

Industrial Hygiene & Containment Conference

Rome May 14-16,
2013

Janssen Pharmaceutica, Cork



Outline

- Use of glove bag to improve exposure control provided by a down flow both when transferring API from 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 $0.74\mu\text{g}/\text{m}^3$
 - now PBOEL HHC 3A and OEL of $6\mu\text{g}/\text{m}^3$
- **Charged to reactor** in Mod 3
 - batch size $\sim 30\text{-}36\text{kg}$ **via IDC** charging system
 - HR092670 was Manufactured in **Plant 1** discharged from **Dryer D6** into **IDC bags** each $\sim 6\text{kg}/\text{bag}$
- **Transferred manufacturing** of the HR092670 to **Plant 3 Mod 2**
 - Discharge from Centrifuge Dryer to **Hecht** high containment bags $\sim 145\text{kg}/\text{bags}$



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 configured 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 – plumbing
 - Needed higher level of control – RPE full suit not adequate
- **Developed flexible glove bag –V4**
 - Reduced exposure to $<0.1\mu\text{g}/\text{m}^3$ funnel & $<0.01\mu\text{g}/\text{m}^3$ scooping
 - Removed ergo issues



Receiving ILC Dover bag attached here

Hecht bag inserted here



#2a) Air classifier Mill filter sock change out

- Mill.005 and Mill.003 air classifier mills
 - Mill.003 $11\mu\text{g}/\text{m}^3$ to $500\mu\text{g}/\text{m}^3$.
 - Mill.005 $2.5\mu\text{g}/\text{m}^3$ to $6\mu\text{g}/\text{m}^3$.
- End of campaign cleaning activity.
- Personal exposure levels
 - Mill.003 – up to $6800\mu\text{g}/\text{m}^3$
 - Mill.005 - up to $1590\mu\text{g}/\text{m}^3$
- RPE required air supplied full suit
 - Added extra difficulty to task

Mill.003 filter sock housing



18 filter socks \sim 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 - 60 $\mu\text{g}/\text{m}^3$
 - PPE required – 1/2 face mask P3 filter



2d) Mill.005 flexible glove bag

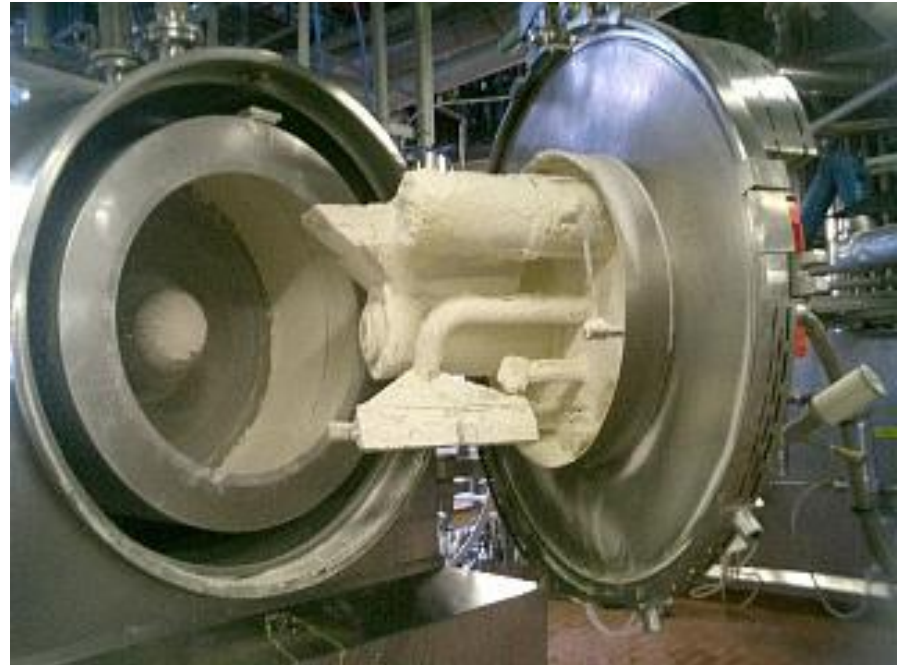
- Mill.005
 - Filter socks $\sim 1\text{m}$



- Personal Exposure levels ranged
 - initially $< 400\mu\text{g}/\text{m}^3$ modified bag
 - 2nd version $< 50\mu\text{g}/\text{m}^3$
 - Final version –awaiting results
- PPE reduced form air supplied full suit

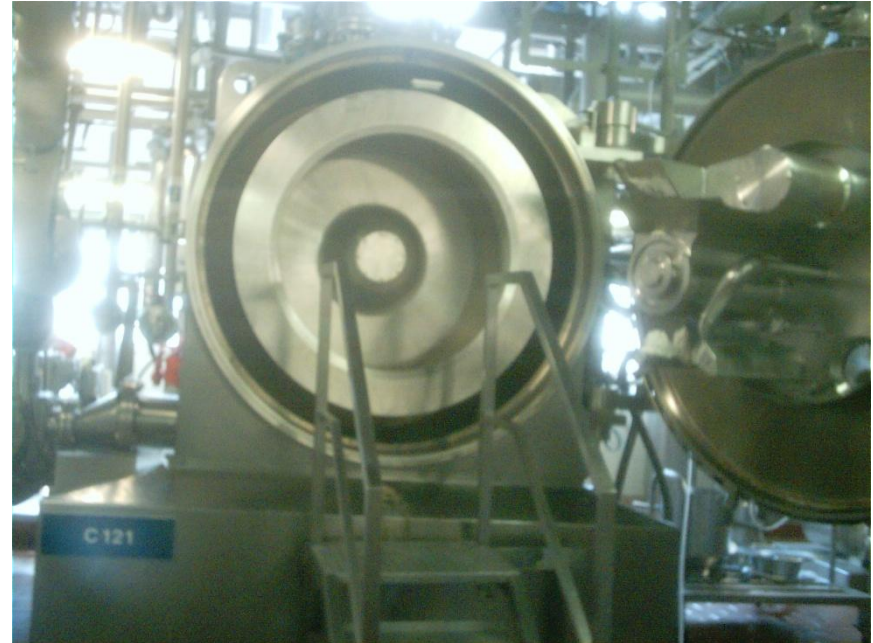
3a) Manual cloth change on Centrifuge

- Centrifuge cloth change at end of campaign – part of manual cleaning activities
- OEL of materials range from 20-1700 $\mu\text{g}/\text{m}^3$
- 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!