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Layer of Protection Analysis on Sterilization Process Using Ethylene Oxide

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Abstract

Layer of protection analysis (LOPA) was conducted on toxic and flammable hazard of sterilization process using ethylene oxide. Hazard associated with the process were studied using HAZOP and scenarios were developed by applying the HAZOP result. For each scenario, independent protection layers (IPLs) were identified and their frequencies were estimated. Three additional IPLs were considered such as personal protection equipment, monitoring device, and ventilation window. By adding such IPLs, the risk was estimated to be reduced to less than chances per million.

Keywords: Layer of protection analysis (LOPA); Sterilization Process; Ethylene Oxide; Independent Protection Layer (IPL); Risk

Abbreviations: LOPA: Layer of protection analysis; IPL: Independent Protection Layer; EO: Ethylene Oxide; FDA: Food and Drug Administration; PSM: Process Safety Management; HAP: Hazardous Air Pollutant; CAA: Clean Air Act; CNS: Central Nervous System; NIOSH: National Institute for Occupational Safety and Health; IARC: International Agency for Research on Cancer; OSHA: Occupational Safety and Health Administration; PEL: Permissible Exposure Limit; STEL: Short-Term Exposure Limit; PPE: Personal Protection Equipment; KETEP: Korea Institute of Energy Technology Evaluation and Planning; MOTIE: Ministry of Trade, Industry & Energy

Introduction

Ethylene oxide (EO) has been widely used as a low-temperature sterilant since the 1950s. It has been the most commonly used process for sterilizing temperature-and moisture-sensitive medical devices and supplies in healthcare institutions in the United States. EO kills microbes by disrupting life-sustaining molecules. Commercially sterilized medical products must meet stringent U.S. Food and Drug Administration (FDA) safety regulations that address product sterility (i.e., microbial levels) and acceptable levels of EO residue. Analytical techniques are used to identify, assess and address risks within the pharmaceutical industry such as HAZOP together with complementary quantitative method [1]. In order to guarantee the safety of pharmaceutical product, some kinds of risk analysis and risk assessment is studied recently [2]. HAZOP analysis is a process hazard analysis method that has been widely applied to the chemical processing industries including EO plant [3].

EO is a hazardous chemical and is both flammable and toxic, listed in 29 CFR 1910.1047in the USA regulation. It is classified as highly hazardous chemicals in the Process Safety Management (PSM) and Hazardous Air Pollutant (HAP) in regulations under the Clean Air Act (CAA). The flammable range of EO/air mixtures is 2.6 -100%under ambient conditions and its flames can accelerate very rapidly [4-6]. It is difficult to design and install reliable explosion control systems, particularly when adding EO to existing process equipment. In order to avoid explosions, facilities must maintain lower EO concentrations entering furnaces below the LFL. National Fire Protection Association (NFPA) codes require facilities to dilute EO concentrations transported to furnaces to less than 25% of the LEL, or 6,500ppm [7]. A typical chamber concentration during sterilization is generally applied between 220,000 and 440,000ppm (400-800 mg/L), which is a very explosive concentration. The acute (short-term) effects of EO to humans is as follows; central nervous system (CNS) depression, irritation of the eyes, and mucous membranes.

The chronic (long-term) exposure may cause irritation of the eyes, skin, and mucous membranesand problems in the functioning of the brain and nerves [8]. A study conducted by the National Institute for Occupational Safety and Health (NIOSH)showed that

long term exposures to EO increases the risk of bone cancer in men and breast cancer among women [9]. EPA has classified ethylene oxide as a probable human carcinogen. International Agency for Research on Cancer (IARC), a part of the World Health Organization, classifies EO as a Group 1 human carcinogen (sufficient evidence of a cause and effect relationship between exposure to the material and cancer in humans). The Occupational Safety and Health Administration (OSHA) of the USA defines permissible exposure limit (PEL) is 1ppm, averaged over an 8-hour workday and short-term exposure limit (STEL) must not exceed 5ppm for 15minutes [10]. In addition, employers are required to take certain actions (e.g., conduct medical surveillance and periodically monitor worker exposures) when employee exposures exceed 0.5ppm averaged over an 8-hour workday.

Evaluating hazard and assessing risk of hazardous facilities are one of the most important activities to keep the site safe. Several studies have been conducted such as on how to review the current methodologies for plant layout optimization and to resolve facility siting issues [11], on how to reduce accidental exposure to various regents that are toxic, explosive, or carcinogenic [12], or on how to apply on an advanced layers of protection analysis (LOPA) method to assess the risk of a chemical process [13]. The layer of protection analysis (LOPA) was introduced in the 1990s as a method for semi-quantitative risk assessment, having advantages of both qualitative and quantitative method of risk evaluation as has been described in the CCPS textbook [14]. LOPA is known to be a powerful analytical tool for assessing the adequacy of protection layers used to mitigate process risk.

EO sterilization process

Because of the variability of products, packaging, load density, etc., each product type (e.g., tubing, catheters, containers, syringes, bandages) requires a unique treatment cycle to ensure sterilization. Figure 1 shows general process of sterilization using ethylene oxide. Cycle variables include EO concentration, duration of exposure, temperature, and humidity, vacuum applied during sterilization, and inerting and gas washing cycles required removing oxygen and residual EO respectively. In the studied case, the ethylene oxide sterilization system comprised of 3m3sterilization chamber equipped with external heating jacket, access door, vacuum system, and humidification system, nitrogen inserting system, EO gas delivery system, exhaust system and ethylene oxide removal system. The equipments are located in separate containment areas equipped with ventilation (Figure 1).

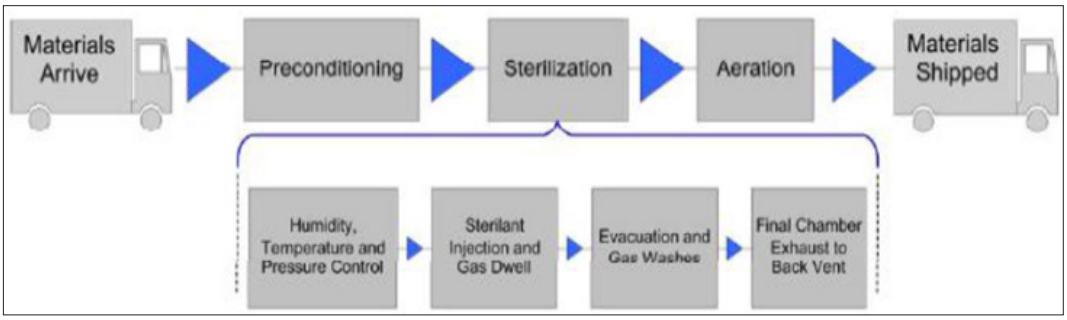

Figure 1: General process of sterilization using ethylene oxide.

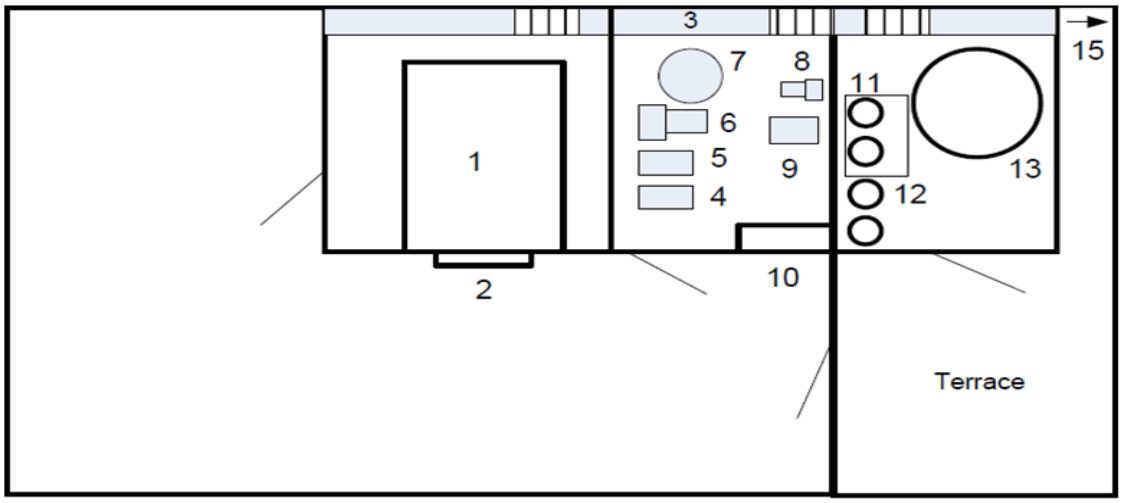

Figure 2: Sterilization System Layout: 1. Sterilization chamber; 2. Sterilization chamber access door; 3. Ventilation system; 4. Hot water system; 5. Steam generator; 6. Liquid ring vacuum pump; 7. Water separator; 8. Reactor-stripper circulation pump; 9. Reactor heater; 10. Control system and monitor; 11. Ethylene oxide cylinder (2 pc) and digital balance; 12. Nitrogen cylinders (2 pc); 13. Stripper-hydrolysis reactor; 14. Ventilations grills (3 pc); 15. Ventilation exhaust.

The Sterilization System

The layout of sterilization department applied to this study is shown in Figure 2.The sterilizer is isolated from the other sections of the production facility. The system is located on the top floor of 3 story building. The confinement, which stores EO, N2cylinders [11,12] and splitter-reactor [13] are located in terrace section out of the building. Three sections of sterilizer are separated by wall and all three sections have separate locked doors against unauthorized access. The air ventilation system has separate grills [14] and negative pressure is applied by ventilation fan which sucks air from all three sections and exhaust is located outside of the building [15]. The process can be monitored and controlled from outside [10] by graphical user interface and PLC system. In addition, the system log is kept by the printer connected to the system. The process parameters and operational mode can 6 only be changed by authorized person, which is assessed by 5-digit user codes. Calibration and major process parameters can only be tuned by service engineer through higher level access codes (Figure 2).

Cycle Phases

The sterilization cycle is initiated by two stepvacuum-N2 cycle for inerting. Steam is injected to achieve desired humidity level within the chamber to condition the products and to improve the sterilization effectiveness. EO is charged from pressurized 80 pound cylinders as 10%-90% ethylene oxide in carbon dioxide housed in cabinets located alongside each chamber. Products are exposed to 400-800 mg/l EO concentration while the chamber is maintained at 37-55oC, 30-80% relative humidity for a pre-determined period between 2-4 hours called the "dwell" phase. The pressure on dwell phase depends on the concentration of ethylene oxide in gas cylinders and adjusted ethylene oxide concentration within the sterilization chamber.

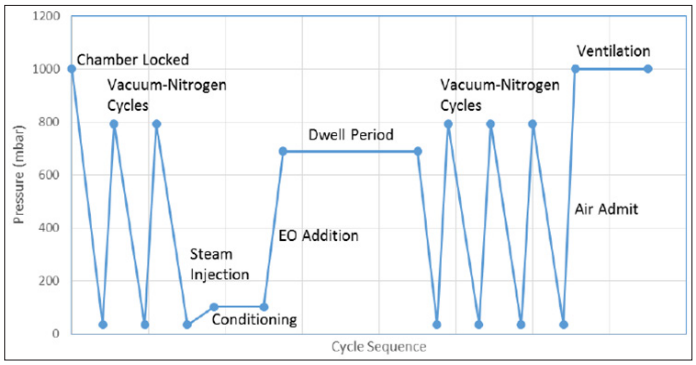

Figure 3: Sterilization cycles and sequencing.

If 90% EO-10% CO2gas mixture is used, the typical dwell phase concentration of 680mg/lis achieved at 600 mbar pressure. Therefore, a positive pressure around 4 bars is applied for 10%EO-90% CO2gas mixture is used. At the end of this phase, the chamber gas mixture is evacuated to the acid scrubber that removes EO. Approximately 60% of the EO is exhausted from the chamber during this phase of the cycle. The chamber then undergoes a series of nitrogen and/or air washes to remove the remaining EO. Figure 3 illustrates the sterilization cycle sequencing described in this section (Figure 3).

Storage, Transportation and Changing EO and N2 Cylinders

The design intent is safely store, transport of EO gas and safely changes EO cylinders. General recommendations for installing new cylinders are as follows;

a. The cylinders [1-2], vent valves and lines, shut off valves, gas regulators, pressure transducers, transducer cables and sockets, pneumatic valves, line heaters and pneumatic tubings-connectors should be labeled and numbered and also indicated in the written operating procedure.

b. EO line from cylinders to the sterilizer cabinet should have vent line which is connected to the exhaust ventilation system.

EO Piping from the Cylinders to the Sterilizer Chamber

The intent of this system is to transfer EO gas to the sterilizer unit.

EO Dosing System

The intent of this system is to vaporize EO gas and dose appropriate amount of EO into the sterilizer chamber.

Operation of Sterilizer

The design intent is to sterilize plastic and metal medical products under controlled conditions without any release of gas into working environment.

EO Stripper and Hydrolysis Reactor

The residual EO is adsorbed in packed adsorption column and catalytically converted into ethylene glycol before disposed.

Utilities and Process Lines in Sterilization System

EO sterilizer involves the flow of air, nitrogen, steam, condensate and water. Consequences of deviation in these flows are considered in this section. Nitrogen is used for inerting the sterilization system and air is used to break the vacuum. The HAZOP analysis of air and nitrogen flow nodes is also essential. In addition, the steam supply, humidification, and heating the sterilization chamber with hot water are also analyzed.

Reliability of Ventilation

The equipment room, loading room, utilities room and storage room are ventilated by a dilution ventilation system. Also the vent stream from EO cylinder changing operation is connected into the ventilation system.

EO Monitoring System

The EO gas detector is placed in EO storage room and continuously detects and monitors EO concentration in air.

Hazard Evaluation

Typical Hazards Associated with the Sterilization Process

Table 1: The typical hazards of EO sterilization process.

Steps to Follow	Remarks
Prevent overfeeding to the reactor	Workers/Employers
Store and handle EO properly	
Deal with leaks and spills	
Be prepared for rescue	Workers
Prevent skin and eye contact	
Use respiratory protection and other PPE	
Analyze and develop written procedures	Employers
Implement engineering controls	
Install emergency equipment	
Provide respiratory protection and PPE	
Provide training	
Prepare workers for rescue	

The typical hazards associated with the sterilization process using EO are listed in Table 1. Both workers and employers are recommended to pay attention to prevent overfeeding of the reactor by EO, to store and handle EO properly, and to deal with leaks 11 and spills. The typical hazards for workers and employers are recommended to follows are in the table (Table 1).

HAZOP Study

The sterilization process was under HAZOP study to find out hazards of the whole system including sterilization, supplying, storage, and ventilation system (Tables 2-4).

Scenario Development

Based on the HAZOP study, the following accident scenarios were developed including overdosing to the reactor, release to loading area, release to equipment area, and leak at storage of EO.

Table 2: HAZOP study EO supply system.

Process	Guideword	Possible cause	Possible Consequence
EO supply cylinders	Safety	High temperature	High pressure
			Decomposition
		Faulty or damaged cylinders	EO release
Piping from the cylinders to the sterilizer chamber	No flow	Closed or faulty valve in line or EO tank is empty	No hazard
		Front line or plugged line	Flow of tapped material into equipment room
	Reverse flow	At least one EO tank is not connected and valves attached to supply system are open.	Flow of trapped material into equipment room
	High flow	Broken line, faulty fitting, accidental break	Flow of EO into equipment room
	Less flow	Near empty cylinder, cold weather, frosting lines	No hazard
	High pressure	EO storage room temperature increases	EO may leak, polymerization may take place
	Low pressure	EO storage room temperature is low Line heaters are not operating	No hazard
	High temperature	High room temperature	High pressure and polymerization risk
	Low temperature	EO storage room temperature is low	No hazard
	Composition	Composition of EO in cylinder is not 90% EO- 10%CO2	Explosion or fire
	Contamination	Dirt and dust contamination in fitting and lines	Polymerization risk
	Relief venting	The blockage in vent line or any failure of vent valves	Depressurization in EO line cannot be done between cylinder and valves

	Maintenance	Leaks from valves, fittings, pressure transducers, regulators, etc.	The EO concentration in working environment increases
	Safety	Major leaks	High concentration of EO in working environment
	Security	Unauthorized entrance into equipment room	Gas leak, explosion, fire
EO transfer into the sterilizer	No flow	Check HAZOP analysis of piping system	
	Reverse flow	Not possible	
	More flow	Failure in valves to the sterilizer	Pressure and EO dose exceeds the set point
		Failure in transducers	Failure of door gasket
	Less flow	Check HAZOP analysis of piping system	Check HAZOP analysis of piping system
	Less pressure	Failure OF LINE HEATERS	Check HAZOP analysis of piping system
		Gas regulators set points are low	No hazard
		Failure of steam valve on evaporator	Pressure and EO dose exceeds the set point
		Failure of steam valve on evaporator	Liquid EO on chamber
		Failure of steam valve on evaporator	Liquid EO on chamber
	Low temperature EO	Same as less pressure	
	Service failure	Power failure	Sequence stops -valve closed
		Air compressor failure	Sequence stops -valve closed
		Steam generator failure	Same as less pressure
		Vacuum service failure	Sequence stops
EO transfer into the sterilizer	No flow	Check HAZOP analysis of piping system	
	Reverse flow	Not possible	
	More flow	Failure in valves to the sterilizer	Pressure and EO dose exceeds the set point
		Failure in transducers	Failure of door gasket
	Less flow	Check HAZOP analysis of piping system	Check HAZOP analysis of piping system
	Less pressure	Failure of line heaters	Check HAZOP analysis of piping system
		Gas regulators set points are low	No hazard
		Failure of steam valve on evaporator	Pressure and EO dose exceeds the set point
		Failure of steam valve on evaporator	Liquid EO on chamber
		Failure of steam valve on evaporator	Liquid EO on chamber
	Low temperature EO	Same as less pressure	
	Service failure	Power failure	Sequence stops -valve closed
		Air compressor failure	Sequence stops -valve closed
		Steam generator failure	Same as less pressure
		Vacuum service failure	Sequence stops

Table 3: HAZOP analysis of EO dosing into the sterilizer.

Process	Guideword	Possible Cause	Possible Consequence
Warm-up, conditioning period	Safety hazards	High set temperature	No safety issues
		Failure of temperature probe	No safety issues
	Evacuation	Vacuum too high	No safety issues
		Vacuum too low	No safety issues
		No water in separator	No safety issues
		Faulty reading of pressure	The oxygen level will be high
Pre-inerting, vacuum, humidifying period	No nitrogen flow	Empty N2cylinder, plugged filter, N2tube or ball valve is closed	No safety issues
	Reverse flow of nitrogen	Not possible	
	High flow of	Nitrogen regulator set point	No safety issues
	Low flow of nitrogen	Nitrogen regulator set point is low	No safety issues
		Faulty reading of pressure	The oxygen residual in the tank will be high
	Evacuation	Vacuum too high	No safety issues
		Vacuum too low	No safety issues
		No water in separator	No safety issues
		Faulty reading of pressure	The oxygen level will be high
	No steam flow	Fault in steam generator, ball valve in steam generator is closed, safety valve plugged	No safety issues
	Reverse steam flow	Not possible	
	High steam flow	Steam generator pressure is not correct	No safety issues
	Low steam flow	Fault in steam generator, ball valve in steam generator is closed, safety valve plugged	No safety issues
	Service failure	No electricity	No safety issues
		Water outage	No safety issues
		No compressed air	No safety issues
EO charging period	No flow	Check EO piping and transfer hazards	No hazard
	Reverse flow	Rupture in evaporator steam coil	EO will flow into steam generator
		Faulty valve into equipment room	EO will flow into equipment room
		Faulty valve to vacuum pump	EO will flow into vacuum pump and separator
	More flow	Check EO piping and transfer hazards	
Sterilization period	Air leakage	Faulty door gasket, dirt, dust in door seal, hole in the chamber	Flammable and explosive mixture forms inside

Table 4: HAZOP analysis of post sterilization period.

Process	Guideword	Possible cause	Possible consequence
Post sterilization period: I- vacuum	Vacuum too high		Surge of EO to separator and stripper
	Vacuum too low	Problem in outlet valve Water in vacuum ring is hot	No safety issues
	No water in separator	Failure in safety valve or water service	No safety issues

1stnitrogen wash	No nitrogen flow	Empty nitrogen cylinder, plugged filter, Nitrogen tube or ball valve is closed	No safety issues
	Reverse nitrogen flow	Not possible	
	High nitrogen flow	Nitrogen regulator set point is high	No safety issues
	Low nitrogen flow	Nitrogen regulator set point is low	No safety issues
2nd- Vacuum	Vacuum too high		Surge of EO to separator and stripper
	Vacuum too low	Problem in outlet valve Water in vacuum ring is hot	No safety issues
	No water in separator	Failure in inlet valve or water service	No safety issues
2nd Nitrogen wash	No nitrogen flow	Empty nitrogen cylinder, plugged filter, Nitrogen tube or ball valve is closed	No safety issues
	Reverse nitrogen flow	Not possible	
	High nitrogen flow	Nitrogen regulator set point is high	No safety issues
	Low nitrogen flow	Nitrogen regulator set point is low	No safety issues
3rd- Vacuum	Vacuum too high		Surge of EO to separator and stripper
	Vacuum too low	Problem in outlet valve Water in vacuum ring is hot	No safety issues
	No water in separator	Failure in inlet valve or water service	No safety issues
Air admit	No air flow	Plugged air filter	No safety issues
	Reverse air flow	Not possible	No safety issues
	High air flow	Not possible	No safety issues
	Low air flow	Plugged air filter	No safety issues

a. Overdosing To The Reactor

i. S01: Failure in valves at inlet part→ Failure in pressure transducer →Pressure and EO dose exceeds the set point → Overdosed

ii. S02: Failure in valve at inlet part→ Failure in pressure transducer → Failure of door gasket → Overdosed

b. Release To Loading Area

i. S11: Small scale leak through sterilizer door gasket → detector malfunction → loading/unloading work exposed to higher than 1.0ppm EO→ workers' exposed probability

ii. S12: Small scale leak through sterilizer door by the process air failure → detector malfunction → loading/unloading work exposed to higher than 1.0ppm EO→ workers' exposed probability

iii. S13: Small scale leak through sterilizer door by the electricity failure → detector malfunction → loading/unloading work exposed to higher than 1.0ppm EO→ workers' exposed probability

iv. S14: Small scale leak at the equipment area → detector malfunction → equipment area exposed to lower than 6,500ppm (25% of the LEL) → sealing failure between the equipment area and loading/unloading room→ workers' exposed probability

c. Release To Equipment Area

i. S21: Small scale leak by pipeline failure → detector malfunction → equipment area exposed to higher than 6,500ppm (25% of the LEL) → ignition

ii. S22: Small scale leak by compartment failure (gasket, joints, or valve stems) → detector malfunction → equipment area exposed to higher than 6,500ppm (25% of the LEL) → ignition

iii. S23: Small scale leak by reverse flow via air inlet → detector malfunction → equipment area exposed to higher than 6,500ppm (25% of the LEL) → ignition

iv. S24: Small scale leak by pressure switch malfunction → detector malfunction → equipment area exposed to higher than 6,500ppm (25% of the LEL) → ignition

v. S25: Small scale leak by electricity failure → detector malfunction → equipment area exposed to higher than 6,500ppm (25% of the LEL) → ignition

vi. S26: Small scale leak by air failure → detector malfunction → equipment area exposed to higher than 6,500ppm (25% of the LEL) → ignition

d. Leak at Storage of EO

i. S31: Small scale leak by piping → bad ventilation →

storage area exposed to higher than 6,500ppm (25% of the LEL) → ignition

ii. S32: Small scale leak by fitting failure → bad ventilation → storage area exposed to higher than 6,500ppm (25% of the LEL) → ignition

iii. S33: Small scale leak by heating pipe line by sunlight → bad ventilation → storage area exposed to higher than 6,500ppm (25% of the LEL) → ignition

iv. S34: Small scale leak by unintended open of valve → bad ventilation → release of trapped EO→ ignition

Likelihoods of Events

The likelihood data are given in Table 5 for the sterilization process (Table 5).

Table 5: Likelihood data for sterilization process using EO Event.

Sterilization process using EO Event	Likelihood	Reference
Valve failure	4.4×10^{-3}	16
Transducer failure	3.0×10^{-4}	18
Gasket failure	4.7×10^{-3}	18
Gas detector failure	1.8×10^{-1}	17
Workers' exposed probability	1.0×10^{-2}	16
Probability of immediate ignition	0.2	17
Pipeline failure	1.0×10^{-3}	16
BPC Sloop failure	1.0×10^{-1}	16
Ventilation failure	0.5×10^{-1}	18

Determining The Frequency of Scenarios

The frequency was determined for each scenario and the results are described below. The frequency ranges from 5.3×10^{-3}(f_{23}) to 8.5×10^{-6} (f_{11},f_{12},f_{13}) are associated with the release to equipment or loading area, ranges from 5.8×10^{-10}(f_{01}) to 6.2×10^{-12}(f_{02}) associated with overdosing to the reactor, and ranges from 1.5×10^{-5}(f_{31}, f_{32}, f33) to 6.5×10^{-6}(f_{34}) associated with leak at the storage.

a. Overdosing to The Reactor

$$f_{01} = (4.4\times10^{-3})(3\times10^{-4})(4.4\times10^{-3})(1.0\times10^{-1}) = 5.8\times10^{-10}$$

$$f_{02} = (4.4\times10^{-3})(3.0\times10^{-4})(4.7\times10^{-3})(1.0\times10^{-1})(1.0\times10^{-2}) = 6.2\times10^{-12}$$

b. Release to Loading Area

$$f_{11} = (4.7\times10^{-3})(1.8\times10^{-1})(1.0\times10^{-2}) = 8.5\times10^{-6}$$

$$f_{12} = (4.7\times10^{-3})(1.8\times10^{-1})(1.0\times10^{-2}) = 8.5\times10^{-6}$$

$$f_{13} = (4.7\times10^{-3})(1.8\times10^{-1})(1.0\times10^{-2}) = 8.5\times10^{-6}$$

$$f_{14} = (1.0\times10^{-1})(1.8\times10^{-1})(1.0\times10^{-2})(4.7\times10^{-3}) = 8.5\times10^{-7}$$

c. Release to Equipment Area

$$f_{21} = (1.0\times10^{-3})(1.8\times10^{-1})(0.296) = 5.3\times10^{-5}$$

$$f_{22} = (4.7\times10^{-3})(1.8\times10^{-1})(0.296) = 2.5\times10^{-4}$$

$$f_{23} = (1.0\times10^{-1})(1.8\times10^{-1})(0.296) = 5.3\times10^{-3}$$

$$f_{24} = (1.0\times10^{-2})(1.8\times10^{-1})(0.296) = 5.3\times10^{-4}$$

$$f_{25} = (1.0\times10^{-2})(1.8\times10^{-1})(0.296) = 5.3\times10^{-4}$$

$$f_{26} = (1.0\times10^{-2})(1.8\times10^{-1})(0.296) = 5.3\times10^{-4}$$

d. Leak at Storage of EO

$$f_{31} = (1.0\times10^{-3})(0.5\times10^{-1})(0.296) = 1.5\times10^{-5}$$

$$f_{32} = (1.0\times10^{-3})(0.5\times10^{-1})(0.296) = 1.5\times10^{-5}$$

$$f_{33} = (1.0\times10^{-3})(0.5\times10^{-1})(0.296) = 1.5\times10^{-5}$$

$$f_{34} = (4.4\times10^{-3})(0.5\times10^{-1})(0.296) = 6.5\times10^{-5}$$

Result and Discussion

Based on the HAZOP study and developed scenario, countermeasures can be obtained to reduce hazards in the sterilization process using EO. Among the developed scenarios, overdosing to the reactor may cause off-specification of the product and is little harmful to workers and facility, and no further analysis is needed. EO release can be very harmful to cause toxic exposure to the workers or became explosive. The EO release to the equipment chamber, loading area, and storage area can intoxicate workers or can be exploded. The scenario associated with the release to loading area has likelihood ranged from 8.5×10^{-6} to 8.5×10^{-7}. The scenario with frequency of 8.5×10^{-6} corresponds to either small scale leak through sterilizer door by the process air failure or by the electricity failure followed by loading/unloading work exposed to higher than 1.0ppm EO with detector malfunction [16-18].

If adequate personal protection equipment (PPE) is available together with monitoring system, then the frequency can be improved to the level of 10^{-6}. The scenario associated with the release to equipment area has likelihood ranged from 5.3×10^{-3} to 5.3×10^{-5}. The scenario with frequency of 5.3×10^{-3}corresponds to small scale leak by reverse flow via air inlet followed by equipment area exposed to higher than 6,500ppm (25% of the LEL) with detector malfunction, then ignited. If adequate ventilation windows are added, then the frequency can be improved to the level of 10^{-6}. The scenario associated with the leak at storage area has likelihood ranged from 1.5×10^{-5} to 6.5×10^{-6}. The scenario with frequency of 1.5×10^{-5} corresponds to small scale leak by fitting failure followed by storage area exposed to higher than 6,500ppm (25% of the LEL) with bad ventilation, then ignited. If adequate ventilation windows are added, then the frequency can be improved to the level of 10^{-6}.

Conclusion

Risk of per 1million is generally acceptable one. Risk of EO gas release followed by EO intoxication or explosion at loading/unloading area and equipment area can be reduced by adding PPE (Personal protection equipment, SIL 1, or) and monitoring system (SIL 2, or) together. Risk of EO gas release followed by EO intoxication or explosion at gas storage facility can be reduced by adding ventilation windows of SIL

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References

1. M Angel de la O Herrera, AS Luna, AC Augusto da Costa, EMB (2015) Lemes, J. Loss Prev. Proc. Ind., 35(5): 1.
2. T Sandle (2016) Pharmaceutical microbiology - essentials for quality assurance and quality control, 233.
3. W Feng, Y Zhaoa, O Yanga, J Cai, M Deng (2013) J. Loss Prev. Proc. Ind, 26(6): 1399.
4. LG Hess, VV Tilton (1950) Industrial & Engineering Chemistry 42(6): 1251-1258.
5. (1994) NFPA 325, Fire hazard properties of flammable liquids, gases and volatile solids.
6. MG Zabetakis (1965) Flammability characteristics of combustible gases and vapors, Bulletin 627, US Bureau of Mines.
7. (2007) NFPA 86, Standard for ovens and furnaces.
8. (2007) American Chemistry Council, EO product stewardship manual (3rd edn).
9. (1981) DHHS (NIOSH) Publication Number 81-130, Ethylene oxide (EO): evidence of carcinogenicity.
10. (2012) OSHA Standards- 29CFR, Part 1910-1047, Ethylene oxide 25.
11. S Jung (2016) Korean Journal of Chemical Engineering 33(1): 1.
12. R Singh, HJ Lee, AK Singh, DP Kim (2016) Korean Journal of Chemical Engineering 33(8): 2253.
13. S Tong, ZZ Wu, RJ Wang, YQ Duo (2016) Korean Journal of Chemical Engineering 33(8): 2291-2297.
14. (2001) CCPS, Layer of protection analysis: simplified process risk assessment, New York, USA, 71.
15. (1989) CCPS, Guidelines for process equipment reliability data - with data tables, New York, USA, 33.
16. (1995) AEA/CS/HSE R1403, BLEVE probability of an LPG road tanker during unloading.
17. C Zhu, J Jiang, X Yuan (2012) Procedia Engineering 45: 435.
18. FP Lees, S Mannan (2012) Loss Prevention in the Process Industry (3rd edn).

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