SfSAP
society for sterility assurance professionals

Pathways to develop expertise in different sterilization modalities by acquiring knowledge, skills, and experiences.

LEARNING FRAMEWORKS AND OUTCOMES

STERILITY ASSURANCE MICROBIOLOGY

Version 1.0-05-23

Sterility Assurance Microbiology Learning Framework

DOCUMENT NUMBER: SAMBLF001
Revision: 1

MODULE	KNOW What are the topics in this module that I need to know and understand?	APPLY How does an expert use (apply) this knowledge?	EXECUTE What experiences should I have where I can apply this knowledge? (Learn by doing; developing a repertoire of experiences)	DEMONSTRATE How can I demonstrate to an incumbent expert that I have the relevant knowledge and skills?	Competence	Acknowledge Competence
Microbial Growth, Isolation, and Identification ISO 11737-1, USP <1113>,						
Aseptic Technique and Good Laboratory Practice ISO 13408-1, ISO 13408-2, ISO 17025						
Bioburden ISO 11737-1						
Bacterial Endotoxin Testing AAMI ST72, (Draft ISO 11737-3)						
Sterility Testing ISO 11737-2, USP<71>						
Environmental Monitoring ISO 14644-1, ISO 14644-2, ISO 14698-1, ISO 14698-2, EN 17141, TIR 52, ISO 8573-1, ISO 8573-3, ISO 8573-5, ISO 8573-7,						
Cleanroom Classification ISO 14644-1						
Cleanroom Operations Principles ISO 14644 series						
Water Systems TRS970 Annex 2, ISPE Baseline Guide, Regional Pharmacopoeia, FDA High Purity Water System (7/93), ISO22519, USP <1231>.						
Cleaning/Disinfection Validation PDA TR70 Fundamentals of Cleaning and Disinfection Programs, ASTM E2614-15 Standard Guide for Evaluation of Cleanroom Disinfectants, ISO 14644-5 Cleanroom Operation						
Cleaning Validation for Reusable Medical Devices AAMI TIR30 (ST98), TIR12, ISO 17664, ISO 15883, FDA Guidance on Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labelling						
Biological Indicators ISO 11138 series						
Radiation Sterilization – Microbiological Elements ISO 11137-2						Acknowledge

Sterility Assurance Microbiology Learning Framework

MODULE	KNOW What are the topics in this module that I need to know and understand?	APPLY How does an expert use (apply) this knowledge?	EXECUTE What experiences should I have where I can apply this knowledge? (Learn by doing; developing a repertoire of experiences)	DEMONSTRATE How can I demonstrate to an incumbent expert that I have the relevant knowledge and skills?	Competence
EO Sterilization – Microbiological Elements ISO 11135, AAMI TIR16 AAMI; TIR 28; ISO 11737-1 & -2; ISO 11138-1 & 2,7					
Moist Heat Sterilization – Microbiological Elements ISO 17665					
Laboratory Equipment – Monitoring, Profiling, Requalification, Calibration and MSA's					

Sterility Assurance Microbiology Learning Outcomes

DOCUMENT NUMBER: SAMBLO001
Revision: 1

This document is to use in conjunction the **Sterility Assurance Microbiology Learning Framework** below to define expected learning out come from each of the modules within the microbiology curriculum.

Sterility Assurance Microbiology Learning Outcomes

Module
Microbial Growth, Isolation, and Identification ISO 11737-1, USP <1113>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Different media types and how to select the most appropriate
  o Liquid media
  o Solid media
• Media preparation and sterilisation
• Moist Heat sterilisation validation relevant to the laboratory
• Sample collection, preparation, and extraction.
• Media QC testing:
  o Media storage and shelf-life qualification and validation.
  o Solid media re-melting qualification/validation.
  o Validation of settle plate exposure time.
  o Growth promotion testing and environmental organisms to use, USP, EP requirements
  o sterility
  o pH and making adjustments for pH.
  o QC testing of control organisms
  o Suspension/sample inoculation
 	
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Microbial Growth, Isolation, and Identification
ISO 11737-1, USP <1113>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Selecting the appropriate conditions for growth, including temperature and time. • Colony counting, manual and electronic counters, • Streak plating, spread plating, spiral plating, pour plating, agar slants, and isolation • Selective culture • Different types of relevant organisms: environmental, human/animal, clinically/industrially significant, moulds, descriptions, gram reaction, morphology, sources, industrial/clinical significance of common organisms. • Different identification methods including macroscopic observation, staining, such as gram and spore stains, Morphology, microscopic observation, catalase/oxidase tests, biochemical ID methods, mass spectrometry, PCR, immunoassay, serotyping, genotypic and rapid methods • Bacterial identification systems: validation requirements: test, equipment, and database.		

Sterility Assurance Microbiology Learning Outcomes

Module
Aseptic Technique and Good Laboratory Practice ISO 13408-1, ISO 13408-2, ISO 17025

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Facility/Laboratory Environment Construction, Layout and Utilities and Ancillaries • Personnel and Resources • Standard Operating Procedures and Protocols/Study Plans • Sample Characterization and Storage • Environmental and Personnel Monitoring Programs • Risk Management application to Laboratory Investigations • Data and Investigation Evaluation • Equipment Qualification and Maintenance • Personnel Qualification/Proficiency • Facilities cleaning and disinfection • Test Methods		

Sterility Assurance Microbiology Learning Outcomes

Module
Bioburden ISO 11737-1

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Bioburden and the potential sources of microorganisms that contribute to the bioburden level • The relationship between bioburden data and different sterilization methods • Selection of product and use of product families • Considerations for establishing a bioburden monitoring program • Sample Item Portion (SIP), its selection, calculation, and use. • Factors to consider when developing a bioburden method including neutralisation of inhibitory substances, removal technique, culture conditions and enumeration. • Low bioburden products and how to improve detection of bioburden • Method selection and recovery techniques using elution and non-elution including MPN • Validation of method including method suitability testing and calculation of recovery efficiency using repetitive rinse or direct inoculation Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Bioburden
ISO 11737-1

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Recording of results, Limit of Detection, and application of recovery efficiency.
• Interpretation of data including spikes, TNTC and characterisation of bioburden isolates
• Requirements for investigation of Out of Specification result
  o Understand the implications of an Out of Specification result for the different sterilization methods
  o Corrective action and effective verification for an Out of Specification result
• Establishing alert and action levels
• The methods available for data analysis and trending
• Maintenance of the bioburden method validation including assessment of changes to product and process, review, and frequency of requalification		

Sterility Assurance Microbiology Learning Outcomes

Module
Bacterial Endotoxin Testing AAMI ST72, (Draft ISO 11737-3)

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• How the device (being tested) will be used and the selection of testing extraction to test for patient contacting portions of a device/material. • Acceptable bacterial endotoxin content based on intended use • Calculation of the maximum valid dilution (MVD) • The requirements for reagent and analyst qualification • The different bacterial endotoxin methods (I.e., gel clot, chromogenic, turbidimetric) • The requirements of the standard curve used for testing • Inhibition and enhancement • When re-assessment of BET shall be executed • Extraction condition requirements (i.e., time and temperature), if applicable • Alternative to batch testing and considerations for establishing • The manufacturing processes or variables that are potential for endotoxin contamination and risk mitigations/risk assessment • Background of the bacterial endotoxin test and how the limit(s) were established. Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Bacterial Endotoxin Testing
AAMI ST72, (Draft ISO 11737-3)

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Factors to consider when establishing product families or test groups
• Items to investigate/consider for out of specifications
  ○ Laboratory Investigations
  ▪ Supplies
  ▪ raw data review
  ▪ Equipment
  ▪ analyst interview
  ▪ Calibration
  ▪ training
  ○ Manufacturing Process
  ▪ Raw materials, components, extrusion
  ▪ Water systems
  ▪ Compressed air systems
  ▪ Cleaning processes
  ▪ Material/product storage conditions
  ▪ Environmental control of manufacturing area
  ○ Corrective action and effective verification for an Out of Specification result		

Sterility Assurance Microbiology Learning Outcomes

Module
Sterility Testing ISO 11737-2, USP<71>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Purpose for performance of sterility test
  o Validation and maintenance of sterilization process
  o Lot release
• Appropriate times for applying sterility test to products or when other tests should be performed instead (e.g., other tests are appropriate for shelf-life testing, to investigate packaging or manufacturing issues)
• Appropriate aseptic technique for test, including use of sterile instruments
• Appropriate gowning for test
• Appropriate environment and testing conditions for test
• Interpreting controls and/or monitors for test
• Selection of appropriate media type and incubation temperatures
• Purpose for method suitability (bacteriostasis/fungistasis)
• Interpretation of method suitability results
• Interpreting positive results
• Determination of turbidity being from product or from microbial growth
 	
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Sterility Testing
ISO 11737-2, USP<71>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Overcoming inhibitory results in method suitability
  o Media additives
  o Rinsing for membrane filtration
• Investigating positive results in different contexts
  o Radiation validations or dose audits
  o EO cycle validation (bioburden comparative resistance/natural product resistance testing)
  o Batch release for aseptically produced products (not for terminally sterilized products)
• Purpose for interim reads
• The need for 14-day incubation
• Why USP requires two media types and ISO only 1
• Change control with respect to sterility testing and method suitability
• Importance of performing identifications of sterility positives
• Establishing proper test instructions
• Selection of appropriate test method (filtration vs immersion vs elution vs fill)
 	
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Sterility Testing
ISO 11737-2, USP<71>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Sample size for testing in different contexts
  ○ Radiation
  ○ EO
  ○ Batch release (USP)
• Potential issues with elution test methods
• Subculturing to verify growth of turbid samples		

Sterility Assurance Microbiology Learning Outcomes

Module
Environmental Monitoring ISO 14644-1, ISO 14644-2, ISO 14698-1, ISO 14698-2, EN 17141, TIR 52, ISO 8573-1, ISO 8573-3, ISO 8573-5, ISO 8573-7

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The three occupancy states for testing • The different airborne particle concentrations • Establishment of sampling locations for nonviable particulate testing • The relationship between the validated sterilization method and the environmental monitoring program requirements. • Environmental conditions and ancillary systems that should be considered/monitored for environmental monitoring • Common factors of the facility design that may impact the controlled environment • Aspects of personal hygiene, clothing, and how behaviours may impact the conditions of the environment • Aspects are to be considered when establishing a routine environmental monitoring plan • What the intention of the risk assessment for the cleanroom is and what it should assess • The different types of air flow (I.e., unidirectional vs. non-unidirectional) • Critical processing zones • Pressure differential concept • Minimum testing frequency for nonviable particulates for periodic classification Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Environmental Monitoring
ISO 14644-1, ISO 14644-2, ISO 14698-1, ISO 14698-2, EN 17141, TIR 52, ISO 8573-1, ISO 8573-3, ISO 8573-5, ISO 8573-7

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Considerations for establishing microbiological alert and action levels or target levels
• Elements for designing a sampling plan
• When the frequency of sampling shall be modified for particular events/cases
• Corrective action as part of investigations of out of specification results, including:
  ○ Resampling
  ○ Evaluate the processes being conducted at time of sampling
  ○ Review of cleaning
  ○ Review of personnel behaviour
  ○ Assessing impact to sterilization / product
  ○ Analyst interview
  ▪ Training
  ▪ Handling of samples
  ▪ Testing anomalies
  ○ Review product bioburden trending
  ○ For compressed air, review preventative maintenance records/completion		

Sterility Assurance Microbiology Learning Outcomes

Module
Cleanroom Classification ISO 14644-1

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The principles and design of a cleanroom • The stages of cleanroom validation IQ, OQ, PQ • The types of airflow e.g., directional, and unidirectional • Occupancy states as built, at rest and in-operation • The factors that impact on cleanroom particle concentration • Airborne particle concentrations and ISO class numbers • Airborne particle concentration and classification as part of a monitoring plan for the cleanroom • Particle counters LSAPC/ test instrumentation function and operation • Selection and number of sampling locations • Sample procedure, sample volume, sample time and classification calculations • Interpretation of results • Investigation of Out of Specification results ○ Corrective action and effective verification for an Out of Specification result • Test Report requirements		

Sterility Assurance Microbiology Learning Outcomes

Module
Cleanroom Operations Principles ISO 14644 series

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• How the cleanroom works, is tested, and monitored • Familiar with the operational procedures • Identify the areas where there is a risk of contamination to the process and determine the method for monitoring those risks. • Training of personnel inside the cleanroom and monitoring their compliance to specified procedures and disciplines • The importance of cleanroom clothing and how to select the appropriate fabric, style, coverage, usage requirements etc. • Good Manufacturing Practices. • How cleanroom personnel should behave to minimise the generation of contamination through good personal hygiene, gowning practices, discipline, and conduct. • The important considerations for developing an effective cleaning program. • Impact of the transfer, installation, maintenance, and use of stationary equipment. • Selection and use of materials and portable equipment in the cleanroom Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Cleanroom Operations Principles
ISO 14644 series

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Safety and emergency response. • The appropriate supporting tests such as air pressure difference, airflow, recovery, temperature, humidity, installed filter system leakage etc (and associated methods and apparatus) that can be used for measuring the performance of a cleanroom. • Importance of maintaining the cleanliness of the cleanroom through systematic cleaning and monitoring procedures • The importance of out of specification results and how to investigate to ensure corrective action and effective verification is carried out.		

Sterility Assurance Microbiology Learning Outcomes

Module
Water Systems TRS970 Annex 2, ISPE Baseline Guide, Regional Pharmacopoeia, FDA High Purity Water System (7/93), ISO22519, USP <1231>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The different pharmaceutical water types and how to select the most appropriate • Specifications and qualities of different water types • Regulatory, guidance and specification documents • The key design philosophies of a water system • The basic microbiology of a water system • Biofilm formation and potential issues • Importance of microbial control methods • The typical design and layout of a pharmaceutical water system • Pre-treatment and the different types/designs, for example ultrafiltration, nanofiltration, media filtration, ion exchange, degasification. • Final treatment and the different options for Purified, Highly Purified Water and Water for Injection for example, ultrafiltration, reverse osmosis, chemical deionization, electro deionization and distillation. • Importance of the storage and distribution systems and designs • The commissioning and qualification essentials for a new pharmaceutical water system Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Water Systems
TRS970 Annex 2, ISPE Baseline Guide, Regional Pharmacopoeia, FDA High Purity Water System (7/93), ISO22519, USP <1231>

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Control and Instrumentation options, required for a Pharmaceutical Water system, for example 'in-line' Conductivity, Total Organic Carbon (TOC), Microbial, pH, Ozone meters and UV lamps / inline flow meters and temperature monitoring. • How to create a URS and the basic ingredients • The role of contractors and contractor management during an installation • Importance of validation planning and the validation cycle – URS, DQ, SQ, FAT, SAT, IQ, OQ and PQ Phases 1-3. • The approach for water system qualification • Devise sampling plan for the PQ phases of the qualification of the water system • Ability to design a routine monitoring program for the site • Methods of water testing and how to get reliable results • The considerations for engineering maintenance and calibrations • Change controls and maintaining the qualified state of the water system • The different types of sanitisation methods (for example Ozone, Temperature and Chemical) and when this should be completed • Importance of out of specification data and know how to investigate • The audit process and how to prepare.		

Sterility Assurance Microbiology Learning Outcomes

Module
Cleaning/Disinfection Validation PDA TR70 Fundamentals of Cleaning and Disinfection Programs, ASTM E2614-15 Standard Guide for Evaluation of Cleanroom Disinfectants, ISO 14644-5 Cleanroom Operation

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The difference between cleaning and disinfection of surfaces • The general types of cleaners and disinfectants • The various tests to demonstrate effectiveness of cleaning and disinfection • Ability to establish acceptance criteria for cleaning and disinfection • Markers for demonstration of cleaning • Chemical composition of cleaning detergent • The compatibility of cleaning detergent with surfaces • How to assess the resistance of microorganisms to the disinfectant • How the concentration and other parameters (e.g., time, temperature, organic matter on the surface, hardness of the water, expected bioburden, porosity of the surface, surface characteristics such as presence of biofilm or cracks, debris on the surface, pH) effect the efficacy • Rotation between disinfectant and sporicidal • How to establish a cleaning and disinfection program (frequency of both, understanding EM, and risk to product) Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Cleaning/Disinfection Validation

PDA TR70 Fundamentals of Cleaning and Disinfection Programs, ASTM E2614-15 Standard Guide for Evaluation of Cleanroom Disinfectants, ISO 14644-5 Cleanroom Operation

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• How to select the disinfectant – spectrum of target microorganisms (e.g., viruses, bacteria, fungi), how quickly it kills (dwell time), required rinsing procedures to remove residuals, corrosive to surfaces, safety of individuals using disinfectant, compatibility of surfaces and with other chemicals used in the area, residual activity (time it resides on the surface and if it should be removed), sporicidal properties – if present, different forms available (ready to use or need to be diluted), sterile vs. nonsterile. • Validation tests and log reduction requirements for different microorganism types • Use of commercially available microorganisms versus environmental isolates from the facility • Different surfaces in the cleanroom and ensure that those are represented in the validation		

Sterility Assurance Microbiology Learning Outcomes

Module
Cleaning Validation for Reusable Medical Devices AAMI TIR30 (ST98), TIR12, ISO 17664, ISO 15883, FDA Guidance on Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labelling

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The difference between cleaning validations for single use device and reusable medical devices • Why a validation is needed for reusable medical devices and who are we validating this for • Common hospital practices that are used to reprocess reusable medical devices in a healthcare/clinical facility • The different steps required prior to cleaning validation (simulated use conditions (disinfection and/or sterilization modalities applicable to the device, repeated use) • How to select test soils to simulate the use of the device in the clinical setting • The different methods of contamination used to soil the devices • What information from the instruction for use (IFU) is used for the validation • The different methods available for cleaning (manual, mechanical, automated) • The type of detergents/disinfectants used for devices based of criticality Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Cleaning Validation for Reusable Medical Devices
AAMI TIR30 (ST98), TIR12, ISO 17664, ISO 15883, FDA Guidance on Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labelling

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The different types of extraction methods used to assess cleanability (manual shaking, swabbing, sonication, orbital shaking, flushing) • If microorganisms are to be used for the testing, selecting the appropriate microorganisms to use for the study, growth conditions and agar for enumeration needs to be understood • Colony counting/enumeration and calculation for log reduction • What cleaning markers/analytes are appropriate to test (protein, haemoglobin, carbohydrate, Total organic carbon) • How cleaning analytes are tested and validated for use in the cleaning validations • The acceptance criteria needed for the validation in respect to regulatory bodies • Interpretation of the controls used in the validation, and how they are applicable • Basic calculations needed to present the data from the cleaning validation		

Sterility Assurance Microbiology Learning Outcomes

Module
Biological Indicators ISO 11138 series

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The different Biological Indicator (BI) types and how to select the most appropriate one for your method of sterilization • The different BI types and how to select the most appropriate one for your process (self-contained, strips etc.) • When to use BI's and not (parametric release) • Supplier selection • Selecting the appropriate conditions for growth, including temperature & incubation times. • Media preparation and sterilisation • Moist Heat sterilisation validation relevant to the laboratory • Media QC testing • Colony counting • Serial dilutions • Streak plating and isolation • Execution of a Reduced Incubation Time (RIT) study, if required • Use of positive & negative controls • Placement & handling of BI's Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Biological Indicators
ISO 11138 series

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Use of BI's as a Process Challenge Device (PCD) • Incoming inspection requirements i.e., sample preparation & population verification • D Value i.e., survivor curve, fraction negative, survivor-kill response • z value • Growth inhibition • Storage requirements • Disposal of BI's • In the case of a BI positive, investigating where a true positive or a false positive & perform identification. • If a false positive a laboratory investigation to be performed of testing practices & techniques. • If a true positive investigates the sterilization process, the BI incoming inspection, preparation & testing. Investigate equipment, process, product & load changes		

Sterility Assurance Microbiology Learning Outcomes

Module
Radiation Sterilization – Microbiological Elements ISO 11137-2

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

Selecting and testing product for establishing the sterilization dose
• The 2 approaches for establishing the sterilisation dose.
  o The principles of dose setting
  o The principles of dose substantiation to verify a preselected dose.
• Product families and how to:
  o define product families
  o designate a product family
  o maintain a product family
• The effect of failure on a product family
• How to define the product to be tested
  o What the product is defined as
  o What a Sample Item Portion is and when it can be used.
• The principles of sampling.
• The general principles of the microbiological testing
• The general principles of the irradiation process.
 	
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Radiation Sterilization – Microbiological Elements
ISO 11137-2

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• How the Bioburden testing is performed to determine the average Bioburden
  o The selection of batches and the batch size needed for the Bioburden phase
  o How the average Bioburden will influence the selection of method for dose establishment.
  ▪ The circumstances in which a method 2 may need to be used. In the case of a BI positive, investigating where a true positive or a false positive & perform identification.		

Sterility Assurance Microbiology Learning Outcomes

Module
Radiation Sterilization – Microbiological Elements ISO 11137-2

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

Methods of dose establishment
Method 1
• The principles of Method 1 and when it is a good choice
  o When a method 1 is a suitable choice
  o The 6 stages for:
  ▪ A method 1 when the average Bioburden is ≥ 1 for multiple production batches & a single production batch.
  ▪ A method 1 when the average Bioburden is 0.1 - 09 for multiple & single production batches.
Method 2
• The rationale and principles of a method 2 and when it is a good choice
  o The difference between method 2A and method 2B and the conditions when a method 2b would be selected for use.
  o The 5 stages of
  ▪ Method 2A
  ▪ Method 2B
 	
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Radiation Sterilization – Microbiological Elements
ISO 11137-2

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

Method VDmax
• The rationale and principles of VDmax and when substantiation of a 15/25Kgy dose is a good choice
  o The 5 stages and confirmatory verification dose experiment for:
  ▪ Method VDmax25 - multiple production batches
  ▪ Method VDmax25 - single production batch
  ▪ Method VDmax15 - multiple production batches
  ▪ Method VDmax15 - single production batch
 	
Sterilization Dose Audit
• The purpose of dose audit
  o The frequency of dose audits
  o The conditions under which the frequency can be reduced
  o Actions to take in the event of failure
• The 4 stages of dose audit using Method 1, Method 2A or Method 2B
  o Actions to take in the event of failure – the augmentation process
• The 4 stages of dose auditing using Method VDmax 25/15kGy
  o Actions to take in the event of failure:
  ▪ Confirmatory dose experiment
  ▪ Augmentation of a sterilisation dose
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Radiation Sterilization – Microbiological Elements
ISO 11137-2

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• The approaches to take when investigating out of specification results – this will include the Requirements for investigation of Out of Specification result in some or all of the following areas: o Out of Specification Investigations - ISO 11737-1 Annex A o Bioburden - ISO 11737-1 o Sterility Testing - ISO 11737-2 o Environmental Monitoring - ISO 14644-1, ISO 14644-2, ISO 14698-1, ISO 14698-2, TIR 52		

Sterility Assurance Microbiology Learning Outcomes

Module
EO Sterilization – Microbiological Elements ISO 11135, AAMI TIR16 AAMI; TIR 28; ISO 11737-1 & -2; ISO 11138-1 & 2,7

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Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Terms and definitions
• Process and equipment characterization
  ○ Sterilization equipment
  ○ Process characterization
  ▪ EO concentration
  ▪ Relative humidity
  ▪ Temperature
  ▪ EO exposure time
  ▪ EO removal system
• Process definition
  ○ Considerations
  ▪ Ethylene oxide exposure parameters
  ▪ Product packaging
  ▪ Selection of the load configuration most challenging to sterilization
  ▪ Load configuration
  ▪ Process development method
  ▪ The role of biological indicators in determining a product Sterility Assurance Level of 10^{-6}
 	
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Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

EO Sterilization – Microbiological Elements
ISO 11135, AAMI TIR16 AAMI; TIR 28; ISO 11737-1 & -2; ISO 11138-1 & 2,7

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
▪ The appropriateness of biological indicators through NPRT (Test of Sterility) ▪ The desired hierarchy of resistance to sterilization between PCD's and natural product bioburden ▪ Sampling considerations for product development studies ▪ Assessment of products for microbiological challenges (BI and NPRT) ▪ Methods for microbial recovery and fraction negative studies **Methods** • Estimating cycle lethality o Cycle lethality determined by Fraction Negative Stumbo-Murphy-Cochran / Holcomb-Spearman-Karber equations o Biological indicator/Bioburden approach o Overkill methods using Half Cycle / Cycle Calculation approaches o Absolute bioburden method • Troubleshooting o Obtaining undesired all BI positive growths o Obtaining undesired all BI negative growths Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

EO Sterilization – Microbiological Elements
ISO 11135, AAMI TIR16 AAMI; TIR 28; ISO 11737-1 & -2; ISO 11138-1 & 2,7

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
○ Obtaining a liner slope in BI lethality ○ NPRT failures ○ Desired hierarchy of resistance is not achieved • Process challenge devices (PCDs) ○ Types of PCDs ○ Appropriateness of PCDs ○ Example of PCDs ○ Know the purpose and use of External versus Internal PCD's • Validation ○ Performance Qualification (PQ) ○ Placement and handling of PCDs, test samples, sensors, etc. ○ Selecting the most challenging load to sterilization - full chamber load / partial chamber load ○ Simulation of anticipated process conditions ○ Release of validation loads as sterile commercial goods ○ Sterilization of small batches or lots for clinical use • Maintenance of process effectiveness ○ Assessment of change ○ Product adoption ○ Requalification ○ Routine sterilization and requalification failure investigation		

Sterility Assurance Microbiology Learning Outcomes

Module
Moist Heat Sterilization – Microbiological Elements ISO 17665

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• Terms and definitions
• Process characterization
  o Product bioburden and sterility test, BI enumeration sterility test
  o Concepts of environmental monitoring
  o Hierarchy of microorganism resistance
  o Selection of a proper indicator microorganism and microorganism characteristics for the validation approach selected (e.g., overkill, BI/bioburden)
  o Principles of method suitability and neutralization
  o Inoculation principles and techniques and how the product can affect inoculation (e.g., liquid product versus solid medical device)
  o Basic understanding of how the following processes affect delivered lethality
  ▪ Saturated steam process
  ▪ Hard good/dry good
  ▪ Liquid loads
  o Air/steam mixture (steam quality)
  o Superheated water spray
  o Temperature
  ▪ Typical sterilization temperatures
  ▪ Low temperature process
Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Moist Heat Sterilization – Microbiological Elements
ISO 17665

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment

• How biological kill relates to chemical indicator response
• Process definition
  o Considerations
  ▪ Moist heat exposure parameters and process type (e.g., gravity, pre-vacuum)
  ▪ Product packaging and its influence on sterilization
  ▪ Load configuration and its effects on lethality
  ▪ Validation approach
  ▪ Overkill
  ▪ BI/Bioburden
  ▪ Bioburden based
  ▪ The role of BIs in determining a product SAL of 10-6
  ▪ Demonstrate the appropriateness of BIs through bioburden characterization
  ▪ Understand the relationship between measurements of biological lethality and physical lethality
  ▪ Use of product family groupings when appropriate and selection of a master product
  ▪ Methods for microbial enumeration and fraction negative studies
 	
Continued on next page		

Module - CONTINUED

Moist Heat Sterilization – Microbiological Elements
ISO 17665

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
○ Methods ▪ Determining cycle lethality ▪ Fraction negative method ▪ Survivor curve method ▪ How does the group want to address this section? ○ Troubleshooting ▪ Obtaining positives when not expected/routine process failures ▪ Obtaining all negatives when not expected ▪ Hierarchy of resistance is not achieved ○ Process challenge devices (PCDs) ▪ Types of PCDs ▪ Appropriateness of PCDs ▪ Example of PCDs ▪ Know the purpose and use of External and Internal PCDs • Validation ○ IQ/OQ/PQ microbiological testing ○ How the placement and handling of PCDs can influence results ○ Selection of sterilization loads for bracketing purposes Continued on next page		

Module - CONTINUED

Moist Heat Sterilization – Microbiological Elements
ISO 17665

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
○ Selecting worst-case parameters ○ Microbiological requirements for release of validation loads/small batches (e.g., half cycle/full cycle exposure) • Maintenance of process effectiveness ○ Assessment of change related to microbiological performance ○ Bioburden test frequency and characterization as part of process monitoring ○ Product adoption and associated microbiological testing/considerations ○ Determining acceptability of BI lots (e.g., D value and spore titre) ○ Routine tests required to demonstrate equipment performance (e.g., dart test, leak test) ○ Understanding requalification requirements • Failure investigation ○ Obtaining BI positives when not expected/routine process failures ○ Obtaining all negatives when not expected ○ Frequency of routine process failures ○ Understand how BI results relate to physical and CI results ○ Understand undocumented changes and how they can affect microbiology/ sterilization effectiveness and/or performance of the equipment		

Sterility Assurance Microbiology Learning Outcomes

Module
Laboratory Equipment – Monitoring, Profiling, Requalification, Calibration and Measurement System Analysis (MSA)

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Asset management • Laboratory/Equipment risk assessments, FMEA, User requirements specification, validation plan, calibration requirements, calibration schedules, • Equipment Commissioning, validation, IQ, OQ, PQ • Maintenance programs, preventative, and corrective. • Inter laboratory comparison programs. • Equipment out of spec/out of tolerance and how to deal with them. • Familiar with Temperature controlled units, Incubators, fridges, heat blocks, water baths ovens, IQ, OQ, PQ, Requalification requirements, thermal mapping. • Laboratory glassware/dishwashers: • Commissioning qualification, validation requirements. • Preventative and corrective maintenance. • Laboratory Autoclave commissioning, validation, IQ, OQ, PQ Thermal and pressure profiling • Routine maintenance • Biological Indicators • Chemical monitoring tests, bowie dick, leak testing, • Routine Monitoring: Thermal controlled units. • Laboratory qualification and routine monitoring, magnahelic gauges, laboratory classification, biohazard levels. • Laboratory facility cleaning and sanitisation. Continued on next page		

Sterility Assurance Microbiology Learning Outcomes

Module - CONTINUED

Laboratory Equipment – Monitoring, Profiling, Requalification, Calibration and Measurement System Analysis (MSA)

Learning Outcome (what person should be able to do with the knowledge and skills)	Outcome met? Y/N	Comment
• Familiar with Laminar airflow units, biological safety cabinets, Isolators: Installation, qualification, routine monitoring, and requalification/certification requirements, HEPA filter maintenance and testing • Laboratory water systems, Installation, commissioning qualification, validation • Preventative and corrective maintenance • Routine monitoring • Laboratory equipment calibration • Calibration curves, verification of calibration curve • MSA when required, accuracy, precision, reproducibility, repeatability, ANOVA, Gage R&R, stability, linearity, • Measurement uncertainty and uncertainty budget • Statistical analysis, variance • Setting tolerance • Dealing with out of tolerance • Laboratory software and requirements: LIMS, Monitoring software, equipment software • Software validation • Laboratory Samplers: particulate samplers, viable air samplers • Qualification/validation/calibration requirements, routine testing/verification requirements. • Maintenance of pH meters, balance, spectrophotometers, shakers, centrifuge, vortex mixers, sonicators, thermocyclers: calibration, qualification and validation, verification requirements, maintenance.		