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	ISSUE DATE:	MONTH 00, YYYY	
	IMPLEMENTATION DATE:	MONTH 00, YYYY	
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TITLE : PROCEDURE – OPERATING – STEAM HEAT STERILIZER – COMPOUNDING PRACTICES

DRAFTED BY:	**SIGNATORY:**			
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APPROVED BY:	**SIGNATORY:**			
	TITLE:	**DESIGNATED PERSON**	SIGNATURE	DATE
APPROVED BY:	**SIGNATORY:**			
☐ n/a	**TITLE:**	**DESIGNATED PERSON**	SIGNATURE	DATE

COMPENDIAL APPLICABILITY OF THE USP GENERAL CHAPTER <800>

"On December 1, 2019, USP's standard on the safe handling of hazardous drugs, General Chapter <800>, became official. General Chapter <800> is informational and not compendially applicable. USP General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings describes practice and quality standards for handling hazardous drugs. USP is committed to maintaining patient access to medicines, while supporting patient safety, healthcare worker safety, and environmental protection when handling HDs (hazardous drugs) in healthcare facilities." (USP Publication: Compendial Applicability of USP 800).

Please see the document titled, compendial-applicability-of-usp-800.pdf in the folder titled, 10 – Supplemental Documentation\References and Standards for additional details.

To determine the regulatory applicability of the USP General Chapter <800>, you must contact your State Board of Pharmacy.

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RELATED LOGS & FORMS

RECORD	SPECIFICATION / DESCRIPTION
USA – STRL – L2.1.1.0	Master Technology ID List
USA – STRL – L2.1.1.0	Technology Calibration Log
	Sheet: Steam Heat Sterilizer
USA – STRL – L3.7.6.0	Steam Heat Sterilizer Cycle History for CSP Log
USA – STRL – L3.7.6.0	Steam Heat Sterilizer Cycle History for Devices Log
USA – STRL – F3.5.7.0	Mapping Strategy Form

RELATED STANDARD OPERATING PROCEDURES

SOP CODE	SOP TITLE
USA – STRL – P0.1.1.0	Preamble – Implementing – Standard Operating Procedures – Compounding Practices
USA – STRL – P0.2.1.0	Preamble – Customizing – Standard Operating Procedures – Compounding Practices
USA – STRL – P0.3.1.0	Preamble – Recording – Good Documenting Practices – Compounding Practices
USA – STRL – P3.5.7.0	Procedure - Managing - Mapping Strategies - Compounding Practices

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RESPONSIBILITIES

1. Designated Person oversees this SOP.
2. Compounding personnel must comply with this SOP.
3. Compounding personnel can perform this SOP.

PURPOSE

1. To ensure appropriate steam heat sterilization of compounded sterile preparations as a viable terminal sterilization method.

SCOPE

1. Applies to non-hazardous and hazardous sterile compounding.
2. Applies to non-hazardous and hazardous compounded sterile preparations.

DEFINITIONS

1. Biological Indicator: Biological indicator that contains integrated growth medium with spores in a crushable glass ampule.
2. Compounded Sterile Preparation (CSP): Compounded medication prepared in a sterile compounding facility.
3. Designated Person: Equivalent to Compounding Supervisor. One or more individuals assigned to be responsible and accountable for the performance and operation of the facility and personnel for the preparation of CSPs.
4. Steam Heat Sterilization: The combination of temperature, pressure and time resulting in microbial lethality.
5. Heat-labile: Destroyed or altered by heat.
6. Physicochemical Indicator: A physicochemical indicator is defined as a device that provides visual evidence of exposure to one or more critical sterilization parameters. Physicochemical indicators do not provide primary evidence of sterilization efficacy.
7. Physicochemical Integrator: A physicochemical integrator is defined as a device that responds to one or more sterilization process critical parameters, which results in a measurable value that can be correlated to microbial lethality.

FREQUENCY

1. Perform terminal sterilization (steam heat or dry heat methods) whenever the selection criteria has been met and there is no potential for damage to the CSP or the container-closure system.
2. Verify sterilization cycle operational parameters and their uniform distribution within the respective chambers each time a sterilization cycle is performed.
    1. Steam Heat: Verify temperature/pressure over time.
    2. Dry Heat: Verify temperature over time.
3. Verify the lethality of the cycle each time a sterilization cycle is performed.
4. Qualify the temperature/pressure distribution over time inside the steam heat sterilizer every six (6) months.

SPECIAL CIRCUMSTANCE

1. This SOP does not apply to filtration of preparations.
2. This SOP does not apply to the irradiation method of sterilization.
3. This SOP does not apply to dry heat sterilization.
4. This SOP does not apply to the sterilization of technology.

PROCEDURE

This SOP is divided into the following sections:

1. Selection of Terminal Sterilization Method
2. Steam Heat Sterilization
3. Steam Heat Sterilizer Maintenance

1. Selection of Terminal Sterilization Method:
    1. CSPs that are terminally sterilized (e.g., dry heat, steam heat, or irradiation) must use a process intended to achieve a probability of a non-sterile unit of 10^{-6}. A probability of a non-sterile unit of 10^{-6} is equivalent to a probability that one unit in a million is non-sterile.
        a. A probability of a non-sterile unit value cannot be applied to CSPs that are aseptically filled into a sterile container following sterilization by filtration because sterilization by filtration is not terminal sterilization.
    2. When selecting the sterilization method for CSPs prepared from one or more non-sterile starting components or using non-sterile supplies or devices, personnel must take into consideration the nature of the component(s), their physical and chemical properties, and the intended container-closure system.
        a. The sterilization method used must sterilize the CSP without degrading its physical and chemical stability (e.g., affecting its strength, purity, and quality) or the packaging integrity.
    3. The following must be considered when selecting an appropriate sterilization method:
        a. Terminal sterilization (e.g., dry heat, steam, or irradiation) is the preferred method unless the specific CSP or container-closure system cannot tolerate terminal sterilization.
        b. Steam sterilization is not an option if moisture, pressure, or the temperatures used would degrade the CSP or if there is insufficient moisture to sterilize the CSP within the final, sealed container-closure system.
        c. Filtration is not an option when compounding a suspension if the suspended drug particles are removed by the filter being used.

d. The sterilization method used must sterilize the CSP without degrading its physical and chemical stability (e.g., affecting its strength, purity, and quality) or the packaging integrity.

4. Select steam heat sterilization when…
    a. CSPs are aqueous, and…
    b. The respective active pharmaceutical ingredients, container-closure system of a preparation are heat stable under conditions of 121^{o}C at 15 psi for 20-60 minutes.
        i. Steam sterilization is not an option if moisture, pressure, or the temperatures used would degrade the CSP.
5. Select dry heat sterilization when…
    a. Items that cannot be sterilized by steam or other means.
    b. Either the moisture would damage the material, or…
    c. The wrapping material is impermeable.

2. <u>Steam Heat Sterilization</u>:
    1. If steam heat sterilization is required, then it must be performed within 6 hours of completion the CSP.
    2. Place sealed container-closures in the steam heat sterilizer allowing for space between items.
    3. Verify that the water reservoir of the steam heat sterilizer contains a sufficient amount of distilled sterile water.
    4. Place chemical indicators for steam heat sterilization in the front and back of the middle shelf of the sterilization chamber.
    5. Package a self-contained biological indicator in a vial.
        a. Place the biological indicator in the sterilization chamber.
        b. Ensure that biological indicators contain 10^6 spores of *Bacillus stearothermophilus.*
    6. Start the steam heat sterilizer.

7. Ensure one of the following sets of conditions are met during the sterilization procedures excluding warm-up or cool-down times:

Steam Heat Sterilization		
Temperature	Pressure	Exposure Time
121°C	15 psi	20-60 Min.

8. Allow for sufficient cooling prior to removal of items from the chamber.
9. Verify that the chemical indicators reached the temperature and time operational parameters requirements.
10. Verify that the biological indicator reached the temperature and time parameters conditions requirements:
    a. Remove biological indicator from the vial.
    b. Crush sterilized biological indicator as specified by the biological indicator manufacturer.
    c. Prepare a positive control by utilizing an unsterilized self-contained biological indicator.
        i. Crush the positive control as specified by the biological indicator manufacturer.
    d. Prepare a negative control as specified by the biological indicator manufacturer instructions.
    e. Incubate sterilized biological indicator, positive and negative control as specified by the biological indicator manufacturer.
    f. Monitor biological indicator and controls daily for microbial growth:
        i. Ensure no microbial growth ensues in the sterilized biological indicator.
        ii. Ensure microbial growth ensues in the positive control within the incubation period, as specified by the biological indicator manufacturer.
        iii. Ensure no microbial growth ensues in the negative control within the incubation period, as specified by the biological indicator manufacturer.

3. Steam Heat Sterilizer Maintenance:
    1. On a weekly basis…
        a. Clean the door gasket with a mild detergent, water and a soft cloth or sponge.
        b. If required by manufacturer, clean the water sensor in the rear of the chamber with a damp cloth or sponge.
        c. Clean and descale the chamber, copper tubes and reservoir using an appropriate cleanser, as per manufacturer.
        d. Remove and clean tray holder and trays, with detergent or a non-abrasive stainless steel cleaner and water, using a cloth or sponge.
        e. Rinse tray holder and trays immediately with water.
        f. Lubricate the door hinges and door-tightening bolt with a few drops of oil.
        g. Clean the exterior of the steam heat sterilizer with a soft cloth.
    2. Monthly:
        a. Clean the strainer or water filter, as per manufacturer instructions.
        b. Check for excessive wear on any hardware, such as door latches.

VERIFICATION

1. Employ a mapping technique using the following SOP to ensure uniformity in the distribution of steam and heat:
    1. **P3.5.7.0 Procedure - Managing - Mapping Strategies - Compounding Practices**
    2. Establish a three-dimensional map of the chamber, indicating sites to test.
    3. Place biological indicators and integrators in strategic locations during cycles.

CORRECTIVE ACTIONS

1. In the event that a chemical indicator or integrator indicates an unsuccessful cycle, discard associated preparations or recall dispensed associated preparations.
2. In the event that the sterilized biological indicator reads positive for microbial growth:
    1. Discard associated preparations.
    2. Recall dispensed associated preparations.

3. Determine root cause and consider:
    a. Verification of proper sterilization chamber function and temperature/pressure distribution.
    b. Verify proper functionality of the water reservoir.
    c. Contact vendor and consider appropriate repair.
    d. Consult manufacturer specifications manual.

PREVENTIVE MEASURES

1. Ensure sterilizing chamber is not overloaded during sterilization cycle.
2. Perform routine maintenance on the wet heat sterilizer:
    1. Verify appropriate selection of water is used to fill the chamber.
    2. Verify frequency of cleaning cycle.
    3. Pressure sensors measure pressure on the inside of the chamber and data is provided via a mechanical or digital pressure gauge.
        a. Verify data recorder used to monitor each cycle and to examine for deviations in temperature or pressure.
    4. Check the safety valve as per manufacturer instructions.

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TECHNOLOGICAL RESOURCES

EQUIPMENT	MANUFACTURER	MAKE	MODEL	SERIAL NUMBER	ID CODE
Medisca United States					

EDUCATIONAL AND SERVICE RESOURCES

AVAILABLE OFFERINGS	
LP3 Network	Medisca Network
	Specialized Consultation Services
	Technical Support Services (TSS)

SPECIFICATION DOCUMENTS

DOCUMENT NUMBER	DOCUMENT NAME	SOURCE	DESCRIPTION

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REVISION HISTORY

REVISION NUMBER	IMPLEMENTATION DATE	TERMINATION DATE	SUMMARY OF CHANGE TO CURRENT VERSION

REGULATORY COMPLIANCE GUIDELINES AND STANDARDS OF PRACTICE

REFERENCE SOURCE	REFERENCE CODE	REFERENCE DATE	SECTION CODE	SECTION DESCRIPTION
USP	797	2008		Pharmaceutical Compounding - Sterile Preparations
USP	800	O1 DEC 19		Hazardous Drugs - Handling in Healthcare Settings
USP	1035	01 AUG 15		Biological Indicators
USP	1209	01 AUG 15		Sterilization – Chemical and Physicochemical Indicators and Integrators
USP	1229	01 AUG 15		Sterilization of Compendial Articles
USP	1229.2	01 AUG 15		Moist Heat Sterilization of Aqueous Liquids
USP	1229.8	01 AUG 15		Dry Heat Sterilization
CDC		01 NOV 08		Guideline for Disinfection and Sterilization