PERFORMANCE QUALIFICATION PROTOCOL FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

Signing of this Performance Qualification Protocol indicates agreement with the Validation Master Plan approach of the equipment. Further if any changes in this protocol are required, protocol will be revised and duly approved.

PREPARED BY:

Organization	Name	Designation	Signature	Date

CHECKED BY:

Organization	Name	Designation	Signature	Date

APPROVED BY:

Organization	Name	Designation	Signature	Date

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

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1 OBJECTIVE

The objectives of this Performance Qualification (PQ) are as follows:

- To verify that the equipment performs in accordance with the design and user requirements as defined by set acceptance criteria and complies with relevant cGMP requirements.
- To demonstrate that the system will perform reproducibly and consistently within its operating range

Following execution of the protocol a summary report will be written and approved. All results, conclusions, exceptions and variances will be addressed and final disposition of the equipment will be stated. Successful completion of this protocol and approval of the summary report will verify that the Process Water Generation & Distribution System meets all the acceptance criteria and is ready for GMP use.

2 SCOPE

This protocol covers all aspects of Performance Qualification for the Process Water Generation & Distribution System serving the .....Tablets, Capsules and Liquid Orals Manufacturing Facility. Scope incorporates qualification of all components starting from Chlorination System, Raw Water Storage & Pumping System, Dual Media Filter, Potable Water Storage & Pumping System, De-chlorination System, and Serial Softeners with Brine Measuring Tank & Salt Saturation Tank, Soft Water Storage & Pumping System and Process Water Storage & Pumping System.

This protocol will define the methods and documentation used to qualify the Process Water Generation & Distribution System for PQ.

3 RESPONSIBILITIES

All work is to be performed under .....over site and according to approved procedures.

Engineering Validation Personnel

The following are the responsibilities of Engineering Validation Personnel:

- Preparation, Review and submission of PQ Protocol.
- Ensures that the protocol is in compliance with current policies and procedures.
- Ensures that the content is sufficient, clearly defined technically sound and accurate.
- Ensures compliance with design specifications.

Validation Personnel

The following are the primary responsibilities of the Validation Personnel:

- Overall cGMP compliance for PQ
- Review and Pre-Approval of PQ Protocol
- Execution of this PQ protocol
- Document Control of PQ Protocol until such document is completed, approved and after.
- Regulatory Compliance Review of the completed PQ Protocol
- Review and Approval of the executed PQ Protocol

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4 SYSTEM DESCRIPTION

The purpose of Process Water Generation & Distribution System is to generate potable water & process water for Potable water distribution system for Formulation & Process Area B, Process water distribution system and feed for Purified water generation system. The Process Water Generation & Distribution comprises of Chlorination System, Raw Water Storage & Pumping System, Dual Media Filter, Potable Water Storage & Pumping System, De-chlorination System, and Serial Softners with Brine Measuring Tank & Salt Saturation Tank, Soft Water Storage & Pumping System and Process Water Storage & Pumping System.

Process Water Generation & Distribution System has been ordered to the following vendors:

- Ion Exchange (India) Ltd.
- Enmax Systemz " Grundfoss"
- AIPA Automation Pvt. Ltd.

Raw Water from Deep bore-well (2 nos.) is taken as a feed for this system. On line chlorination is done through NaOCl dosing. Chlorinated water is stored in Raw Water storage tanks. Chlorination is carried out for water before being stored in Tank to protect water from bacterial growth. Raw Water from water storage tanks are pumped by Raw Water transfer pump (1W+1S) to 1 No. Multi-grade filter. Filtered water coming from Multi-grade filter is stored in 3 Nos. potable water storage tank. Potable Water from Potable Water storage tank is pumped by potable water pumps (1W+1S) to 2 Nos. of softners. Online $Na_2S_2O_5$ (Sodium Meta Bi-Sulphite) dosing is done on Potable Water coming from water transfer pump to remove dissolved chlorine in water. De-chlorination is carried out for water entering to softeners for protection of resin against residual chlorine. Tapping for supply to Potable Water Distribution System (Hydro Pneumatic System) for Formulation Plant is done before De-chlorination.

Water coming from softner is stored in 2 Nos. soft water tank Soft Water from one tank is pumped by soft water transfer pump (1W+1S) to feed as make up water for Cooling Tower HVAC, make up water for Cooling Tower DG sets, make up water for Hot Water HVAC, make up water for Chilled Water HVAC & make up water Boiler.

Soft Water from second soft water storage tank is pumped through process water transfer pumps (1W+1S) to feed for Purified Water Generation and to Process Water Distribution. Online chlorination is done after transfer pump (P804 A/B).

Process Water Generation and Distribution System is being supervised and controlled by Panel mounted microprocessor stand alone indicator & controllers alarm with annunciation.

5 DOCUMENTATION REQUIREMENTS

The PQ File should include:

- This PQ Protocol.
- All laboratory test results or their referenced location.
- All executed routine check sheets.
- Any change control actions that may have occurred during the qualification activities.
- Any variances, exceptions or investigation reports generated during the qualification activities.

6 DATA COLLECTION

All personnel shall have suitable documented training or experience.

All approvals shall be made in *BLUE* ink.

All data entry shall be made in *BLUE* ink.

All corrections to this Protocol, which are not retyped, are to be made in *BLUE* ink. All written corrections to this Protocol or to data entered in this Protocol should be made by using a single line to delete the error. The person who makes the correction shall initial and date it and add comment to explain reason for correction.

After performing the qualification tests, collect all relevant printouts, check sheets, Laboratory test results and certificates and retain for inclusion in the PQ File. If more Data Sheets or Variance Sheets are required, they are to be attached to this Protocol as *Appendices* and to be listed in *Section 13. List of Appendices*.

7 CHANGE CONTROL

Any changes or modifications to the system shall be performed in accordance with the Project Change Control Procedure.

Change Control Forms raised during the execution of this PQ will be filed along with the protocol. An assessment will be made for each change to determine whether or not any re-validation is required.

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8 PRE-QUALIFICATION REQUIREMENTS

The results of any tests should meet the limits and acceptance criteria specified in the test documents. Any deviations or issues should be rectified and documented prior to PQ commencing. Open action items resulting from these tests shall be listed in the Comments section.

8.1 System Pre-requisites

S.No.	Description of Pre-requisite	Completed [Yes / No]	Verified By	Date
1	Verify that the OQ of the Process Water Generation and Distribution System has been executed and approved.	Yes/No*		

Note:- * -Circle one, which is appropriate.

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9 TESTS AND CHECKS

9.1 Water system monitoring, sampling and testing

9.1.1 Purpose

The objective of the test is to ensure that the Process Water Generation & distribution system can consistently, over a 28 day period (14 days phase I and 14 days phase II), meet the following at all sample points

- Microbiological standard
- Specifications from the IS – 10500-1991.

9.1.2 Method

The strategy for water system monitoring, sampling and testing as defined below is used to:

1. Establish documented evidence for consistent operation of the treatment stages.
2. Establish a reference for the action and alert limits based on the plant microbial performance at intermediate process stages.
3. Confirm that the overall plant operates to specification over a prolonged period of time when operated and maintained to the SOP's

Monitoring, sampling and testing will take place over a 28day (14 days phase I and 14 days phase II), Sampling for testing will be as per sampling plan described below as sampling Plan (Table-2) covering all the sampling points listed in Test location (Table-1)

Test locations -Table-1

Description	Sample Points
Outlet of Bore well Pump I	RW01
Outlet of Bore well Pump II	RW02
Post Online Chlorination System	RW03
Before MGF	RW04
After MGF	RW05
Before Softner	RW06
After Softener	SW01
Post Tank T- 802 B	SW02

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Sample Points	Description	Sample Points	Description
SW07	Process Water Tank	SW25	Coating III
SW08	Liquid Filling (Syrup Preparation) (a)	SW26	Solution Preparation – Coating III & IV
SW09	Liquid Filling (b)	SW27	Dry Compaction (a)
SW10	Liquid Filling (Bottle Cleaning) (c)	SW28	Dry Compaction (b)
SW11	Media Destruction	SW29	Solution Preparation – Coating I & II
SW12	Chemical Testing	SW30	Coating I
SW13	Hot Area	SW31	Coating II
SW14	Chemical Wet Lab (a)	SW32	Hose Keeping (PM)
SW15	Chemical Wet Lab (b)	SW33	Sifting & Milling III
SW16	TOC / GC Room	SW34	Granulation II (a)
SW17	Glassware Washroom	SW35	Granulation III
SW18	Chemical Shower	SW36	Granulation II (b)
SW19	House Keeping (RM Store)	SW37	Granulation II (c)
SW20	Wash Room (Sifting)	SW38	Sifting and Milling I
SW21	Wash Room (Coating)	SW39	Sifting and Milling II
SW22	Bin Washing (Ist Floor)	SW40	Granulation I (a)
SW23	Small Volume	SW41	Granulation I (b)
SW24	Coating IV	SW42	Wash Room (RM)

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Sampling plan – Table-2

Test day	RW01/ RW02	RW03	RW04	RW05	RW06	SW01	SW02	SW07 – SW42
1	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	Refer Table 3 on Page 11 of 18
2	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
3	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
4	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
5	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
6	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
7	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
8	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
9	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
10	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
11	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
12	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
13	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
14	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
15	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
16	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
17	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
18	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
19	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
20	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
21	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
22	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
23	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
24	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
25	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
26	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
27	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	
28	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H, TDS, pH, P	M, H	M, H	

M = Microbial Test
P = Potability Test
H = Hardness
TDS = Total Dissolved Solids

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Sampling plan – Table-3

Phase	Test day	Sample Points						Tests
Phase I	1	---		---		---		Description, Total Viable Count, Pathogens and Total Hardness
	2	SW07		SW08		SW09		
	3	SW10		SW11		SW12		
	4	SW13		SW14		SW15		
	5	SW16		SW17		SW18		
	6	SW19		SW20		SW21		
	7	SW22		SW23		SW24		
	8	SW25		SW26		SW27		
	9	SW28		SW29		SW30		
	10	SW31		SW32		SW33		
	11	SW34		SW35		SW36		
	12	SW37		SW38		SW39		
	13	SW40		SW41		SW42		
	14	---		---		---		
Phase II	15	---		---		---		
	16	SW07		SW08		SW09		
	17	SW10		SW11		SW12		
	18	SW13		SW14		SW15		
	19	SW16		SW17		SW18		
	20	SW19		SW20		SW21		
	21	SW22		SW23		SW24		
	22	SW25		SW26		SW27		
	23	SW28		SW29		SW30		
	24	SW31		SW32		SW33		
	25	SW34		SW35		SW36		
	26	SW37		SW38		SW39		
	27	SW40		SW41		SW42		
	28	---		---		---		
Phase III	Ist Month	RW01	RW02	RW03	RW04	RW05	RW06	Analysis as per Table No. 2 – Page No. 10
	IInd Month	RW01	RW02	RW03	RW04	SW01	SW02	
	IIIrd Month	RW01	RW02	RW05	RW06	SW07	SW08	
	IVth Month	RW01	RW02	SW09	SW10	SW11	SW12	
	Vth Month	RW01	RW02	SW13	SW14	SW15	SW16	
	VIth Month	RW01	RW02	SW17	SW18	SW19	SW20	
	VIIth Month	RW01	RW02	SW21	SW22	SW23	SW24	
	VIIIth Month	RW01	RW02	SW25	SW26	SW27	SW28	
	IXth Month	RW01	RW02	SW29	SW30	SW31	SW32	
	Xth Month	RW01	RW02	SW33	SW34	SW35	SW36	
	XIth Month	RW01	RW02	SW37	SW38	SW39	SW40	
	XIIth Month	RW01	RW02	SW41	SW42	---	---	

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

Attach the laboratory worksheets in the appendix and transcribe the results in results section 9.1.5 and 9.1.5 as applicable.

9.1.3 Acceptance Criteria

Sampling and testing to follow sampling plan in Table –2.

Description (For all Points) Clear, colorless, odorless and tasteless liquid.

Potability Test (RW01 – RW06) Coliform should be absent

Microbial limit – Table 4

Sample Points	Alert Level (CFU/ml)	Action Level (CFU/ml)
RW01	NMT 300	NMT 500
RW02	NMT 300	NMT 500
RW03	NMT 300	NMT 500
RW04	NMT 300	NMT 500
RW05	NMT 300	NMT 500
RW06	NMT 300	NMT 500
SW01	NMT 200	NMT 300
SW02	NMT 200	NMT 300
SW07-SW42	NMT 200	NMT 300

Pathogen Test (For all Points) Pathogens: *E. coli, Salmonella, S. aureus, P. aeroginosa* should be absent

Chemical limit – Table 5

<table>
<tr><th>Sample Points</th><th colspan="2">Hardness (ppm)</th><th colspan="2">TDS (ppm)</th><th>pH</th></tr>
<tr><td>RW01</td><td rowspan="6">Desirable Level: Max. 300</td><td rowspan="6">Permissible Level: Max. 600</td><td rowspan="6">Desirable Level: Max. 500</td><td rowspan="6">Permissible Level: Max. 2000</td><td>6.5 – 8.5</td></tr>
<tr><td>RW02</td><td>6.5 – 8.5</td></tr>
<tr><td>RW03</td><td>6.5 – 8.5</td></tr>
<tr><td>RW04</td><td>6.5 – 8.5</td></tr>
<tr><td>RW05</td><td>6.5 – 8.5</td></tr>
<tr><td>RW06</td><td>6.5 – 8.5</td></tr>
<tr><td>SW01</td><td colspan="2">NMT 10</td><td colspan="2">NA</td><td>NA</td></tr>
<tr><td>SW02</td><td colspan="2">NMT 10</td><td colspan="2">NA</td><td>NA</td></tr>
<tr><td>SW07-SW42</td><td colspan="2">NMT 10</td><td colspan="2">NA</td><td>NA</td></tr>
</table>

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

9.1.4 Results of Daily sampling and testing for System

Comments:

Reviewed by		Date	

9.1.5 Results of Daily sampling and testing of User's Point

Comments:

Reviewed by		Date	

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

10 CHECKLIST OF ALL TESTS AND CHECKS

This checklist is provided to ensure that all tests or checks required for this protocol have been executed.

Reference No.	Tests or Checks	Executed [Y/N]	Comment
9.1.4	Sampling and testing of system		
9.1.5	Sampling and Testing of User's Point		

11 VARIANCE SHEET

Report any deviations from the acceptance criteria or exceptions from protocol instructions in the Record Sheet as described in SOP–"Handling of Deviations". Record the total number of exceptions / deviations reported during the qualification activities of this Protocol. Record the Deviation Number and Title in the Table below. Include all Deviation Record Sheets in the IQ File.

TOTAL NO. OF VARIANCES = _____

Variance No.	Variance Title	Status

Comments:

Reviewed by		Date	

12 REFERENCES

The Principle Reference is the following

- Master Validation Plan.
- Schedule – M – "Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products."
- WHO Essential Drugs and Medicines Policy, QA of Pharmaceuticals, Vol 2 – Good Manufacturing Practices and Inspection.

The following references are used to give addition guidance

- FDA/ISPE Baseline Pharmaceutical Engineering Guide-Volume 5:- Commissioning and Qualification Guide, First Edition / March 2001.
- Code of Federal Regulations (CFR), Title 21, Part 210, *Current Good Manufacturing Practice (cGMP) in Manufacturing, Processing, Packing, or Holding of Drugs*, General. April 1, 1998.
- Code of Federal Regulations (CFR), Title 21, Part 211, *Current Good Manufacturing Practice (cGMP) for Finished Pharmaceuticals*, April 1, 1998.
- EU Guide to Good Manufacturing Practice, Part 4, 1997.
- European Commission's working party on control of medicines and inspections document, *Validation Master Plan, Design Qualification, Installation & Operational Qualification, Non Sterile Process Validation, Cleaning Validation*, October 1999.
- GAMP Guide, Validation of Automated Systems in Pharmaceutical Manufacture, Version 4.0, December 2001.
- Handling of Deviations.
- Change Control Procedure.
- USP-28

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13 LIST OF APPENDICES

Appendix No.	Document Title

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

14 SUMMARY

PERFORMANCE QUALIFICATION FOR PROCESS WATER GENERATION & DISTRIBUTION SYSTEM

15 APPROVALS

The following approvals signify that the PQ is complete and acceptable.

EXECUTED BY:

Organization	Name	Designation	Signature	Date

REVIEWED BY:

Organization	Name	Designation	Signature	Date

APPROVED BY:

Organization	Name	Designation	Signature	Date