Industrial Hygiene & Containment Conference
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Janssen Pharmaceuticaal,Cork
Outline

• Use of glove bag to improve exposure control provided by a down flow both when transferring API form one type of flexible container to another - short term requirement.

• How we met the challenges of changing mill filter socks with the aid of a flexible barrier system.

• Finally an example of how a change in the cleaning sequence significantly reduced exposure levels during the changing of centrifuge cloths.
1a) Transferring API in Warehouse Booth

- **Background to situation** - Plant 3 Module 3 – Aseptic plant for manufacture of sterile Paliperidone Palmitate ZR092670
  - PBOEL HHC 3B and OEL of 0.74µg/m³
  - now PBOEL HHC 3A and OEL of 6µg/m³

- **Charged to reactor** in Mod 3
  - batch size~30-36kg **via IDC** charging system
  - HR092670 was Manufactured in **Plant 1** discharged from **Dryer D6** into **IDC bags** each ~6kg/bag

- **Transferred manufacturing** of the HR092670 to **Plant 3 Mod 2**
  - Discharge from Centrifuge Dryer to **Hecht** high containment bags ~145kg /bags
1b) Immediate Challenges

1) Charge batch ~ 36-42kg to Reactor R331 in Mod 3
2) Transfer from Hecht container to ??? & how much??
3) Transfer in a contained manner in GMP Low Bioburden area??
4) Charge to reactor R331 via ???????
5) Mod 3 Plant in aseptic mode with sterile production in progress
   - No opportunity for obtrusive retrofitting of equipment or
   - Any type of construction related activity
   - Did not have time to achieve GMP approval for ‘new’ bag material (up to 18mths).
1c) Where to from here?

Options

1) Short term to keep production schedule on track
   a. What charging system?
   b. What type of container / bag?
   c. What Quantities?
   d. How to transfer/ dispense HR API from hecht bags to new bags?

2) Long term - need to find a satisfactory solution – IH & GMP, & inline with production planning – campaigning operations.
1d) Short term Charging system selected

- A) Short term option selected – EZIDOCK
  - Relatively easy to configure an interface funnel which could be docked with the existing IDC Valve.
    - Minimal disturbance to aseptic plant

- B) Container choice
  - Use current (GMP) approved 25L ILC Dover ‘seed’ bags with EZIDOCK attachment - already on site

- C) Use ~6kg in each bag –
  - Batch size required 5-6 bags.
1e) Dispensing form hecht to ILC Dover seed bag

- API weigh booth
  - approved GMP Low Bioburden Area.

- 2 person task
  - One at Hecht bag scooping
  - One at funnel filling seed bag

- Exposure levels not satisfactory
  - Funnel side – pluming
  - Needed higher level of control – RPE full suit not adequate

- Developed flexible glove bag – V4
  - Reduced exposure to <0.1µg/m³ funnel & <0.01µg/m³ scooping
  - Removed ergo issues
#2a) Air classifier Mill filter sock change out

- Mill.005 and Mill.003 air classifier mills
- API OEL range
  - Mill.003 11µg/m³ to 500µg/m³.
  - Mill.005 2.5µg/m³ to 6µg/m³.
- End of campaign cleaning activity.
- Personal exposure levels
  - Mill.003 – up to 6800µg/m³
  - Mill.005 – up to 1590µg/m³
- RPE required air supplied full suit
  - Added extra difficulty to task

Mill.003 filter sock housing

18 filter socks ~ 2m in length
2b) Mill.003 filter sock change out

- Placed flexible glove bag in place around top of filter housing unit.
- 18 socks removed individually rolled up and put into the bag out sleeve on the flexible system.
2c) Mill.003 filter sock change out

- Waste bag is tie wrapped and the Flexible bag is removed tie wrapped labelled for disposal.
  - A number of improvements to the bag design made along the way.
  - Final design in place.

- Personal Exposure levels
  - Ranged from 2 - 60µg/m$^3$
  - PPE required – ½ face mask P3 filter
2d) Mill.005 flexible glove bag

- Mill.005
  - Filter socks ~1m

- Personal Exposure levels ranged
  - initially < 400µg/m³ modified bag
  - 2nd version < 50µg/m³
  - Final version – awaiting results

- PPE reduced form air supplied full suit
3a) Manual cloth change on Centrifuge

- Centrifuge cloth change at end of campaign – part of manual cleaning activities
- OEL of materials range from 20-1700µg/m³
- High personal exposure levels
3b) Centrifuge Cloth change

- Trailed Cleaning In Place (CIP) to determine if this would be effective.
  - Cleaning solvent pumped through cleaning nozzles on door and cloth.

- Significant reduction in personal exposure levels

- Improvements resulting from trials
  - Additional step to remove solvent prior to opening centrifuge to remove cloth.
  - Optimising process for all materials going through the centrifuge is underway.
Thank You!