SafeBridge CONSULTANTS, INC.

A Process Hazard Analysis Concept for Pharmaceutical Operations

Introduction

Pharmaceutical manufacturing operations utilize physical processes, machinery and drug substances that present risks of fire, explosion, and injury or illness to people, plant and environment. These risks can only be properly managed by the application of thorough engineering analysis and mitigation of the hazards by knowledgeable and qualified professionals working as a team to review all aspects of the design of a new process. To do less invites an incident or disaster that can have serious financial effects on the company through interruption of manufacturing, destruction of physical plant and injury to people.

Discussion

Process hazard analysis consists of a methodical, comprehensive review of all aspects of a process design using the combined knowledge and efforts of specialists that represent all disciplines that necessarily must be brought to bear on the problem. Normally, the interests and viewpoints of management, manufacturing, process engineering, employee health and safety, maintenance and environmental protection must be heard, evaluated and accommodated in this process. It is not a single shot approach but is rather a series of reviews beginning at the conceptual stage of a process design, through design development, to pre-startup review and post operational validation. Each stage builds on the information and risk management decisions made by the team at the preceding stage.

At the **conceptual** stage, all process safety information is gathered and evaluated, and decisions are made about the need for any additional information to allow the PHA to be properly conducted. Data needed at this stage are:

- Proposed equipment list
- Proposed process flow description
- Preliminary instrumentation and control diagrams
- Chemical and physical hazard characteristics of the materials to be processed, including:
    - Animal and human toxicology
    - Occupational exposure limits (OELs)
    - Airborne contaminant sampling and analysis methods
    - Reactivity and stability

- Explosion severity
- Minimum explosive concentration
- Ignition temperature
- Minimum ignition energy
- Volume resistivity
- Environmental fate and effects

A questionnaire has been developed by SafeBridge to guide this information gathering effort. Some information gaps will undoubtedly be identified at the conceptual stage and plans should be made to conduct the necessary testing to obtain the information.

At the **design development** stage, the information from the conceptual stage is evaluated and used to guide the proposed design. At this point, the suitability of the specific machinery proposed is evaluated, ergonomic factors are checked, mitigation measures are decided upon, and the basis of safety is agreed upon. For example, the basis of safety for the hazard of explosion in a fluidized bed dryer/granulator could be explosion suppression, or inerting, or venting or containment. This is sometimes referred to as the "Safety Case". The process design is then finalized in accordance with the Safety Case and constructed or installed, and procedures and batch sheets are written. The final review at this stage consists of a look at the procedures and batchsheet to ensure that the necessary operational controls required by the Safety Case are provided.

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