



## STERILIZATION VALIDATION

All sterilization processes require validation of the efficacy and reproducibility of the process. Depending on the type of sterilization, this may be accomplished by partial, sub-lethal, or repetitive processing, using representative product and/or biological challenges. WuXi AppTec offers a full range of services in this area, from testing alone to full management of the validation.

## REUSABLE MEDICAL DEVICE VALIDATION

The FDA expects manufacturers to validate all instructions for reusable devices, including cleaning, disinfection, sterilization parameters and aeration times, if applicable. WuXi AppTec offers a comprehensive program for evaluation of cleaning and sterilization processes for reusable medical devices.

*Your WuXi AppTec Account Manager can provide you with initial information regarding any of these testing programs. Also working closely with you will be a highly trained and knowledgeable technical expert.*

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## EO STERILIZATION VALIDATION

For validation of ethylene oxide (EO) sterilization, certain steps must be followed as outlined in ISO and AAMI standards. As part of the performance qualification, a microbiological challenge must be performed to demonstrate the adequacy of the process to achieve the desired sterility assurance level (SAL). One of the most utilized methods is the half-cycle (overkill) method, which uses a biological indicator (BI) challenge, typically  $10^6$  spores of *Bacillus atrophaeus*. Complete EO validation studies can be designed for a particular product and process, and all aspects of the studies follow the requirements of ISO and AAMI standards.

**ESTIMATED TOTAL TESTING TIME: 4 - 6 weeks**

### FRACTIONAL CYCLE STUDIES

**1203000**

#### Inoculated Biological Indicators

Samples will contain the microbial challenge system (process challenge device) inoculated in the device's most difficult area to sterilize. The BI seeded samples can be simulated products if they are wholly representative of the actual finished product.

**SAMPLE REQUIREMENTS** Dependent on load size

#### USP Product Sterility Test

**1220010**

Extra Small [ $\leq$  100 mL of media]

**1220000**

Small [100 and 200 mL of media]

**1226000**

Medium [300 and 400 mL of media]

**1227000**

Large [500 and 600 mL of media]

**1228000**

Extra Large [800 and 1000 mL of media]

**1228010**

Jumbo [1200 and 1500 mL of media]

**1128010**

Extra Jumbo [2000 mL of media]

At least 20 - 40 product samples from the processed load are tested for sterility. (A minimum of 40 extra samples should be retained in the event a retest is required.)

**SAMPLE REQUIREMENTS** 20 - 40 products

**190105** Immersion

**190104** Membrane Filtration

#### Sterility Method Suitability Test (B/F) – Two Media [USP]

Sample device or material in the sterility test medium is tested for growth inhibition using the current USP organisms for Soybean-Casein Digest Medium (SCDM) and Fluid Thioglycollate Medium (FTM). (Additional organisms available upon request.)

**SAMPLE REQUIREMENTS** 6 sterile product samples

**TURNAROUND TIME** 7-10 days

**DETERMINATION OF BIOBURDEN**

*For more information on these tests, see Page A-2 and A-3.*

Devices are selected at random for the bioburden recovery validation. They need not be identified with the production batches being used for validation.

**SAMPLE REQUIREMENTS** 3-5 products

**1601000**

**Bioburden Recovery Efficiency  
– Repetitive Recovery Method**

**OR**

**1602000**

**Bioburden Recovery Efficiency  
– Spore Inoculation Method**

Non-sterile devices are tested for bioburden.

**SAMPLE REQUIREMENTS** Minimum 10 products

**1603010**

**Aerobic Bioburden Panel**

Non-sterile devices are tested for bioburden.

**SAMPLE REQUIREMENTS** Minimum 10 products

**1605000**

**Total Bioburden Panel**

**TERMINAL STERILIZATION STUDIES**

At least 10 BI samples per cycle will be tested for sterility according to client specifications and/or the USP.

**SAMPLE REQUIREMENTS** Per client specifications

**1201000**

**Biological Indicators**

Product samples from the terminal sterilization cycle will be tested for ethylene oxide residuals at incremental time periods. Samples should be representative of the various materials of the product(s).

**SAMPLE REQUIREMENTS** Varies

**195000**

**EO Residual Panel –  
Water Extraction**

**OR**

**194500**

**EO Residual Panel –  
Headspace Extraction**

# RADIATION STERILIZATION VALIDATION

For validation of radiation (gamma, electron beam or x-ray) sterilization, certain steps must be followed as outlined in ISO and AAMI standards. As part of the performance qualification, a dose-setting or dose substantiation study must be performed to demonstrate the adequacy of the minimum dose to achieve the desired sterility assurance level (SAL). Several methods are available for validation of the minimum SAL dose, and the choice of method is dependent on a number of variables. Complete radiation validation studies can be designed for a particular product and process, and all aspects of the studies follow the requirements of ISO and AAMI standards.

***WuXi AppTec offers different levels of service programs for sterilization validations, as well as for dose audits. For more information, see Page H-6.***

## ANSI / AAMI / ISO 11137 Method 1 Validation

TOTAL TURNAROUND TIME: 5-7 weeks

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Total Bioburden Panel	10 products from three batches	Page A-3
Bioburden Recovery Efficiency Test	3-5 products from any batch	Page A-3
Sterility Method Suitability Test (B/F) – One Medium	3 products from any batch	Page G-3
Product Test of Sterility	100* samples from one batch	Page G-4

*NOTE: Single batch validations are also available.*

## Dose Audit

TOTAL TURNAROUND TIME: 3-5 weeks

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Aerobe or Total Bioburden Panel	10 products from one batch	Pages A-2, A-3
Product Test of Sterility	100* samples from one batch	Page G-4

## ANSI / AAMI / ISO 11137 Method 2 Validation

TOTAL TURNAROUND TIME: 6-10 weeks

*The requirements of Method 2 are not outlined here because of the complexity of the sampling scheme. Please contact the laboratory for more information.*

## Dose Audit

TOTAL TURNAROUND TIME: 3-5 weeks

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Aerobe or Total Bioburden Panel	10 products from one batch	Pages A-2, A-3
Product Test of Sterility	100* samples from one batch	Page G-4

\* Reduced number of samples may apply, based on specific criteria. Contact laboratory.

# RADIATION STERILIZATION VALIDATION

## ANSI / AAMI / ISO 11137 Vdmax 15 kGy or 25 kGy Validation and AAMI TIR 33

TOTAL TURNAROUND TIME: 5-7 weeks

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Total Bioburden Panel	10 products from three batches	Page A-3
Bioburden Recovery Efficiency Test	3-5 products from one batch	Page A-3
Sterility Method Suitability Test (B/F) – One Medium	3 products from any batch	Page G-3
Product Test of Sterility	10 samples from one batch	Page G-4

*NOTE: Single batch validations are also available.*

## Quarterly Dose Audit

TOTAL TURNAROUND TIME: 3-5 weeks

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Aerobic or Total Bioburden Panel	10 products from one batch	Pages A-2, A-3
Product Test of Sterility	10 samples from one batch	Page G-4

## **SERVICE OPTIONS FOR RADIATION STERILIZATION VALIDATION PROGRAMS**

To help clients get their products through the validation process, WuXi AppTec offers different levels of service options for validation studies and for dose audits – with varying degrees of involvement.

Your choice of service levels would depend on how much of your company's time, manpower and expertise you want to commit to your validation program. For example, WuXi AppTec can provide only the testing services while you schedule and manage all aspects of the irradiation services and develop all the documentation to present an organized study. Or, in addition to the testing, we can handle all the irradiation services for you, and you would be responsible only for producing the final documentation. Or we can take care of everything. You simply choose the validation method, give us your product samples, and 5 to 7 weeks later we give you a completed validation and finished manual.

## **SERVICE OPTIONS FOR DOSE AUDIT PROGRAMS**

Most products that are validated for radiation sterilization require periodic dose audits. As with validations, WuXi AppTec offers varying levels of service options for dose audits.

## **DOSE AUDIT REMINDER PROGRAM**

Dose audits are typically performed every three (3) months. However, the dose audit requirements for Method 1, Method 2 and VDmax validations may allow for a reduction in the frequency and – in the case of Method 1 and 2 – a reduction in the number of verification samples required, based on certain criteria. WuXi AppTec offers a dose audit reminder program that informs clients of their options, and issues reminders when dose audits are due for each product or family of products.

**Contact your Account Manager for more information about these programs.**

When reusable medical devices are cleaned and sterilized in a health care facility, manufacturers are responsible for providing their customers with complete and comprehensive written instructions for handling, cleaning, disinfection and sterilization. The FDA expects manufacturers to validate all reuse instructions including cleaning and disinfection procedures, sterilization parameters, and aeration times, if applicable.

WuXi AppTec offers a comprehensive program for evaluation of cleaning and sterilization processes for reusable medical devices. Testing follows the guidelines outlined in *AAMI TIR No. 12* and *AAMI TIR 30* (“Designing, Testing & Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: A Guide for Device Manufacturers”). This program assists the manufacturer in meeting the requirements of the FDA Reviewer Guidance: “Labeling Reusable Devices for Reprocessing in a Health Care Facility.”

## Protocol Development

A custom protocol is written for each study, tailored specifically to the device and the manufacturer’s instructions for reuse. WuXi AppTec’s scientific staff assists clients in assessing cleaning processes and developing protocols.

## Cleaning Efficacy Studies

Manufacturers must verify the efficacy of their recommended cleaning processes. Following the manufacturer’s cleaning instructions, this study tests those processes using simulated soil inoculated with an appropriate marker. Those markers can be microbial (Gram positive, Gram negative, spore-forming) and/or physical markers (such as protein, carbohydrate and TOC), which are representative of typical contamination.

## Sterilization Efficacy Studies

Manufacturers must provide health care facilities with detailed sterilization instructions for their particular medical device. Sterilization parameters are tested to determine capability of producing a sterility assurance level of at least  $10^{-6}$ . Studies are available for evaluating the following sterilization processes:

- Liquid chemical sterilants
- Ethylene Oxide (EO)
- Pre-vacuum, steam (132-135°C)
- Gravity, steam (121-123°C and 132-135°C)

## Support for Functionality Studies

These studies involve exposure to multiple cleaning and/or sterilization cycles as part of the functionality studies required to determine the useful life of a device.

**For more information on reusable device validation testing,  
contact Technical Services at the WuXi AppTec – Atlanta facility.**