PERFORMANCE QUALIFICATION PROTOCOL FOR PURIFIED WATER STORAGE & DISTRIBUTION SYSTEM

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PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

PERFORMANCE QUALIFICATION PROTOCOL FOR PURIFIED WATER STORAGE & 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

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PERFORMANCE QUALIFICATION PROTOCOL FOR PURIFIED WATER STORAGE & DISTRIBUTION SYSTEM

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 Purified Water Storage & 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 Purified Water Storage & Distribution System serving the .....Orals Manufacturing Facility. Scope incorporates qualification of all components starting after Valve V44 up to all user points, consisting of Purified Water Storage Tank, Sanitary Grade Pumps, UV Unit, Point of Use and Inter connecting Piping inside battery limit as marked in P&I Diagram for Storage & Distribution System.

This protocol will define the methods and documentation used to qualify the Purified Water Storage & 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

4 SYSTEM DESCRIPTION

Purified Water from Purified Water Generation System is used as feed to this system. Purified Water is stored in SS 316L storage tanks. This tank is designed for full vacuum and is fully drainable. The tank is having the internal finish of 240grit and surrounded by limpet coil and jacket. Chilled water at 5.5°C is circulated through limpet coil to maintain temperature of Purified Water at 15-27°C. Purified water is heated to 80°C + 5 °C using steam in Jacket of Purified Water Storage Tank during sanitization. Hot Water

is circulated at 80°C throughout the distribution loop covering all the user plants.

Purified Water is distributed through SS 316L pipes having 2" diameter. These pipes have 0.5 Ra internal finishes and have slope of 1:100 to make the system fully drainable. Purified Water before being distributed to different user points is subjected to Ultra Violet light to have microbial control.
Purified Water is pumped through sanitary grade Centrifugal Pumps. Casing and Impeller of these pumps are in SS316L. One Cold standby pump is provided for the system. Pump has been provided with VFD and with a closed loop control from flow meter installed at the return. The control logic is to maintaining a minimum velocity of 1m/sec by changing speed of pump as the demand increases or reduces.

Non-Metallic parts like gaskets, 'O' rings, diaphragms coming in contact with Purified Water is of food grade quality.

Purified Water is re-circulated through return loop, sprayed into the Storage Tank through 360° shadow free spray ball. Purified Water shall be maintained between 15-27°C and its velocity should not fall below acceptable limit that is 1m/sec in return loop. The distribution network shall not have dead leg > 6d (as per Article 8.7.1.6 of ISPE Base Line, Volume-4, Water & Steam Systems). All the joints are connected with triclover clamps. The system does not have any direct connection to drains or sewers to prevent bacteria entry into the system. Sampling points are provided after each equipment and in return loop.

Associated System components comprise:

- **Control System:** The Purified Water Storage and Distribution System is controlled and monitored via a Siemens PLC (Programmable Logic Controller) and Industrial type Man Machine Interface (MMI), with an external PLC Interface to a printer. All the major parameters including Alarms, and Valves will be through control panel of the PLC.

- **Safety system:** The following Safety systems are incorporated:

    - Emergency push button is provided
    - Mechanical guard for all rotating parts are provided
    - The system is checked for any leakages present
    - Electrical panels is properly grounded with no un sec used joints
    - Double earthing is provided for all electrically operated equipment
    - Overload relay for motors provided in pump feeder in MCC
    - Noise pollution is under 80db at 1M from source.
    - Tagging and naming of all electrical wires and pneumatic tubing is done
    - Drain and effluent from the system is complying to local code of practice

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 Purified Water Storage 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 Purified Water Storage and Distribution System can consistently, over a 28 day period(14 days for phase I and 14 days for phase II), meet the following at all sample points.

- High microbiological standard
- Current USP (USP 28) monograph.

Weekly sampling and analysis with location from distribution system i.e. user's points for Phase-III study will be carried out as per the plan given in Table 2 and Table 3.

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 distribution system.
2. Establish a reference for the action and alert limits based on the system microbial performance at various distribution stages.
3. Confirm that the overall system 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 28days (14 days for Phase I and 14 days for 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

<table>
<tr><th rowspan="2">Description</th><th rowspan="2">Sample ref.</th><th colspan="2">Sampling and Testing</th></tr>
<tr><th>Phase I & II</th><th>Phase III</th></tr>
<tr><td>Outlet of Purified Water Storage Tank</td><td>PW02</td><td rowspan="5">Daily</td><td rowspan="4">Refer Table -2</td></tr>
<tr><td>Outlet of Pump P-201</td><td>PW03</td></tr>
<tr><td>Outlet of UV unit</td><td>PW04</td></tr>
<tr><td>User Points (35 Numbers)</td><td>PW05 to PW39</td></tr>
<tr><td>Return loop to Purified Water Storage Tank</td><td>PW40</td><td>Daily</td></tr>
</table>

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Test locations and sampling plan* for Phase - III -Table-2

Sampling Points	Location	Sampling Day	Sampling Points	Location	Sampling Day
PW02	Outlet of Purified Water Storage Tank	Mon	PW21	Granulation-II (c)	Wed
PW03	Outlet of Pump P-201	Mon	PW22	Granulation -III	Thurs
PW04	Outlet of UV unit	Mon	PW23	Granulation -III (GPCG 300)	Thurs
PW05	Active mixing & Syrup preparation	Mon	PW24	Sifting-I	Thurs
PW06	Liquid filling line	Mon	PW25	Sifting-II	Thurs
PW07	Decartoning & Bottle washing	Mon	PW26	Process Area B	Thurs
PW08	Media destruction	Mon	PW27	Washing room - RM warehouse	Thurs
PW09	Wash room Q.C.	Mon	PW28	Wash room sifting & dispensing	Fri
PW10	Chemical testing	Tues	PW29	Sifting –III	Fri
PW11	Glass ware wash room	Tues	PW30	Small batch area (a)	Fri
PW12	Wet chemical Lab	Tues	PW31	Small batch area (b)	Fri
PW13	TOC/GC lab	Tues	PW32	Bin washing	Fri
PW14	Granulation I (a)	Tues	PW33	Wash room coating	Fri
PW15	Granulation I (b)	Tues	PW34	Coating –IV	Sat
PW16	Granulation I (c)	Wed	PW35	Coating –III	Sat
PW17	Dry Compaction (a)	Wed	PW36	Solution preparation coating III/IV	Sat
PW18	Dry Compaction (b)	Wed	PW37	Solution preparation coating I/II	Sat
PW19	Granulation II (a)	Wed	PW38	Coating –II	Sat
PW20	Granulation II (b)	Wed	PW39	Coating-I	Sat

* **This sampling plan is for Phase-III; however for Phase –I and Phase-II, daily sampling from all above mentioned points will be carried out.**

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Sampling plan – Table-3

Test day	PW02	PW03	PW04	PW05 to PW39	PW40*
1	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
2	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
3	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
4	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
5	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
6	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
7	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
8	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
9	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
10	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
11	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
12	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
13	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
14	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
15	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
16	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
17	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
18	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
19	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
20	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
21	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
22	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
23	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
24	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
25	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
26	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
27	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH
28	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC	M,D,C,TOC, Pathogens, pH

D = Description TOC = Total Organic Carbon
M = Microbial Test C = Conductivity (off-line)

* Including Acidity or Alkalinity, Ammonium, Calcium and Magnesium, Chloride, Nitrate, Sulphate, Oxidizable Substances and Residue on Evaporation

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Attach the laboratory worksheets in the appendix and transcribe the results in results section 9.1.5 and 9.1.6 as applicable.

Prior to each day's sampling of the Purified Water, record the conductivity from at CT 201 and CT 202 in section 9.1.4 of this protocol.

9.1.3 Acceptance Criteria

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

Laboratory worksheets attached in the appendix.

Description:	Clear, colorless, odorless and tasteless liquid.
Microbial limit:	
All Sample points	Absence of *E.coli, Salmonella, S.aureus & P.aeroginosa* Alert limit: 25 cfu/ml Action limit: NMT 100 cfu/ml
Chemical limit:	
Acidity or Alkalinity	To comply test
Ammonium	NMT 0.2 ppm
Calcium and Magnesium	To comply test
Chloride	To comply test
Nitrate	NMT 0.2 ppm
Sulfate	To comply test
Oxidizable Substances	To comply test
Residue on Evaporation	NMT 0.001 %
Conductivity -	≤ 1.3 µS/cm
Total organic carbon	≤ 500 ppb
pH	4.5 – 7.0

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9.1.4 Results – Daily On-line monitoring

Test day/ Date	On-line conductivity - µ S/cm		Acceptable (Y/N)	Initial/ Date
	CT 201	CT 202		
1/				
2/				
3/				
4/				
5/				
6/				
7/				
8/				
9/				
10/				
11/				
12/				
13/				
14/				
15/				
16/				
17/				
18/				
19/				
20/				
21/				
22/				
23/				
24/				
25/				
26/				
27/				
28/				

Comments:

Reviewed by		Date	

PERFORMANCE QUALIFICATION PROTOCOL FOR PURIFIED WATER STORAGE & DISTRIBUTION SYSTEM

9.1.5 Results – Daily sampling and testing

Attach the Quality Control reports of daily testing as Appendices 2.

Comments:

9.1.6 Results - Record of distribution system sanitisation

Date of sanitisation	Time of sanitisation -hrs	Operator Signature	Completed successfully (Yes/No)

Comments:

Reviewed by		Date	

PERFORMANCE QUALIFICATION PROTOCOL FOR PURIFIED WATER STORAGE & 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	Water system monitoring, sampling and testing		

11 VARIANCE SHEET

Report any deviations from the acceptance criteria or exceptions from protocol instructions in the Record Sheet as described in SOP for "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	

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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 PROTOCOL FOR PURIFIED WATER STORAGE & DISTRIBUTION SYSTEM

14 SUMMARY

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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