Technical Report No. 48
Moist Heat Sterilizer Systems: Design, Commissioning, Operation, Qualification and Maintenance

Module Four

User Requirements (C):
Sterilizer Design, Functional and Design Specifications
(Section 4.3, 4.4, Appendix A)

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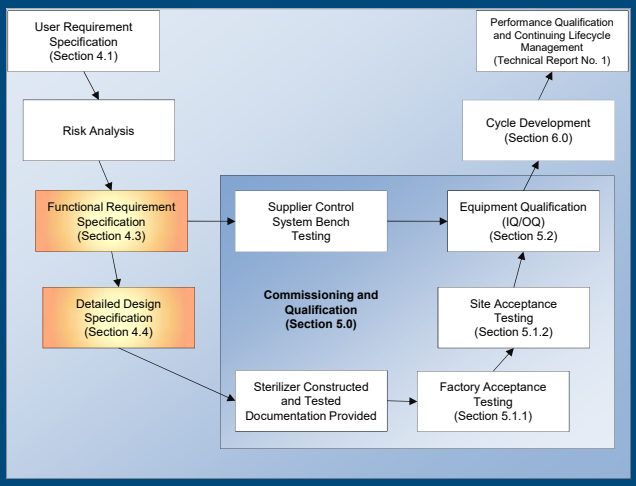
Validation Lifecycle Activities



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2

Sterilizer Design (4.0)

Design of sterilizer system begins with end use in mind and leads to creation of User Requirement Specification (URS), Functional Requirement Specification (FRS), and Detailed Design Specification (DDS) documents

3

Sterilizer Design (4.0)

- Define relevant process outputs, features and functions (URS)
- Specifications are then used to develop FRS
- Functional requirements may then be turned into DDS

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Functional Design Considerations

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Sterilizer Design

Functional Design Considerations

The intended use of the autoclave dictates the size, shape, construction materials, control system, required utilities, cycles available and accessories to be supplied with the unit

EXAMPLE-Media Bottles

(Section 4.3)

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Sterilizer Design

Functional Design Considerations

- Functions are defined first by the purpose of the system and then are defined in more detail as a series of individual functions. The FRS includes both manual and computer controlled functions.
- Requirements are described in terms of quality needs (i.e., instrument accuracy), hardware and software needs, system interfaces (i.e., particular programmable logic controller model should interface to particular distributed control system model), operator/product safety and performance.
- Utilities specifications should be included

(Section 4.3)

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Sterilizer Design

Functional Design Considerations

These attributes are defined in the functional requirement specification (FRS). FRS examples may include:

- If clean steam is required but not available at the installation site, a clean steam generator may be installed on the sterilizer skid.
- A decontamination cycle may be required for use in applications where chamber effluents may contaminate the sterilizer drain line or building drain system.

(Section 4.3)

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Sterilizer Design

Functional Design Considerations

- A requirement to roll heavy tanks or equipment into the chamber may dictate a pit-mounted installation, in which the floor of the chamber aligns with the floor of the room.
- Steam sterilizers used for decontamination of equipment may be manufactured from Ni-Clad material rather than stainless steel due to the corrosive nature of the effluent.

(Section 4.3)

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Sterilizer Design

Functional Design Considerations

- Media Bottle Example:
  - *What features do I need to make the unit function based on the URS?*
  - *URS-I want to sterilize 200 media bottles per day. Media bottles are glass and sealed with a plastic cap. I need to capture data for validation records.*
  - *Chamber -Throughput, time temp, cooling*
  - *Loading Equipment-rack, transfer cart, load cart*
  - *Cycle type- time/temp, Fo, overpressure, cooling*
  - *Utilities-clean steam/house steam, water, air, electrical*
  - *Data-electronic, Paper, remote historian*

(Section 4.3)

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Detailed Design Considerations

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Sterilizer Design

Detailed Design Specification

The DDS includes basic elements common to all sterilizers as well as specific requests intended to satisfy operation requirements

Basic elements include sterilizer description, size and configuration, sterilization cycle types required and maximum load size or mass.

(Section 4.4)

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Sterilizer Design

Detailed Design Specification

- Control system type as well as validation requirements should be specified
- Typical options include: special cycle requirements, load probes for internal temperature measurement, loading carts and spare parts
- Specifications might also include project milestones
- Cleaning requirements suitable to the environmental classification(s)
- Utility piping requirements should be specified

(Section 4.4)

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Sterilizer Design

- Consider this for detail design:
  - Don't get too caught up in the details.
  - Avoid the boilerplate or previous project temptation
  - Go back to your URS and FRS.

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GMP versus non-GMP Sterilizers

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Sterilizer Design

GMP and Non-GMP Sterilizers

It is commonly understood that a "GMP sterilizer" is a unit designed for moist heat sterilization, and built in accordance with current pharmaceutical industry sanitary design standards.

(Section 3.4)

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Sterilizer Design

GMP and Non-GMP Sterilizers

"Non-GMP" sterilizers are generally used for sterilization of items not used for processing product, product contact items, microbiological test items or items contacting primary product packaging. These sterilizers may include some "GMP" features, but may not have the precise control or recording of temperature and pressure that "GMP" sterilizers provide

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GMP and Non-GMP Comparison Chart

GMP Sterilizer	NON-GMP Sterilizer
Typical applications include sterilization of products used in the testing or manufacturing of drug products, and terminal sterilization of liquids in sealed containers.	Typical applications include sterilization of products used for laboratory work (not supporting a production area or product testing) or sterilization of waste materials prior to disposal.
Piping and chamber are designed to accommodate clean utilities such as pure or clean steam and process air. This includes stainless steel clamped and welded designs, proper slopes and deadlegs.	Piping and chamber are designed as appropriate (e.g., copper piping) for the sterilizer's intended use.
Materials of construction are compatible and appropriate (e.g., non-particle generating) with products and processes ensuring no contamination (e.g., product or environmental). May be supported by certificates of inspection and traceability.	Materials of construction appropriate (e.g., ensure no adverse reaction with load items to be sterilized) for the sterilizer's intended use.
Product contact utilities (e.g., water, steam, air) supplied to the sterilizers are suitable for its intended use and meet applicable Compendial expectations.	Load contact utilities (e.g., water, steam, air) supplied to the sterilizer are suitable for its intended use.
Control and monitoring systems meets regional regulatory expectations for data security and integrity	Control and monitoring systems data security and integrity meets internal organization requirements
Temperature monitoring and control devices (e.g. drain probes) are independent of one another.	Temperature monitoring and control may be from a single device.
Performance meets requirements and specifications with Quality Unit oversight is expected.	Performance meets requirements and specifications. Quality Unit oversight may not be required.

(Section 3.4)

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Equipment and Process Considerations

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Sterilizer Design

Equipment and Process Considerations

- Cycle time and throughput requirements
- Load configuration (e.g., item size, type and number of loads)
- Loading and unloading requirements (e.g., walk-in or reach-in)
- Specify location, number, size and type of temperature probes ports for validation studies
- Door gasket medium (e.g., clean steam or pharmaceutical air) requirements. Determine if a backup door gasket is required.

(Section 4.1.2)

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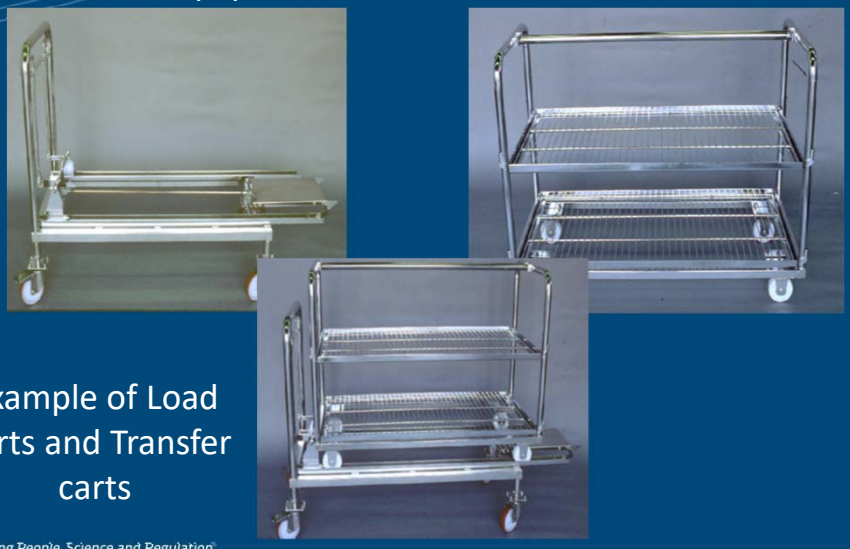
Sterilizer Design

Equipment and Process Considerations



Example of Load Carts and Transfer carts

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Sterilizer Design

Equipment and process considerations

- Air removal is critical for optimum heat transfer to the porous/hard goods load. Steam should be saturated, not introduce contaminants and meet Compendial requirements
- For liquid loads, the steam acts principally as an agent for heat transfer. Therefore, air removal and steam attributes are not of equal significance as compared to porous/hard goods loads.

(Section 4.1.2)

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Equipment and Process Considerations

For terminal sterilization of products in final packaging, the major concern is the identification of a sterilization cycle that ensures that sufficient lethality has been achieved in all locations of the load without compromising item or product. Due to these factors, care must be taken to ensure that the air over-pressure (where utilized) is sufficient to minimize the breakage or distortion of containers.

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Sterilizer Design

Equipment and Process Considerations

Consider the number of cycles needed for the range of items being sterilized. Include additional cycles to be used with the sterilizer (e.g., chamber leak test, vent filter sterilization, air removal test).

Describe the requirements for the steps/phases that are required for the range of the sterilization cycles to be used.

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Sterilizer Design

Equipment and Process Considerations

Identify the critical control parameters for each cycle phase. For example:

- Heat-Up Phase:
  - Number of vacuum pulses
  - Time to attain vacuum
  - Vacuum hold time
  - Vacuum and pressure level
  - Temperature and pressure ramp rates

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Sterilizer Design

Equipment and Process Considerations

- Exposure Phase:
  - Temperature Set Point
  - Pressure Ranges / Set Point
- Cool-Down Phase:
  - Evacuation level (if vacuum drying is used)
  - Hold Time
  - Heat input (if drying is accomplished using heat)
  - Exhaust Rate
  - Pulse Drying
  - Pressure Equalization
  - Vacuum Relief Phase (if required)
  - Liquid Cooling Temperature and method used
  - Temperature and Pressure Ramp Rates

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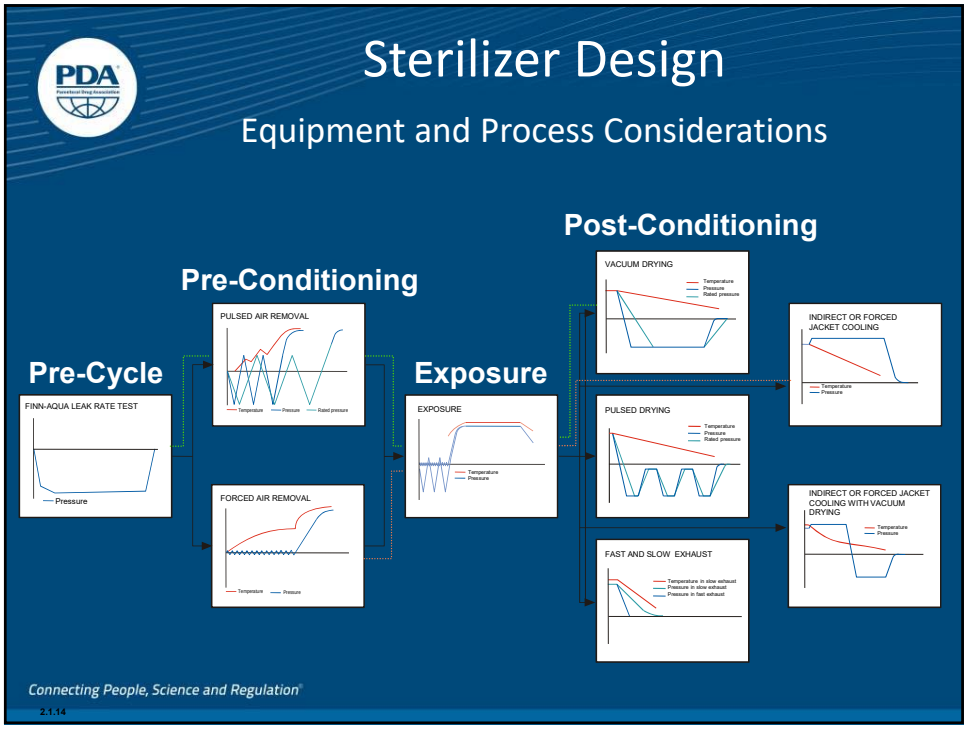
Sterilizer Design
Equipment and Process Considerations
Post-Conditioning
Pre-Conditioning
Pre-Cycle
Exposure
FINN-AQUA LEAK RATE TEST
Pressure
PULSED AIR REMOVAL
FORCED AIR REMOVAL
EXPOSURE
VACUUM DRYING
PULSED DRYING
FAST AND SLOW EXHAUST
INDIRECT OR FORCED JACKET COOLING
INDIRECT OR FORCED JACKET COOLING WITH VACUUM DRYING
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2.1.14

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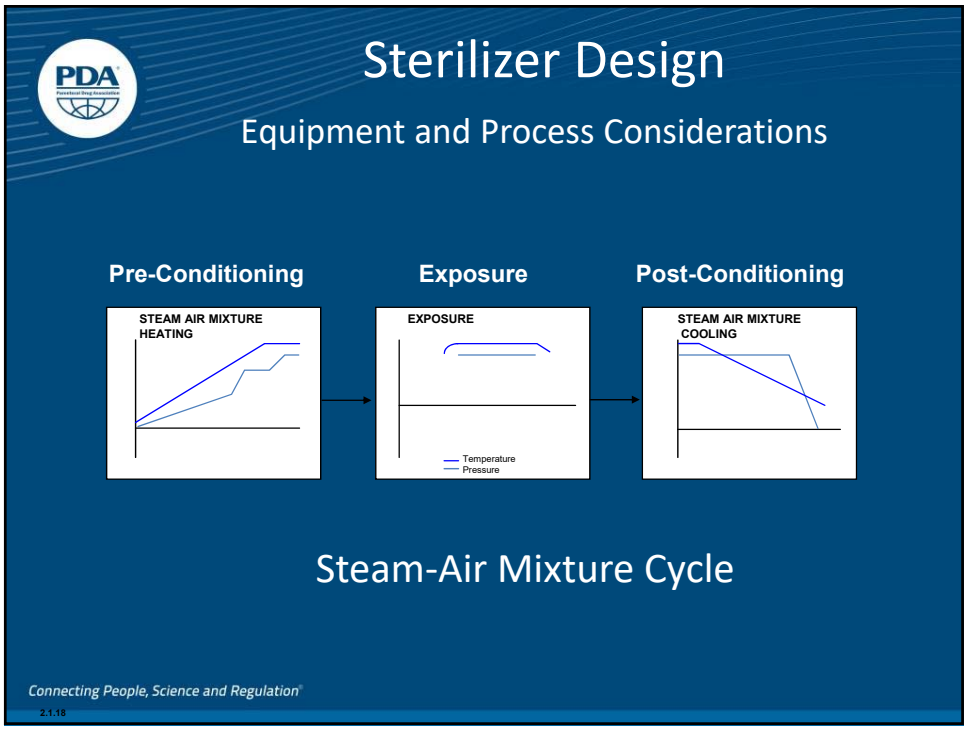
Sterilizer Design
Equipment and Process Considerations
Pre-Conditioning
Exposure
Post-Conditioning
STEAM AIR MIXTURE HEATING
EXPOSURE
STEAM AIR MIXTURE COOLING
Temperature
Pressure
Steam-Air Mixture Cycle
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2.1.18

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Design Considerations

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Sterilizer Design

Control System Considerations

Remember how simple it used to be….

(Section 4.2)

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Sterilizer Design

Control System Considerations

Good manufacturing practice with regard to the specification, build, testing and operation of sterilization equipment requires a systematic approach to ensure that the equipment as designed, meets specifications and is fit for intended use. Many choices may be evaluated during definition of the control system design.

(Section 4.2)

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Sterilizer Design

Instrumentation and Controls Considerations

A local control panel may include:

- start / stop
- emergency stop
- door control
- pressure indication (chamber, jacket)
- temperature indication (chamber, jacket)
- a local printer provides numerical data of the cycle
- a chart recorder that provides a graphical representation of the cycle
- audible / visible alarm indicator

(Appendix A)

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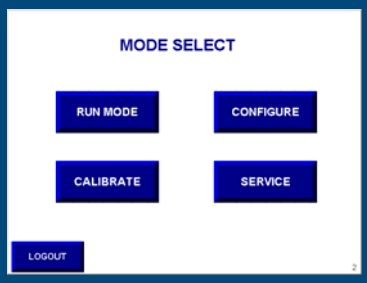
Sterilizer Design

Instrumentation and Controls Considerations

- a local Human Machine Interface (HMI) that allows :
  - selection and start of different type of cycles,
  - cycle programming
  - maintenance functions
  - Cycle status and alarms scanning
  - a cycle report print initiation



(Appendix A)

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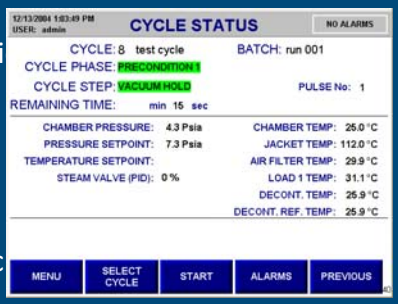
Sterilizer Design

Instrumentation and Controls Considerations

- Critical parameter data should be controlled or monitored and documented (e.g., printout, electroni storage) according to applicable regulations
- This critical parameters data may include:
  - date, time, load, lot number, batc information, program, temperature, pressure, cycle phases, duration, alarms



(Appendix A)

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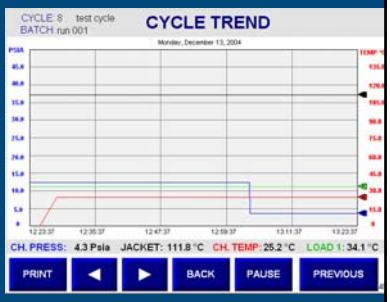
Sterilizer Design

Control System Considerations

Control System considerations include:

- Define the list of process variables to be recorded and frequency of recording (e.g., chamber pressure, chamber temperature, jacket temperature, run time)
- If the system provides a report, define the expectations for information to be included in the report



(Section 4.2)

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Sterilizer Design

Control System Considerations

CPU address	Notes	Data Type	Signal name
REAL_to_SCADA[0]		REAL	Chamber pressure measurement (mbar)
REAL_to_SCADA[1]		REAL	Chamber pressure measurement (Psia)
REAL_to_SCADA[2]		REAL	Chamber drain temperature measurement
REAL_to_SCADA[3]		REAL	Jacket temperature measurement
REAL_to_SCADA[4]		REAL	Filter temperature measurement
REAL_to_SCADA[5]		REAL	1. load temperature measurement
REAL_to_SCADA[6]		REAL	2. load temperature measurement
REAL_to_SCADA[7]		REAL	3. load temperature measurement
REAL_to_SCADA[8]		REAL	4. load temperature measurement
REAL_to_SCADA[9]		REAL	Air detector temperature measurement
REAL_to_SCADA[0]		REAL	Decontamination temperature measurement
REAL_to_SCADA[7]	0= not in use	REAL	Pressure set point (mbar)
REAL_to_SCADA[8]	0= not in use	REAL	Temperature set point

(Section 4.2)

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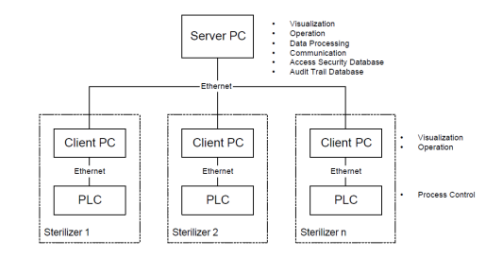
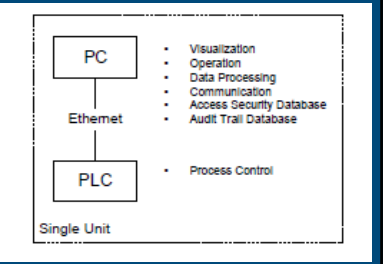
Sterilizer Design

Control System Considerations

- How complex or simple a control system is needed. Describe the control system requirements in terms of manual, semi-automatic and automatic operation.
- Possible interfaces of the control system with other systems available in the area





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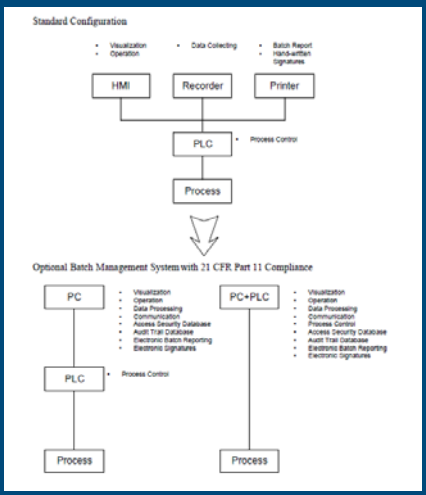
Sterilizer Design

Control System Considerations

- Data collection should be based on company requirements (e.g. local printer report, network printer report, building control system report, historical trending).



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Sterilizer Design

Control System Considerations

- Whether the operation and control of the system is to be performed at an operator interface panel on the sterilizer or at an external control system. State whether the access is provided through a data-communication link.
- Specify security access levels for operation, cycle programming, and maintenance activities. Security access is typically local and may be server verified.

(Section 4.2)

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Sterilizer Design

Temperature Control System Considerations

- Load probes
- Drain probes
- Pressure control system
- Proportional steam control valve (optional)
- Dual temperature probes
  - Temperature Recording
  - Temperature Control

(Appendix A)

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Sterilizer Design

Control System Considerations

- Control type should be taken into consideration – on/off or analog. Digital (on/off) and Proportional (analog) valves are both successfully used in the establishment of steady state conditions within a chamber and load.
- Orifice plates and/or flow control valves positioned on the chamber inlet and / or outlet. Their settings or dimensions therefore become key control parameters.

(Section 4.2)

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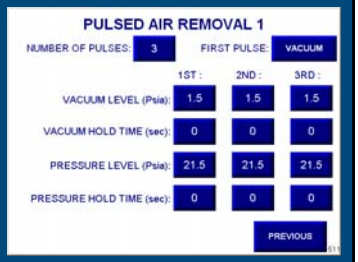
Sterilizer Design

Control System Considerations

- A temperature and/or pressure control system
- A thermostatic steam trap (open when cool, closed when hot) to remove air and/or condensate from the chamber
- A cycle timer and (usually) a sequencing controller
- The ability to configure cycle parameters (e.g., add or subtract number of pulses, vacuum levels, exposure time)
- System valves and instruments should be accessible for maintenance and calibration



(Section 4.2)

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Sterilizer Design

Critical/Key Process Instruments Considerations

- Instruments identified in the risk assessment as critical and/or key to the process should be designed for calibration and should be easily accessible.
- Instruments should have the correct range, resolution, accuracy and precision for calibration and be designed to meet the needs of the process.
- Prior to qualification activities, instruments should be calibrated.

(Section 4.2)

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Sterilizer Design

Control System Considerations

Interlocks:

- The door cannot be sealed before it is closed and locked
- The cycle cannot be initiated until the door is sealed
- The cycle can be initiated only if there are no active alarms.
- The door cannot be unsealed before the sterilization cycle is completed and the chamber pressure has equalized to atmospheric pressure
- In case the cycle is aborted but the exposure phase was not completed, only the loading side can be opened.

(Section 4.2)

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Sterilizer Design

Control System Considerations

Interlocks:

- The chamber steam valve cannot be opened by the controller if a door is open or unsealed.
- Specify the placement of the Emergency Stop (E-Stop) button(s) according to local requirements. A double door sterilizer should have E-Stop buttons on both sides of the sterilizer.

(Section 4.2)

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Sterilizer Design

Control System Considerations

Interlocks:

- Requirements for the system response to an operator initiated cycle abort. Describe the final state the autoclave needs to be in at the conclusion of the abort sequence.
- System alarm requirements, both critical and informational.

(Section 4.2)

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Sterilizer Design

Chamber and Jacket Considerations

- Pressure vessel
  - should be positioned so condensate flows toward the drain
- Minimize Condensate Pooling
  - Sloped floors
- Location and Number of validation ports to insert thermocouples or load probes as required
- Meet applicable regional pressure vessel requirements

(Appendix A)

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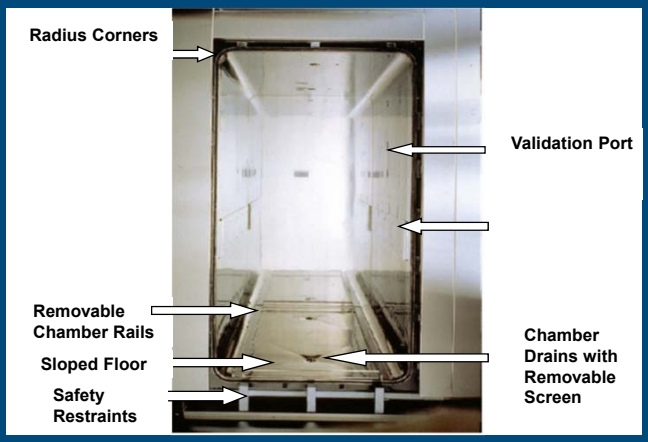
Sterilizer Design

Chamber and Jacket Considerations



(Appendix A)

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Sterilizer Design

Chamber and Jacket Considerations

- Chamber Door
  - Sliding door
  - Swing door
- Door Gaskets
  - should be lubricated and/or changed as required to provide proper operation
  - Active gaskets may be monitored for integrity using pressure devices

(Appendix A)

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Sterilizer Design

Piping Design Considerations

- Materials of construction and internal surface finish should meet the needs of the process
- Piping should be sufficiently sized to provide adequate flow to meet process requirements and standards
- Valves should meet process requirements
- Steam piping should be insulated for safety and to minimize heat loss and condensate formation
- Insulation should be non-shedding and chloride-free if stainless steel piping is used

(Appendix A)

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Sterilizer Design

Piping Design Considerations

- Pipe slopes should be adequate to promote drainage and condensate removal
- Deadlegs should be minimized
- If process requires WFI, deadleg piping should allow purging
- Utility cross contamination risk should be minimized
- Welds should meet applicable materials and joining standards

(Appendix A)

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Sterilizer Design

Piping Design Considerations

- If the incoming steam pressure is above the manufacturer's recommendations, additional valves (e.g., modulating steam, pressure reducing, pressure relief, shut-off) should be considered
- An appropriate thermostatic steam trap combined with floating ball should be used to quickly remove large quantities of air and/or condensate from the chamber

(Appendix A)

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Sterilizer Design

Sterile Air Filter Considerations

- Use of a sterilizing air filter for atmospheric vacuum break or overpressure cycles filtration may be determined through a risk assessment for available tools to perform risk assessment
- Terminal sterilization processes typically do not require an air sterilizing filter
- Sterilizing air filters should be considered if unloading into an aseptic environment

(Appendix A)

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Sterilizer Design

Sterile Air Filter Considerations

- Filters should be integrity tested (method and frequency according to the manufacturers' recommendation)
- Filter housings may be stainless steel or disposable
- Filters may be sterilized in place (in-situ) based on application
- Redundant or serial filtration should be determined through a risk assessment
- A separate filter should be used on the vacuum pump for the heat up phase of an effluent decontamination process

(Appendix A)

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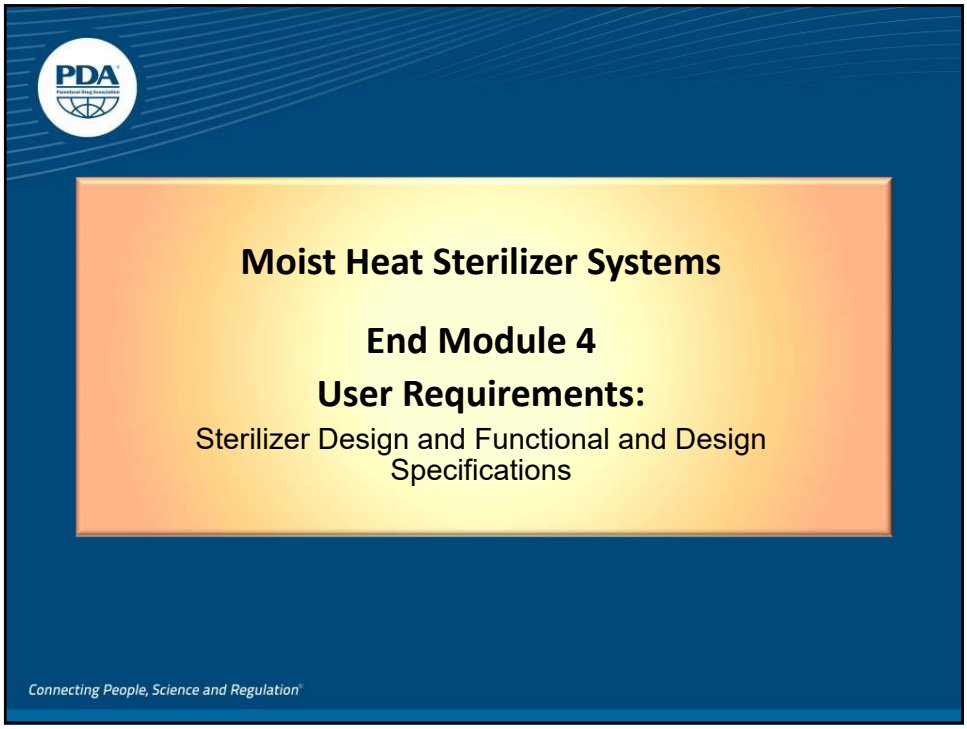
Sterilizer Design

Vacuum Pump Considerations

- Vacuum pumps aid in efficient air removal mechanically
- Vacuum pumps are typically a liquid ring type
- A condenser may be used to decrease steam volume before the pump
- Closed water circuits with cooling reduces water consumption
- Water temperature and elevation impacts vacuum depth and process efficiency

(Appendix A)

Questions / Discussion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User Requirements:
Sterilizer Design and Functional and Design Specifications
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