



PHARMA DEVILS

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QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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1.0 PROTOCOL PRE 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:

SERIAL No.	ITEM DESCRIPTION	PAGE No.
1.0	PROTOCOL APPROVAL	3
2.0	OVERVIEW:	4
2.1	Objective	4
2.2	Purpose	4
2.3	Scope	4
2.4	Responsibility	5
2.5	Execution Team	5
3.0	GENERAL CONSIDERATION/PREREQUISITE	6
4.0	REQUALIFICATION CRITERIA	6
5.0	PERFORMANCE QUALIFICATION PROCEDURE	7
5.1	Procedure	7
5.2	Third phase validation	9
5.3	Acceptance criteria	12
6.0	ACTION TO BE TAKEN IN CASE OF FAILURE	15
7.0	DEFICIENCY AND CORRECTIVE ACTIONS	16
8.0	ANNEXURE (S)	17
9.0	PERFORMANCE QUALIFICATION FINAL REPORT	18
9.1	Summary	18
9.2	Conclusion	18
9.3	Final report approval	19



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

2.0 OVERVIEW:

2.1 OBJECTIVE:

The objective of developing and executing this protocol is:

- To establish and confirm that the generation and distribution system shall operate within specified operating ranges at phase – III validation.
- To demonstrate reliable performance over an extended period and to evaluate the impact of seasonal variations over an extended period.
- 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 validate and establish sanitization and regeneration procedures
- To evaluate the effects of seasonal changes on quality of purified water.

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



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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-III validation, Execution team comprises of:

DEPARTMENT	DESIGNATION	NAME	SIGNATURE	DATE
PRODUCTION				
ENGINEERING				
QUALITY CONTROL				
QUALITY ASSURANCE				



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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 phase – I and Phase - II of the system shall be successfully completed before the execution of the phase – III performance qualification.
- 3.4 The impact analysis of the system shall be recoded in the summary sheet.
- 3.5 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.
- 3.6 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 addition, deletion or replacement of components of the system.



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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 incoming 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 – II and phase - III.

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 SOP's. 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 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.



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

PHASE	PRIMARY OBJECTIVES	DURATION
I	<ul style="list-style-type: none">• Develop appropriate operating ranges• Develop and finalize operating, cleaning, maintenance procedures and sanitization frequency.• Demonstrate production and delivery of water of the required quality.	21 Working Days
II	<ul style="list-style-type: none">• Demonstrate consistent operation within established ranges.• Demonstrate consistent production and delivery of water of the required quality.	21 Working Days
III	<ul style="list-style-type: none">• Demonstrate extended performance and quality of water.• Ensure that potential seasonal variations of feed water are evaluated and treated.• To verify the impact of seasonal variations on alert and action limit.	One year



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

5.2 Third phase validation:

5.2.1 Objective:

The objective of this phase is to demonstrate reliable performance over an extended period and to evaluate the impact of seasonal variations over an extended period.

5.2.2 Procedure:

- Third phase Qualification shall be carried out for one year.
- The Purified Water system shall be Operated/Regenerated/Sanitized as per respective Standard Operating Procedures.
- 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 – III validation of all data / trend shall be reviewed and attached to this protocol.



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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	Weekly
SP -2C	After ADS dosing system	As per soft water specification	Weekly
SP -3C	After pH dosing system	As per soft water specification	Weekly
SP -4C	After cartridge filter (CF-201)	As per soft water specification	Weekly
SP -5C	After cartridge filter (CF-202)	As per soft water specification	Weekly
SP -6C	Permeate line of ROH-201	As per RO water specification	Weekly
SP -7C	Permeate line of ROH-202	As per RO water specification	Weekly
SP -8C	Permeate header of RO pass I	As per RO water specification	Weekly
SP -9C	Permeate line of ROH-203	As per RO water specification	Weekly
SP -10C	After cartridge filter (CF-203)	As per RO water specification	Weekly
SP -11C	Permeate line of EDI-201	As per Purified water specification	Weekly
SP -12C	Feed line of post UF system	As per Purified water specification	Weekly
SP -13C	Outlet of post UF system	As per Purified water specification	Weekly
SP -14C	Outlet of PW storage tank	As per Purified water specification	Daily
SP-15C	Before UV	As per Purified water specification	Weekly
SP-16C	After UV	As per Purified water specification	Weekly
SP-17C	Roll compactor VII (second floor)	As per Purified water specification	Weekly
SP-18C	IPQC (Second floor)	As per Purified water specification	Weekly
SP-19C	Wash room (second floor)	As per Purified water specification	Weekly
SP-20C	Sifting & milling V (Second floor)	As per Purified water specification	Weekly
SP-21C	Sifting & milling VI (Second floor)	As per Purified water specification	Weekly
SP-22C	PW tank of bin washing m/c (Second floor service area)	As per Purified water specification	Weekly
SP-23C	Wash room store area (second floor)	As per Purified water specification	Weekly
SP-24C	Janitor room store area (third floor)	As per Purified water specification	Weekly
SP-25C	Janitor room store area (second floor)	As per Purified water specification	Weekly
SP-26C	Granulation XII (Second floor)	As per Purified water specification	Weekly
SP-27C	Granulation XI (Second floor)	As per Purified water specification	Weekly
SP-28C	Granulation X (Second floor)	As per Purified water specification	Weekly



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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.	<i>Escherichia coli</i> ,	Should be Absent
b.	<i>Staphylococcus aureus</i>	Should be Absent
c.	<i>Pseudomonas aeruginosa</i>	Should be Absent
d.	<i>Salmonella species</i>	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.	<i>Escherichia coli</i> ,	Should be Absent
b.	<i>Staphylococcus aureus</i>	Should be Absent
c.	<i>Pseudomonas aeruginosa</i>	Should be Absent
d.	<i>Salmonella species</i>	Should be Absent



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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 Not more than 1.2 µS/cm 2. #For offline monitoring Stage 1: NMT 1.3 µS/cm Stage 2: NMT 2.1 µS/cm Stage 3: NMT 4.7 µS/cm
4.	Acidity/ Alkalinity	For acidity, the resulting solution should not be red 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) (Alternative Test) **Oxidisable Substances	NMT 500ppb The solution should remain faintly pink
9.	Total Viable Count (cfu/ml)	NMT 100
10.	Test for specified microorganism	
A..	<i>Escherichia coli</i> ,	Should be Absent
B..	<i>Stapylococcus aureus</i>	Should be Absent
C.	<i>Pseudomonas aeroginosa</i>	Should be Absent
D.	<i>Salmonella species</i>	Should be Absent
E.	<i>Burkholderia cepacia</i>	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.



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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 III study shall be extended for further 3 weeks. During this period production activity shall be carried out.

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



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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:

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

Reviewed By:

Date



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

9.0 PERFORMANCE QUALIFICATION FINAL REPORT:

9.1 SUMMARY:-----

9.2 CONCLUSION:-----

Reviewed By:

Date



PHARMA DEVILS

PHARMA DEVILS
QUALITY ASSURANCE DEPARTMENT

PROTOCOL No.:

PERFORMANCE QUALIFICATION (Phase-III)

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 – III) 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		