OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION SYSTEM

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

Signing of this Operational 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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QUALITY ASSURANCE DEPARTMENT

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

TABLE OF CONTENTS

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

1. OBJECTIVE

The objectives of this Operational Qualification (OQ) are as follows:

- To verify that the equipment operates 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 operate reproducibly and consistently within its operating range.
- To confirm the suitability of the Standard Operating Procedures for all routine activities associated with the system.

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 Generation System meets all the acceptance criteria and is ready for PQ.

2. SCOPE

This protocol covers all aspects of Installation Qualification for the Purified Water Generation System serving the .....Tablets, Capsules and Liquid Orals Manufacturing Facility. Scope incorporates qualification of all Purified Water Generation components from Feed water inlet, upstream of Sample valve SV1, up to and including Product three way diverter valve V44 in the water treatment stream and oil free filtered Instrument air downstream of V32.

This protocol will define the methods and documentation used to qualify the Purified Water Generation System. Successful completion of this protocol will verify that the Purified Water Generation System meets all acceptance criteria and is ready for Operational Qualification.

3. RESPONSIBILITIES

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

Jacobs Engineering Validation Personnel

The following are the responsibilities of Engineering Validation Personnel:

- Preparation, Review and submission of OQ 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 OQ
- Review and Pre-Approval of OQ Protocol
- Execution of this OQ protocol

- Document Control of OQ Protocol until such document is completed, approved and after.
- Regulatory Compliance Review of the completed OQ Protocol
- Review and Approval of the executed OQ Protocol.

4. SYSTEM DESCRIPTION

The Purified water generation system is fed by Chlorinated soft water complying with IS Standards as filtered through 5.0 µ cartridge filter to control SDI. The quantity of the free chlorine in Feed water shall be kept within 0.02 ppm by SMBS dosing before entering to Purified Water Generation Skid. The Purified Water Generation System shall produce Purified water in compliance with current USP 28, at flow rate of 4 m^3/hour and pressure of < 1.5 bar. Pre conditioning skid consists of heat exchanger, SMBS dosing and NaOH dosing which controls temperature, Conductivity and pH of water respectively. Feed to the purified water system shall be at 7.0 bars from the pre conditioning skid. Pre conditioning skid consists of heat exchanger, SMBS dosing and NaOH dosing which control temperature, chlorine and pH of water respectively. The system comprises of pre-treatment and final treatment section. The pre-treatment section of Generation skid consists of Two Base Exchange Softeners, to reduce total hardness in feed water, and a 5.0 µ cartridge filter to reduce particulate loading on final treatment section. The pre treated feed water is fed to storage to in feed water tank TK1. The pre-treatment section is followed by Reverse Osmosis and Continuous De-Ionization process to generate required grade Purified water. The treated water, which meets the quality requirements specified, enters as Purified Water into the Purified Water storage tank and distributed to manufacturing premises through Distribution skid.

Qualification activities for the PW Generation System incorporate the following system components as listed below in order of process:

- **Two Base Exchange Softeners**: BES-1 and BES-2. The Softener is used to reduce total hardness in feed water
- **5.0 µm cartridge filter FLT 1**: This cartridge filter is used to reduce particulate loading on final treatment section
- **Chlorine Monitor**: Free chlorine will be monitored by chlorine monitor before entrance to the Purified Water generation skid by taking sample at frequency to be determined in Phase 1 & 2 trials and will be a part of operating SOP.
- **Feed water Tank TK1**: Filtered water from the 5.0 µm cartridge filter is stored in this Tank. The Feed water Tank is of 100 Litre capacity and provided with a electric heater. This tank serves as a multipurpose break tank, heating chamber for hot water sanitisation, CIP tank for final treatment section and an expansion tank during hot water sanitisation
- **RO feed pump PU 1**: This pump is variable speed driven and feeds RO unit. This pump's speed is set by PLC to achieve pre-set flow and pressure.
- **RO Unit R01**. This is a two-pass arrangement comprising high pressure Stainless Steel vessels fitted with hot water sanitisable RO elements. The RO feed pump force feeds the feed water to RO unit; the RO unit is designed to have recovery rate of 75%, producing permeate at 4m^3/hour.
- **Degasser DEG A/B**: Degasser enhances the performance of downstream Continuous De-ionization units. Degasser module(s) contain thousands of fine Hydrophobic hollow tubes that will allow only the gases and not the water to pass through. A stream of oil free filtered Instrument air is used to strip out excess levels of Carbon-di-oxide from RO permeate
- **CDI-LX Units CDI-LX A/B**: Process water leaving the RO unit is passed to the CDI System which consists of alternating cation and anion exchange modules. High voltage Direct Current is

applied to the electrodes located at either end of the CDI modules, this action will remove ions from the feed water and regenerate ion resins inside the modules continuously. The module produces consistent, predictable water quality which is better than 95% removal with a feed water conductivity of 50 µ S/cm

- **Saturator for regenerating Softeners with brine solution**. A multi port valve located on each softener controls the regeneration process. Softeners are interlocked so that only one can be regenerated at a time.
- **CIP systems (chemical):** As the chemical cleaning requirements of various parts of final treatment are different, they can be isolated for chemical cleaning in place as three different circuit namely CIP1 (low pressure chemical cleaning of RO unit) and CIP 2 (high pressure cleaning of RO unit) by isolating RO unit from Degasser and CDI; CIP 3 is for CDI-LX Units cleaning. They are all semi-automatic process selected and prompted by PLC**.**
- **Control System**. The PW Generation System is controlled and monitored via a Siemens S7-300 PLC (Programmable Logic Controller) and Human Machine Interface (HMI), with an external PLC Interface to DCS/SCADA using Modbus Protocol and status control system
- **Alarms and Safety Interlocks.** Three different alarm types are incorporated namely warning, non-critical alarm and critical alarms. Emergency stop is hardwired independently from the control system and can thus override control of the PLC.

Hot water sanitization: Final treatment section including the feed water tank is hot water sanitisable up to 85 ° C on automatic control set via HMI. It can be either manually initiated or run automatically at a pre-set day and time via time clock

5. DOCUMENTATION REQUIREMENTS

The OQ File should include:

- This OQ Protocol.
- Any laboratory test results or their referenced location.
- 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 and certificates and retain for inclusion in the OQ 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*.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

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 OQ 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.

8. PRE-QUALIFICATION REQUIREMENTS

Refer to .....*Procedure* for the pre-qualification activities, tests and/or procedures that should be carried out on the Purified Water Storage and Distribution System prior to the execution of OQ. Any variances or issues which occur when reviewing the pre-requisites should be raised by following, ... *Procedure* for Validation Variance Report'.

8.1 System Pre-requisites

S. No.	Description of Pre-requisite	Completed Yes or No	Verified By	Date
1	Verify that the IQ of the Purified Water Generation System has been executed and approved. IQ Protocol Document No:	Yes/No*		
2	Verify that Site Acceptance Tests (SAT) of the Purified Water Generation System has been executed and approved.	Yes/No*		
3	Verify that the safety walk through has been completed and that the system is safe to use.	Yes/No*		
Verify that authorised drafts of the following procedures (SOP / PMI) relevant to operation of the Purified Water Storage and Distribution System are available.				
4	SOP-Purified Water Generation system Operation	Yes/No*		
5	SOP-Purified Water Generation system Maintenance.	Yes/No*		
6	SOP-"Sanitisation of Purified Water Generation System	Yes/No*		
7	SOP "Filter Integrity Test for Water & Compressed air System"	Yes/No*		

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

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

8.2 Test Equipment Calibration

Review the calibration status for the test equipment to be utilised and record the calibration due dates in the table below. All equipment / instrumentation must remain within the calibration due date for the duration of OQ test for which the item is used. If a due date potentially occurs during the testing period then the instrument must be recalibrated before it can be utilised.

Equipment Name	Equipment Owner	Equipment Number	Due Date	Signature	Date

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9. TESTS AND CHECKS

9.1 SOP Verification

9.1.1 Purpose

To verify the accuracy of Standard Operating Procedures applicable to the Purified Water Generation System.

9.1.2 Method

Obtain a controlled copy of each SOP referenced within section 9.1.4. During the course of OQ testing, perform each operation according to the instruction indicated within the appropriate SOP. Mark with a highlighter pen each instruction or statement within the SOP which is verified and in accordance with the actual practice. Write any differences from actual practice in red ink on the copy of the SOP. On completion, write "Operational Qualification - SOP Verification" on the marked-up copy of the SOP, sign & date it and attach as an appendix to the OQ protocol together with any other raw data such as printouts. Ensure all SOP's identified in Section 9.1.4 are evaluated and checked.

9.1.3 Acceptance Criteria

At the completion of OQ testing, all standard operating procedures referenced within section 9.1.4 will be annotated to correctly reflect the applicable method instruction(s) required to obtain intended operation or function result.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.1.4 Results

Enter the SOPs into the table below and verify that they have been evaluated and checked. Incorporate the marked up SOPs as an appendix to the OQ report together with any other raw data such as printouts

SOP Number	SOP Description	SOP accurate after check [Y/N]	Initial / Date
	Preventive Maintenance of Purified water Generation System		
	Cleaning of RO membrane		
	Calibration of conductivity sensors		
	Calibration of conductivity indicators		
	Calibration of pressure transmitters		

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.2 Generation System Security Test

9.2.1 Objective

To verify that access to system programs and data are protected in an adequate manner.

9.2.2 Method

Follow instructions in the Test Method column in section 9.2.4 to test security of the system. Record all observations in the actual results column in section 9.2.4 and attach any raw data printouts as an appendix to this protocol.

9.2.3 Acceptance Criteria

Access to control system and software is to authorised personnel only. Specific acceptance criteria for each test are provided in section 9.2.4.

9.2.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
<< Enter test methods for testing in-built security access to the control system (level 0, level 1, level 2, etc – refer Functional requirement specification and FAT report>>	<< Enter expected result of each test >>			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

9.3 Generation System Start-Up and Shutdown Test

9.3.1 Objective

To verify that the system components will power-up and start as defined by the design documentation.

9.3.2 Method

Follow instructions in the Test Method column of section 9.3.4 to test the start-up and shutdown of each system component. Obtain approval from the Production, Electrical and Mechanical Departments (where applicable) prior to this test and attach the approval slip as an appendix to this protocol. Record all observations in section 9.3.4 and attach any raw data printouts as an appendix to this protocol.

9.3.3 Acceptance Criteria

All Start-up and Shutdown functions operate correctly as specified in the following document:

- *System Operating and Maintenance Manual Purified Water Package: <<Document Ref>>>*

Specific acceptance criteria for each test are provided in the tables in section 9.3.4.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.3.4 Results

Shutdown Procedure

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
While the system is operating, cease operation by assigning the following mode on the Human Machine Interface (HMI):				
Heat exchanger with dosing system	The unit will stop functioning			
Purified Water Central Control Panel Main Isolator Turn OFF	CDI Unit will stop operating.			
	Degasser Unit stop operating.			
	RO Unit will stop operating.			
	Circulation Pump will STOP operating.			
	Softener Unit will stop operating << enter the unit stopped indication e.g. valve status, regeneration status, soft water throughput etc>>			
	Central Control Panel Unit is switch off. Alarm is activated.			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.3.4 Results (cont'd)

Power-Up and Start Test

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Start heat exchanger with dosing system	The dosing pump will start and the value of chlorine, pH and temperature will be shown.			
Start operation by turning on the main power isolator at the Purified Water Package Control Panel and power up the RO Unit.	Power is distributed to electrical components. System returns to operation mode.			
Softener unit selected for operation	<< Enter the indication of softener unit operation – e.g. regeneration status, soft water throughput etc>>			
Start the RO unit and select service command to start	Pump will start operation. PS-1 indicates positive reading and Pump speed XY3A indicates minimum value.			
	Power light is ON ON/OFF light is ON RO Unit will start.			
	Degasser unit started operation. <<Enter the indication of Degasser unit operation – e.g. valve V-31 status, FI-1/FSL-1 status etc>>			
	Degasser unit started operation. <<Enter the indication of Degasser unit operation – e.g. valve V-31 status, FI-2/FSL-2 status etc>>			
	CDI –LX A unit started operation.			
	CDI –LX B unit started operation.			

Equipment Operated By		Date	

Comments:

Reviewed by		Date	

9.4 Operator Data Entry Test

9.4.1 Objective

To verify system response following Operator Data Entry and to ensure that the system will only accept approved inputs and that all other inputs are rejected in a controlled manner.

9.4.2 Method

Follow the instruction within the test method column of section 9.4.4 to test the data entry of the system. Record all observations in the actual results in section 9.4.4 and attach any raw data printouts as an appendix to this protocol.

Ensure that upon test conclusion, all parameter set points are returned to normal operating status.

9.4.3 Acceptance Criteria

Operator inputs with limits / formats associated with them will accept values as stated in column “System accepts Input as Valid”. Entered value or format stated in column “System rejects Input as invalid” will be rejected by the system.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.4.4 Results

System Variable	Limits		Value Smaller than Min	Value Greater than Max	Expected Result Met?	
	Min	Max			Yes / No	Initial & Date
Expected Result	**System accepts Input as Valid**		**System rejects Input as Invalid**			
<<enter list of Operator Data and their acceptable range in appropriate unit to verify that the system will only accept approved inputs and that all other inputs are rejected in a controlled manner>>						
Feed water Tank contents Temperature TS-4 Set point	10	40	9	41		
Feed water Conductivity/ temperature CS/TS-1 Set point	10	40	9	41		
RO feed pressure- PS/PT-1 set point (bar)	0	40	-1	41		
RO feed pressure- PS/PT-2 set point (bar)	0	40	-1	41		
RO recycle flow FS/FT-2 set point – m/sec	0.1	10	0	10.1		
RO concentrate to drain flow FS/FT-3 set point - lpm	6	60	5	61		
Permeate line flow FS/FT-4 set point - lpm	18	180	17	181		
CDI-LX feed pressure- PS/PT-3 set point (bar)	0	10	-1	11		
CDI-LX A concentrate line flow sensing FS/FT-5A set point -lpm	2	20	1	21		
CDI-LX B concentrate line flow sensing FS/FT-5B set point -lpm	2	20	1	21		
CDI-LX A concentrate pressure- PS/PT-5A set point (bar)	0	10	-1	11		
CDI-LX B concentrate pressure- PS/PT-5B set point (bar)	0	10	-1	11		
CD-LX product water Conductivity/ temperature CS/TS-2 Set point	0	45	-1	1.4		
CD-LX product water Conductivity/ temperature CS/TS-3 Set point	0	1.3	-1	0.3		
CDI-LX concentrate outlet pressure- PS/PT-6 set point (bar)	0	10	-1	11		
CDI-LX product water pressure- PS/PT-7 set point (bar)	0	10	-1	11		
Pure water recycle temperature TS/TT-5 set point - °C	0	40	-1	41		

Equipment Operated by		Date	
Comments:			

Reviewed by		Date	

9.5 Generation System Functionality Tests

9.5.1 Objective

To verify purified water Generation system components functionality.

9.5.2 Method

Prior to this test, power up and start-up each component as described in Section 9.5.4: *Power Up and Start Test*. Operate each item as described in Section 9.5.4 to test the functionality of the system. Record all observations in the Actual Results column in Section 9.5.4.

9.5.3 Acceptance Criteria

All aspects of control for individual components integrated within the purified water Generation system shall function as specified in the expected results column in Section 9.5.4.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.5.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Heat exchanger with dosing system				
Increase the temperature of water and put HCl to increase the pH and chlorine level.	First the system will dump the water, then the temperature, pH level and chlorine level will slowly decrease and after some times it will maintain.			
Base Exchange Softener –1				
Initiate manual regeneration. Record the stages of regeneration.	Regeneration starts and continues in an automatic sequence as, without any fault alarm listed below: 1. Media backwashing. 2. Brine solution dilution. 3. Passing brine through media. 4. Displacing regenerant and hardness salt. 5. Rinsing excess brine solution. 6. Completion of regeneration			
Initiate Automatic regeneration by simulating the volume of soft water produced. Record the stages of regeneration.	Regeneration starts and continues in an automatic sequence as, without any fault alarm listed below: 1. Media backwashing. 2. Brine solution dilution. 3. Passing brine through media. 4. Displacing regenerant and hardness salt. 5. Rinsing excess brine solution. 6. Completion of regeneration			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.5.4 Results (Contd)

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Feed water Tank TK-1				
Record the value of level switch by varying the water level	Level switch shows value of low and high water level			
Record the temperature by heating the water	Recorded			
Spray ball is working satisfactory	Satisfactory			
Position of the feed water Inlet valve	Normally open			
Position of three way valve	Depends upon water level			
Position of drain valve	Normally close			
Position of outlet valve	Normally open			
RO Feed Pump PU-1				
Direction of rotation	Clockwise			
Output current	15 ampere			
Interlocking with purified water generation skid	Interlocked			
Inlet pressure	0			
Outlet pressure	40 bar			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.5.4 Results (Contd)

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Press Emergency Stop button at the RO Unit.				
RO Unit RO-01: Reset the Emergency Stop button. Press 'ACK' at the HMI and press the reset pushbutton at the Central Control Panel. Ensure feed pump is in service. Switch on the ON button at the RO Control Panel.	The RO Unit is stopped an alarm is raised at the Control Panel.			
	The alarm at HMI will clear once it is acknowledged. The RO unit will restart once the reset pushbutton at the Central Control Panel and 'ON' button at the RO Control Panel are pressed. The RO Unit will restart and alarm at HMI will clear once the reset pushbutton at the HMI is pressed.			
Degasser Unit DEG -A	Supply air to Degasser unit stops.			
	Air supply to Degasser unit established. Air supply pressure: ≥2 bar (g). Air flow: ≥ 5 m^3/hr			
CDI-LX –A unit	Power supply to CDI-LX A interrupted.			
CDI-LX –B unit	Power supply to CDI-LX B interrupted.			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.5.4 Results (Contd)

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Return/Service diverter valve V-44				
Generation unit is in continuous generation mode and Purified water demand exists. Record Product water conductivity (CS/TS-3) and Product 3 way Diverter V-44.	Product water conductivity (CS/TS-3) is less than or equal to 1.3 µ S/cm. Product 3 way Diverter V-44 is in "Feed" position.			
Simulate Product water conductivity monitored at CS/TS-3 to attain more than 1.3 µ S/cm.	"Final water high-high conductivity" alarm activates.			
	Product 3 way Diverter V-44 forced to "Recycle" position.			
Feed water tank heater HT-1				
Initiate Hot water Sanitisation. Confirm heater HT-1 is enabled. Reduce Tank TK-1 level below LSL-1 level.	Feed water tank level low alarm activates.			
	Heater HT-1 disabled.			
	Feed pump PU-1 trips			
	Generation unit shuts down			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

9.6 Generation System Functionality Tests for Feed Water Tank Heater

9.6.1 Objective

To verify purified water Generation system components functionality.

9.6.2 Method

Prior to this test, power up and start-up each component as described in Section 9.6.4: *Power Up and Start Test*. Operate each item as described in Section 9.6.4 to test the functionality of the system. Record all observations in the Actual Results column in Section 9.6.4.

9.6.3 Acceptance Criteria

All aspects of control for individual components integrated within the purified water Generation system shall function as specified in the expected results column in Section 9.6.4

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.6.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Initiate Hot water Sanitisation. Confirm heater HT-1 is enabled. Reduce Tank TK-1 level below LSL-1 level.	Feed water tank level low alarm activates.			
	Heater HT-1 disabled.			
	Feed pump PU-1 trips			
	Generation unit shuts down			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.7 Generation System Emergency Shutdown Stop

9.7.1 Objective

To verify that the emergency stop function activation shuts down the system in an appropriate manner.

9.7.2 Method

Ensure system is running under normal operating procedures. Press the emergency stop button and follow instructions in the Test Method column in section 9.7.4. Record all observations in the Actual Result column in section 9.7.4 and attach any raw data printouts as an appendix to this protocol.

9.7.3 Acceptance Criteria

Component comprising the Generation system shut down in a safe and controlled manner when the emergency stop button is pressed. All pumps and motors will disengage. An alarm condition is registered with audible alarm.

9.7.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Press Emergency Stop Button while the system is running in normal operating mode	The system shuts down in a safe and controlled manner. 1. PU-1 stops 2. Tank heater HT-1 de-energises. 3. CDI-LX de-energises. 4. Emergency push button illuminates. 5. “Emergency stop tripped” alarm displayed. 6. Audible alarm sounds. 7. Generation unit shuts down.			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

9.8 Generation System Power Failure and Recovery Test

9.8.1 Objective

To ensure that system integrity is maintained in the event of power loss, that the system operates in accordance with specified acceptance criteria during failure and that the system can be recovered back to a satisfactory operational state without the loss of data.

9.8.2 Method

Perform a simulated power loss while the systems operating normally without any faults. Verify the capability of the system to safely recover and resume normal operation. Verify that the system is able to retain the original program without data corruption. Also, verify that the system can prevent loss or corruption of stored data.

Follow instructions in the Test Method column in Section 9.8.4. Record all observations in the Actual Results column in section 9.8.4 and attach any raw data printouts as an appendix to this protocol.

9.8.3 Acceptance Criteria

Upon loss of power the system shuts down safely without causing damage to equipment components and can automatically restart following a power failure event without the need for application of additional resetting procedures. The system is able to retain the original program upon a loss of power.
The system is able to prevent the loss or corruption of stored data during a power failure.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.8.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Copy the list of set parameters from the HMI at the Configuration Menu before power failure test in Section 9.8.4.1 'Parameter Settings'. Perform a simulated power loss while the system is operating normally without any faults.	The system will automatically restart upon restoration of electrical power. The system will choose from which phase the plant has restart, depending on the parameters conditions at the power ON moment.			
Restore electrical power to the system.	The system steps through the start-up and normal operation phases identical to start-up test.			
After the restoration and recovery of electrical power, copy the list of set parameters from the HMI at the Configuration Menu in Section 9.8.4.1 'Parameter Settings'. Check the set parameters value before and after power failure. Verify that the system is able to retain original program without data corruption in case of power failure.	Parameters settings before and after power failure are the same.			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.8.4.1 Parameter settings

System Variable	Prior to Power Failure	Following power restoration	Initial / Date
Feed water Tank contents Temperature TS-4 (°C)			
Feed water Conductivity/ temperature CS/TS-4			
RO feed pressure- PS/PT-1 (bar)			
RO feed pressure- PS/PT-2 (bar)			
RO recycle flow FS/FT-2 (m/sec)			
RO concentrate to drain flow FS/FT-3 (lpm)			
Permeate line flow FS/FT-4 (lpm)			
CDI-LX feed pressure- PS/PT-3 (bar)			
CDI-LX A concentrate line flow sensing FS/FT-5A (lpm)			
CDI-LX B concentrate line flow sensing FS/FT-5B (lpm)			
CDI-LX A concentrate pressure- PS/PT-5A (bar)			
CDI-LX B concentrate pressure- PS/PT-5B (bar)			
CD-LX product water Conductivity/ temperature CS/TS-2			
CD-LX product water Conductivity/ temperature CS/TS-3			
CDI-LX concentrate outlet pressure- PS/PT-6 (bar)			
CDI-LX product water pressure- PS/PT-7 (bar)			
Pure water recycle temperature TS/TT-5 (°C)			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.9 Filter Integrity Test

9.9.1 Objective

To verify that installed filters have been integrity tested, and that certification remains valid within the period set forth for operational use.

9.9.2 Method

Review filter integrity test documentation for filters listed in section 9.9.4.

9.9.3 Acceptance Criteria

All filters have been issued is valid for the period of operational use.

9.9.4 Results

Filter Installation location/description and Filter Tag No	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
FLT 1	Integrity test should comply			

Comments:

Reviewed by		Date	

9.10 Operator Interface and Screen Graphics Testing

9.10.1 Objective

To verify the operation of all push buttons, touch buttons, switches and screen graphics associated with the Purified Water Generation and Distribution System.

9.10.2 Method

Verify that all push buttons touch buttons and switches and screen graphics operate as defined in the tables. Document the results of the test in the table below. Record the results in section 9.10.4 of this protocol.

Verify and mark-up a copy of the following operator screens and attach the copy to the protocol

- Main Menu
- Softener
- Feed water Tank
- RO unit
- Degasser
- CDI-LX
- Sanitisation Set up Screen
- Set point Screen #1
- Set point Screen #2
- Set point Screen #3
- Set point Screen #4
- Set point Screen #5
- PID Set-up Screen #1
- PID Set-up Screen #2

Append the marked up screen graphics printouts in appendix.

9.10.3 Acceptance Criteria

The push buttons touch buttons and switches operate as defined in the tables. The screen graphics appear as defined in the table.
The actual results meet the expected results as defined in the test table(s) provided.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.10.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Control panel:				
Alarm sounder reset: Generate an alarm and press the Alarm sounder reset	The Audible alarm silences, but raised alarm is still active.			
Reset Fatal alarm button: Generate an alarm and press the Reset Fatal alarm button when the alarm condition has been lifted.	The alarm is reset and the alarm disappears from the alarm status 'active alarms' screen.			
Display or print each of the screens containing critical data, from the system HMI. Verify the screens against those specified.	The screens printed or displayed from the system, accurately represent the screens specified by the vendor documentation			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.11 Valve Operational Test

9.11.1 Objective

To ensure that valves located at sample points throughout the purified water system operate correctly and can be accessed safely.

9.11.2 Method

Locate each valve listed in Section 9.11.4. Perform the test by manually opening and closing the valve. Verify that all valves can be accessed safely and that each valve can be fully opened and closed. Record results following testing in section 9.11.4.

9.11.3 Acceptance Criteria

Each valve can be accessed safely.
Each valve can be operated at full open and full closed positions.

9.11.4 Results

Valve Check	Expected Result	Valve Tag No	Actual Result	Acceptable [Y/N]	Initial / Date
Verify that each valve can be assessed safely. Verify that each valve operates and seals correctly.	Valve can be accessed safely. Valves operate and seal correctly.	SV-1			
		SV-2A			
		SV-2B			
		SV-3			
		SV-4			
		SV-5			
		SV-8			
		SV-9			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.12 Confirmation of Critical Parameter and Full Function Testing

9.12.1 Objective

To confirm that the critical parameter and full function of the Purified Water Generation System are as defined below:-

- Feed water Free Chlorine is not more than 0.02 ppm at Softener inlet
- Feed water pressure to RO (PS/PT-1)
- Feed water pressure to CDI-LX (PS/PT-3)
- Feed water temperature at Feed water tank (TS/TT-4) on unit service mode
- RO recovery is between 75 % and 77 %
- Permeat conductivity (CS/TS-2)
- Product water, to Purified water Storage tank, conductivity (CS/TS-3)
- Product water flow velocity at CDI-LX downstream
- Generation unit Capacity.

9.12.2 Method

Follow the test methods described in section 9.12.4 for various parameters under test.
Record the observation in 9.12.4 actual results column.
Attach supporting documents, as applicable, in the appendix.

9.12.3 Acceptance Criteria

The critical operational parameters and full function testing on the Purified Water Generation system has been identified and completed satisfactorily.

Unit shuts down when feed water pressure to RO unit ≥ 8 barg for more than 30 sec.
Unit shuts down when feed water pressure to CDI-LX unit ≥ 6 barg for more than 30 sec.
Unit shuts down when feed water tank water temperature ≥ 40 ° C.
Unit shuts down when Permeat conductivity at RO exit ≥ 1.0 µ S/cm @ 25 °C for more than 30sec.
Product 3 way diverter (V-44) recycles product water to feed tank TK-1 when Final water ≥ 1.3 µ S/cm.
Product water flow velocity at downstream of CDI-LX ≥1 m/sec.
Generation unit Capacity ≥ 4 m^3/hr

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.12.4 Results

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Feed water pressure to RO (PS/PT-1)				
Generation unit is in continuous generation mode. Record feed water pressure to RO unit (PS/PT-1)	Feed water pressure to RO unit is ≤ 7.5 bar (g).			
Simulate pressure monitored at PS/PT-1 to attain more than 25 bar (g).	"RO feed high-high pressure" alarm activates.			
	Feed water pump PU-1 stops.			
	Generation unit shuts down.			
Feed water pressure to CDI-LX (PS/PT-3)				
Generation unit is in continuous generation mode. Record feed water pressure to CDI-LX unit (PS/PT-3)	Feed water pressure to CDI-LX unit is less than ≤ 2.0 bar (g).			
Simulate pressure monitored at PS/PT-3 to attain more than 5 bar (g).	"CDI-LX feed pump high-high pressure" alarm activates.			
	CDI-LX unit shuts down.			
Feed water temperature at Feed water tank (TS/TT-4)				
Generation unit is in continuous generation mode. Record feed water temperature at Feed water tank (TS/TT-4)	Feed water temperature at Feed water tank (TS/TT-4) is less than or equal to 25 °C			
Simulate temperature monitored at TS/TT-4 to attain more than 40 °C.	"Feed water tank high-high temperature" alarm activates.			
	Generation unit shuts down.			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.12.4 Results (Contd…)

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Permeat conductivity (CS/TS-2)				
Generation unit is in continuous generation mode. Record Permeate conductivity (CS/TS-2)	Permeat conductivity (CS/TS-2) is less than or equal to 1.0 µ S/cm			
Simulate Permeat conductivity monitored at CS/TS-2to attain more than 1.0 µ S/cm.	"RO permeat conductivity high-high" alarm activates.			
	Generation unit shuts down.			

Equipment Operated by		Date	

Comments: **** Product 3 way diverter valve V-44 automatically recycles to TK-I for 1 minute in a cycle of 60 minutes feeding to Purified water storage tank.**

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.12.4 Results (Contd…)

Test Method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Generation unit Capacity				
Generation unit is in continuous generation mode and Purified water demand exists. Arrange to storage around 800 litres to 1000 litres in Purified water storage. Record the Purified water storage tank level/ water capacity at the start of the test. Record the Purified water storage tank level/ water capacity at the completion of 10 minutes of the test.	Tank level/storage at start of test: 100 %/mm/litres. Tank level/storage at end of test: 500 liters.			
Estimate the amount of Purified water generated and stored in 10 minutes continuous operation. Calculate the generation capacity for one hour continuous operation. Attach the calculation in the appendix.	Purified water generated in continuous operation is ≥ 4 m^3/hr			

Equipment Operated by		Date	

Comments: Note :-

Reviewed by		Date	

9.13 Loss of Utilities

9.13.1 Objective

To verify the loss of utilities supplies will not affect or damage the Purified Water Generation System and that the subsequent return of any failed utility does not pose a threat to the system, the system's operator and the product quality.

9.13.2 Method

- **Feed water supply to the Purified Water Generation System**
  Run the Purified Water Generation system in normal operation.
  Isolate the supply of feed water to the Purified Water Generation system. Record the system's reactions and any alarms generated in the result table below.
  Reinstate the supply of feed water to the Purified Water Generation system and record the systems reactions in the result table 9.15.4 as the system returns to normal operation
- **Compressed Air Supply to the Purified Water Generation System**
  Run the Purified Water Generation system in normal operation.
  Isolate the supply of compressed air to the Purified Water Generation system. Record the system's reactions and any alarms generated in the result table below.
  Reinstate the supply of compressed and record the systems reactions in the result table 9.15.4 as the system returns to normal operation

9.13.3 Acceptance Criteria

The Purified Water Generation system shall raise an alarm and revert to the scenario's listed in the results section below on the isolation of:

- Feed water supply
- Compressed air

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.13.4 Results

Test method	Expected Result	Actual Result	Acceptable [Y/N]	Initial / Date
Shut off the feed water supply to the Purified Water Generation system by closing valve V-1. Record the system's reactions in the actual result column.	<<enter softener response – any alarm?>>			
	Feed tank low level alarm LSL-1 activates			
	Feed pump PU-1 shuts down			
Restore feed water supply to the Purified Water Generation system by opening valve V-1. Record the system's reactions as the system returns to normal operation.	<<enter softener response – any alarm?>>			
	Feed tank low level alarm LSL-1 activates			
	Feed pump PU-1 shuts down.			
Turn off compressed air supply to the Purified Water Generation system by closing valve V-32. Record the system's reactions in the "actual result" column.	"Compressed air flow low" alarm activates.			
	All actuated valves fail-safe			
Restore compressed air supply to the Purified Water Generation system by opening valve V-32. Record the system's reactions as the system returns to normal operation.	"Compressed air flow low" alarm resets.			
	System reverts to normal status.			

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.14 Temperature Distribution during Hot Water Sanitisation

9.14.1 Objective

To verify that the temperature distribution in the Purified water Generation System are meeting the specified sanitisation time and temperature.

9.14.2 Method

Pre-calibrate the thermal data logging equipment and attach the pre-calibration report in appendix.
Position 10 thermocouples around the Purified water Generation System at the positions listed in the table below.
Attach each thermocouple to a clean smooth surface, on the outside of the pipe work in a drop of thermostatic paste. Fix the thermocouple with some autoclave tape. Insulate the thermocouple by placing a piece of Armaflex over the fixed thermocouple and make sure the Armaflex is tightly attached to the pipe work.
Obtain copies of the verified P&ID drawing of the Purified water Generation System and mark up the drawing with the selected locations for the thermocouples and attach the drawing in appendix.
Start the thermal data logging equipment and initiate Generation loop sanitisation sequence. Record the start and end times in the result section.
Stop the thermal data logging equipment and attach the printouts in appendix.
Repeat the above test two more times and complete the result section
Post-calibrate the thermal data logging equipment and attach the post-calibration report in appendix.
Attach all print outs from the system's chart recorder in appendix.

9.14.3 Acceptance Criteria

All test locations must show a minimum sanitisation temperature of 80°C± 1°C for a duration of at least 1 hour for 3 consecutive hot water sanitisation cycles.

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.14.4 Results

Thermocouple Number	Location Description	Installed (Y/N)	Initial / Date
1	Final water temperature near V-44/TS-3		
2	Product water return Feed water tank		
3	Tank top near the strainer connection		
4	Tank temperature near TS-4		
5	RO recycle line		
6	CDI –LX concentrate line		
7	Feed pump inlet		
8	RO outlet		

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

9.14.4 Results (Contd…)

Test Run	Expected Results	Actual Results	Acceptable [Y/N]	Initial / Date
1	All temperatures in the Purified Water Generation System have maintained a minimum temperature of 80°C± 3°C for at least 60 minutes during the first hot water sanitisation cycle.	Start time: ……. End time: …….		
2	All temperatures in the Purified Water Generation System have maintained a minimum temperature of 80°C± 3°C for at least 60 minutes during second the sanitisation cycle.	Start time: ……. End time: …….		
3	All temperatures in the Laboratory Purified Water System have maintained a minimum temperature of 80°C± 3°C for at least 60 minutes during the third hot water sanitisation cycle.	Start time: ……. End time: …….		

Equipment Operated by		Date	

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

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	SOP Verification		
9.2	Generation System Security Test		
9.3	Generation System Start-Up and Shutdown Test		
9.4	Operator Data Entry Test		
9.5	Generation System Functionality Test		
9.6	Generation System Alarm and Interlocks Test		
9.7	Generation System Emergency Shutdown Test		
9.8	Generation System Power Failure and Recovery Test		
9.9	Filter Integrity Test	N/A	Not Applicable
9.10	Operator interface and Screen Graphics Testing		
9.11	Valve Operational Test		
9.12	Confirmation of Critical parameter and full function testing		
9.13	Loss of utilities		
9.14	Temperature distribution during hot water sanitisation		

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

11. VARIANCE SHEET

Report any deviations from the acceptance criteria or exceptions from protocol instructions in the Record Sheet as described in SOP No:.....-" 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 EXCEPTIONS / DEVIATIONS = _____

Exception / Deviation No.	Exception / Deviation Title	Status

Comments:

Reviewed by		Date	

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

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.
- SOP No BQA)-017-"Handling of Deviations".
- SOP No BQA)-011-"Change Control Procedure".

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

13. LIST OF APPENDICES

Appendix No.	Document Title

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

14. SUMMARY

OPERATIONAL QUALIFICATION PROTOCOL FOR PURIFIED WATER GENERATION

15. APPROVALS

The following approvals signify that the OQ is complete and acceptable and that the system is ready for PQ Execution.

EXECUTED BY:

Organization	Name	Designation	Signature	Date

REVIEWED BY:

Organization	Name	Designation	Signature	Date

APPROVED BY:

Organization	Name	Designation	Signature	Date