QUALIFICATION AND VALIDATION DOCUMENT

PROTOCOL

Title: Stopper Cleaning Process Validation

Issue Date: **System No.: N/A**

APPROVAL SIGNATURES

Written by:	_____	_____ **Date**
Reviewed and Approved by:	_____ **Manufacturing Manager (Responsible Department Head)**	_____ **Date**
	_____ **QA/QC Manager**	_____ **Date**
	_____ **Facilities Manager**	_____ **Date**
	_____ **VP of Development and Operations**	_____ **Date**

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1. PURPOSE

1.1. The objective of this validation protocol is to define the requirements for completing the Process Validation (PV) for cleaning stoppers using the Stopper washer (system no. 02-422) in Room 1 of Building 1. The specific objectives of this PV are to:

1.1.1. Verify the effectiveness and reproducibility of the cleaning process relative to the process requirements.

1.1.2. Collect data to support established operating parameters of the system used in the cleaning process.

1.1.3. Evaluate the standard operating procedures and other documentation pertaining to the monitoring, maintenance and operation of the system relative to the process requirements.

2. ACCEPTANCE CRITERIA

2.1. Endotoxin: report for evaluation; see Section 2.4.

2.2. Bioburden: report for evaluation; see Section 2.4.

2.3. Particulates: report for evaluation; see Section 2.4.

2.4. The Validation Committee will review the results for this and other aseptic processing-related validations to determine the suitability of the existing Stopper cleaning process and establish acceptance criteria for recertification. If the committee determines that the existing Stopper cleaning process is not suitable, the validation will be repeated, using the new acceptance criteria, after the appropriate modifications have been made to the process.

2.5. All standard operating procedures pertaining to the monitoring, maintenance and operation of the system and the cleaning process must be approved or drafted and reviewed for completeness.

3. SYSTEM DESCRIPTION AND HISTORY

3.1. The stopper washer, on-station in room 108, is used for cleaning stoppers which are to become primary product closures. The stopper washer is a stainless steel unit and comprises the following major components assembled on a portable frame:

- glass process vessel
- valved utility service connections (for WFP, clean compressed air, clean steam)
- single setpoint temperature controller/indicator

3.2. The water used in the wash- and rinse-cycle steps is WFP. The temperature of the WFP is regulated during the wash (agitate/heat) step via passage of clean steam directly into the water in the process vessel, which also achieves the agitation required.

3.3. The pressures of the water, air and steam to the unit are regulated via valves on the utility lines (V517, V708 and V410, respectively) and the flow rates to the process vessel are controlled with separate, manually operated, pressure adjusting valves on the unit (V103, V105, V106 and V111) which are currently fully open during operation.

3.3.1. The speed of rotation for the process vessel (through its -20° to +20° movement from TDC) is controlled with a manually operated electric motor.

3.4. The stopper washer is operated in a manually loaded, manually controlled, discrete batch mode described by the following cycle for each batch:

- Cycle Step 1 - load process vessel
- Cycle Step 2 - fill vessel with WFP (valve V103)
- Cycle Step 3 - agitate/heat with CCA, then CS (valves V105 then V106)
- Cycle Step 4 - drain
- Cycle Step 5 - rinse with WFP (valve V103) while rotating vessel
- Cycle Step 6 - dry with CCA (valve V111)
- Cycle Step 7 - unload process vessel

  where: WFP = water for production, CS = clean steam, CCA = clean compressed air

3.5. No equipment modifications have been made since installation.

3.6. No prior process validation has been performed.

4. RESPONSIBILITY

4.1. Execution of the Validation Procedures in sections 9.1. through 9.4. shall be performed by Validation Dept, with all sampling and testing performed by QC Dept.

4.2. Completion of the QVD report shall be the responsibility of Validation Dept.

4.3. Review and approval of the QVD report shall be the responsibility of QA Dept.

5. REFERENCES AND APPLICABLE DOCUMENTS

5.1. 11-0006-SOP-1.0, Operation and Maintenance of the SMEJA Stopper Washer (CL-003).

5.2. 02-0033-SOP-1.0, Cleaning and Autoclaving of the Teflon Coated Rubber Stoppers.

5.3. 09-0158-SOP-1.0, Endotoxin Determination using ThermoMax Microplate Reader.

5.4. 09-0099-SOP-1.0, Bioburden Testing RM-Subassemblies/Final Assemblies.

5.5. USP XXII, <788> Particulate Matter in Injections, Small Volume Injections.

5.6. 11-0031-IOP-1.0, Stopper Washer Installation/Operational Qualification.

6. MATERIALS AND EQUIPMENT

6.1. Teflon faced rubber stoppers (P/N 400030-01); 500 each run x 3 runs = 1500 stoppers.

6.2. Calibrated electronic stopwatch.

7. HEALTH AND SAFETY CONSIDERATIONS

7.1. Clean steam pipes and valves are extremely hot - operators should avoid direct contact with exposed pipe and valve surfaces and wear protective apparel to avoid contact injury.

7.2. Always make sure the expansion valve (#104) is open during steam, air and water inlet to prevent pressurization of the system.

8. GENERAL REQUIREMENTS

8.1. Attachments #1 through #4 are forms that are to be photocopied for execution of the PV protocol. Do not write on the original forms.

8.2. The relevant data, observations and evaluations shall be entered directly onto the appropriate form in a legible manner and may not be transcribed to other forms at a later date.

8.3. Entries and signatures shall be made with indelible, waterproof black or blue ink. Erroneous entries must be struck through with a single line, dated and initialed. Erroneous entries may not be erased or obscured.

8.4. Unused sections of the form shall be struck through with a single line, dated and initialed. If the information requested in a particular section of the form is not applicable for a specific instance, the abbreviation "N/A" shall be entered. The abbreviation "N/A" shall not be used if the information cannot be verified or obtained. In these instances, an explanation shall be provided to justify omission of the information.

8.5. Several copies of some forms may be required. Each set of copies shall be sequentially numbered in the space provided in the upper right corner of the form (*e.g.*, if two copies of a particular form are required, they shall be numbered "Page 1 of 2" and "Page 2 of 2."

8.6. Some attachments require that supporting documentation be affixed. Each page of supporting documentation included with the attachments in the final report shall be identified with protocol number, attachment number and page number (using the "page __ of __" numbering format). This information may be handwritten, stamped or typed.

8.7. The "Completed By" signature shall be entered at the bottom of each form immediately after the form has been completed. The forms shall be reviewed and the "Reviewed By" signature shall be entered within two week of the date of the "Completed By" signature, prior to the approval of the PV summary report.

8.8. If the Reviewer requests additional information and/or clarification, new form copies shall be prepared, completed and resubmitted to the Reviewer with the original forms attached.

8.9. The completed, signed forms shall become part of the PV summary report.

8.10. The PV protocol execution shall be deemed complete when all forms, functional tests and the written evaluation have been completed, reviewed and signed.