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A STERIGENICS WHITE PAPER

Pros, Cons and Considerations of Using a Developmental Chamber During Ethylene Oxide Validation

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Abstract

A developmental chamber is usually smaller than a production chamber and used to perform studies to support Ethylene Oxide validation. This white paper discusses use of a developmental chamber for Process Definition performed as part of a validation, in adherence with ISO 11135:2014, using the Overkill Approach. Project Management and Quality Assurance personnel within the medical device, pharmaceutical, commercial and food industries will learn what to consider when contemplating either a developmental or production chamber, as well as advantages and disadvantages of using a developmental chamber. As an example, one advantage of using a developmental chamber is that smaller sample sizes in the smaller developmental chamber will often mean lower laboratory testing costs.

Introduction

When it comes to performing runs, there are two (2) main parts to an Ethylene Oxide (EO) sterilization validation. The first part is Process Definition. This part addresses fractional work that includes (but is not limited to) confirming Biological Indicator (BI) appropriateness, determining the resistance of different internal Process Challenge Devices (PCDs), determining an appropriate external PCD, and calculating the theoretical half-cycle gas dwell time.

The second part to an EO sterilization validation (traditionally performed after Process Definition) is Performance Qualification (PQ). This part addresses the Microbiological Performance Qualification (MPQ) work (half cycles) and Physical Performance Qualification (PPQ) work (full cycles). The production chamber must be used for the MPQ and PPQ runs; however, ISO 11135:2014 allows the use of a developmental or production chamber for the Process Definition work.

The authors of this white paper guide readers through the use of a developmental chamber for Process Definition in adherence with ISO 11135:2014. The authors provide both advantages and disadvantages of using the developmental chamber. And, finally, the authors offer considerations to guide decision-making as to whether to use a developmental chamber or production chamber for EO validation.

A **developmental chamber is usually a smaller chamber than the production chamber** and can be used to perform studies to support validation.

Requirements and Guidance for Using a Developmental Chamber for Process Definition

ISO 11135:2014 provides the following requirements, information and guidance should you chose to use a developmental chamber for Process Definition.

- Section 8.3 states that the developmental chamber has to have undergone an Installation Qualification (IQ) and Operational Qualification (OQ).
    - Documentation demonstrating the Installation Qualification (IQ) and OQ have been performed successfully should be on site at the facility in which the chamber is located. Confirmation that the IQ and OQ have been performed and were found to be acceptable satisfies this requirement.

- Section 9.4.2.4 states that if a developmental chamber is used for Process Definition, the MPQ should include at least three (3) fractional or three (3) half cycles performed in the production chamber to confirm the data from the developmental chamber.
    - For validations performed utilizing the Half-Cycle Overkill Approach, the half cycle runs must be performed in the production chamber. For validations performed utilizing the Cycle Calculation Overkill Approach, the Process Definition runs performed to determine the D-value and full-cycle gas dwell time must be performed in the production chamber. These runs cannot be performed in a developmental chamber. To satisfy this requirement, when validating using either method, a minimum of three (3) MPQ runs must be performed in the production chamber.

- Section D.8.3 states that using a developmental chamber does not preclude confirmation of PQ in a production chamber.
    - The PQ runs must be performed in the production chamber. To satisfy this statement, when validating using either method, the PQ runs must be performed in the production chamber.
- Section D9.4.2.4 provides the following guidance: If a developmental chamber is used for Process Definition, consideration should be given to establish the relationship between data from the developmental chamber studies and data from the production chamber.
    - Inactivation curves can be developed in a developmental chamber that can deliver equivalent parameters—especially EO concentration used in the production chamber.
        - Due to the size of a production chamber and the time required to inject and remove EO in the chamber, often times a microbial inactivation curve is not possible in the production chamber. The longer injection and evaluation times can limit the ability to obtain fractional growth of the indicator organism in the production chamber. This is why, traditionally, fractional runs are performed in a developmental chamber.
        - To use a developmental chamber, the chamber must be able to perform equivalent parameters compared to the parameters performed in the production chamber. This can include (but is not limited to) showing the developmental chamber's ability to reach the same vacuum depths, use specified rates, inject specific amounts of gas (i.e., EO, Nitrogen and Air), and provide similar humidity conditions. Note that alteration of some parameters during Process Definition is common to obtain fractional growth (i.e., gas dwell time, rates). One should show equivalent parameters can be performed in both chambers. This can be done by comparing the cycle parameters used for runs performed in the production chamber and runs performed in the developmental chamber. If the cycle parameters performed in the developmental chamber can be considered equivalent, and the developmental chamber can create similar conditions in the chamber to those used in the production chamber, this guidance has been met.
    - Methods for demonstrating a relationship between the data developed in the developmental chamber and a production chamber involve a physical profile comparison and load density comparison.
        - It is recommended to compare the temperature and relative humidity (RH) profiles from both chambers. This is done to evaluate the ability of both chambers to yield similar conditions using equivalent parameters. The same or similar cycle should be performed in both chambers and the profiles (temperature and RH) from these runs can be compared. Showing the developmental chamber can provide similar temperature and RH profiles compared to the production chamber when using an equivalent cycle complies with this guidance.
        - The reference load used for Process Definition work should consist of the same load configuration as the reference load used for PQ runs performed. This includes the way shipper boxes are arranged on the pallet, the way the material is configured in the shipper boxes and the actual material used to configure the reference load. During a validation, one should use material and a load configuration that is representative of the routine process. This means regardless of the run type performed (i.e., fractional, half cycle, full cycle), the same load configuration should be used. As density is a very important aspect of the load configuration, it is very important to make sure the density of the product used for Process Definition work is the same as that used for the PQ work and ultimately routine processing.

    - Due to the size of the developmental chamber, the number of layers on the pallet may need to be reduced for the Process Definition runs. As long as the difference is determined to be insignificant, there should be no issue with the slight load configuration change. Evaluation must be performed to confirm the load configuration size change does not impact the ability of the developmental chamber to deliver equivalent conditions as full-load configuration used in the production chamber.
  - During the development of the sterilization process in a developmental chamber, it is important to place PCDs inside the finished product case or in the routine configuration to provide a relationship of the dynamics of the products within the case against the PCD during process development.
    - It is common practice at Sterigenics to place all samples (excluding external PCDs) inside the shipper box next to the product. If there is not enough space in the shipper box for the sample and the product, the sample will take the place of the product in certain locations. When samples are placed in the same location as the product, they will see the same conditions as the product, which allows for an accurate comparison.

Advantages of Using a Developmental Chamber for Process Definition

Process Definition work does not have to be performed in a developmental chamber; however, there may be benefits to using a developmental chamber. Below are some advantages to using a developmental chamber for Process Definition.

- Sample quantities are usually smaller when using a developmental chamber because the chamber itself is smaller. The smaller sample sizes will often mean lower laboratory testing costs as well.
- When using a smaller chamber, shorter pull times may be able to be utilized. This would be determined after additional evaluation from Environmental Health & Safety (EHS).
- It is often easier to get fractional growth in a smaller chamber than in a larger chamber. This could mean performing less runs during Process Definition. Often times, additional parameter adjustments may be needed when performing fractional runs in a production chamber due to the size of the chamber.

Disadvantages of Using a Developmental Chamber for Process Definition

Performing Process Definition work in a developmental chamber is not always the best option. Below are some disadvantages to using a developmental chamber for Process Definition.

- One must confirm the requirements and guidance listed in ISO 11135 for using a developmental chamber are met.
- One must determine the amount of scale up needed for the sterilization cycle when moving to the PQ runs in the production chamber. Scale up are the adjustments made to the sterilization cycle when increasing the load size or moving to a larger chamber to make sure the required lethality can still be achieved. The larger load size or using a larger chamber may create a condition in which it is harder to get lethality throughout the load so scale up must be taken into consideration.
- If the size difference between the production chamber and the developmental chamber is very large, more consideration may be needed when determining the scale up needed to move into the production chamber.

Additional Considerations to Determine When to Use a Developmental Chamber

Considerations must be made when determining the appropriate situations for using a developmental chamber for Process Definition. Below are some additional items one should consider before using a developmental chamber.

- Evaluate the type of sterilization cycle being validated. Certain cycles may make it more difficult to determine the appropriate amount of scale up when moving into the production chamber. Types of cycles that may fall into this pitfall are shallow vacuum cycles and low temperature cycles. These are typically cycles that may have a flatter inactivation curve than traditional cycles.
- Take the size of the final load into consideration. If there is a large difference between the size of the developmental chamber and the production chamber, there may be additional issues when determining the amount of scale up needed. Options are to use a larger developmental chamber or to perform the process definition work in the production chamber.
- The ratio of the load to chamber size should be evaluated. Changes in the amount of head space in the chamber can impact the microbiological results and process dynamics (i.e., absorption of temperature and EO) when moving from a developmental chamber to a production chamber.

Conclusion

A developmental chamber can be used for Process Definition work as long as certain criteria are met. Ultimately, the developmental chamber must be working appropriately and be able to provide equivalent conditions compared to the production chamber. In most cases, it is beneficial to use a developmental chamber when performing fractional runs (if the option is available); however, when fractional runs are not available, additional evaluation should be done before making a decision to use a developmental chamber.

Reference

ISO (International Standards Organization) 11135:2014, Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices.

About Sotera Health

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Sterigenics is a global leader in mission-critical sterilization solutions and expert advisory services. Its 1,600 engineers, scientists and safety specialists provide deep expertise in Gamma, EO, E-Beam and X-ray sterilization technologies for the medical device, pharmaceutical, food and commercial safety, and high-performance materials industries. Its network of 47 facilities in 13 countries put its services close to customers' production and distribution points, ensuring it is the "point of safe" for customers around the world.

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