Pharmaceutical Regulatory Affairs: Open Access

Shintani, Pharmaceut Reg Affairs 2015, 4:2
DOI: 10.4172/2167-7689.1000e152

Editorial Open Access

Performance of Qualification of Ethylene Oxide Gas Sterilization Process

Hideharu Shintani*

Chuo University, Tokyo, Japan

There are several different methods for performance qualification of an ethylene oxide gas (EOG) process for sterilization of a medical device or component. They are half cycle method, overkill method, combined BI (biological indicator)/bioburden method and absolute bioburden method. The most popular procedure is overkill method as described in ISO 14161. This is the most popular and cost-effective method utilized in the industry today. ISO14161 and ISO 11135 describe the qualification process for an overkill method as follows: This method involves determination of the minimum time of exposure to EOG, with all other process parameters held constant, at which there are no survivors of BIs. A short duration from which survivors can be recovered should also be run to demonstrate the adequacy of the recovery technique. Initial population is 10^6 CFU (colony forming unit)/carrier and SAL (sterility assurance level) of 10^{-6}, so as a whole 12 log reduction exposure time is the overkill method. The qualification method described above is very similar to a half cycle method. In overkill method, one half of the gas exposure times were conducted in which a 10^6 CFU/carrier BI is reduced to SAL of 10^0 spores when it is placed in the most difficult to sterilize location within the medical device and within the sterilizer load and this 6 log reduction doubled and as a whole 12 log reduction (Figure 1).

The BI used for EOG sterilization is *Bacillus atrophaeus* ATCC 9372, which is defined in ISO 11138-2. Also as a benefit, the fractional cycle may be utilized to establish a relationship between a BI placed on the outside surface (external) of a pallet and the BI placed in the most difficult to sterilize location (internal). This data may allow routine monitoring using only external BIs, thus preventing internal BI monitoring. This is a great advantage since the cartons do not have to be opened which prevents potential operator exposure to elevated levels of ethylene oxide.

Monitoring of internal load temperatures and relative humidity is also a requirement of performing qualification process which complies with the guidelines established in ISO11135. The total number of sensors required is load size dependent. The actual number can be calculated using the formulas and procedures identified in the respective documents. The parts of a simple EOG validation, assuming qualification of a single device of simple design, are presented below.

AAMI TIR No. 14-19975, titled "Contract Sterilization for Ethylene Oxide" recommends that all qualifications be performed using a written action plan in the form of a protocol. It further recommends that the protocol be reviewed and approved by qualified personnel prior to its execution.

Two types of biological testing are utilized for qualifications. One is natural product sterility testing (bioburden sterility testing) and the other is BI sterility testing. Natural product sterility testing is performed after each half cycle to assure the product is rendered sterile by the process. BI sterility testing when successfully performed demonstrates a 6-log reduction of the BI at half exposure, which yields a theoretica1 12-log reduction at full exposure (thus the reference to overkill).

Internal process challenge devices (IPCDs) are prepared by placing BI in the most difficult to sterilize area of the health care products. This "sporing" location is selected utilizing data generated during process/product development or by examination by a sterilization specialist who is familiar with the type of device and the sterilization process. The number of IPCDs required is dependent upon the load size (ISO 11135).

Additional BIs are prepared to be utilized as external process challenge devices (EPCDs). The EPCDs will be placed on the exterior surfaces of the load and will ultimately be used as the routine biological process monitor.

A reference load is defined in 11135 as specified sterilization load made up to represent the most difficult combination of products to be sterilized. Working with the customer, a reference load will be identified which will result in a challenge of the maximum load density. Once the load configuration is identified, all PCDs (internal and external) are placed on the load along with the product sterility samples and temperature/relative humidity monitoring instruments.

Most of the sterilization processes of conditioning of the products are qualified the sterilization recovery process. Preconditioning is usually performed in a room which has been specially designed to heat and humidify the products to a stable internal temperature and moisture content prior to entering the chamber.

The product is placed into the preconditioning room and held for a time (dwell) which has been selected by the EOG sterilization specialist to represent the minimum time which will be allowed during routine production.

Once the preconditioning dwell time is complete, the products are moved to the sterilizer for processing the half or fractional cycle. Fractional cycle means that the load is processed in a sterilization cycle which has been selected or designed by the EOG sterilization specialist to deliver less lethality at a fraction of the routine cycle exposure time, as compared to the cycle which will be used for routine processing.

Half cycle means that the load is then processed in a cycle which has been selected or designed by the EOG sterilization specialist to deliver less lethality at one half the routine cycle exposure time, as compared to the cycle which will be used for routine processing.

After sterilization, the load is placed in a heated room for additional removal of EOG residue. The room is maintained at elevated temperatures and the outgassed residues are continuously removed from the room and scrubbed. The products are resident in the aeration room for a maximum of 6 hours. Then it is moved to the sampling area.

Biological samples are removed from the load and sent to the laboratory for sterility testing. All BIs are aseptically transferred to tubes of growth media and placed into incubation for at least 10 days. All product sterility test units are aseptically transferred to growth media and placed into incubation for14 days.

Sterility testing can be conduced as follows;

***Corresponding author:** Hideharu Shintani, Faculty of Science and Engineering, Chuo University, 1-13-27, Kasuga, Bunkyo, 112-8551, Tokyo, Japan, Tel: +8142592233; Fax: +81425922336; E-mail: shintani@mail.hinocatv.ne.jp

Received March 25, 2015; **Accepted** March 26, 2015; **Published** April 02, 2015

Citation: Shintani H (2015) Gas Plasma Exposure to Bacterial Spore, Endotoxin and Prion. Pharmaceut Reg Affairs 4: e152. doi:10.4172/2167-7689.1000e152

Fractional cycle (l each) is that the cycle, if successful, will produce growth of some or all of the BIs, yet yield zero growth of the product sterility test units. BI growth will serve to validate the BI recovery process.

Half cycles (3 each) is that these cycles, if successful, will result in total sterility of all IPCDs and product sterility test units. Depending on the resistance of the EPCD, some growth may be observed due to the short duration of the selected.

Full cycles performed at the routine exposure time will be utilized as part of the qualification process to appraise product functionality, packaging integrity, and EOG residue. These will be performed and ultimately be part of the performance qualification data set.

A final report will be prepared which contains all data and a summary which identifies the success of the validation process. Approvals for the final report are typically those individuals who approved the testing protocol. A copy of the final report and all data should be maintained on file.