



# Shipping of Infectious Substances and Diagnostic Specimens



**International Biological Threat Reduction  
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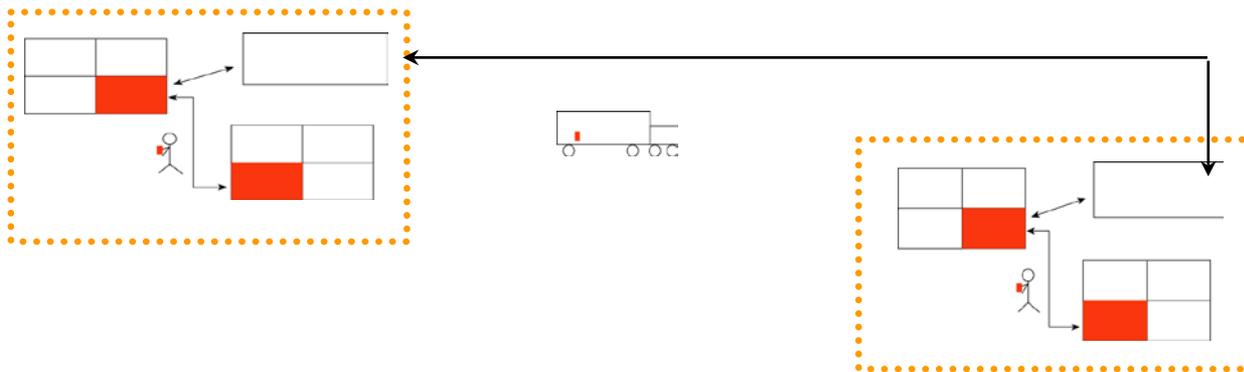
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# Infectious Substance Transport

- **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





# Material Transfer Agreement (MTA)

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- **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



Model Regulations on the Transport of Dangerous Goods



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



National Regulations





# 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>





# 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**



# 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

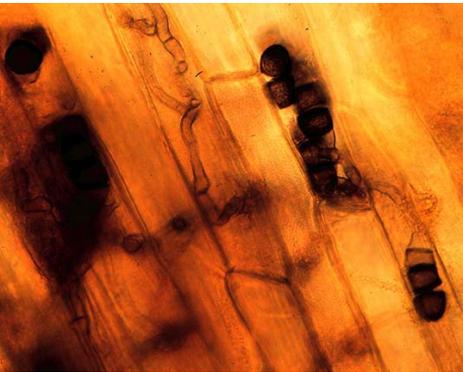


# Definitions



- **Infectious Substances**

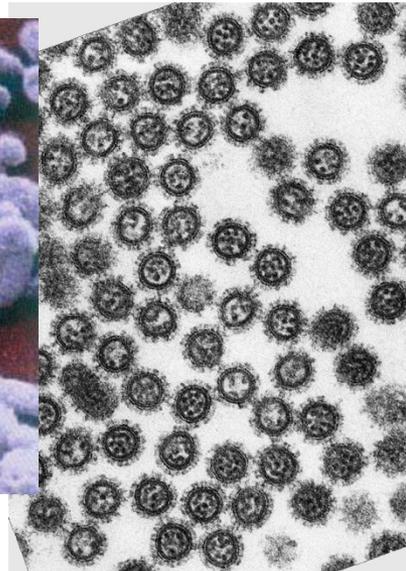
- Substance known or which is reasonably expected to contain pathogens
- Pathogens are microorganisms (including bacteria, viruses, rickettsiae, parasite, fungi, and other agents such as prions), which can cause disease in humans or animals
- Divided into 2 categories: Category A and Category B



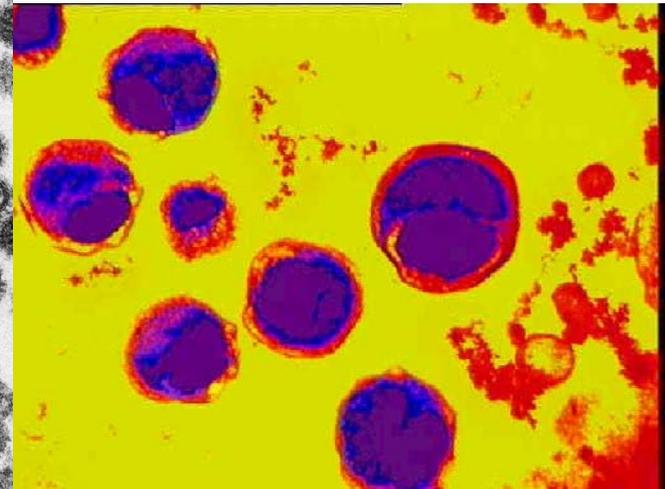
*Thielaviopsis*



*Coxiella burnetii*



Influenza A



*Chlamydia*



# 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 SUBSTANCES, 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.



# 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



# 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



# 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
<b>UN 2814</b>	<i>Bacillus anthracis</i> (cultures only)
<b>Infectious substance affecting humans</b>	<i>Brucella abortus</i> (cultures only)
	<i>Brucella melitensis</i> (cultures only)
	<i>Brucella suis</i> (cultures only)
	<i>Burkholderia mallei</i> – <i>Pseudomonas mallei</i> – Glanders (cultures only)
	<i>Burkholderia pseudomallei</i> – <i>Pseudomonas pseudomallei</i> (cultures only)
	<i>Chlamydia psittaci</i> – avian strains (cultures only)
	<i>Clostridium botulinum</i> (cultures only)
	<i>Coccidioides immitis</i> (cultures only)
	<i>Coxiella burnetii</i> (cultures only)
	Crimean-Congo hemorrhagic fever virus
	Dengue virus (cultures only)
	Eastern equine encephalitis virus (cultures only)
	<i>Escherichia coli</i> , verotoxigenic (cultures only)
	Ebola virus
	Flexal virus
	<i>Francisella tularensis</i> (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
	<i>Mycobacterium tuberculosis</i> (cultures only)
	Nipah virus
	Omsk hemorrhagic fever virus
	Poliovirus (cultures only)
	Rabies virus (cultures only)
	<i>Rickettsia prowazekii</i> (cultures only)
	<i>Rickettsia rickettsii</i> (cultures only)
	Rift Valley fever virus (cultures only)
	Russian spring-summer encephalitis virus (cultures only)
	Sabia virus
	<i>Shigella dysenteriae</i> 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)
	<i>Yersinia pestis</i> (cultures only)
<b>UN 2900</b>	African swine fever virus (cultures only)
<b>Infectious substances affecting animals</b>	Avian paramyxovirus Type 1 – Velogenic Newcastle disease virus (cultures only)
	Classical swine fever virus (cultures only)
	Foot and mouth disease virus (cultures only)
	Goatpox virus (cultures only)
	Lumpy skin disease virus (cultures only)
	<i>Mycoplasma mycoides</i> – 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 B Infectious Substances

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

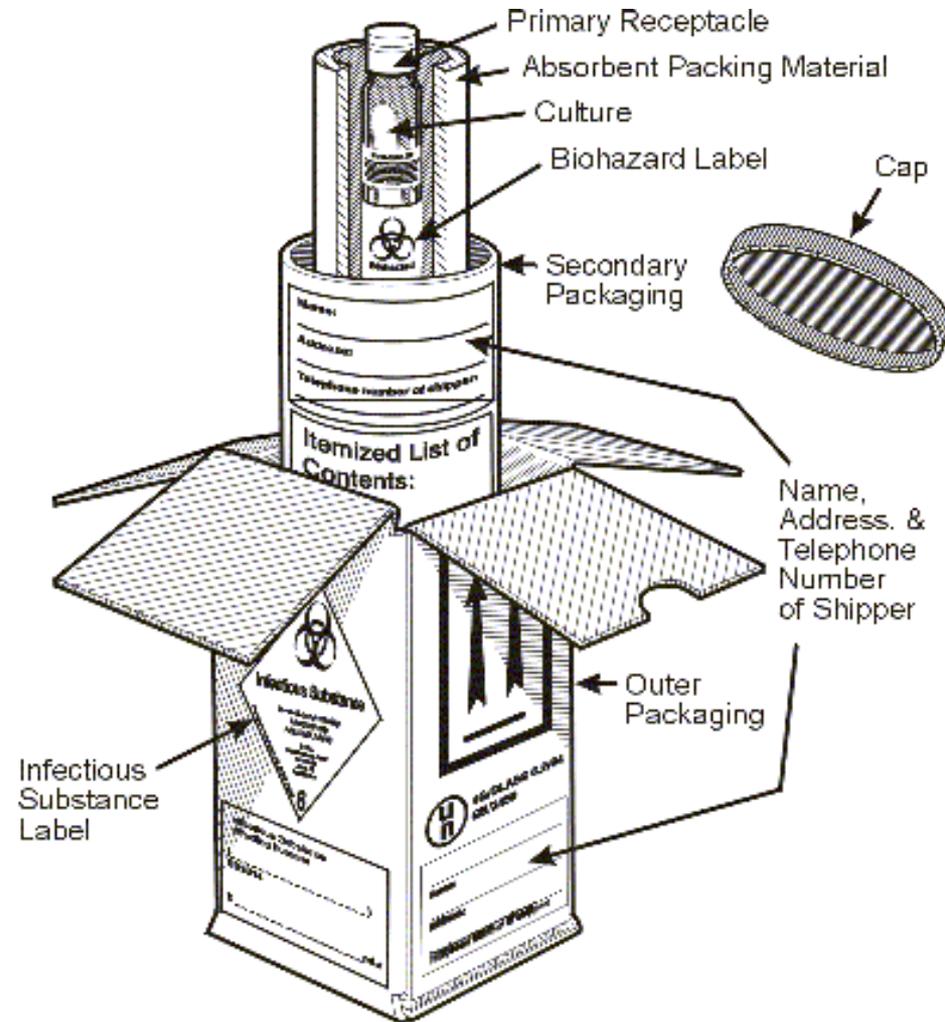
## Category A Infectious Substances

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



# 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





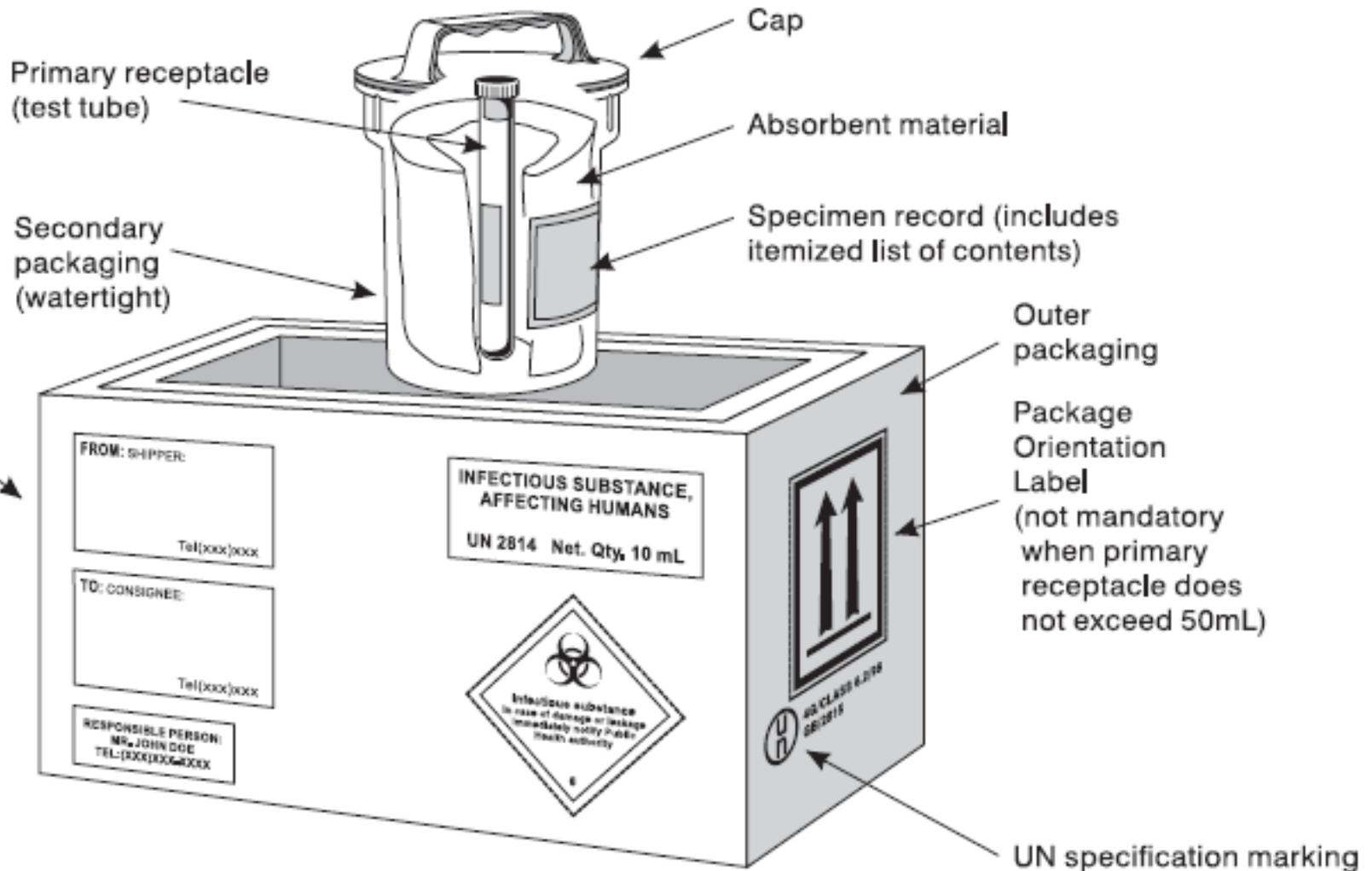


# Packaging, Labeling, Marking for Category A

- **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**



# Category A Packaging





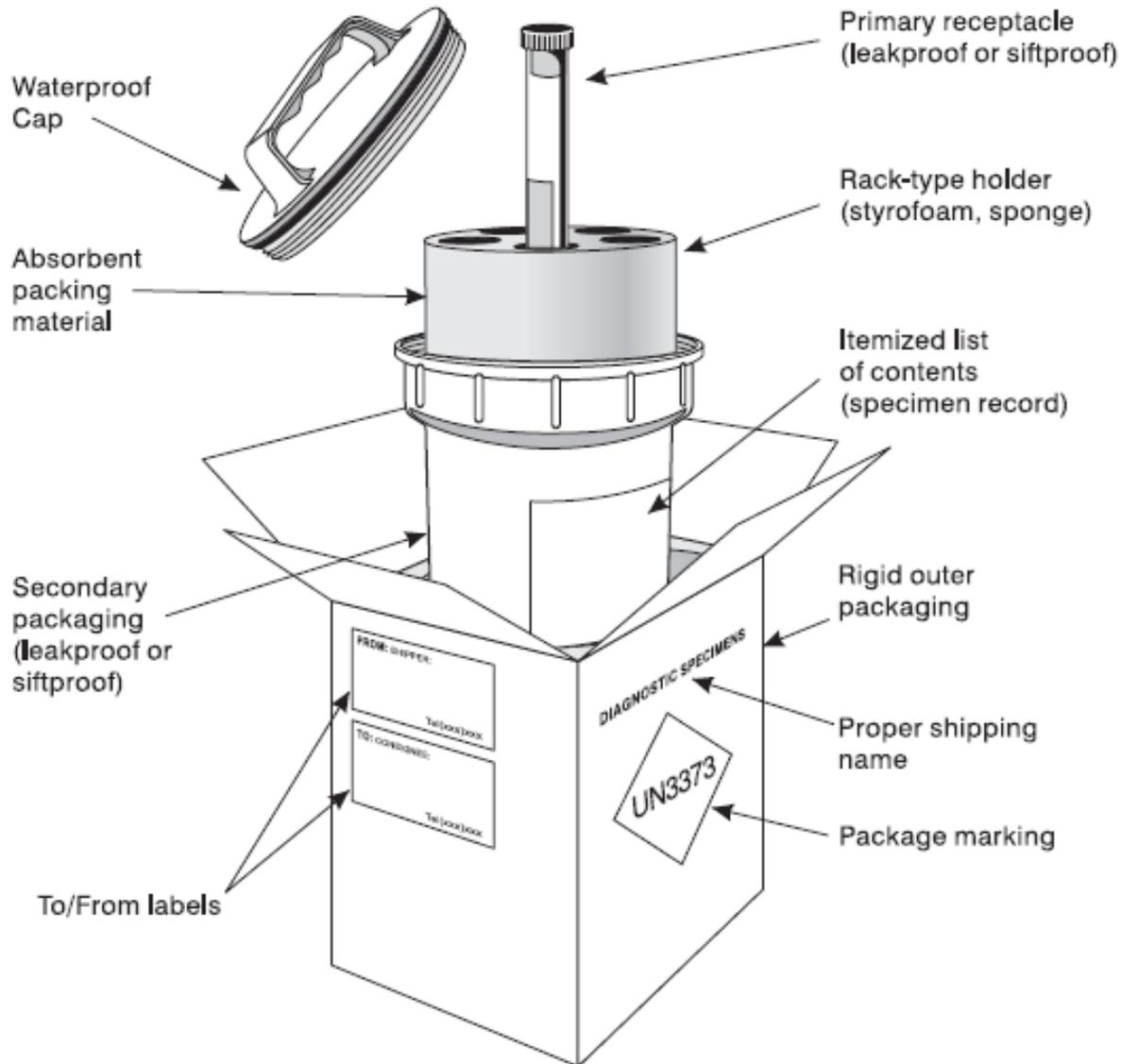
# Packaging, Labeling, Marking for Category B

- **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**





# Category B Packaging

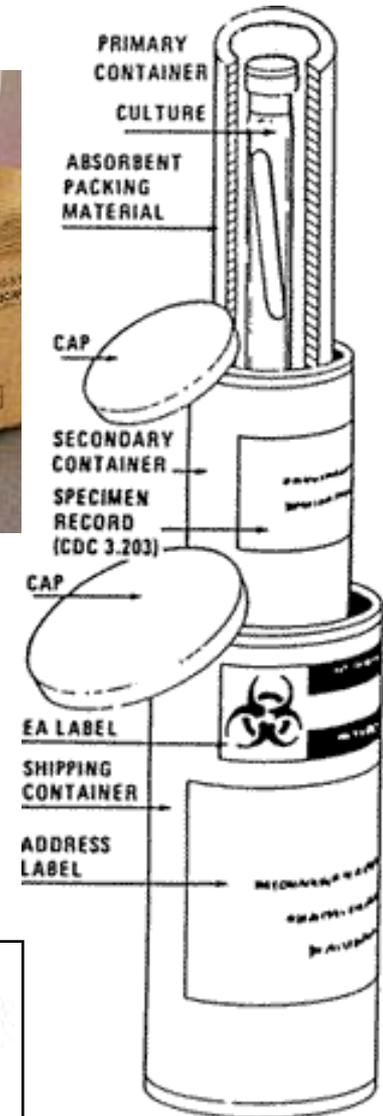


# Shipping Infectious Substances with Dry Ice



## • 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



# 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

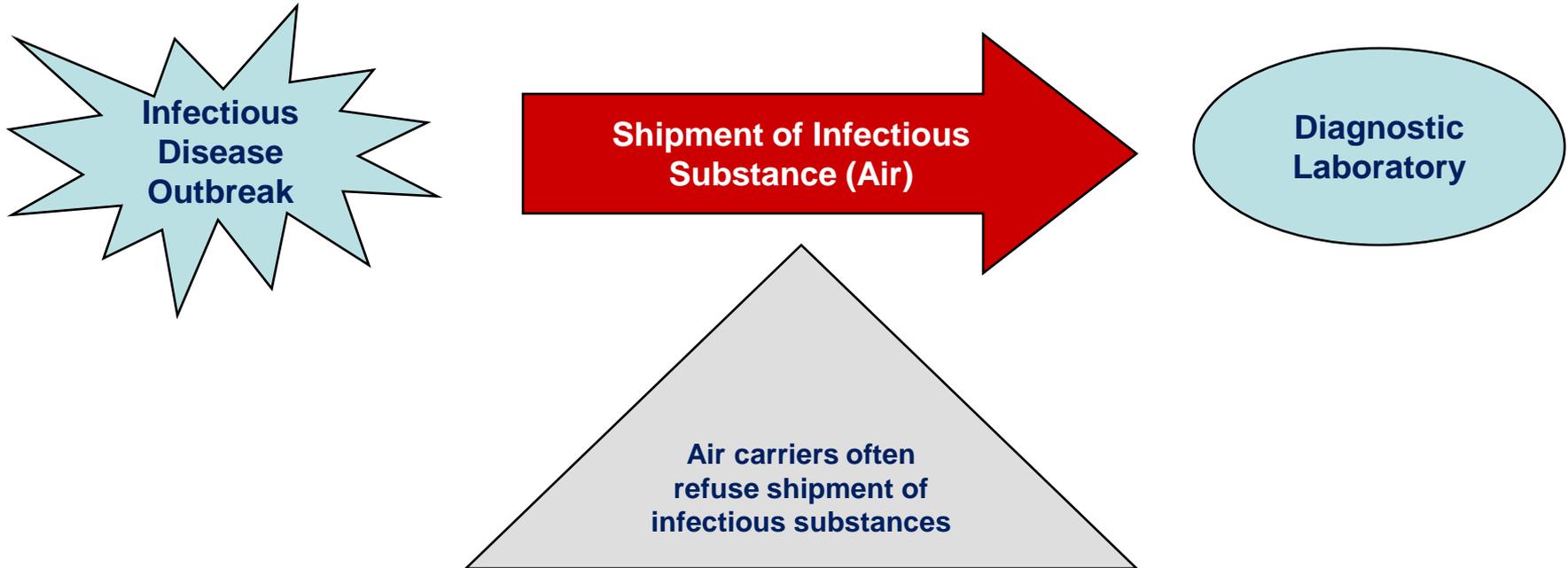


# Facility Responsibilities in Shipping, continued

- **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**