# PERFORMANCE QUALIFICATION

# (Phase-II)

# PERFORMANCE QUALIFICATION (Phase - II)

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## 1.0 PROTOCOL APPROVAL:

Signing of this approval page of Protocol indicates agreement with the qualification approach described in this document. If modification to the qualification approach becomes necessary, an addendum shall be prepared and approved. The protocol cannot be used for execution unless approved by the following authorities.

This performance qualification protocol of Purified Water System has been reviewed and approved by the following authorities:

| FUNCTION | NAME | DEPARTMENT | SIGNATURE | DATE |
|---|---|---|---|---|
| PREPARED BY | | QUALITY ASSURANCE | | |
| REVIEWED BY | | PRODUCTION | | |
| REVIEWED BY | | ENGINEERING | | |
| REVIEWED BY | | QUALITY CONTROL | | |
| APPROVED BY | | QUALITY ASSURANCE | | |

# PERFORMANCE QUALIFICATION (Phase - II)

## 2.0 OVERVIEW:

### 2.1 OBJECTIVE:

The objective of developing and executing this protocol is to

- To establish and confirm that the generation and distribution system shall operate within specified operating ranges at phase – II validation.
- To develop and evaluate the system operation, sanitization and maintenance procedures.
- To verify that the water produced and delivered to the points of use consistently meets the required quality specifications and acceptance criteria.

### 2.2 PURPOSE:

The purpose of this protocol is to establish documentary evidence to ensure that the Purified water system Provides purified water of pre-determined quality consistently.

### 2.3 SCOPE:

The scope of this protocol is to verify the Purified water system for the following boundaries and establish the operating ranges and procedures.

- To ensure that purified water meets the pre-determined requirements.
- To confirm the appropriateness of critical parameters and the operating ranges.
- To establish reproducibility and reliability of the systems
- To establish Alert and Action levels
- To validate and establish sanitization and regeneration procedures

### 2.4 RESPONSIBILITY:

The following shall be responsible;

- Quality assurance officer/Executive – For Preparation of Protocol /Execution
- Execution team- For execution of protocol
- Engineering head – For execution support and review of protocol
- Production Head – For execution support and review of protocol
- Quality control head – For analysis of samples and review of protocol
- Quality Assurance Head – For adequacy and final approval

## 2.5 EXECUTION TEAM:

The satisfactory performance of the Purified water system shall be verified by executing the qualification studies described in this protocol. The successfully executed protocol document that the Purified water system is installed and satisfactorily operational. Execution team is responsible for the execution of performance qualification of Purified water system at phase-II validation, Execution team comprises of:

| DEPARTMENT | DESIGNATION | NAME | SIGNATURE | DATE |
|---|---|---|---|---|
| PRODUCTION | | | | |
| ENGINEERING | | | | |
| QUALITY CONTROL | | | | |
| QUALITY ASSURANCE | | | | |

## 3.0 GENERAL CONSIDERATION/PREREQUISITE:

3.1 Approved standard operating procedure of the system shall be available.

3.2 Approved analytical methods for testing the samples collected during the processing.

3.3 The installation and operational qualification of the system shall be successfully completed before the execution of the performance qualification.

3.5 The impact analysis of the system shall be recoded in the summary sheet.

3.6 All the deficiencies and discrepancies related to the system which affect the product quality and corrective action taken shall be recorded in the appropriate section of the protocol.

3.7 The analytical test results and other reports related with the system shall be attached with the performance qualification of the system and finally verified.

## 4.0 REQUALIFICATION CRITERIA:

The system shall be revalidated if

- There are any major changes, which affect the performance of the system.
- After major changes in the components of the system.

## 5.0 PERFORMANCE QUALIFICATION PROCEDURE:

### 5.1 Procedure:

The performance Qualification of purified water system shall be done in three phases. The purpose and sampling plan is described as below:

The initial phase (phase-one) typically begins only after successfully completion of operational qualification. After successfully completed first phase the water shall be used for the manufacturing Process.

**PHASE- I**

During this phase appropriate operating ranges shall be established. Sampling should be after each step in the treatment process and from each point of use. The in coming feed water shall also be tested to verify the compliance with the specifications. The detailed sampling plan is mentioned in the Protocol. At the end of this phase alert and action limits shall be established. This alert and action limits will be used during phase two and beyond.

**PHASE- II**

This phase is to demonstrate that the system consistently operates within predetermined operating ranges and delivers the water of the required quality (as specified) when operated in accordance with the SOPs. The sampling plan shall be same as phase-I.

**PHASE- III**

This phase will be continued for one year after completion of second phase to verify the extended performance of system procedures, quantity and quality of water despite possible seasonal variations of feed water.

At the end of this phase the performance qualification is considered as completed and on going monitoring will be established a continuous record of water quality.

## PERFORMANCE QUALIFICATION (Phase - II)

| PHASE | PRIMARY OBJECTIVES | TYPICAL DURATION |
|---|---|---|
| I | • Develop appropriate operating ranges<br>• Develop and finalize operating, cleaning, maintenance procedures and sanitization frequency.<br>• Demonstrate production and delivery of water of the required quality. | 21 consecutive Days |
| II | • Demonstrate consistent operation within established ranges.<br>• Demonstrate consistent production and delivery of water of the required quality. | 21 consecutive Days |
| III | • Demonstrate extended performance<br>• Ensure that potential seasonal variations of feed water are evaluated and treated | One year |

## 5.2 Second Phase Validation:

### 5.2.1 Objective:

The objective of this phase is to establish appropriate operating ranges and provide data for the development of cleaning and sanitization procedures, regeneration procedures and frequencies.

### 5.2.2 Procedure:

- The phase second Qualification shall be carried out for 21 consecutive days.
- The Purified water system will be will be Operate/Sanitized/maintained as per respective Standard Operating Procedures at frequencies recommended in phase I.
- Sample shall be collected and analyzed from all the specified points at a specified frequency as per protocol.
- Record the results of the validation phase of each sampling points in respective data sheets as per sampling plan describe in the protocol.
- After completion of the Phase – II validation all data / trend shall be reviewed and attached to this protocol.

### 5.2.3 Sampling points and sampling frequency:

The sampling points and their sampling frequencies are mentioned as below.

| Sampling point No. | Sampling points Description | Testing Parameter | Frequency |
|---|---|---|---|
| SP -1C | Before ADS Dosing system | As per soft water specification | Daily |
| SP -2C | After ADS dosing system | As per soft water specification | Daily |
| SP -3C | After pH dosing system | As per soft water specification | Daily |
| SP -4C | After cartridge filter (CF-201) | As per soft water specification | Daily |
| SP -5C | After cartridge filter (CF-202) | As per soft water specification | Daily |
| SP -6C | Permeate line of ROH-201 | As per RO water specification | Daily |
| SP -7C | Permeate line of ROH-202 | As per RO water specification | Daily |
| SP -8C | Permeate header of RO pass I | As per RO water specification | Daily |
| SP -9C | Permeate line of ROH-203 | As per RO water specification | Daily |
| SP -10C | After cartridge filter (CF-203) | As per RO water specification | Daily |
| SP -11C | Permeate line of EDI-201 | As per Purified water specification | Daily |
| SP -12C | Feed line of post UF system | As per Purified water specification | Daily |
| SP -13C | Outlet of post UF system | As per Purified water specification | Daily |
| SP -14C | Outlet of PW storage tank | As per Purified water specification | Daily |
| SP-15C | Before UV | As per Purified water specification | Daily |
| SP-16C | After UV | As per Purified water specification | Daily |
| SP-17C | Roll compactor VII (second floor) | As per Purified water specification | Daily |
| SP-18C | IPQC (Second floor) | As per Purified water specification | Daily |
| SP-19C | Wash room (second floor) | As per Purified water specification | Daily |
| SP-20C | Sifting & milling V (Second floor) | As per Purified water specification | Daily |
| SP-21C | Sifting & milling VI (Second floor) | As per Purified water specification | Daily |
| SP-22C | PW tank of bin washing m/c (Second floor service area) | As per Purified water specification | Daily |
| SP-23C | Wash room store area (second floor) | As per Purified water specification | Daily |
| SP-24C | Janitor room store area (third floor) | As per Purified water specification | Daily |
| SP-25C | Janitor room store area (second floor) | As per Purified water specification | Daily |
| SP-26C | Granulation XII (Second floor) | As per Purified water specification | Daily |
| SP-27C | Granulation XI (Second floor) | As per Purified water specification | Daily |
| SP-28C | Granulation X (Second floor) | As per Purified water specification | Daily |

## PERFORMANCE QUALIFICATION (Phase - II)

| Sampling point No. | Sampling points Description | Testing Parameter | Frequency |
|---|---|---|---|
| SP-29C | IPQC (ground floor) | As per Purified water specification | Daily |
| SP-30C | IPQC (first floor) | As per Purified water specification | Daily |
| SP-31C | Auto-coater XIII (first floor) | As per Purified water specification | Daily |
| SP-32C | Auto-coater XIV (first floor) | As per Purified water specification | Daily |
| SP-33C | Auto-coater XV CIP system (first floor service area) | As per Purified water specification | Daily |
| SP-34C | Janitor room (ground floor) | As per Purified water specification | Daily |
| SP-35C | Auto-coater XV (first floor) | As per Purified water specification | Daily |
| SP-36C | Solution preparation IV (first floor) | As per Purified water specification | Daily |
| SP-37C | Janitor room store area (first floor) | As per Purified water specification | Daily |
| SP-38C | Wash room bin washing area (first floor) | As per Purified water specification | Daily |
| SP-39C | Solution preparation V (first floor) | As per Purified water specification | Daily |
| SP-40C | Wash area (ground floor) | As per Purified water specification | Daily |
| SP-41C | Janitor room (first floor) | As per Purified water specification | Daily |
| SP-42C | Return Loop | As per Purified water specification | Daily |

## 5.3 Acceptance criteria:

Water, which is collected from different locations from distribution system, shall meet the specified acceptance limits mentioned in given below tables.

### 5.3.1 Acceptance criteria for Soft water

| S.No. | Test | Specification |
|---|---|---|
| 1. | Description | Clear, color less and odorless liquid |
| 2. | Total Hardness(ppm) # | Not more than 10 |
| 3. | Free Chlorine (ppm) $ | Not more than 0.2 |
| 4. | Total Aerobic microbial counts** cfu/ml | Not more than 250 |
| 5. | **Test for specified microorganism**** | |
| a. | *Escherichia coli* | Should be Absent |
| b. | *Staphylococcus aureus* | Should be Absent |
| c. | *Pseudomonas aeroginosa* | Should be Absent |
| d. | *Salmonella species* | Should be Absent |

#: Total hardness test shall be applicable for after softener only.

$: Test of free chlorine shall be done after SMBS dosing only.

**: Microbiological analysis shall not perform after SMBS dosing after pH correction.

### 5.3.2 Acceptance criteria for RO water

| S.No. | Test | Specification |
|---|---|---|
| 1. | Description | Clear color less and odorless liquid |
| 2. | pH | 5.0 to 7.0 |
| 3. | Total aerobic microbial Counts (cfu/ml) | NMT 250 |
| 4. | **Test for specified microorganisms** | |
| a. | *Escherichia coli* | Should be Absent |
| b. | *Staphylococcus aureus* | Should be Absent |
| c. | *Pseudomonas aeroginosa* | Should be Absent |
| d. | *Salmonella species* | Should be Absent |

**5.3.3 Acceptance criteria for Purified water:**

| S.No. | Test | Specification |
|---|---|---|
| 1. | Description | Clear color less and odorless liquid |
| 2. | pH | Between 5.0 to 7.0 |
| 3. | Conductivity at 25°C (µS/cm ) | 1. *For online monitoring<br>Not more than 1.2 µS/cm<br>2. #For offline monitoring<br>Stage 1: NMT 1.3 µS/cm<br>Stage 2: NMT 2.1 µS/cm<br>Stage 3: NMT 4.7 µS/cm |
| 4. | Acidity/ Alkalinity | For acidity, the resulting solution should not be red<br>For alkalinity, the resulting solution should not be blue. |
| 5. | Nitrate (ppm) | Not more than 0.2 |
| 6. | @Nitrite content (µg/ml) (by HPLC) | Not more than 0.1 |
| 7. | Heavy Metals (ppm) | Not more than 0.1 |
| 8. | *Total Organic Carbon (ppb)<br>(Alternative Test)<br>**Oxidisable Substances | NMT 500ppb<br>The solution should remain faintly pink |
| 9. | Total Viable Count (cfu/ml) | NMT 100 |
| 10. | **Test for specified microorganism** | |
| A.. | *Escherichia coli* | Should be Absent |
| B.. | *Stapylococcus aureus* | Should be Absent |
| C.. | *Pseudomonas aeroginosa* | Should be Absent |
| D. | *Salmonella species* | Should be Absent |
| E. | *Burkholderia cepacia* | Should be Absent |

* Online measurement.

** In case of instrument breakdown, perform oxidisable substance in place TOC.

# In Case of instrument breakdown, perform online conductivity measurement.

@ shall be performed only on return loop point.

## 6.0 ACTION TO BE TAKEN IN CASE OF FAILURE:

In case of any failure investigation shall be carried out and rectification or modification shall be done if required. In such case the sampling and test period of Phase II study shall be extended for further 21 days. During this period production activity shall be carried out.

Alert and action limit for Microbiology test shall be as per first phase validation.

## 7.0 DEFICIENCY AND CORRECTIVE ACTION (S) REPORT (S):

Following deficiency was identified and corrective actions taken in consultation with the validation team.

**Description of deficiency:**

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**Corrective action(s) taken:** ----------

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**Reviewed By:**

**Date**

## 8.0 ANNEXURE (S):

| S.No. | Annexure No. | Title of Annexure |
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## 9.0 PERFORMANCE QUALIFICATION FINAL REPORT:

### 9.1 SUMMARY ----------

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### 9.2 CONCLUSION: ----------

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**Reviewed By:**

**Date**

## 9.3 FINAL REPORT APPROVAL:

It has been verified that all tests required by this report are completed, reconciled and attached to this protocol or included in the qualification summary report. Verified that all amendments and discrepancies are documented, approved and attached to this protocol (If applicable).

Signature in the block below indicates that all items in this qualification report of Purified Water System (phase – II) has been reviewed and found to be acceptable and that all variations or discrepancies have been satisfactorily resolved.

| NAME | DESIGNATION | DEPARTMENT | SIGNATURE | DATE |
|---|---|---|---|---|
| | | PRODUCTION | | |
| | | ENGINEERING | | |
| | | QUALITY CONTROL | | |
| | | QUALITY ASSURANCE | | |