Packaging Challenges for Drug/Device Combo Products In The Cold Chain Distribution System

Presented By:

Anthony Alleva
Technical Services Manager, TCP Reliable, Inc.
SPEAKER INFORMATION

Anthony Alleva
Technical Services Manager

TCP Reliable, Inc.
551 Raritan Center Parkway
Edison, NJ 08837

Tel: 732-346-9200 x 107

Email: aalleva@tcpreliable.com
TCP PRODUCTS AND SERVICES

*a single source center for cold chain management*

**Regulatory Compliance Services**
Expert technical support for regulatory gap analysis, temperature profile mapping, training, validation and qualification

**Testing and Design** Validated testing of temperature-sensitive packaging and medical devices

**Quality Management Systems**
Hardware and software platforms to monitor storage facilities and transportation systems; track and monitor shipments and products

**Cold Chain Packaging Systems and Materials** Refrigerants and insulated shippers designed for off-the-shelf solutions and custom needs

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Package Needs Assessment

- Temperature Controlled Packaging is Needed if
  - The item to be shipped is only stable within a specific range of temperatures.
  - The stable temperature range is such that at temperatures naturally experienced during shipping are likely to cause damage to the product.
  - The shipping routes for the product are such that it is not practical to control the environmental conditions.
TEMPERATURE CONTROLLED PACKAGING 101

- The purpose of a temperature controlled package is to maintain an interior thermal environment sufficient to meet the product’s temperature requirements.

- Refrigerant packs in combination with insulated containers make up the bulk of temperature controlled packages.

- Most commonly employed refrigerant material is water often with some additives to alter its properties.

- Most packages are shipped overnight through the small parcel system.
DEFINING PROJECT SPECIFICATIONS

- **Product Description**
  - Size, Make-up
  - Stable Temperature Range
  - Excursions to Temperature Range
  - Product Load – Min/Max Quantity Requirements

- **Shipping Logistics**
  - Where is it going, for how long, and how does it get there?
  - Ambient Temperature Profile
PACKAGE DESIGN PROCESS

- Develop a prototype based on the requirements.
- Test the prototype and analyze the results.
- If results are unacceptable, refine design and repeat test.
- If the results are acceptable, perform triplicate qualification and write report.
PACKAGING INSULATIONS

- Insulation is used to slow down the heat transfer from the environment into the payload.

- The most widely used insulations for packaging applications are (in order of ascending thermal resistance)
  - Expanded Polystyrene (EPS, aka Styrofoam)
  - Closed Cell Urethane Foam
  - Extruded Polyisocyanurate (PIR)
  - Vacuum Panels

- Biodegradable Insulations are being developed
  - Corn Starch Based
  - Recycled blue-jeans
REFRIGERANTS

- Refrigerants provide the energy source for the package and will maintain a specific temperature while melting and freezing.

- The most widely used refrigerant for packaging applications is water usually in gelled form and packaged in various ways.
  - Flexible Film Gel Pack
  - Rigid Bottle
  - Flexible Film Gel Blanket
  - Phenolic Foam Brick
PHASE CHANGE MATERIALS (PCM’S)

- A PCM is a material chosen for its phase change properties applicable for use in a certain application. Normally it is the solid-liquid phase change that is utilized.

- While water is correctly referred to as a Phase Change Material, the packaging industry usually excludes water from the category when discussing PCM’s.

- The goal is to match the phase change temperature with the product temperature requirements.
WATER IS THE STANDARD OF COMPARISON

- Most current temperature control packaging applications are based on using water as the PCM and the industry is used to those systems.
  - Water has:
    - Consistent, repeatable, reliable phase change temperature.
    - High Enthalpy of Fusion, long time to melt.
    - Safe, Non-Toxic (Inhalation of large amounts is fatal though)
    - Easily packaged into “gel packs” or “cold pack bottles”.
    - Very inexpensive and easy to obtain.
  - A “good” PCM will mimic these properties but change phase at a desired temperature.
PCM DESIGN EXAMPLE: WATER / ETHYLENE GLYCOL MIXTURE

- Water mixed with Ethylene Glycol is commonly referred to as “antifreeze” and is used in cars as the engine coolant.

- Phase Change Temperature: Eutectic Point is approximately -50°C at just under 60% Ethylene Glycol concentration.

- Enthalpy of Fusion: Ethylene Glycol is 160 kJ/kg and water is 334 kJ/Kg (mixture will be between those values).

- Toxicity: Moderate to Low (drinking Ethylene Glycol can result in death but the toxicity is mitigated by water).

- Packaging: Can be contained in any material that is able to contain water.

- Ease of Manufacture: Antifreeze is very commonly available.

- Cost: Approximately $0.50 per pound.

(Diagram from http://www.uwgb.edu/dutchs/petrolgy/BEUTECT.HTM)
DRY ICE AS A PHASE CHANGE MATERIAL

- Dry Ice is Carbon Dioxide in its Frozen State.

- Phase Change Temperature is -78.5°C, best for keeping materials deep frozen.

- The phase change it undergoes is called “Sublimation” which means it changes phase directly from solid to gas, skipping the liquid phase.

- Dry Ice has a very high Enthalpy of Sublimation at 571 kJ/kg. (Water’s Enthalpy of Fusion is 334 kJ/kg)
EXPERIMENTAL EXAMPLE OF PCM PERFORMANCE

- Payload temperature vs PCM temperature
  - Water Gel: Phase change at 0°C
  - Phase 5: Phase change at 5°C
  - Phase 22: Phase change at 22°C
  - Cube of PCM encased in Cube of Polystyrene
PCM TEMPERATURE VS SHIPMENT DURATION (FREEZING)

Comparison of Freezing of Three PCM's

-40
-30
-20
-10
0
10
20
30
40
0 6 12 18 24 30 36 42 48
Time(h)

Temperature(°C)

Ambient Phase 5 Water Gel Phase 22

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PCM TEMPERATURE VS SHIPMENT DURATION (MELTING)

Comparison of Melting of Three PCM's

Temperature (°C) vs. Time (h)

-40 -30 -20 -10 0 10 20 30 40

48 54 60 66 72 78 84 90 96

Time (h)

Ambient Phase 5 Water Gel Phase 22
DESIGN CONSIDERATIONS FOR A PCM BASED PACKAGE

- The primary drivers for a temperature control package design are:
  - Payload volume and temperature requirements
  - Expected ambient temperatures during transit
  - Duration of the shipment

- Basic design steps:
  - Select a PCM that will maintain the proper temperature and cover as much of the payload as possible.
  - Determine the balance of insulation quality and PCM amount so as to overcome the amount of heat flow into or out of the package.
  - The goal is for the PCM to not complete its phase change until the shipment is delivered and unpacked.
Medical devices can be temperature sensitive for a variety of reasons.

- Some examples:
  - The device contain a liquid that will damage the device if it freezes and expands.
  - The materials expand or contract at differing rates causing misalignments.
  - There is a biological component that must be controlled even though the rest of the device is temperature stable.
GOOD DESIGN PRACTICES

- Temperature controlled packaging gets more complicated and expensive as the size of the controlled volume increases and the width of the required temperature range decreases.

- Try to isolate the temperature sensitive portion of the product whenever possible.

- Understand the temperature stability of the product enough to know the effects of excursions outside of the intended storage range.
Challenge

• To design a shipper for use in sending drugs to free clinics.
• Cost is a major factor since the product is not being paid for.
• Product Information:
  • Payload = 11” x 8.5” x 6”
  • Temp Range = 2°C to 8°C

• Shipping Information:
  • Continental US 24 hours, ISTA 7D Profile
CASE STUDY: FREE CLINIC PACKAGE

- Project Review
  - Design concept created to meet the initial customer requirements was too heavy, complex and expensive.

  - Going into greater detail with the customer requirements came the breakdown of the 11” x 8.5” x 6” payload to included Four 100 dose vials & *Four Hundred* 11” x 8.5” sheets of paper

  - Since the paper wasn’t temperature sensitive the design concept was changed to remove it from the temperature controlled payload area.

  - By isolating the temperature sensitive item from the temperature stable items, the resulting design was far simpler and less expensive.
CASE STUDY: FREE CLINIC PACKAGE

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CASE STUDY: BIOPSY KIT

- **Challenge**
  - To design a kit for operating room use in harvesting cells for biopsy.
  - Outbound shipment includes all of the items needed to perform the harvest.
  - Inbound shipment contains the harvested cells along with blood ampules.
  - Must be compact and easily portable.
CASE STUDY: BIOPSY KIT

- Project Review
  - Items included in the kit were fragile to shock and vibration so the kit needed to be designed with individual cavities for each item.
  
  - To simplify their use in the cell harvesting the items were arranged in the kit in the same order that they would be used in the process.
  
  - The largest challenge with the system is that the harvested cells need to be maintained below -20°C while the blood ampules must be maintained above 0°C.
  
  - The large variance in temperature ranges of the two items combined with the need for compactness meant that the cavities needed to be separated by more than just foam insulation.
CASE STUDY: BIOPSY KIT: PROTOTYPE
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CASE STUDY: BIOPSY KIT: TEST RESULTS

Temperature (°C) vs. Time (H)

- Ambient
- Thermos
- Dry Ice Cavity

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Questions?

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