Flexible Containment Solutions

Leigh Barratt – Pfizer
Rome, May 2013
Containment Project – Containment Best Practice

• Introduction
  – Overview of Issues
  – Scope of Project
  – Improvements Made
  – Project Summary
Historical Risk Control Issues

- Pre-Improvement Facility Designs & Equipment
- Historical levels OC > 1,000 X OEL
- Cross Contamination Potential
- Potential Pharmaceuticals In the Environment risk (PIE)
Real Risks
Guideline: Scope

- R&D API Manufacturing & Handling
- Pharmaceutical Manufacturing
- BioPharmaceutical Manufacturing
- New Products Facilities and Areas
- Renovated Facilities and Areas
- Third Party Manufacturing

Requires project-specific hazard interpretation - The focus is to design to meet OEL!
PSC RBEC Criteria Table & Gap Checklist

- Facility Design for Containment
- Room & Work Surfaces
- HVAC Systems
- Local Exhaust Ventilation
- Process Equipment
- Unit Operations: milling, blending, sieving, etc.

- Product Transfers
- Maintenance & Cleaning
- Medical Surveillance
- Work Methods & SOPs
- PPE & Respirators
- Waste Containment & Disposal
- cGMP & Regulatory conformance
PDC CONTAINMENT PROJECT
AN OVERVIEW

Designed for handling OEB 4 compounds
# Flexible Containment Systems Summary

<table>
<thead>
<tr>
<th>Process Equipment</th>
<th>Equipment Modifications/Containment Hardware</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet Press</td>
<td><strong>SMI MiniPress MII</strong> Mobile device support cart with integral enclosure attachment flange, bag-in canister, product staging table and external enclosure support frame</td>
</tr>
<tr>
<td>Korsh XL100 PRO</td>
<td>Press attachment flange, Bag-in canister mounted on mobile stand with integral product staging table, Enclosure external support frame</td>
</tr>
<tr>
<td><strong>Fluid Bed Gran</strong></td>
<td><strong>Glatt GPGC2</strong> Cabinet attachment flange, Bag-in Canister mounted on left side filler plate, Enclosure external support frame</td>
</tr>
<tr>
<td>Extrusion</td>
<td><strong>Nica E140</strong> Cabinet attachment flange with rigid tray containment box, Bag-in canister on mobile stand with integral product staging table, Enclosure external support frame</td>
</tr>
<tr>
<td>Spheronization</td>
<td><strong>Nica S450</strong> Cabinet attachment flange, Bag-in canister mounted on enclosure external support frame</td>
</tr>
<tr>
<td>Coating Pan</td>
<td><strong>O’Hara LC M</strong> Cabinet attachment flange around product and/or cleaning door, Bag-in canister on mobile stand with integral product staging table, Enclosure external support frame</td>
</tr>
<tr>
<td>Blender</td>
<td><strong>GlobePharma</strong> Mobile device support cart with integral enclosure attachment flange, bag-in canister, product staging table and external enclosure support frame</td>
</tr>
<tr>
<td>Fluid Bed Drier</td>
<td><strong>Strea 1 Pro</strong> Column base and cabinet flanges for enclosure attachment, bag-in canister, utility pass through ports and external enclosure support frame</td>
</tr>
<tr>
<td>Wet Granulation</td>
<td><strong>Procept Mi-Pro 1900</strong> Vessel base with enclosure attachment flange, bag-in canister, utility pass through ports and external enclosure support frame</td>
</tr>
<tr>
<td>10 L collette</td>
<td>Granulator cabinet mounted enclosure attachment flange, Bag-in canister on mobile stand with integral product staging table, Enclosure external support frame</td>
</tr>
<tr>
<td>25 L collette</td>
<td>Granulator cabinet mounted enclosure attachment flange, Bag-in canister on mobile stand with integral product staging table, Enclosure external support frame</td>
</tr>
<tr>
<td>Roller Compactor</td>
<td><strong>Gerteis Mini-Pactor</strong> Compactor cabinet mounted enclosure attachment flange, Bag-in canister on mobile stand with integral product staging table, Enclosure external support frame</td>
</tr>
<tr>
<td>Milling</td>
<td><strong>LB Bohle Cone mill</strong> Enclosure attachment canisters (two), Bag-in canisters (two) mounted on mobile stand with integral staging and collection container tables.</td>
</tr>
</tbody>
</table>
Flexible Containment Concept Designs

Note: Glove-ports not shown on all concept sketches.
Blender and Mi-Pro & SMI system not shown
Transfer Systems

- All isolator systems provided with a Bag in/out canister to allow contained transfer in and out of materials. The canister is 11.73” internal diameter.

- This canister also serves the duel purpose of allowing connection of the In-Process Isolator. Canisters are mounted at standard height to allow easy connection.

- The only isolators that the In-Process isolator cannot connect to directly are the Extruder and Spheronizer systems (due to height issues). A connection can be made using a length continuous liner if it is required.
In-Process Isolator

The In-Process Isolator is a general purpose piece of equipment designed to allow any number of tasks to be carried out. It can be used independently or connected to other flexible isolator systems, as shown.
Typical Process Flow

Subdivision/Weighing:
In-process isolator can be directly connected to Granulator or Blender or used independently. Place materials & tools required into In-process isolator using pass in ports and carry out subdivision & weighing process. After process is complete, pass materials directly to granulator or blender (if connected) or out via bag out port.

Granulation
Pass weighed materials/tools required into granulator isolator using pass in ports and process. After process is complete pass materials out via bag out port.

Blender
Pass weighed materials/tools required into blender isolator using pass in ports and process. After process is complete pass materials out via bag out port.

Mill
Pass weighed materials/tools required into Mill isolator using pass in ports and process. After process is complete pass materials out via bag out port.
Typical Process Flow

**FBD**
Pass materials/tools required into FBD isolator using pass in ports and process. After process is complete, pass materials out via bag out port.

**Extruder/Spheronizer**
Pass materials/tools required into Extruder or Spheronizer isolator using pass in ports and process. After process is complete, pass materials out via bag out port.

**Mill**
Pass materials/tools required into Mill isolator using pass in ports and process. After process is complete, pass materials out via bag out port.

**Roller Compaction**
Pass materials/tools required into Roller Compactor isolator using pass in ports and process. After process is complete, pass materials out via bag out port.
Typical Process Flow

Compression
Pass materials/tools required into Compression isolator using pass in ports and process. After process is complete, pass materials out via bag out port. The In-process Isolator can be connected for testing of tablets and for use as a staging area for tools, etc.

Coating
Pass tablets/tools required into Coating isolator using pass in ports and process. After process is complete, pass materials out via bag out port. The In-process Isolator can be connected for testing of tablets and for use as a staging area for tools, etc.

O-Hara Coater

END
Extruder & Spheronizer Design Progress

- Finalized 3D Design Drawing
- Flange Mock Up
- Flanges Installed
- Enclosure Installed
Glatt GPCG1 Design Progress

Finalized 3D Design Drawing

Ergonomic & Flange Mock Up

Enclosure Installed
Korsch Design Progress

Finalized 3D Design Drawing

Enclosure Installed
Procept & SMI Press

Procept Final Design

SMI Press Flange Installed

Enclosure Installed
Strea Design Progress

Finalized 3D Design Drawing for Flange

Enclosure Installed
Roller Compactor Design Progress

Gerteis Mini-Pactor

Finalized Design Concept
Final Assembly Shipped
Bohle BTS-100 Cone Mill

Finalized 3D Design Drawing

Enclosure Installed
Collette UltimaGral 10 – 25 Liter

Finalized 3D Design Drawing

Enclosure Installed
Industrial Hygiene Data

- Real time IH data (not lactose) collected
  - IH method and OEG in existence (2008)

- Two sets of IH data for OEB 4 compounds
  - TWA8 and task specific samples
  - Outside PPE (PAPR)

- All results None Found < limit of detection

- Respirator Requirements would have been Removed

- Based on Pfizer OEL of 1.0 ug
  - would need to re-sample to verify result
Summary

- Successful containment of API at source
- Flexible Isolation allowed ‘flexibility’ desired by operators
- Designed for individual pieces of equipment
- Relatively easy to assemble/disassemble
- Successful use of hierarchy of controls
- Disposable after completion of campaign
- User Acceptance
- Respirators not required
- Total cost for PDC approx $1,000,000
  - Flexible Isolation/retrofits for 20 pieces of equipment
  - Misting booth
  - Portable ventilation & Tiger Vac
Questions?
Acknowledgements

- Steve Meszaros – Pfizer
- Michael West – Pfizer