Process Safety Fundamentals for Pharmaceutical Operations
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Introduction to the EPSC Pharma Group

Working group comprising safety engineers and leaders from 14 Pharma companies specifically interested in sharing learnings from incidents, best practices and collaborating on projects relevant to our industry.

Previous projects:-
• Process Safety Hazards associated with Pharma Unit Operations
• Fluid Bed Drying Hazards
• Best Practice Guide on Electrostatics
Background: EPSC Fundamentals

• EPSC Project group developed the “Process Safety Fundamentals” in 2020 based on a concept introduced in Shell.

• The objective was to produce a set of key concepts which could be discussed with front-line staff who are directly engaged in activities which could lead to (or prevent) Major Accident Hazards.
Purpose:
- Highlight hazardous conditions and when they are typically presented
- Emphasising good practices with a specific focus on operation and maintenance aspects.
- Intended to be used on site, to support coaching and development of frontline staff.
- Based on established practices, not something new!

Key Themes:
- Plant integrity,
- Process control,
- Ignition risk management and
- Reporting/escalation processes
Process Safety Hazards in the Pharmaceutical Industry

**API Manufacture**
- Making the “Active"
- Traditionally batch operations.
- 50kg to 1000kg scales
- Highly potent chemicals
- Reaction, Distillation, Evaporation, Crystallisation
- Filtration (Centrifugation) and Drying
- Solvent based chemistry in multiple stages.
- Recovery of solvents by distillation/drying

**Drug Product Formulation**
- Formulation and filling technologies depend on the dose form – oral, topical, inhaled, pastes.
- Handling the pure API and excipients.
- Combustible dusts are the major hazard.
- Equipment might include mixing vessels, granulators, fluid bed dryers, filling machines
- Some solvent based processes.
Evolving the Fundamentals for the Pharma Environment

- Incorporated double isolation, open drain, plugs/blockages and first line break into “Safe isolation and draining”
- Added ventilation in hazardous areas since most facilities are indoors and ventilation is critical to hazardous area, toxic gas and asphyxiant management
- Added combustible dust housekeeping as significant hazard specially in secondary/formulation plants
- Added electrostatics since these are a prevalent and often transient risk of ignition in our facilities.
- General refocus on guidance towards batch manufacturing / high frequency turnarounds / multipurpose plant
Process Safety Fundamentals for Pharma Industry

1. Safe Isolation and Draining
2. Leak Tightness and Testing
3. Connections and Unloading
4. Use of Flexible Hoses
5. Operating Limits
6. Overrides
7. Report Issues with Critical Equipment
8. Report Process Safety Incidents
9. Line of Fire
10. Ventilation in Hazardous Areas
11. Dust Housekeeping
12. Electrostatics
13. Splash Filling
14. Run Away Reaction
Process Safety Fundamentals for Pharma Industry

Plant Integrity
- Safe Isolation and Draining
- Leak Tightness and Testing
- Connections and Unloading
- Use of Flexible Hoses
- Configuration and Line Walks

Operating Discipline
- Operating Limits
- Overrides
- Report Issues with Critical Equipment
- Report Process Safety Incidents
- Line of Fire

Fire/Explosion Hazards
- Ventilation in Hazardous Areas
- Dust Housekeeping
- Electrostatics
- Splash Filling
- Run Away Reaction
1. Safe Draining and Isolation

Hazards:
Hazardous fluids such as steam, solvents, and pressurised gases present a significant risk of injury, fire or explosion. Follow good isolation and draining practices.

When important:
During draining, sampling and other non-routine activities such as line-breaks.

Challenges in the field:
- Two levels of isolation should be used.
- In older plants this standard may be difficult to apply and aseptic plant design reduces number of isolation points.
- Blind flanges not put back after maintenance work or flanges not fully tightened.
- Drain valves left open.
- Valve handles that can be opened accidentally.

Options to get it right:
- Clearly define/label plant where hazardous fluids are present.
- Where possible drain and flush hazardous fluids from plant before working on it.
- Apply two points of isolation for highly hazardous or pressurised services.
- “Prove” the isolation, by checking valves hold through a drain point before disconnecting pipework.
- Ensure all points of isolation are locked-out & tagged.
- Fit routine points of isolation with spectacle blinds, valve locking kits etc.
- Point of isolation as close as possible to where you are working (visible).
- Do not accept missing blind flanges or missing bolts on blind flanges.
- Ensure there is an emergency plan if an isolation leaks.
11. Ventilation in Hazardous Areas

Hazards:
Accumulation of flammable concentrations of vapours or dusts leading to an explosion
Toxic gases and vapours and Asphyxiants such as nitrogen or carbon dioxide.

When important:
Plants areas where flammable, toxic or asphyxiant materials are handled.

Challenges in the field:
➢ Technical assessments of ventilation e.g. Hazardous Area Calculations or Asphyxiation calculations may not be available.
➢ Ventilation systems may not have monitoring instrumentation e.g. to detect failure of fans/motors/belts
➢ Systems are often designed to recirculate air to reduce energy demands therefore hazardous materials can accumulate.
➢ Some powders can be difficult to remove/collect through basic ventilation
➢ Changes to HVAC settings can compromise the safety function if the MoC process is not robust.

Options to get it right:
➢ Minimise sources of release – keep materials in the plant or operate outside!
➢ Provide good local ventilation near release points (sample points, charge ports, manholes etc)
➢ Conduct Hazardous Area Assessments and specify suitable equipment in these zones.
➢ Robust change control for HVAC equipment, changes to air flows, Hazardous Area Reviews.
➢ Install low flow alarms/trips on critical ventilation systems.
➢ Use of gas detection systems e.g. oxygen depletion, flammable gas detection.
➢ Where spillages could occur, minimise the floor/spill area to reduce evaporation.
➢ Ventilation systems should be considered safety (and quality) critical devices with planned preventative maintenance programmes.
➢ Provide a basis of safety for asphyxiation, flammable gas/dust and toxics to enable design of right ventilation system and train plant operators and engineers.
**Process Safety Fundamentals and Life Saving Rules**

**Life Saving Rules**
- Apply for all company personnel and typically contractors
- All in all settings; occupational safety and areas of high severity risk.
- Rules - considered “non negotiable”

**Process Safety Fundamentals**
- Designed for front-line staff managing or working with Major Accident Hazards
- Emphasise key hazards, risk factors and good practices
- Primarily for coaching/developing/training of operators, supervisors, technicians
Next Steps

Final copy editing & update pictograms
Integrate with Pharma Unit Ops Guidance (tbc)
Brochure/pdf format
Publish to EPSC website

Thank You!