NOTE: We are in the process of updating the contents of this catalog. Please contact your WuXi AppTec Account Manager for the most accurate information, especially regarding turnaround times and test codes.

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.

REPROCESSING VALIDATIONS FOR REUSABLE MEDICAL DEVICES

The FDA expects manufacturers to validate all instructions for reusable devices, including cleaning, disinfection, sterilization parameters and dry 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.

IN THIS SECTION

Radiation Sterilization Validation

Method 1, Method 2, and VDmax + Dose Audits

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Overview

Cleaning Efficacy Studies

Inoculated Product Tests

Sterilization Efficacy Studies

Contact your Account Manager for the most accurate information regarding test codes and turnaround times.

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.

ANSI / AAMI / ISO 11137 Method 1 Validation

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Total Bioburden Panel	10 products from three batches	Page C-5
Bioburden Recovery Efficiency Test	3-5 products from any batch	Page C-5
Sterility Method Suitability Test (B/F) – One Medium	3 products from any batch	Page C-15
Product Test of Sterility	100* samples from one batch	Page C-16

NOTE: Single batch validations are also available.

Dose Audit

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Aerobe or Total Bioburden Panel	10 products from one batch	Page C-5
Product Test of Sterility	100* samples from one batch	Page C-16

ANSI / AAMI / ISO 11137 Method 2 Validation

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

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Aerobe or Total Bioburden Panel	10 products from one batch	Page C-5
Product Test of Sterility	100* samples from one batch	Page C-16

*** Reduced number of samples may apply, based on specific criteria. Contact Atlanta facility.**

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

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Total Bioburden Panel	10 products from three batches	Page C-5
Bioburden Recovery Efficiency Test	3-5 products from one batch	Page C-5
Sterility Method Suitability Test (B/F) – One Medium	3 products from any batch	Page C-15
Product Test of Sterility	10 samples from one batch	Page C-16

NOTE: Single batch validations are also available.

Quarterly Dose Audit

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Aerobic or Total Bioburden Panel	10 products from one batch	Page C-5
Product Test of Sterility	10 samples from one batch	Page C-16

Contact your Account Manager for the most accurate information regarding test codes and turnaround times.

ETHYLENE OXIDE (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.

SUB-LETHAL CYCLE STUDIES

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Total Bioburden Panel	10 products	Page C-5
Bioburden Recovery Efficiency Test	3-5 products from any batch	Page C-5
Inoculated Biological Indicators	Dependent on load size	Page C-11
Sterility Method Suitability Test (B/F) – Two Media	6 products from any batch	Page C-15
Product Test of Sterility	Dependent on load size	Page C-16

TERMINAL STERILIZATION STUDIES

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Biological Indicators	Per client specifications	Page C-14
EO Residual Panel	Varies	Page B-6

VALIDATION PROGRAMS – SERVICE OPTIONS

SERVICE OPTIONS FOR VALIDATION PROGRAMS

To help clients get their products through the validation process, WuXi AppTec offers different levels of service options for validation studies – 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 sterilization services and develop all the documentation to present an organized study. Or, in addition to the testing, we can handle all the sterilization 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 PROGRAMS

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.

REPROCESSING VALIDATIONS FOR REUSABLE MEDICAL DEVICES

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 dry 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, hemoglobin 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
- Gravity, steam

DRY TIME VALIDATION STUDIES

Manufacturers must provide heath care facilities with an effective dry time to be used in conjunction with the required steam sterilization cycle for reusable devices that are manufactured and supplied non-sterile to the user. Dry time validations will be based on the standard, full cycle steam sterilization cycle recommended by the manufacturer for the specified device in healthcare facilities as previously validated. At the conclusion of the sterilization cycle the devices will be exposed to the specified dry time for the evaluation of the effectiveness of that time to remove all residual moisture from the device as well as the sterilization wrap.

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 reprocessing validations, contact Technical Services at the WuXi AppTec – Atlanta facility.

STERILIZATION EFFICACY – STEAM GRAVITY OR PRE-VAC CYCLES

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Product Inoculation	4 samples (3 test samples, 1 positive control)	Page F-10
Autoclave Cycles	3 cycles, minimum	Page F-12
Biological Indicators	Varies per test article	Page F-10
Inoculated Product Sterility	Varies per test article	Page F-10

STERILIZATION EFFICACY – EO CYCLES [Hospital Cycles]

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Product Inoculation	4 samples (3 test samples, 1 positive control)	Page F-10
EO Cycles	3 cycles, minimum	Page F-12
Biological Indicators	Varies per test article	Page F-10
Inoculated Product Sterility	Varies per test article	Page F-10

CLEANING EFFICACY – MICROBIAL / PHYSICAL CHALLENGE [Manual or Automated]

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Soiling	5 samples (3 test samples, 1 positive control, 1 negative control)	Page F-8
Cleaning		Page F-8
Spore Count for Inoculated Product		Page F-8
Residual Protein – Cleaning Efficacy		Page F-9
Residual Carbohydrates – Cleaning Efficacy		Page F-9
Residual Total Organic Carbon (TOC) – Cleaning Efficacy		Page F-9
Residual Hemoglobin – Cleaning Efficacy		Page F-9

DRY TIME VALIDATION – STEAM GRAVITY OR PRE-VAC CYCLES

TEST NAME	SAMPLES REQUIRED	TEST DESCRIPTION
Autoclave Cycles	3 cycles, minimum	Page F-12
Dry Time Evaluation	3 cycles, minimum	Page F-12

REPROCESSING VALIDATIONS

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, hemoglobin and TOC), which are representative of typical contamination.

180115

Soiling

Simulated soil is used to inoculate the devices prior to cleaning the devices per manufacturer's instructions. Various soils are available and the intended use of a device will determine which soil is most appropriate.

SAMPLE REQUIREMENTS 4 product samples (1 to be used as positive control)

180116 Manual

180117 Automated

Cleaning

The manufacturer's instructions for cleaning are followed to determine the effectiveness of the process after devices are soiled. Cleaning may be performed manually or using an automated washer/disinfector.

SAMPLE REQUIREMENTS 4 product samples (1 to be used as positive control)

160210

Spore Count for Inoculated Product

After devices are cleaned per manufacturer's instruction, a bioburden test is performed to evaluate the effectiveness of the cleaning. Results are reported as a log reduction.

SAMPLE REQUIREMENTS 4 product samples (1 to be used as positive control)

400443 Residual Protein

400442 Residual Carbohydrates

400363 Residual Total Organic Carbon (TOC)

400444 Residual Hemoglobin

Tests for Physical Markers

See next page for descriptions of these individual tests.

After devices are cleaned per manufacturer's instruction, these tests are used to determine the residual concentration of various physical markers to evaluate the effectiveness of the cleaning.

SAMPLE REQUIREMENTS 10 to 50 mL extract from cleaned product samples

This test is used to determine the residual concentration of Total Organic Carbon (TOC) on reprocessed devices. **SAMPLE REQUIREMENTS** 50 mL extract	**400363** **Residual Total Organic Carbon (TOC) – Cleaning Efficacy**
This test is used to determine the concentration of carbohydrates on reprocessed devices. A colorimetric method is used. **SAMPLE REQUIREMENTS** 10 mL extract **E**	**400442** **Residual Carbohydrates – Cleaning Efficacy**
This test is used to determine the concentration of protein on reprocessed devices. The Modified Lowry Protein Assay, a colorimetric method, is used. **SAMPLE REQUIREMENTS** 10 mL extract	**400443** **Residual Protein – Cleaning Efficacy**
This test is used to determine the concentration of hemoglobin on reprocessed devices. **SAMPLE REQUIREMENTS** 10 mL extract	**400444** **Residual Hemoglobin – Cleaning Efficacy**

REPROCESSING VALIDATIONS

INOCULATED PRODUCT TESTS

Inoculated product consists of actual devices or materials that have been inoculated with a specified level of a liquid biological indicator (BI) suspension. Inoculated products are used to validate and / or monitor certain sterilization processes. Testing is performed by product immersion using either the BI manufacturer's parameters or those found in USP, ISO or AAMI standards.

Biological indicators (BIs) are carriers, such as a paper strip, that are inoculated with a specified level of a particular organism (typically *bacillus* species). BIs are used to validate and/or monitor certain sterilization processes.

1902000 *B. atrophaeus*
1902100 *G. stearothermophilus*

Product Inoculation

Devices are inoculated (usually in a location determined as most difficult to sterilize) with an indicator organism appropriate to the sterilization system in use.

SAMPLE REQUIREMENTS No minimum.

Indicate required population and sterilization method.

1204100 **Laminar Flow Hood Only**

Biological Indicator Direct Transfer

Individual spore strips are transferred from their primary package to SCDM and incubated for recovery of the indicator organism.

SAMPLE REQUIREMENTS Spore strips
(Client-provided positive control recommended.)

SHIPPING Overnight air. Protect from temperature extremes.

1205100 **Laminar Flow Hood Only**

Biological Indicator Within Product

Spore strips that have been placed within a product or its package are retrieved from the product or package and transferred to SCDM for recovery of the indicator organism.

SAMPLE REQUIREMENTS Spore strips
(Client-provided positive control recommended.)

SHIPPING Overnight air. Protect from temperature extremes.

Product that has been inoculated with a liquid spore solution and exposed to a sterilization process is tested in SCDM to detect surviving organisms.

SAMPLE REQUIREMENTS Dependent on method and sterilizer volume.

Inoculated Product Sterility

1221010
Extra Small [≤ 100 mL of media]

1221000
Small [100 & 200 mL of media]

1221210
Medium [300 & 400 mL of media]

1221410
Large [500 & 600 mL of media]

1221610
Extra Large [800 & 1000 mL of media]

1221620
Jumbo [1200 & 1500 mL of media]

1221630
Extra Jumbo [2000 mL of media]

Liquid samples, including spore suspensions and inoculated liquids, are enumerated to confirm spore population.

SAMPLE REQUIREMENTS Dependent upon expected population.

190501

Liquid Sample Population Confirmation

Before using a new lot of BIs for sterilization load monitoring, the average population per unit should be independently confirmed per USP regulations.

SAMPLE REQUIREMENTS Dependent on selected test.

190300 3 Sample Composite
120200 Single Sample

Biological Indicator – Total Viable Spore Count

REPROCESSING VALIDATIONS
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}.

800445

Autoclave Cycle

Steam sterilization cycle run per client specifications. Gravity and pre-vacuum cycles are available

SAMPLE REQUIREMENTS Dependent on study protocol

180112

Data Logger Use for Validation Cycle

Data loggers utilized during a steam sterilization cycle run per client specifications. Gravity and pre-vacuum cycles are available

SAMPLE REQUIREMENTS Dependent on study protocol

180111

Dry Time Evaluation

Steam sterilization cycle run per client specifications. Gravity and pre-vacuum cycles are available

SAMPLE REQUIREMENTS Dependent on study protocol

800446

EO (Hospital) Cycle

Ethylene oxide sterilization cycle run per client specifications.

SAMPLE REQUIREMENTS Dependent on study protocol

180110

Disinfection Cycles Cycle

Samples processed per client specified disinfection instructions.

SAMPLE REQUIREMENTS Dependent on study protocol

1801500

Decontamination of Test Samples

Samples are processed between validation cycles. The method of decontamination varies per client specifications.

SAMPLE REQUIREMENTS Dependent on study protocol