Packaging & Shipping of Human Cell and Tissue Products

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Transporting HCT/Ps

- Vendor qualification/selection
- Containers
- Validation of the shipping container
- Shipping Regulations
- Personnel training

Shipping

- An extension of storage conditions
- Consider:
  - Temperature
  - Duration
  - Monitoring
  - Periodically review to ensure compliance
  - Corrective action plan for failures

Vendor Qualification

- Specifications: selecting the right equipment
  - Appropriate for use
  - Hazardous Materials
  - Shipping Regulations
  - Control (security of vessel)
  - Monitoring
  - Review of previous shipping issues (complaint file)
- Select the best courier

Containers

- Validated or verified as appropriate
- Follow equipment regs 21 CFR 1271.200
  - Prevent cross contamination
  - Sanitization and cleaning on established schedule
  - Inspection
  - Records
  - Product Log

cGTPs 1271 CFR 265(d) Packaging and Shipping

- Package and container designed to protect product from contamination
- For each product type must establish appropriate shipping conditions to be maintained during transit

Some options….

- Dry “vapor” shippers
- Styrofoam boxes – specially designed
- Coolers (hand carried)
- Other options (different material, shape, etc)
  - Aluminum conducts heat better that steel;lighter

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Dry shippers for liquid nitrogen

- Absorbent material – measure by “weight”
- Validate: curve to predict amt of time remaining before warming (10-14 days)
- Lose vacuum if damaged
- Inspect before use
- Temperature monitoring device (FACT requirement)
- Measure (QC) and compare to initial performance periodically
- Similar model for dry ice (evaporation rate)

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Validation of Shipping Containers

- Would apply for all conditions, not just liquid nitrogen
- Test extremes
- Maintain data to perform risk evaluation in an “event”
- Clean (cross contamination) between products

GTPs Transport Documentation

- Prior to transport:
  - “Predistribution availability” based upon record review and release criteria 1271.265 (b) and (c)
  - Summary of records and donor eligibility (if applicable) 1271.55
- Document traceability from donor to final product disposition 1271.290 (e)
  - Transport logs
  - Labels
- Labeling – comply w/ GTPs, FACT, AABB

Regulations for Shipping Biological Material

- U.S Department of Transportation (DOT)
  - 49 CFR Part 171-180 Hazardous Material Regulations
- International Air Transport Association (IATA)
  - Dangerous Goods Regulations
- Others
  - World Health Organization
  - Postal Service
    - Hazardous Materials Domestic Mail Regulations

US DOT
Shipping Regulations

- Apply to biological material being transported in commerce by railcar, aircraft, vessel and motor vehicle
- Steps to properly ship biologic material include
  - Classification
  - Packaging
  - Labeling
  - Documentation

US DOT
Classifying Biological Material

- Packaging & labeling requirements dependent upon whether biological material is considered Division 6.2 Infectious Substance

- Division 6.2 Infectious Substance Classification
  - Category A
  - Category B
  - Materials exempt from Division 6.2

49 CFR 171-180

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Division 6.2 Infectious Substance Classification

- Category A
  - Materials which are known or reasonably expected to contain pathogens (bacteria, viruses, parasites, fungi, prions).
  - Refer to 49 CFR 171 for complete list
- Category B
  - Do not meet criteria for inclusion in Category A.
  - Pathogens are expected to be present
  - Ship as Diagnostic Specimens, Clinical Specimens or Biological Substances

Division 6.2 Infectious Substances Exemptions

- Determination of exemption is based upon professional judgment
- Judgment based upon
  - Known Medical History
  - Symptoms
  - Individual circumstances of the source, human or animal
  - Endemic local conditions
- If there is reason to suspect the material contains a pathogen, it can not be shipped as exempt from class 6.2

Packaging Known Infectious Substances Category A

- Inner Packaging Requirements
  - Primary & secondary receptacles must be watertight.
  - Absorbent material must be placed between receptacle(s) be of sufficient quantity to absorb the entire contents
- Outer Packaging Requirements
  - Must be rigid
  - Package must be at least four inches in the smallest overall external dimension.
- Accompanying Documentation
  - Shipper's Declaration for Dangerous Goods
- Labeling
  - “Infectious Substance” label UN2814

Packaging Known Infectious Substances Category B

- Packaging
  - Durable – withstand handling, vibration, temp change, humidity
  - Leak-proof primary receptacle not containing more than 1 liter or 4 kg
  - Leak-proof secondary package
  - Rigid outer package not containing more than 4 liters or 4 kg
- Pass a drop test of at least 1.2 meters.
- Documentation
  - No Shipper's Declaration for Dangerous Goods Required
- Outer Package Labeling
  - “Clinical Specimen” or “Biological Substance, Category B”
  - One surface having dimensions of 100mm x 100mm

Packaging Non-Infectious Biological Material

- Packaging
  - Leak-proof primary and secondary receptacle
  - Absorbent material between receptacles
  - Outer package of adequate strength, capacity, mass for intended use
  - One surface having dimensions of 100mm x 100mm
- Documentation
  - No Shipper's Declaration for Dangerous Goods Required
- Labeling
  - Outer package “Exempt Human Specimen” (FedEx)

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US DOT Training

- If you ship Category A or B Infectious Substances you must participate in training (initial and ongoing) to fulfill US DOT shipping requirements
- More than one-third of the DOT's enforcement actions pertaining to violations of the hazardous materials transportation regulations involve the failure of hazmat employers to provide training or maintain test records.
- No training required for non-infectious biological material

US DOT Training Requirements….

- Anyone involved in transport process
- Every 3 yrs 49 CFR (172.700, 173.1, 175.200, 177.800)
- Every 2 yrs under ICAO/IATA
- As often as regulations change
- Trainer can be employer or outsourced
- Training modules available at:
  - http://hazmat.dot.gov/training/training.htm

Final Note… LN_2 Dry Shippers

- Properly filled dry shippers are not subject to US DOT Hazardous Material regulations

  however…

- Improperly filled dry shippers present a risk of LN_2 leaking and are subject to regulations should a spill occur
  - Violation of US DOT shipping regulation may result in civil/criminal penalties

Be sure to remove all free liquid nitrogen!

References

- Hazmat List: http://www.myregs.com/dotrspa/
- Hazmat Training: http://hazmat.dot.gov/training/rmgmt/InfectSubstances.pdf
- Training Requirements/ Q&A/Class info: http://hazmat.dot.gov/training/trainreq.htm www.fda.gov
- **University of Minnesota Biosafety** http://www.ibc.umn.edu/Shipping.html

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