Hole Committee Update

For Presentation to:
The IoPP Medical Device Packaging Committee
March 27, 2003

Agenda

- Members and technical help
- Charter statement and objectives
- Current Thinking
- Things that still need to be decided
- Items tabled for later study

Hole Committee Members

- Brett Baker – Sabin, Corp.
- Laura Bix- Michigan State University
- Steve Bunnell- Mocon
- Matt Caldemeyer- Michigan State University
- Steve Good - Abbott Laboratories
- Varsha Kalynakar- Cardinal Health
- Hugh Lockhart- Michigan State University
- Jordan Montgomery- Medtronic
- Tom Misik- Belco Packaging Systems
- Dave Morris- iTi Qualitek
- George Young- GWY Technologies, Inc.

Technical Assistance

- Vangie Alocilja- Biosystems Engineering, MSU
- Gary Burgess- Engineering Mechanics, MSU
- Nick Fotis- Director, Packaging Technology Center, Cardinal Health
- Dennis Gilliland- Statistician, MSU
- Earl Hackett Jr.- Research Associate, Dupont
- Bruce Harte- Food Science and Human Nutrition, MSU
- John Linz- Microbiology, MSU
- Mike Rich- Composite Center, MSU
- Paul Singh- Agricultural Engineering, MSU

Charter Statement

We are attempting to answer the question "What hole size presents a danger in medical device packages"? so that:

- Manufacturers can make informed decisions about the appropriate sensitivity for integrity tests
- Informed decisions can be made in the event of a potential recall situation
- Patient safety is maximized, while costs are minimized

Current Objectives

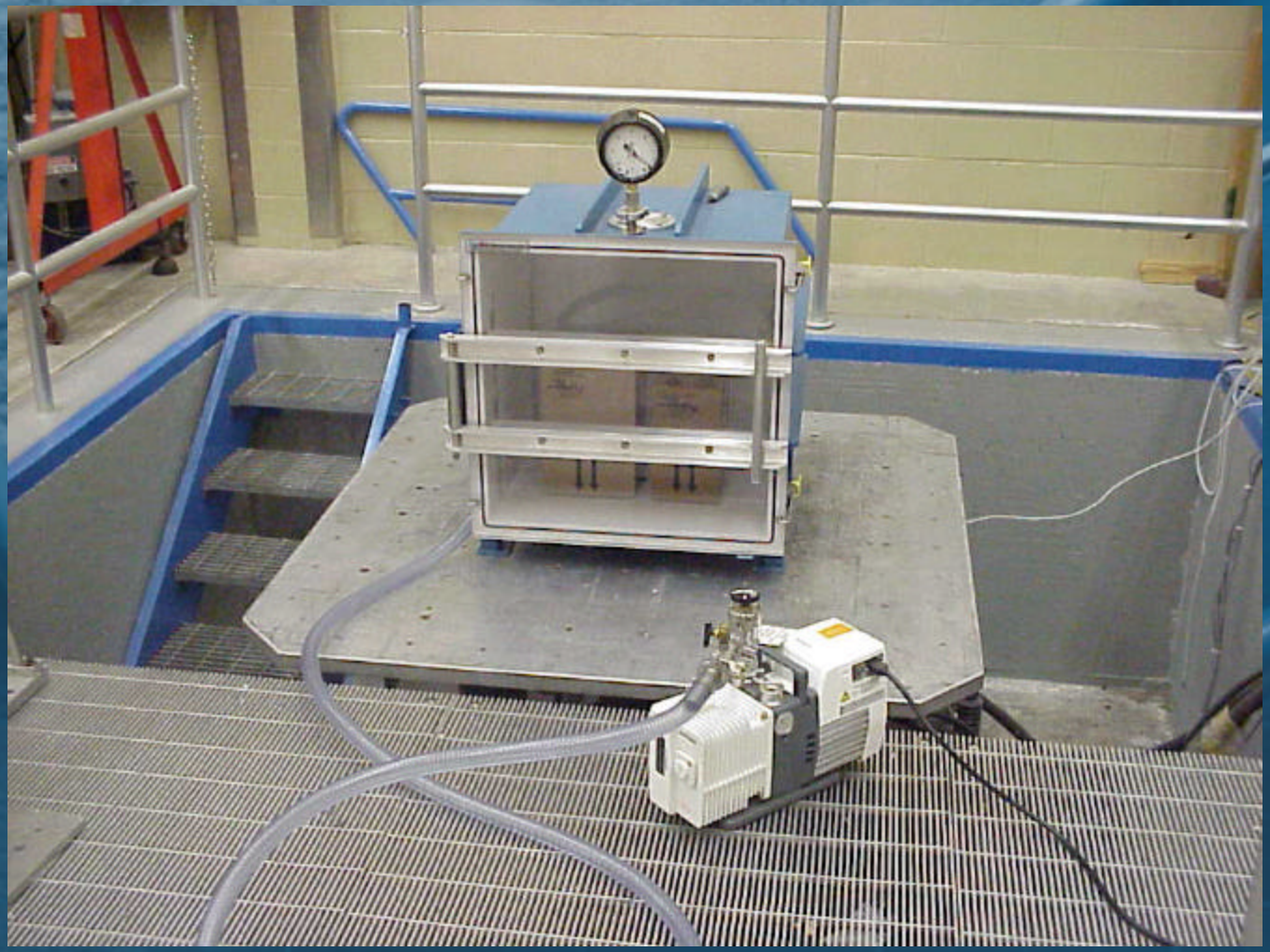
1. Identify the minimum hole size(s) through which Bacillus subtilis and E. coli K-12 penetrate a rigid tray when temperature and RH are standard and gravity serves as the driving force across the breached barrier

2. Identify the minimum hole size(s) through which Bacillus subtilis and E. coli K-12 penetrate a rigid tray when temperature and RH are standard and the package is subjected simultaneously to vibration and pressure differentials that simulate those recorded during flight

Current Thinking- 3 Experiments

1. "Aseptically" filling sterile rigid trays
   - Will not result in unwanted contamination
   - Will result in the ability to measure package integrity after packages are subjected to a microbial challenge
2. The effect of defect size on microbial penetration when no other driving force than gravity is present
3. The effect of defect size on microbial penetration when simulating pressure and vibration experienced during flight

Flight Simulation



What we have decided

- Pinholes only
- Small, rigid trays that do not contain product
- Heavily coated Tyvek ® lid
- Bacillus subtilis and E. coli K-12 as the "challenge"

Decision making

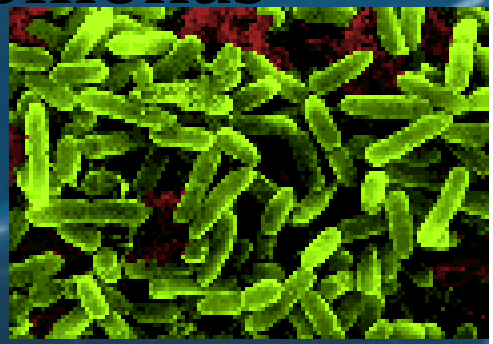
- Rigid trays with a heavily coated Tyvek® lid were chosen because they represent a worst case scenario in terms of the pressure differentials experienced
- Pinholes were chosen because they represent a worse case than channels, due to the short pathway through materials
- Small trays were chosen because more packages will be able to be tested per “run” and less agar will be required per package
- To learn about the smallest defects that microbes penetrate, the best indicator is a microbe

Decision making- The microbes

- Bacillus subtilis
  - Harmless
  - Used in current standards (ASTM F1608-00) and previous studies (Hansen et. al; Jones et. al)
  - Typically used in the spore form
  - Cells are rod-shaped and straight and range from 0.5-2.5 * 1.2-10 µm

Decision making The microbes, cont'd.

- Vegetative form of E. coli K-12
  - Harmless
  - Smaller than Bacillus subtilis 1.1-1.5 * 2.0-6.0 μm
  - Likely to accurately mimic Pseudomonas aeurginosa (0.5-1.0 * 1.5-5.0 μm)
    - Environmental versatility
    - Ability to cause disease in those susceptible
    - Resistance to antibiotics



Things that still need to be decided

- Defects
  - What sizes?
    - Relative size of hole and organism
    - Previous studies- Literature
  - How many different sizes?
  - How to produce them?
    - Laser?
    - Mechanically?
    - Calibrated leaks?

Things that still need to be decided

- Aerosolizing the microbes
  - Concentrations
    10^6 CFU/mL? (Keller, 1996)
  - Exposure time?
  - How to assure uniformity
  - Particle size
    - How to measure particle size
  - This issue gets more complicated as we talk about Experiment 3

Items tabled for later study

- Pouches
- The issue of channel defects
  - Defect size
  - Seal width
- The effect of secondary and tertiary packaging on penetration when gravity is the predominant driver and when flight is simulated
- The effect of relative humidity on microbial penetration
- Filled packages
- The penetration of viruses?


Questions?
Comments?