample transfers are necessary for diagnosis and analysis
- **Transport can occur**
  - Across international borders
  - Within a country
  - Within a facility



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Material Transfer Agreement (MTA)

- **A material transfer agreement is a contract between the sender and recipient organizations**
  - Defines the rights and responsibilities of each
  - Provides a record of the transfer

- **Issues with sharing materials that may be addressed in a MTA include:**
  - Ability to publish / academic freedom
  - Ownership of materials to be shared
  - Ownership of intellectual property
  - Further distribution of materials
  - Liability

Import, Export, and Biosecurity Regulations

- **Many countries have import regulations requiring recipients to get a permit prior to importation**
  - Helps expedite clearance of infectious materials through customs
- **Export controls and export licensing help facilitate legitimate trade and ensure compliance with international treaties**
  - Some countries abide by Australia Group recommendations for export controls
  - Biological and Toxin Weapons Convention requires State Parties to:
    - **Prevent the transfer of materials which might assist the manufacture, or any means of acquiring biological weapons (Article III)**
  - United Nations Security Council Resolution 1540 requires all States to:
    - **Establish and maintain appropriate effective national export and trans-shipment controls**
- **National biosecurity regulations**
  - Typically require approval of recipient prior to shipment

Regulations That May Impact Shipping

- **Regulations that impact approvals and process**
  - Biosecurity regulations
  - Export and import control regulations
- **Regulations that impact shipping process**
  - UN Model Dangerous Goods regulations
  - Regional regulations
    - **European rail and road regulations, NAFTA**
  - National shipping regulations
  - Local shipping regulations
  - Regulations for each mode of transportation
    - **Air, Road, Rail, Sea**
  - Postal regulations
  - Carrier requirements
  - WHO recommendations

Development of Regulations for Transport of Infectious Substances

UN Transport of Dangerous Goods Sub-Committee

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Model Regulations on the Transport of Dangerous Goods

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ADR (road) | **RID (rail)** | **IMO (sea)** | **ICAO (air)** → **IATA (air)**

National Regulations

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UN : Transport of Dangerous Goods Sub-Committee

- **Meets 4 times in every 2 year period**
- **Develops Model Regulations on the Transport of Dangerous Goods**
- **27 countries with voting status**
  - Argentina, Australia, Austria, Belgium, **Brazil**, Canada, China, Czech Republic, Finland, France, Germany, India, Iran, Italy, Japan, Mexico, Morocco, Netherlands, Norway, Poland, Portugal, Russian Federation, South Africa, Spain, Sweden, UK, and US
- **Non-voting observers (numerous countries and non-governmental organizations), including**
  - ICAO (International Civil Aviation Organization)
  - IATA (International Air Transport Association)
  - EBSA (European Biological Safety Association)
  - ABSA (American Biological Safety Association)
  - WHO (World Health Organization)

- **UN Transport Secretariat's Website**
  - http://www.unece.org/trans/main/dgdb/dgsubc/c3age.html

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What are Dangerous Goods?

- **Definition from DGR**
  - "Dangerous goods are articles or substances which are capable of posing a risk to health, safety, property, or the environment and … which meet the criteria from one or more of the nine UN hazard classes"

- **Dangerous goods are classified into:**
  - 9 hazard groups
  - Some classes are further divided into divisions
  - Some classes or divisions have packing groups to identify how dangerous a substance is
    - **Packing Group I – highest danger**
    - **Packing Group II – medium danger**
    - **Packing Group III – low danger**

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Nine Classes of Dangerous Goods

- **Class 1 Explosives**
- **Class 2 Gases**
- **Class 3 Flammable Liquids**
- **Class 4 Flammable Solids**
- **Class 5 Oxidizing Substances and Organic Peroxides**
- **Class 6 Toxic and Infectious Substances**
  - 6.1 Toxic substances
    - **Includes toxins**
  - 6.2 Infectious substances
    - **Includes cultures, pathology specimens**
- **Class 7 Radioactive Material**
- **Class 8 Corrosives**
- **Class 9 Miscellaneous Dangerous Goods**
  - Includes dry ice

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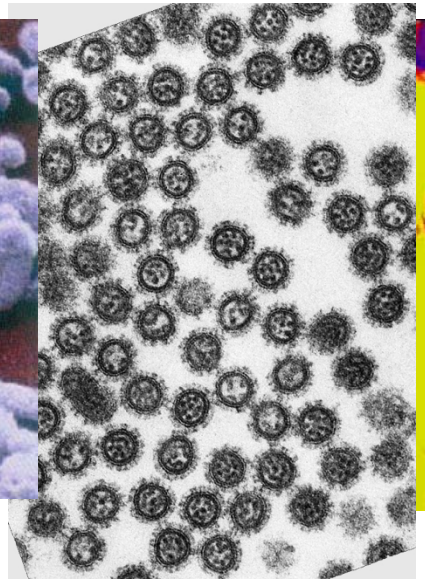
Definitions

- **Infectious Substances**
  - Substance known or which is reasonably expected to contain pathogens
  - Pathogens are microorganisms (including bacteria, viruses, rickettsiae, parasite, fungi, and other agents such as prions), which can cause disease in humans or animals
  - Divided into 2 categories: Category A and Category B

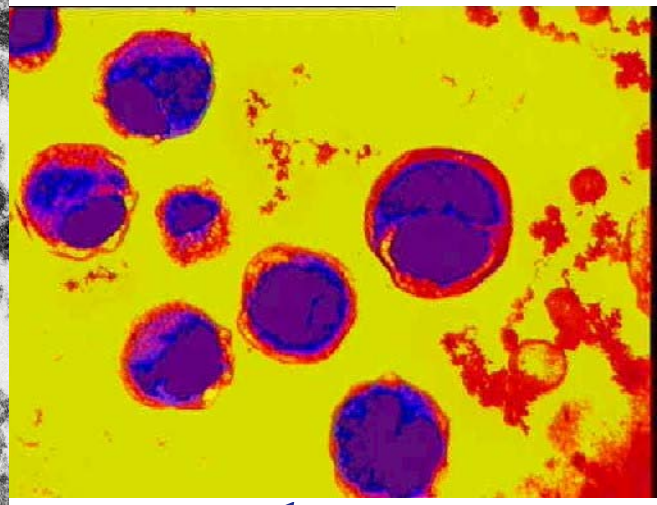
Thielaviopsis

Coxiella burnetii



Influenza A

Chlamydia



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Classifying and Identifying Samples for Shipping

- **The United Nations assigns a number to every type of dangerous goods**
- **The Proper Shipping name must be used**
  - If not exactly as in regulations, airlines will reject the package
- **Classification determines requirements and which Packing Instructions must be followed**

- **Examples:**
  - UN 2814 INFECTIOUS SUBSTANCES, AFFECTING HUMANS
  - UN 2900 INFECTIOUS SUBSTANCES, AFFECTING ANIMALS ONLY
  - UN 3373 BIOLOGICAL SUSBSTANCES, CATEGORY B
  - UN 1845 CARBON DIOXIDE, SOLID or DRY ICE

- **If samples of GMOs, patient specimens, regulated medical waste, or biological products also meet the definition of infectious substances, classify as UN 2814, 2900, or 3373.**
  - Otherwise, refer to the regulations for UN numbers and shipping requirements.

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Determining if a Sample is Category A or Category B

- **Risk-based classification**
  - Risk from a shipping perspective, not a laboratory biosafety perspective
    - **Damage to Package**
    - **Pathogens Released**
    - **Exposure Incident**
    - **Entry to Host**
    - **Infectious Dose**
    - **Host Susceptibility**
    - **Infection**

- **Tables of Indicative Samples of Category A; Tables not exhaustive**
  - New or emerging pathogens meeting same criteria shall be classified as Category A
  - Cultures may be Category A or B depending on microorganisms

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Category A Infectious Substances

- **An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals**

- **Examples of Category A infectious substances are given in a list**
  - List is not exhaustive

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Examples of Category A Infectious Substances

Table 3.6.D
Indicative Examples of Infectious Substances Included in Category A in Any Form Unless Otherwise Indicated (3.6.2.2.2.1)

UN Number and Proper Shipping Name	Micro-organism
UN 2814	*Bacillus anthracis* (cultures only)
Infectious substance	*Brucella abortus* (cultures only)
affecting humans	*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
	Hantavirus causing hemorrhagic fever with renal 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

UN Number and Proper Shipping Name	Micro-organism
	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 (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)
	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	African swine fever virus (cultures only)
Infectious substances	Avian paramyxovirus Type 1 – Velogenic Newcastle disease virus (cultures only)
affecting animals	Classical swine fever virus (cultures only)
	Foot and mouth disease virus (cultures only)
	Goatpox 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)
	Swine vesicular disease virus (cultures only)
	Vesicular stomatitis virus (cultures only)

Exemptions - Examples

- **Blood or blood products for transfusion**
- **Tissues or organs for transplant**
- **Materials with low probability of containing infectious substances (foodstuffs, water samples, living persons)**
- **However, WHO recommends that all specimens of human or animal origin be packaged in P650 as a minimal standard!**

Infectious Substances Packaging

Category A Infectious Substances

- Most durable triple packaging
- Full dangerous goods documentation
- Packing Instruction 602

Category B Infectious Substances

- Less stringent triple packaging
- No dangerous goods documentation required
- Packing Instruction 650

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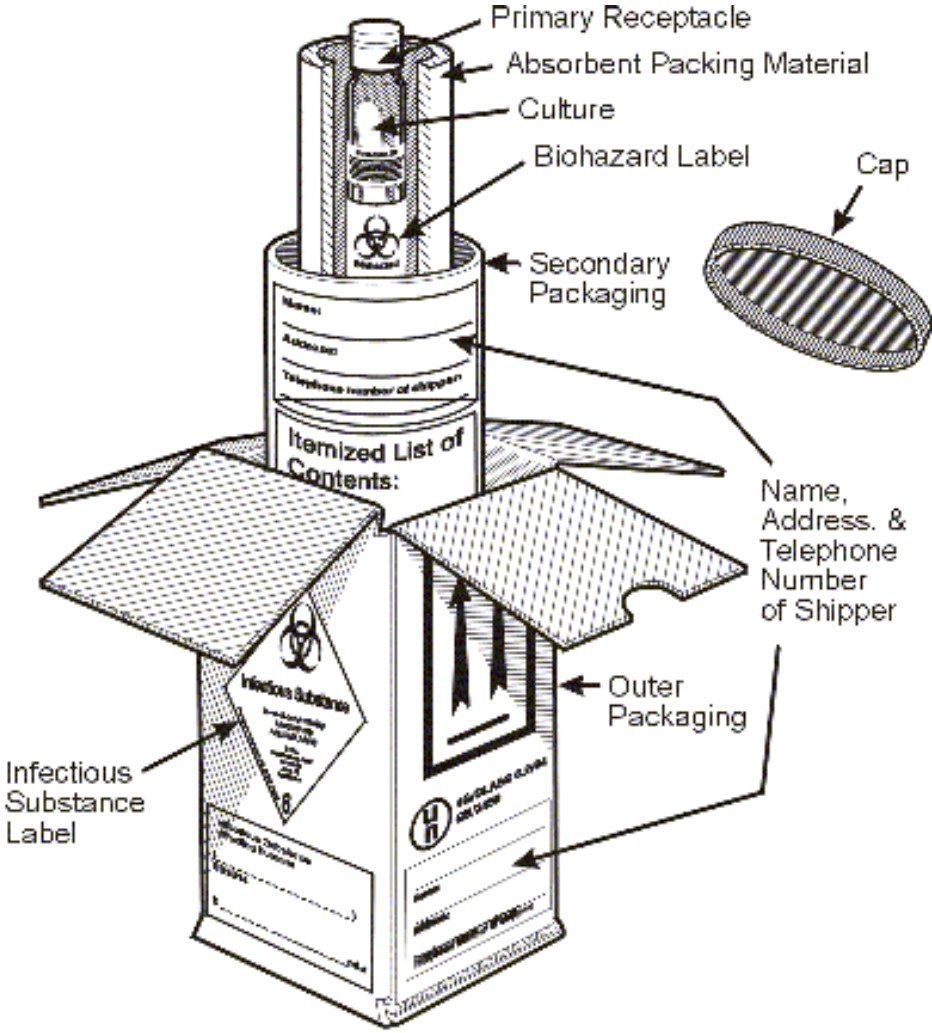
Overview of Packaging

- **Triple packaging required for Category A and B**
- **Primary receptacle**
  - A primary watertight, leak-proof receptacle containing the specimen
- **Secondary packaging**
  - A durable, watertight, leak-proof package to enclose and protect the primary receptacle(s)
  - Absorbent material shall be used to absorb all fluid in case of breakage
- **Outer packaging**
  - Secondary packagings are placed in outer packagings with cushioning material
  - Outer packagings protect their contents from physical damage while in transit
  - At least one external surface with a minimum dimension of 10x10 cm



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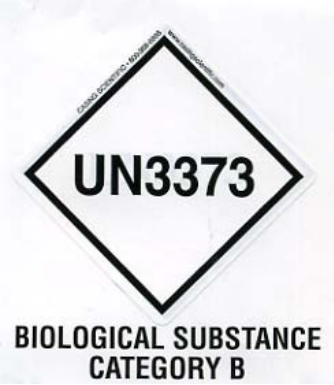
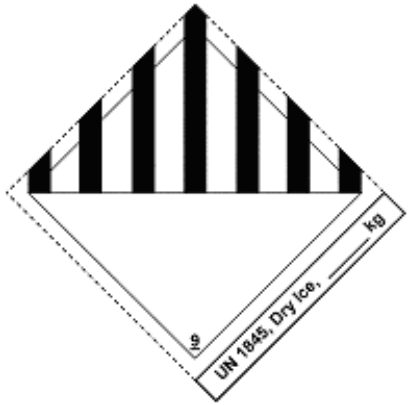
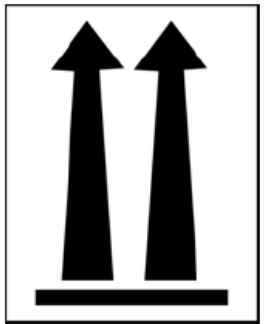
Overview of Marking and Labeling

- **Markings provide information on**
  - Contents of package
  - Nature of hazard
  - Applicable packaging standards
  - Must be clearly visible
- **Labels – two types**
  - Hazard labels required for most dangerous goods
    - **Diamond-shaped**
  - Handling labels required for some dangerous goods
    - **Various shapes**
  - Affixed to outside of each package







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Packaging, Labeling, Marking for Category A

- **Packaging must meet UN Class 6.2 specifications (UN Specification marking) and comply with Packing Instruction P620 (PI602)**
- **Tests**
  - 9 m drop test (dry, wet, -18°C, dry ice)
  - Puncture test
  - Stacking test
  - Internal pressure test – 95 kPa
- **Air Transport Maximum Net Quantity**
  - 50 ml or 50 g per package for passenger aircraft
  - 4 l or 4 kg for cargo aircraft
- **Markings on outer packaging or overpack**
  - Shipper's name, address
  - Phone # of responsible person for the shipment
  - Receiver's name, address, phone #
  - UN number followed by proper shipping name
    - **Technical names no longer required – consider security issues before including**
  - Temperature storage requirements (optional)
  - If dry ice or liquid nitrogen is used: UN number and proper shipping name of refrigerant and net quantity
- **All applicable labels**

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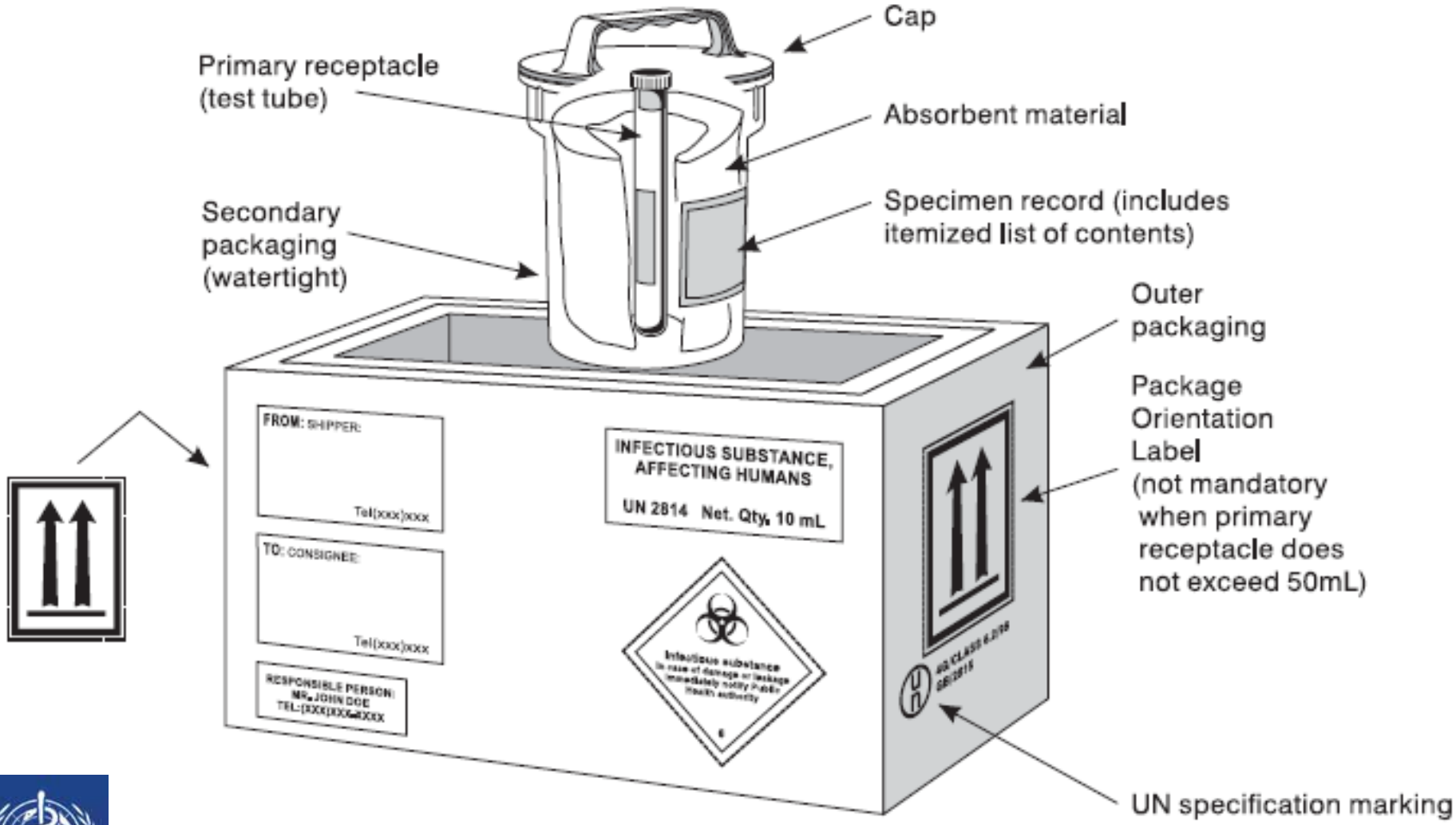
Category A Packaging



Packaging, Labeling, Marking for Category B

- **Packaging must comply with Packing Instruction P650 (PI650)**
- **No test documentation needed**
  - 1.2 m drop test (dry, wet, -18°C, dry ice)
- **Air Transport Maximum Net Quantity**
  - 1 l (liquids) or 1 kg (solids) per primary receptacle
  - 4 l or 4 kg total per package

- **Markings on outer packaging or overpack**
  - Shipper's name, address
  - Phone # of responsible person for the shipment
  - Receiver's name, address, phone #
  - UN number followed by proper shipping name
    - **Technical names no longer required – consider security issues before including**
  - Temperature storage requirements (optional)
  - If dry ice or liquid nitrogen is used: UN number and proper shipping name of refrigerant and net quantity
- **All applicable labels**

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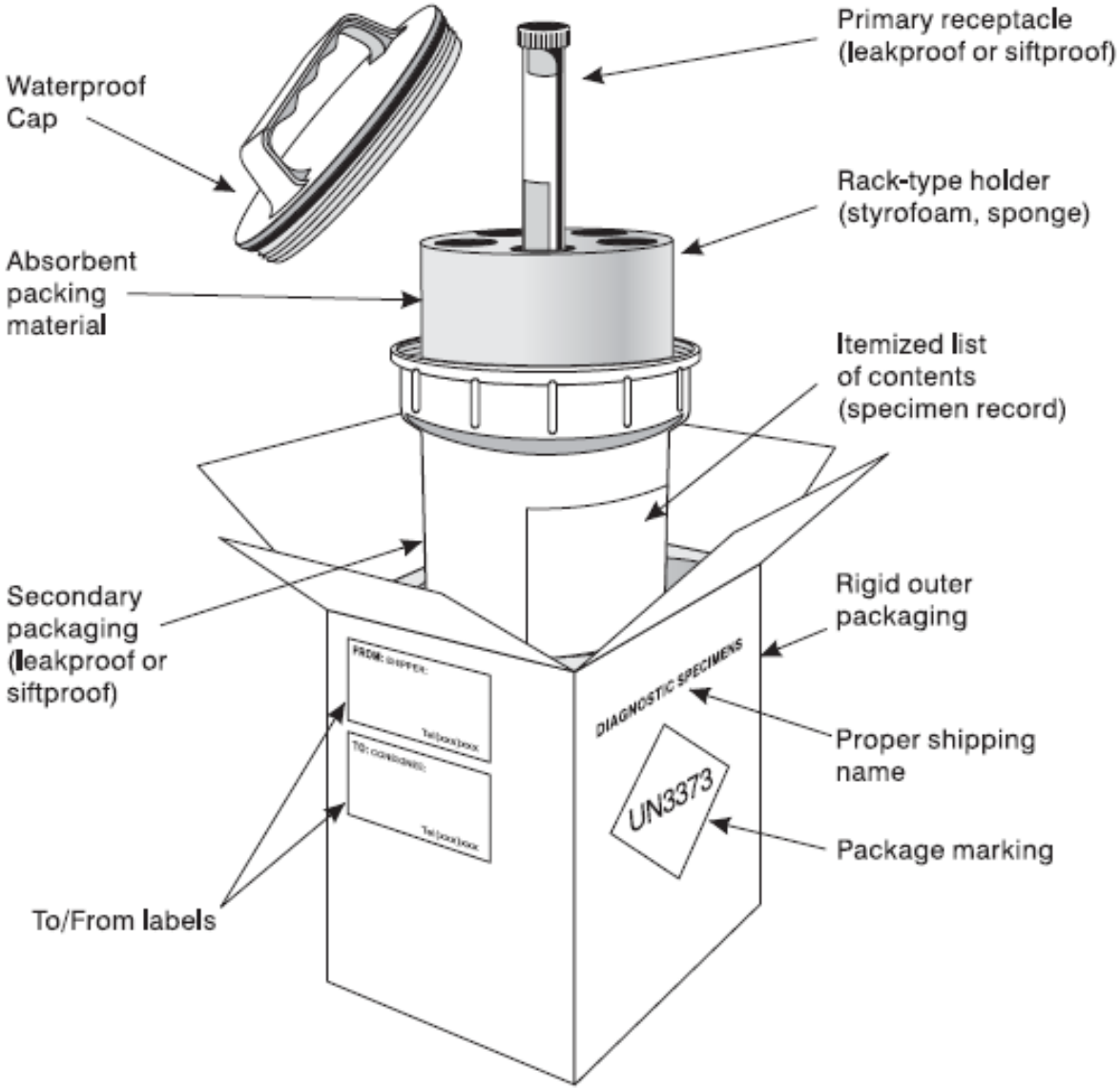
Category B Packaging



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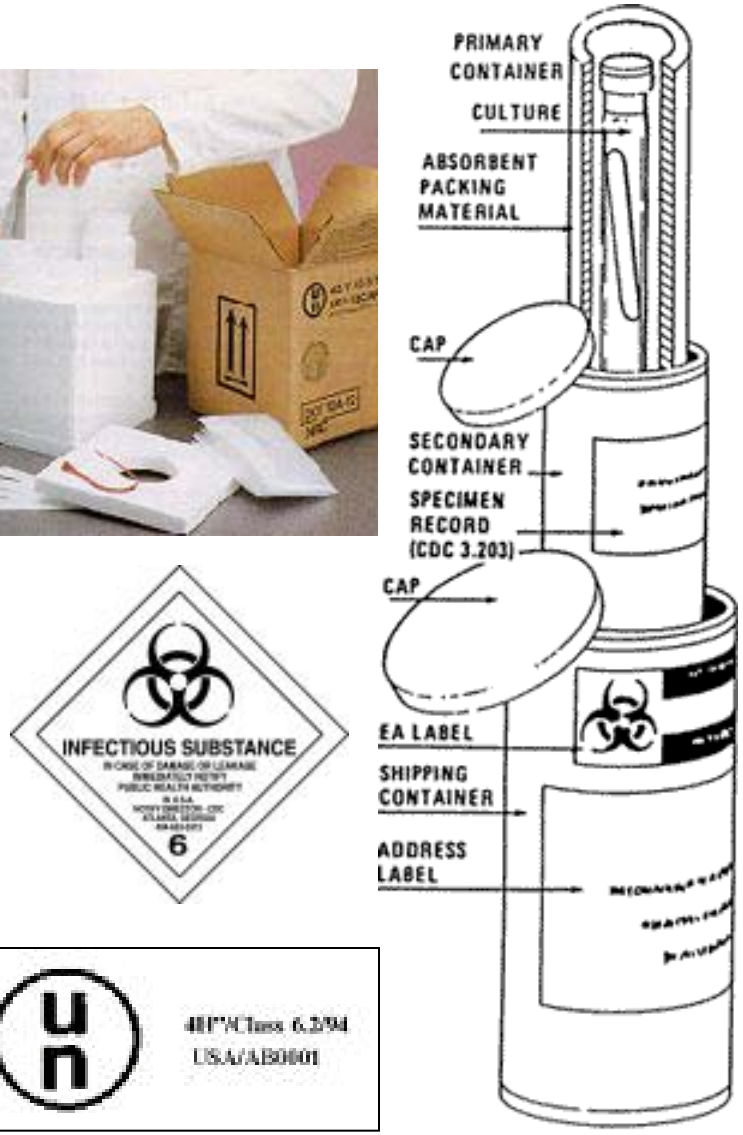
Shipping Infectious Substances with Dry Ice

- **Two options**
  - "All packed in one fibreboard box"
    - UN Specification Box that holds both the samples and the dry ice in one outer package. UN Specification markings are visible on outside of this box
  - "Overpack used"
    - Infectious substances packaged in a smaller UN Specification Box that does not hold the dry ice
    - This smaller UN Specification Box is placed in an outer box or overpack that can hold the dry ice
    - Overpack is not a UN Specification Box but must be marked
      - "Inner packages comply with prescribed specifications"
      - All markings and labels on inside box must also be on overpack
      - Outside box must be marked with word "overpack"
    - Overpacks used when several packages are combined to form one unit and sent to the same destination by a single shipper



Remember, dry ice is a Class 9 dangerous good

Required Documentation

- **For all shipments, consider**
  - Is an import and/or an export permit needed?
  - Material transfer agreement or other agreement to share materials prior to shipping?
  - Documentation indicating recipient is authorized to have material?
  - Packing list / proforma invoice, which includes
    - **Receiver's address**
    - **Number of packages**
    - **Detail of contents**
    - **Weight**
    - **Value (for customs purposes, indicate a minimal value if items supplied free of charge)**
  - Shipping waybill
- **Category A packages also require**
  - Shipper's Declaration for Dangerous Goods
  - An itemized list of contents (e.g. packing list) which is enclosed between the secondary and outer packaging

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Facility Responsibilities in Shipping

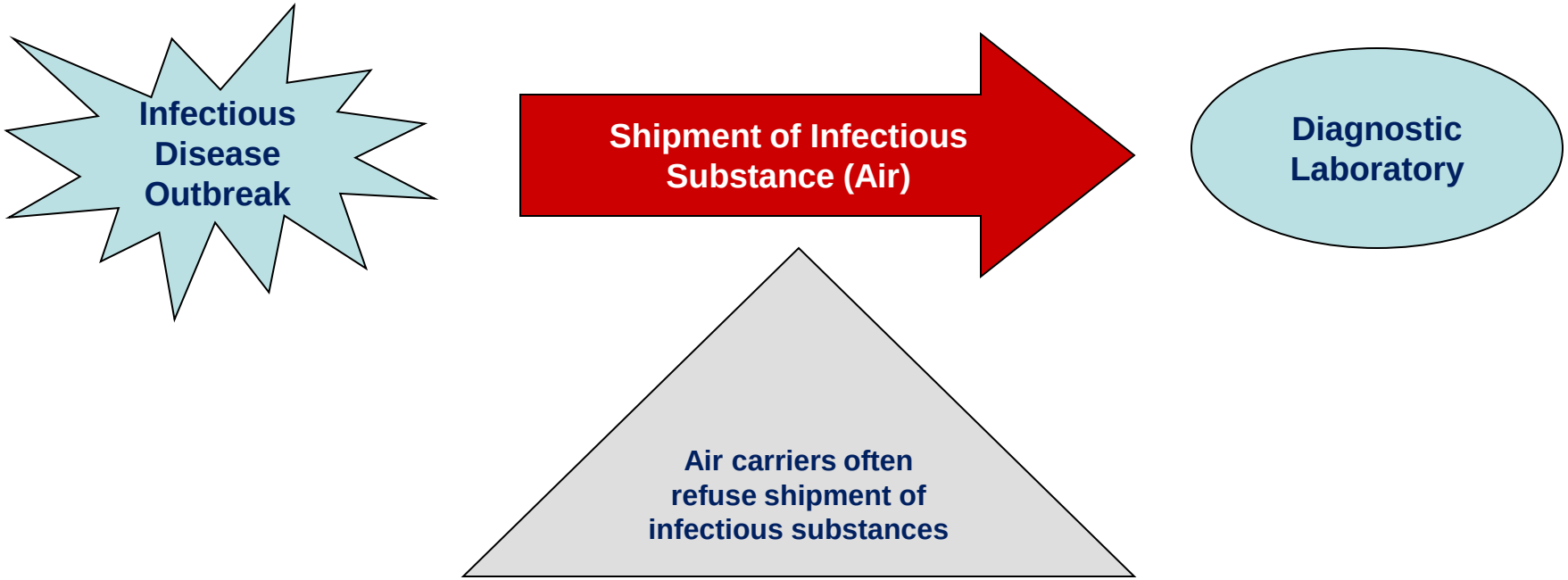
- **As discussed at beginning, institution's need system to:**
  - Ensure appropriate approvals and paperwork in place prior to shipping
- **Ensure that packages are prepared in such a manner that they arrive at their destination in good condition and present no hazard to persons or animals during transport**
  - Classification, Packaging, Labeling, Marking, Documentation
- **Control of samples prior to shipping**
  - Which personnel are authorized to have access to the materials and information
  - Limited access to packages prior to hand over to carrier
    - **E.g. secure storage for packages waiting to be picked up by carrier**
  - Using a chain of custody may be appropriate for transport of higher security risk materials
    - **Record all individuals who have contact with the dangerous pathogens and toxins up until moment package turned over to carrier**

Facility Responsibilities in Shipping, continued

- **Selection of an appropriate carrier that can provide appropriate security by**
  - Ensuring reliable and trustworthy people handle the package
  - Controlling access to transport facilities, docks, and vehicles
  - Tracking shipping progress
  - Providing ongoing security training for employees

- **Verification that recipient receives package as expected**
  - Email or fax preferred since receipt is documented

Risk Perception in Transportation



Time Delay = Increase in deaths and greater economic damage

Summary

- **Many factors affect the transportation of infectious substances**
  - Security becoming a more important concern issue
- **UN Model regulations revised every two years**
- **Specific packaging requirements for international shipments**
  - Category A vs Category B
- **Training requirements**