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A structural approach to the HAZOP – Hazard and operability technique in the biopharmaceutical industry

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ABSTRACT

Recently, the use of analytical techniques to identify, assess and address risks within the pharmaceutical industry is increasing from the initial and operating phases until the final use of products aiming to eliminate or reduce the severity of deviations. The hazard and operability studies – HAZOP establish that accidents are the result of failure modes in process variables out of operational parameters. In this paper, the HAZOP methodology was used to assess risks in the system for recombinant protein production where a multidisciplinary group used the brainstorming strategy to identify the risk level and deviations in nodes defined by functionality in the system. Nineteen critical nodes were identified, deviations were established in based on knowledge, and experience by the group, thus precluded the need of deviation's records to estimate frequency and impacts of events. It was also shown that in the pharmaceutical industry the most-critical risks are those that have adverse impacts on production like partial and total losses and when noncompliance of regulations are involved. The HAZOP risk assessment tool can be easily followed by people who are interested in starting to use this technique to improve the security environment within the institution and when required by regulatory agencies.

1. Introduction

The HAZOP study was first developed in the United Kingdom for use in its chemical industry during the 1960s. Imperial Chemical Industries, Ltd. (ICI) is credited for developing this standardized approach to the analysis of process hazards associated with basic operating conditions of their facility. Its use and development were encouraged by the Chemical Industries Association – CIA Guide published in 1977 (CIA, 1977). Then, using the HAZOP and "what-if" methodologies, changes to individual control protocols were introduced (on paper) one at a time to allow the review group to evaluate the subsequent (albeit hypothetical) consequences. Over time, this analysis method evolved into a standard practice, first at ICI and then into the chemical industry in general. Although it should be stated that HAZOP was not uniformly or consistently applied, the concepts still form the basis of the HAZOP approach that is in general use today. With the implementation of hypothetical changes into the operating system, the potential consequences can be better understood, and, if necessary, actions can be taken to prevent any possibility of realizing such consequences under real-world operating conditions (Vincoli, 2005; Mentzer et al., 2014).

HAZOPs evolution allowed increasing its use over the years, however, there are several tools used for risk assessment like FMEA (Failure Mode and Effect Analysis). It is a risk assessment tool used in the chemical industry and is characterized by an inductive approach for defining failure effects in system elements. Another risk assessment tool commonly used is the FTA (Fault-Three Analysis). In this case, it uses a deductive process where an unwanted final event is analyzed defining the different deviations that could lead to that event aiming to eliminate them or reduce their impact and is very helpful to define probability to define routes of the most-likely events (Wang et al., 2012; Wang and Gao, 2012). Nevertheless, the HAZOP methodology main feature is that it can

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be defined as an intermediate methodology between a deductive and inductive approach. Since it is possible to define the result of unwanted events as the FTA using guide words, which is a unique characteristic of this methodology and later analyze these events formulating possible causes that originated deviation, in the same way as the FMEA procedure (Rahman et al., 2009). Aiming to satisfy the ICH Q9 purpose to offer an approach to ensure a systematic quality risk management, the HAZOP methodology address deductive and inductive approaches simultaneously (ICH, 2005). This particular feature allows the responsible to use this tool to perform a quick and objective work reducing time and, therefore, reducing both economic and human resources when HAZOP studies are performed.

1.1. The HAZOP methodology

Before defining the HAZOP methodology, it is important to remember that there is no a particular technique demanded by regulatory entities to assess risks. The HAZOP methodology is usually modified depending on the user's interests and it can be used also as a complementary tool for other Process Hazard Analysis (PHAs) techniques as explained previously. Successful implementation of HAZOP studies depends on information used and organization's requirements. Thus, the organization first move before run the analysis of deviations is defining the hazard identification (nodes) detail level, the number of nodes that will be studied, available time to perform the study, number working meetings and total time required for the study (Dunjó et al., 2011; Wang et al., 2013). Therefore, is important to define a general procedure to follow during a study regardless if the application target is to assess risks originated in material or infrastructure issues and especially when the human factor is considered as the origin of deviations. Moreover, a team of specialists established basic requirements for the HAZOP methodology. In their work was suggested that before starting deviations analysis a multidisciplinary team of professionals directly involved with the process is necessary to be responsible for performing a risk analysis (Ilangkumaran and Thamizhselvan, 2010). Although the list of experts can be extensive depending on the depth of the research, an essential group of members should be considered according to their specialty (BS IEC 61882, 2001). An efficient multidisciplinary team should have at least the following members:

- *Study leader;* the leader's primary roles are to conduct the research, organize and delegate responsibilities to the group.
- *Recorder;* responsible for recording data and all information generated during the meetings
- *Process designer;* aiding to define deviations and the effect on the system
- *User;* sharing his experience identifying and evaluating the severity level of deviations,
- *Specialists*, *engineers, maintenance staff*; this group will be called only in particular situations, when their experience is needed avoiding crowded meetings and focus loss.

Whereas the HAZOP study must be based in process data and technical information, P&I diagrams, material balances, process parameters, instrumentation diagrams, plot plans, line arrangement and safety valves lists should be available for the multidisciplinary group before the start the analysis.

Once all process and technical information are available, the group should be able to apply the HAZOP methodology for identification and treatment of risks using the brainstorming technique (Khan and Abbasi, 1997). The method analyzes the whole process and uses failure knowledge and experience of past events in similar systems to identify deviations and effects in the system under study (Kidam and Hurme, 2013). Fig. 1 shows a procedure that can be easily followed to identify and treat deviations. However is important to notice that this methodology is an iterative process and although the steps are easy to follow, the leak of the proper experience in processes may result in defining improbable situations or in higher level of impacts than the actual.

The HAZOP technique systematically analyzes system nodes and defines qualitatively how operational deviations could occur, and whether further protective measures, operating procedures upgrade or design changes are required to reduce or eliminate their effects. The main feature of this methodology is that the group can use guide words that represent a number process parameters derived from HAZOP methodology. A list of the standard and most common process parameters deviations used in HAZOP analysis are detailed in Table 1 (DOE-HDBK, 2004). In addition, the HAZOP group can propose more deviations if required, in this case, the group must use standard criteria aiming to maintain the veracity of facts and avoid guesswork of unlikely events. For example, if the line is over-pressured, a plausible cause of this deviation and subsequently consequences should be estimated. When high-pressure values may be within the line acceptance rate, consequences could be considered as trivial, however, if pressure rate is exceeded out of operation limits, deviations may result in a line rupture and therefore it can be considered as a hazardous occurrence. Consequences may be trivial or significant; however, in both cases the group must evaluated and decide if deviations constitute a potential hazard for their process or not.

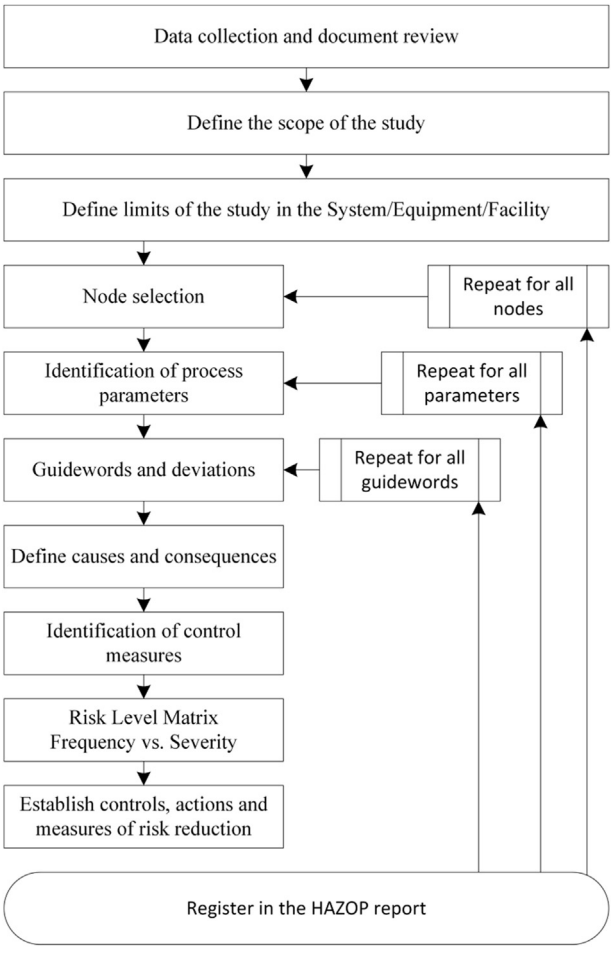

Fig. 1. Application procedure of the HAZOP methodology for risk identification.