SUSTAINABLE EO® STERILIZATION SERVICES

ADVANCING STERILITY ASSURANCE THROUGH SCIENCE, TECHNOLOGY AND INNOVATION

Frequently Asked Questions

Q **Why should I consider optimizing the amount of sterilant in my existing EO sterilization cycle?**

A Ethylene oxide (EO) is a universally accepted sterilization technology that has delivered sterile healthcare products for patient care since the 1960s. However, with the use of EO as a sterilant, human safety and environmental challenges must be considered.

As part of our commitment to providing innovative and sustainable solutions, STERIS AST has developed the **Sustainable EO® sterilization services** program. Our Sustainable EO services provide Customers with strategies to reduce the EO sterilant used in their sterilization process to achieve their prescribed Sterility Assurance Level (SAL).

The program includes innovative approaches to EO sterilization including establishing the most appropriate process challenge device design (PCD, cycle design and validation strategy; all focused on the reduction of EO residuals on healthcare products).

Optimized sterilant input provides several benefits, including:

- Lower product residuals that meet current and potential future patient safety requirements
- Improved occupational safety
- Improved supply chain efficiencies due to reduced aeration (off-gassing) of EO gas

Q **Is the Sustainable EO program a validation approach using alternative bioburden-based methods?**

A While bioburden-based methods per ISO 11135:2014 may be used at any time, the focus of the Sustainable EO program is to predominantly utilize use an Overkill approach. Successfully qualified Sustainable EO cycles using overkill approachs have demonstrated delivery of the required SAL of 10^{-6} , minimizing the level of over-processing seen on legacy cycles.

Q **Does ISO 11135:2014 specify that the biological indicator (BI) should be placed within the most challenging location of the product?**

A No. The specific requirement of clause 8.6 c) of ISO 11135:2014 is that the BI “be placed in a PCD” and that “the PCD shall present a challenge to the sterilization process that is equivalent or greater than the challenge presented by the **natural bioburden** at the most difficult to sterilize location within the product.”

In the original version of ISO 11135 (issued in 1994), the guidance in Annex B suggested that BIs should be located in the most challenging location. However, this recommendation changed with subsequent revisions of the standard. In the 2007 revision of the standard, clause 8.6 c) required that the BI be placed in the most challenging location **or** within a PCD. Whereas, the 2014 revision simply requires that it be “placed within an appropriate PCD.”

The guidance offered in clause D.8.6 of ISO 11135:2014 outlines approaches that can be used to demonstrate the appropriateness of a process challenge device (PCD), with “Approach 2” having been widely adopted to establish relative resistance data between the BI/PCD and the product bioburden.

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Q **Does my cycle need to use the same EO concentration as that used to establish the D-value of the BI?**

A No. The D-value (Decimal Reduction Value) of any BI is the defined resistance of that BI at a given set of conditions. This is established in a Biological Indicator Evaluation Resistometer (BIER) vessel. A BIER vessel needs to meet specific criteria with prescribed limits on process parameterscontributing to lethality in accordance with the requirements of ISO11138: EO concentration, temperature, injection and evacuation times.

While the D-value of BIs is typically established with an EO concentration of 600 mg/L at 54°C, industrial EO processes may be qualified at a range of temperatures and EO concentrations based on specific product limitations. Furthermore, studies have been published demonstrating that although lethality increases with higher EO concentrations, the increased lethality tails off after 400 mg/L and has little impact above 500 mg/L (Caputo, Rohn, Odlaug, 1981).

Q **Given the criticality of the Test of Sterility on products with natural product bioburden in the proposed method, are there particular considerations regarding sampling for this assay?**

A Comparative studies should be performed using product bioburden that is representative of that expected from normal production and that will be the sterilization challenge during routine sterilization processing. Refer to sections 5.1 and 7 of ISO 11737-2:2009 for the selection of samples and assessment of test method for the Test of Sterility used in this approach.

Q **My bioburden upper control limit is 1,000 CFUs. However, it can vary and be as low as 50 CFUs. What do I use in my comparative study?**

A Samples with bioburden that are typical of routine production should be selected for both Test of Sterility and bioburden testing. Where there is expected to be variability in the bioburden data, samples with bioburden close to the upper limit should be selected. Refer to sections 5.1.1 and A.5.1.1. of ISO 11737-1:2018 and 5.1 of ISO 11737-2:2009 regarding the selection of bioburden and Test of Sterility samples.

Q **How do I perform a comparative resistance study?**

A A comparative resistance study is performed early in the overall validation program and involves the performance of a sublethal fractional exposure time process. PCDs and product Test of Sterility units are placed in the load and tested for recovery after the exposure to a fractional cycle. The results from the testing of the PCDs and the Test of Sterility provide data to compare the relative resistance of each against each other. The desired outcome is no growth from the Test of Sterility and some level of growth from the PCDs. This provides evidence that the PCD is a greater challenge than the bioburden on the product; including the location that is the most challenging to sterilize.

Q **What do I do if I get no growth from the both the product Test of Sterility and the IPCD?**

A No growth from both the IPCD and the product Test of Sterility units would indicate that there is an opportunity to further reduce cycle lethality by lowering the EO concentration and/or the EO dwell time to obtain some level of growth from the IPCDs.

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ADVANCING STERILITY ASSURANCE THROUGH SCIENCE, TECHNOLOGY AND INNOVATION

Q **What do I do once I have my IPCD determined and demonstrated as appropriate?**

A Once an IPCD is defined, the validation progresses to Performance Qualification (PQ) cycles to confirm that the process can deliver the required minimum SAL of 10^{-6}.

Q **Do I need to demonstrate that my EPCD (if used) is more challenging that my IPCD?**

A A PCD, internal or external, only needs to demonstrate that it presents "a challenge to the sterilization process that is equivalent or greater than the challenge presented by the natural bioburden at the most difficult to sterilize location within the product."

Only when looking to accept growth of an EPCD from a half cycle exposure (as per ISO 11135:2014, section 9.4.2.5) does the EPCD need to have "demonstrated greater resistance than the internal PCDs providing a "worst-case challenge" for routine processing."

Q **If I have a legacy process and re-design to a Sustainable EO process, is it considered a change?**

A Yes. Any change needs to be reviewed and subjected to verification and/or validation. A recommended approach would be to perform a risk assessment of any changes. Typically, the change will be a reduction in the current process such as reduced EO concentration, reduced processing time, and/or reduced EO exposure time. Hence, the legacy process will remain a worst case as parameters such as temperature, humidity and vacuum depth will be unchanged. As the Sustainable EO program involves a full validation compliant with ISO 11135:2014, a minimum SAL will be demonstrated and EO residuals will be assessed per ISO 10993-7:2008.

Q **What notification do I need to make to my Notified Body?**

A Having documented a risk assessment described above, a sterilization expert should then consult with their Regulatory Affairs or directly with their Notified body regarding required regulatory filings. STERIS AST has already presented the Sustainable EO approach to a number of the Notified Bodies, demonstrating how it fully complies with both normative and informative references in ISO 11135:2014.

Q **Does the Sustainable EO process use a mixed gas technology?**

A While STERIS AST offers a mixed gas (EO:CO_2) technology through our proprietary EO+ service, the primary focus of Sustainable EO is on 100% EO gas processes, where EO concentrations are typically in range of 500-700 mg/L. EO+ by nature of process design is typically in the range 250-350 mg/L. Thus, the benefits of further reduction can be limited. However, the benefits of a clear definition of relative resistance can be realized for all processes.

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ADVANCING STERILITY ASSURANCE THROUGH SCIENCE, TECHNOLOGY AND INNOVATION

Q **Does Sustainable EO affect my ability to use parametric release?**

A No. Sustainable EO is focused on the validation and the demonstration of lethality, which is a requirement of ISO 11135:2014, irrespective of the process release mechanism used. At the PQ stage, lethality to IPCDs would be quantified and conditions extrapolated to a Full cycle with process monitoring for parametric release.

Q **Does Sustainable EO affect my ability to process products a second time (2X) ?**

A No. In fact, a Sustainable EO process, using less EO and a shorter duration, may provide an opportunity for products that are currently only capable of being processed once (1X) in an existing process to allow for processing a second time (2X) with a Sustainable EO process.

Q **I have multiple product SKUs that require multiple processing cycles. Does Sustainable EO allow for standardization of the EO sterilization process?**

A Yes. Often, legacy processes per SKU were the result of the ISO 11135:1994 approach of validating with a BI in the worst-case conditions. A Sustainable EO validation can be used to define a standard IPCD with relative resistance demonstrated for many products and subsequently combined into a single process.

Q **Does STERIS AST have examples of Sustainable EO validations?**

A YES. STERIS AST has been successful in qualifying Sustainable EO processes, which have delivered significant improvements in Customer outcomes. We have documented these in case study papers, which may be shared with Customers on request.

Q **Will my validation take more time if performing a Sustainable EO validation?**

A No. Sustainable EO follows the same overkill approach already utilized, which is comprised of fractional, half and full cycles. If looking to convert an existing EO process, any changes would require full ISO11135 validation, but opportunities such as annual re-qualification or product adoptions could be used to minimize the extent of the validation.

Q **My EO residuals are already demonstrated as compliant to ISO10993-7:2008. Why would I need to perform a Sustainable EO validation?**

A As noted in the first question in this document, there are many benefits to optimizing sterilant input through a Sustainable EO validation.

While EO residuals are currently compliant, there is an opportunity for meeting further guidance provided in Europe on neonatal products (ANSM, TUV) and, more importantly, an opportunity to future-proof processes for any potential changes to the limits outlined in ISO10993-7.

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Q **I am a low frequency user of EO sterilization. Why should I consider a Sustainable EO validation?**

A The benefits of Sustainable EO are relevant to all manufacturers that utilize the technology, regardless of the frequency of processing.

Q **Will a Sustainable EO process require a higher processing temperature time?**

A No. Any loss of lethality through reduction in EO concentration does not need to be offset by an increase in process temperature.

Q **Will a Sustainable EO process require a longer EO process?**

A No. A significant amount of time in an EO process is devoted to removing the EO gas after the inactivation of the microorganisms. This aeration may consume hours in the sterilizer itself and days in additional aeration of products. By reducing the amount of EO sterilant being inputted to the process, there is often potential to optimize aeration times while maintaining compliance to the EO residual standard (ISO10993-7) requirements.

Q **I'd like to move to a Sustainable EO process but have limited technical resources to engage in such a project. How can STERIS help?**

A The STERIS EO TechTeam® technical experts can assist with optimizing your sterilization process. Learn more at www.steris-ast.com/techteam.

TechTeam®
We're Here to Help

STERIS
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