



**PHARMA DEVILS**

QUALITY ASSURANCE DEPARTMENT

Document No.:

Revision No.:

**WATER SYSTEM  
VALIDATION MASTER PLAN**

Effective Date:

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**WATER SYSTEM  
VALIDATION MASTER  
PLAN**



**PHARMA DEVILS**



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### APPROVALS:

Signatures in this page indicate that this document has been Initiated, Reviewed, Approved and Authorized by the concerned personnel's. It shall be signed and dated as shown below.

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**1.0 INTRODUCTION:**

.....is a professionally engaged Pharmaceutical company, manufacturing various dosage forms and has emerged as a reputed pharmaceutical formulation manufacturer. Water Manual is related to manufacturing facility of ..... The site manufactures Tablets, Capsules, Liquid Injectable, Dry Syrup & Dry Injectable in General category.

**2.0 OBJECTIVE:**

The main objective of this manual is to provide the complete details related to raw water, purified water and water for injection for cleaning of equipment and manufacturing of Tablets, Capsules, Liquid Injectable, Dry Syrup & Dry Injectable in General category.

**3.0 SCOPE:**

The scope of this document is for the Water Generation & and Distribution at .....

**4.0 RESPONSIBILITY:**

In order to achieve the objective for the collection of complete details of raw water, purified water and water for injection, following shall be the responsible.

Department	Responsibility
<b>Quality Assurance</b>	<ul style="list-style-type: none"> <li>• Shall Prepare &amp; Review the manual.</li> <li>• Collection and attachment of all required documents with manual.</li> </ul>
<b>Quality Control</b>	<ul style="list-style-type: none"> <li>• Review the manual for correctness, completeness and technical excellence.</li> <li>• Support to QA for collection and attachment of QC related documents.</li> </ul>
<b>Engineering</b>	<ul style="list-style-type: none"> <li>• Review the manual for correctness, completeness and technical excellence.</li> <li>• Support to QA for collection and attachment of utility related documents.</li> </ul>
<b>Production</b>	<ul style="list-style-type: none"> <li>• Review the manual for correctness, completeness and technical excellence.</li> <li>• Support to QA for collection and attachment of production related documents.</li> </ul>



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**5.0 WATER MANUAL POLICY:**

**WATER MANULA POLICY**

“Water” forms the most important ingredient in the pharmaceutical manufacturing process and also finds a major use in cleaning of equipment before and after processing. However due to its tendency to give way to microbiological proliferation during storage and distribution, it becomes a “critical” ingredient as well. Thus emphasis is given on water system maintenance and further checks are required during storage, distribution and use.

The document provide a detailed view into the technical aspects, testing, validation and reporting pattern for “water”. It further reinforces the company’s commitment to maintain GMP.

The plant is to provide the total amount of Purified water & water for Injection required for the Formulation Plant of ..... plant produces water suitable for pharmaceutical use, i.e. so-called Purified water & water for Injection quality as per WHO specifications which must quality pH, Calcium & Magnesium, Heavy metals, Chloride, Nitrate, Sulphate, TOC, Conductivity, Microbial counts, Bacterial Endotoxin Test etc. by means of new Generation Plant.

The plant must comply with the requirements of the pharmacopoeia and the cGMP regulations as well as with WHO inspection regulations for plants producing Purified water & water for Injection.



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**6.0 TYPE OF WATER AND ITS INTENDED USE:**

**RAW WATER**

- As input for making Treated water
- For cleaning purpose in change rooms, Toilets, Drinking water (By Used by RO).

**TREATED WATER–**

- For component cleaning Manufacturing area. (It consists of Pretreatment upto outlet of RO-II.)
- For equipment cleaning & Boiler feed water.(It consists of Pretreatment upto softener Plant).

**PURIFIED WATER –**

- For the preparation of batch of Tablets & capsules.
- For final rinsing of washed components & equipment used for the manufacturing of Tablets & Capsules.

**WATER FOR INJECTION–**

- For the preparation of batch of Injections.
- For final rinsing of washed components & equipment used for the manufacturing of Liquid Injectable & Dry Injectable in General & Cephalosporin category.
- For final rinsing of primary packing materials used for the packing of Liquid Injectable, Dry Injectable in General & Cephalosporin category.

**7.0 PURIFIED WATER & WATER FOR INJECTION PLANT:**

Source of water supply is from 2 bore wells with depth 160 feet. Freshly drawn water from the bore well is collected into underground RCC tank (60KL) by pump with online dosing of 2-3ppm chlorine with the solution of Sodium Hypochlorite. The water then passed through multigrade filter to remove suspended matter if any. Raw water then transferred through softener to reduce the hardness to below 5 ppm. The soft water is then stored in soft water storage tank (capacity 5KL).The water then treated with Sodium Metabisulphite solution with a online dosing to oxidize excess of chlorine and monitored through ORP meter oxidation up to less than 400 mv. The ORP meter (oxidation Reduction Potential) is installed in the feed line to RO to check for chlorine free water. Chlorine free water is supplied along with anti scaling dosing to RO- 1 & RO- 2 then to Mixed bed & UV for making Purified Water. The capacity of the RO System is 3000 Ltr./hr. To check the conductivity, the conductivity sensor is installed in the supply and return loop of the distribution system. The conductivity of the purified water is continuously monitored through Programmable Logic Control panel and in the event of variation in the conductivity; it automatically drains the water instead of going into the storage tanks with help of online dumping valve. Finally conductivity passed purified water is stored in Purified water storage tank. The capacity of the Purified water storage SS316L tank is 3KL. This water system is installed in general block and distributed through a closed recirculation loop inside the plant for appropriate user points at ambient temperature. One point of loop is going to cephalosporin block with proper slope and controlled manner to fill the purified water storage tank of cephalosporin block. Purified water storage tank capacity is also 3KL for cephalosporin block. Stored Purified water recirculated in closed loop and distributed through loop with appropriate user point at



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ambient temperature in cephalosporin block separately. The conductivity monitoring sensor is installed at the return loop. The conductivity of the purified water is continuously monitored through Programmable Logic Control panel and in the event of variation in the conductivity; it automatically drains the water instead of going into the storage tanks with help of online dumping valve.

Purified water is used to produce Water For Injection. To get high quality Water For Injection, installed 1 Multi Column Distillation Plant at general block. The capacity of the Multi Column Distillation Plant is 1000Ltr./hr. This unit is fully automatic and Micro processor based. Water for injection stored in water for injection tank (Capacity 3KL). This water for injection system is installed in general block and distributed through a closed recirculation loop inside the plant for appropriate user points at temperature 80-90°C. One point of loop is going to cephalosporin block with proper slope and controlled manner to fill the water for injection storage tank of cephalosporin block. Water for injection storage tank capacity is 1KL for cephalosporin block. Stored water for injection recirculated in closed loop and distributed through loop with appropriate user point at temperature 80-90°C in cephalosporin block separately.

Vent filters provided to Purified water storage tanks and Water for Injection storage tanks. Storage tank temperatures are continuously monitored through temperature thermograph. Fresh WFI is always taken for final rinsing of Vials/Ampoules and rubber stoppers for dry injections.

Sanitization of water for injection plant, storage tank and loop system to be done as per frequency mentioned in SOP. Sanitization functions of the system available in the plant on auto mode as well as on manual mode.

**7.1 WATER SYSTEM BASIC DESIGN:**

**7.1.1 BORE WELL PUMP:** Bore well pump is transfer water from bore well to underground raw water storage Tank.

**7.1.2 ON LINE NaOCl DOSING SYSTEM:** Sodium Hypo chloride is dosed to reduce the bacteria, microorganism of Bore well water stored in underground raw water storage tank.

**7.1.3 MULTI SAND FILTER:** Multi Sand filtration is considered for removal of suspended solids and turbidity in the water. Chlorinated water helps Sand filter less prone for microbial growth.

**7.1.4 UNDER GROUND RAW WATER STORAGE TANK:** Chlorinated Raw water is stored in underground raw water storage tank.

**7.1.5 RAW WATER TRANSFER PUMP:** Raw water transfer pump transfers water from underground raw water storage tank to Softner system.

**7.1.6 SOFTENER:** Softener is provided for to reduce the hardness of water using the principle of ion exchange. The substances in the incoming water which causes hardness (calcium & magnesium ions) are replaced by sodium ions.

**7.1.7 SOFT WATER STORAGE TANK:** soft water is stored in soft water storage tank in water system.

**7.1.8 SOFT WATER TRANSFER PUMP:** Soft water transfer pump transfers water from soft water storage tank to RO system.

**7.1.9 SMBS DOSING SYSTEM:** The de chlorination is carried out with the help of Sodium Meta Bi-Sulphite, which removes the presence of chlorine in RO feed water.

**7.1.10 ANTISCALENT:** Dosage of antiscalent solution into outlet water of Softener to control the scaling of RO membrane due to presence silica in raw water.

**7.1.11 RO LOW PRESSURE PUMP:** RO Low Pressure pump transfers soft water from soft water storage tank passing through to 5 micron cartridge filter to RO -1 for infeed.



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**7.1.12 BEFORE REVERSE OSMOSIS 5 MICRON CARTRIDGE FILTER:** The soft water passed through 5 micron cartridge filter which remove the presence of dissolve solids & particles.

**7.1.13 RO HIGH PRESSURE PUMP:** RO high pressure pump transfers water from RO-1 to RO-2.

**7.1.14 RO SYSTEM:** The water from the Soft water storage tank transferred to Reverse Osmosis System. RO unit works on principle of reverses osmosis which separates water from dissolve salt in solution by filtering through a semi permeable membrane. The concentrate form of reverse osmosis system, which carries a high salinity, goes to the drain.

**7.1.15 MIXED BED SYSTEM:** Mixed Bed system contributes for the removal of dissolved solids. Single column mixed bed system, in which the Cation and anion resins are mixed to obtain the desired quality of Purified water by using the same principle as ion exchange resin.

**7.1.16 ULTRA VIOLET DISINFECTANT SYSTEM-1:** Now the Purified water is passed though the Ultra Violet Disinfectant system which disinfects the water & kills the bacteria. This water is stored in Purified water storage tank.

**7.1.17 PURIFIED WATER STORAGE TANK:** The Purified water from the Purified storage tank in 3000 Liters Cylindrical, Vertical, Jacketed storage tank. From the storage tank the water is supplied to various user point. The water level in the purified water tank shall be controlled by the help of level controller, which performs necessary actions of high levels to low level to maintain sufficient water level in the tank, and avoids dry running of purified water distribution pump.

**7.1.18 WATER FOR INJECTION FUNCTIONAL DESCRIPTION:**

The WFI system consists of MCDP plant & WFI Storage & Distribution System.

The Water for Injection is generated by Multi Column Distillation Plant, this water is stored in 3000 Liters WFI Storage tank and distributed to all user points by means recirculation pump and distribution loop.

The WFI Storage and Distribution system designed for continuous recirculation, if there is shutdown or system fails. System sanitization has to be done during restarting of the system.

This Generation, Storage and distribution system is controlled by centralized control panel, critical parameters viz. Tank Level, Return line Conductivity, Return line Temperature and Return line Flow will be continuously monitored.

The Distribution loop is pressurized and continuously under recirculation. The minimum velocity to be maintained in the return line during consumption is 1.2 m/sec.

System to be passivation and sanitized during start-up. Sanitization procedure manually.





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**8.0 WATER SOURCE, PRETREATMENT, POST TREATMENT, STORAGE SYSTEM, OPERATIONAL, CLEANING & SANITIZATION PROCEDURE.**

**8.1 RAW WATER SOURCES:**

<b>BORE WELL PUMP:</b>		
<b>BOREWELL</b>	<b>I</b>	<b>Stand by II</b>
Bore size	8'' Dia	8'' Dia
Bore depth	160 Feet.	160 Feet.
<b>BORE WELL PUMP</b>		
Make	Pluga	Pluga
Type	Vertical Multistage	Vertical Multistage
Flow rate	10.0 m3/hr	5.0 m3/hr
Discharge Head	35 Meter	35 Meter
Volt	415 V	415 V
Power	10 HP	5 HP
Quantity	One	One

<b>CHLORINE DOSING PUMP:</b>	
Type	Horizontal
Capacity	6 LPH

**ON LINE NaOCl DOSING SYSTEM:** Sodium Hypo chloride is dosed to reduce the bacteria, microorganism of Bore well water stored in underground raw water storage tank.

**MULTI SAND FILTER:** Multi Sand filtration is considered for removal of suspended solids and turbidity in the water. Chlorinated water helps Sand filter less prone for microbial growth.

<b>MULTI SAND FILTER:</b>	
Cartridge Type	Sand
Micron Rating	25 Micron
Housing MOC	FRP
Size of the filter vessel	24'' diameter x 65'' height.
Softner vessels qty.	2 No's

**OPERATION, CLEANING & SANITIZATION OF SAND FILTER:**

**PROCEDURE:** Start the back wash of sand filter after a 8 hour of normal running of sand filter Start the bore well pump and flush the water for 20 minute in Back wash mode of sand filter. Change the position of multiport valve from backwash to Rinse mode. Start the bore well pump and run the sand filter for 10 minute at Rinse mode. Stop the bore well pump from starter panel after rinsing and change the position of multiport valve from rinse mode to service mode. Take 98 liter raw water in HDPE tank and install the circulation pump in the tank. Add the 2 liter H<sub>2</sub>O<sub>2</sub> (Hydrogen peroxide) with above 98 liter water and mix properly. Open the inlet & outlet valve of sand filter. Start the circulation pump from electrical panel board. Keep the continuation of circulation for 45 minute. After 45 minute of circulation of solution, switch OFF the circulation pump from panel board. Change the position of multiport valve from service to rinse mode. Close the solution tank inlet valve. Open the bore well outlet valve. Start the bore well



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pump for 20 minute at Rinse Position of Multi Port Valve and drain the water. Change the position of multiport valve rinse to services mode. Starts the bore well pumps to fill the underground raw storage tank.

**STORAGE TANKS:**

<b>UNDER GROUND RAW WATER STORAGE TANK:</b>	
Make	Internal finish with Acid proof tiles with smooth finish & epoxy grove filled.
Type	RCC
Quantity	Two
Capacity	30 KL each tank

**CLEANING & SANITIZATION OF RAW WATER STORAGE TANKS:**

(Frequency: Once in 3 months).

**PROCEDURE:** Pump out or drain the existing filled water from the storage tank and ensure that the tank is empty for cleaning. Clean the walls and floor of the tank with help of wire brush and cleaned clothes. Take 20 liter fresh water in a bucket and add 8 Kg sodium hypochlorite and mix properly. Apply the above solution on the wall surface and floor of the tank and hold for 30 minutes. After 30 Minutes wash the walls and floor of tank with fresh water. After proper washing & flushing, collect the fresh water in storage tank by switch ON the bore well pumps.

**8.2 TREATED WATER**

**SOURCE:**

The water generated by passing raw water through the water pretreatment system ( sand filtration & NaOCl Dosing ) is called Treated water.

**STORAGE TANKS:**

<b>SOFT WATER STORAGE TANK</b>	
Make	
Capacity	5 KL
MOC	HDPE
Operating temperature	Ambient
Quantity	Two

**CLEANING & SANITIZATION OF SOFT WATER STORAGE TANKS**

(Frequency: Once in One months)

**PROCEDURE:** Clean the walls and floor of tank with help of nylon brush and clean clothes. Flush the tank with fresh water for 10 minutes and drain the wash water from the tank. Take 20 liter fresh water in a bucket and add 8 Kg sodium hypochlorite and mix properly. Apply the above solution on the wall surface and floor of the tank and hold for 30 minutes. After 30 Minutes, wash the walls and floor of tank with fresh water. After proper washing & flushing, collect the fresh soft water in storage tank by softener.

**SOFTENER:** Softener is provided for to reduce the hardness of water using the principle of ion exchange.



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The substances in the incoming water which causes hardness (calcium & magnesium ions) are replaced by sodium ions.

SOFTENER	
Type	Vartical
Capacity	Liter 700
MOC (over head)	FRP
Size of the filter vessel	24'' Diameter x 65''Height.
Softener vessel qty.	2 No's

**OPERATION, REGENERATION & SANITIZATION OF SOFTENER**

**PROCEDURE:** After rinsing of softener for 5 minutes check the hardness of soft water with help of hardness test kit it should be less than 5 PPM.. If it more than 5PPM start the regeneration of softener as per procedure of regeneration of softener plant.

Make the regeneration solution of Softener by adding the 30 kg salt in 100 Liters of fresh water in the soft water regeneration tank. Check the hardness of water, it should be less than 5 PPM, if it is not in the limit, keep continuation of rinsing of water till the hardness comes in the limit. After getting the permissible result, fill the soft water storage tank up to high level of soft water storage tank.

**Cleaning & Sanitization Procedure of Softener (frequency-Monthly):**

Take the 98 Liters soft water in a sanitization solution tank and mix 2 Liter H<sub>2</sub>O<sub>2</sub> and install a circulation pump. Open the inlet valve of Softener and connect with discharge of circulation pump with help of PVC flexible pipe. Open the outlet valve of Softener and connect the flexible pipe from out let of softener and dip in sanitization solution tank. Start the circulation pump from panel board for 40 minutes. After 40 minutes, stop the circulation pump. Remove the circulation pump from softener and connect the line of softener as per previous position. Start the raw water transfer pump from electrical starter panel of softener plant. Change the position of multiport valve from service mode to Rinse mode. Rinse the softener for 30 minutes. Check the hardness of water, it should be less than 5 PPM, if it is not in the limit, keep continuation of rinsing of water till the hardness comes in the limit.

**SMBS DOSING SYSTEM:** The de chlorination is carried out with the help of Sodium Meta Bi-Sulphite, which removes the presence of chlorine in RO feed water.

**PROCEDURE (Frequency: after complete use of solution or idle condition of 48 hours)**

Before preparation of SMBS solution, clean the solution dosing tank by fresh water.

Take 50 litres fresh water in solution dosing tank. Add the 250 gram SMBS in tank and mix properly with help of Stainless steel Rod.

**SMBS DOSING PUMP:**

Capacity : 6.0 LPH

**ANTISCALENT:** Dosage of antiscalent solution into outlet water of Softener to control the scaling of RO membrane due to high amount of silica in raw water. Sodium hexametaphosphate (NaPO)<sub>6</sub> dosing is considered for this purpose.

**PROCEDURE: (After complete use of solution or not in use within 48 hours)**



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Before preparation of solution, clean the HDPE dosing tank by fresh water.  
Take 50 litres fresh water in solution preparation tank.  
Add the 150 gram Anti Scalant Chemical in tank and mix properly with help of S.S. Rod.  
If solution not comes in use within 48 hours drain the solution and prepare fresh solution as per above.

**ANTISCALENT DOSING PUMP:**

Capacity : 6.0 LPH

**BEFORE REVERSE OSMOSIS 5 MICRON CARTRIDGE FILTER:** The soft water passed through 5 micron cartridge filter which remove the presence of dissolve solids & particles.

<b>MICRON CARTRIDGE FILTER</b>	
Micron Rating	5μ
Cartridge MOC	Poly Propylidine
Cartridge Make	MDI
Housing MOC	PVC
Housing End Connection	Threaded End
Make	MDI
Size	• 18 Inch

**RO SYSTEM:** The water from the Soft water storage tank transferred to Reverse Osmosis System and RO water storage tank. RO unit works on principle of reverses osmosis which separates water from dissolve salt in solution by filtering through a semi permeable membrane. The concentrate form of reverse osmosis system, which carries a high salinity, goes to the drain.

<b>RO Membrane</b>	
Housing Size	3100mm Length,200mm Dia
	2100mm Length,200mm Dia
	2100mm Length,200mm Dia
	2100mm Length,200mm Dia
Type	CIP
MOC of the membrane	Poly Amide
Area of the membrane	Ro - Housing
Construction	SS316
End port	Flanch to Flanch
Maximum pressure	28 kg/cm <sup>2</sup>
Maximum operating temperature	25-40 kg/cm <sup>2</sup>
Sanitization temperature	Ambient
Operating pH range	4.0 to 9.0
Cleaning pH range	4.0 to 9.0
Maximum allowable SDI	4 PPM
Salt rejection	20%
Model no. of membrane	Make: Daw, Mode: BW30-365 IG
Quantity	09 Nos.



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**MIXED BED SYSTEM:** Mixed Bed system contributes for the removal of dissolved solids. Single column mixed bed system, in which the Cation and anion resins are mixed to obtain the desired quality of Purified water by using the same principle as ion exchange resin.

### REGENERATION OF MIX BED

#### PROCEDURE

**Action and Alert Limit:** When the conductivity of outlet of Mix Bed is goes up to  $1.0\mu\text{s}/\text{cm}$ , prepare for regeneration of mix bed.

When the conductivity of Mix bed outlet goes up to  $1.20\mu\text{s}/\text{cm}$  stop the RO system and start the regeneration of Mix Bed.

After completion of 12 hour in running mode after regeneration of Mix bed start the regeneration of Mix Bed

If idle condition of mix bed is more than 36 hours after regeneration start the regeneration.

#### Pre Start Up:

**Take 30 Liter R.O water in mix bed regeneration tank.**

**Add 6 Lit HCL of 33% concentration and make the HCL solution.**

**Take the 30 Lit R.O water in a mix bed regeneration tank.**

**Add 4 kg NaOH of 99% and make the NaOH solution.**

#### Start up:

##### Back wash mode :

For backwash open the valve No. 5,8 and 4 and Close the valve No. 1,2,3,6,7,9,10,11,12&13 .

Start the RO plant to feed the water in Mix Bed and done back wash of Mix Bed for 15minute .

Stop the R.O plant .

After completion of backwash of mix bed rinse the mix bed for 5 minute.

For rinsing of mix bed open the valve No 3, 5 & 7 and Close the valve No. 1,2,4,6,8,9,10,11,12,13.

After completion of rinsing of mix bed stop RO plant .

##### NaOH Injecting Mode :

For NaOH Injection open the valve No. 1,2,3,7 & 12 and Close the valve No. 4,6,8,9,10,11, & valve No.13

After complete injection of NaOH solution, close the solution injection valve No -12 and Switch off the RO plant.

Open the valve No. 3,5 & 7 and Close valve No. 1,2,4,6,8,9,10,11,12 & 13 for Rinse the mix bed .

##### HCl Injecting Mode:

For HCL Injection open the valve No. 1,2,6,11 & 12, Close the valve No. 3,4,5,7,8,9,10 & valve No.13

After complete injection of HCL solution, close the solution injection valve No -12 and Switch off the RO plant.

Open the valve No.5, 6 & 11and close the valve No. 1.2.3.4, 7,8,9,10,12 &13 for rinse the mix bed.

Check the pH at drain water, when pH comes up to 5.5-7 pH then stop the RO plant.

Stop the RO system and open the valve No. 3, 5 & 11, close the valve No. 1,4,6,7,8,9,10,12 &13 for final rinse of mix bed.

Start the RO system and done final rinse of mix bed for 5 minute.

After 5 minute stop the RO system and go for air mixing mode.



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**Air Mixing Mode:**

Open the valve No. 10 & 13 for air mixing.  
Open the compressed air valve (1.5 to 2kg/cm<sup>2</sup>) valve and done the air mixing of mix bed for 15 minute  
After air mixing close the compressed air valve and air mixing valve 10 & 13 of Mix Bed.

**Service in mode**

Open valve No. 5, 3, 9 & 14 (Auto dump valve), Close the Valve No. 1.2.4.6.7.8.10.11.12&13.  
Start the RO plant  
Drain the water from auto dump valve of mix bed by manually.  
Collect the sample from mix bed outlet and send the sample to Quality Control for testing of final parameter of conductivity and pH.  
After collect the passed results of Purified water from Quality Control, Run the RO plant in service mode as per requirement.  
Clean the solution tanks and prepare the solution for next regeneration of mix bed and keep the lid of solution tanks in closed condition.

**ULTRA VIOLET DISINFECTANT SYSTEM-1:** Now the Purified water is passed though the Ultra Violet Disinfectant system which disinfects the water & kills the bacteria. This water is stored in Purified water storage tank.

**OPERATION, CLEANING AND REPLACEMENT OF UV SYSTEM INSTALLED IN WATER SYSTEM PROCEDURE**

**Operation of UV System:**

Switch "ON" the UV System by pressing main switch provided on main electrical panel.  
Check the intensity of UV Lamp it should be between 30-50W/m<sup>2</sup>.  
Note the reading of burning hour.

**Procedure of cleaning of quartz jacket (frequency-monthly):**

If the intensity of UV lamp comes between 30-50W/m<sup>2</sup>, stop the system where UV system is installed.  
Switch off UV system form control panel of UV system.  
Open the drain nut of UV hosing, provided on bottom of UV housing.  
Remove the UV light from UV housing carefully.  
Open the end cover of UV housing and remove UV quartz carefully.  
Clean the UV quartz with help of clean cloth.  
Installed the UV quartz and fit the end cover of UV housing as previous fitted.  
Install UV light in UV housing as previous fitted.  
Start the system and Open the inlet valve and drain the water for 2- 3 minutes. Close the drain port by using the drain nut.  
Switch on the UV system control panel and check the intensity of UV lamp.

**Replacement of Lamps: (Every Running hours of 9000 Hours or out of working or intensity is less than 30W/m<sup>2</sup>)**

Stop electrical power supply from UV System control panel and display the under maintenance board. Unscrew socket and remove end covers of lamp holder. Remove the old lamps from quartz jacket carefully. Now fix the new ultraviolet lamp carefully in the quartz jacket, then and fix end cover of the lamp holder as previous. Switch ON electrical power supply from UV system electrical control panel.





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**8.3 PURIFIED WATER**

**SOURCE:** The water generated by passing Treated water through the reverse osmosis system, Mixed bed & UV (Post treated is called purified water).

**STORAGE:**

<b>Purified water storage tank</b>	
Type	Jacketed
Nominal Capacity	3000 Liter
Design Pressure (Shell)	-1.0 to 3.0
Operating Pressure (Shell)	1.5 kg/cm <sup>2</sup>
Test Pressure (Shell)	3.9 kg/cm <sup>2</sup>
Design Pressure (Jacket)	2.5 Kg/sq cm.
Operating Pressure (Jacket)	1.5 Kg/sq cm.
Test Pressure (Jacket)	3.9 kg/cm <sup>2</sup>
Maximum Operating Temperature (Shell)	80°C - 90°C
Maximum Operating Temperature (Jacket)	80°C - 90°C
Design Standard	USP
Process Fluid-Shell Side	3.0 kg/cm <sup>2</sup>
Make	Pharmalab
MOC	SS 316L
Internal Finish	Polishing
External Finish	Polishing

**Operation and Sanitization of Purified Water Generation System:**

**PROCEDURE**

Check and ensure the flow of RO-I recycle water between 1000 to 1400 LPH, for reject water between 1600 to 2200 LPH, RO-1 feed water between 2-5 Kg/cm<sup>2</sup> and pressure of RO-I recycle water is 2-4 Kg/cm<sup>2</sup> .

Check and ensure the flow of RO-II recycle water between 1200 to 1600 LPH, for reject water (recycle water for RO-I) between 2500 to 3500 LPH and inlet pressure of RO-II feed water between 2-5Kg/cm<sup>2</sup>, RO-II outlet pressure between 1.5 – 3.0 Kg/cm<sup>2</sup> and pressure of Recycle is 2-4 Kg/cm<sup>2</sup>.

Check and ensure the flow of RO-II permeate water between 3000 to 4000 LPH.

Check and ensure that conductivity of RO -II permeate is should be less than 40µs/cm.



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Ensure and check the Conductivity in conductivity meter of Mix Bed outlet, it should be less than 1.29µs/cm and water is being stored in purified water storage tank. If conductivity is not in the limit FDV of Mix Bed outlet will be opened automatically and water will be drained.

If conductivity of outlet water of Mix bed is more than the limit 1.29µs/cm, stop all the system and start the regeneration of Mix Bed .

Ensure and check the level of PW storage tank and after getting the high level alarm, stop the RO system. After getting the Middle level indication of PW storage in PLC of distribution skid, start the RO and fill the PW up to High level.

If middle level of PW Tank not comes within 12 hour after filling or RO system stop time is more than 8 hour then flush the RO system for 1 hour.

**Sanitization of RO: (Frequency: Fortnightly or whenever Microbial Load is more than the limit and QC intimation.)**

Start the RO system and check the conductivity of RO-II permeate water.

Stop the RO system.

Stop the softener and drain the soft water from the storage tank

Collect 500 liter fresh water in soft water storage tank.

Add 50 liter H<sub>2</sub>O<sub>2</sub> to prepare the H<sub>2</sub>O<sub>2</sub> solution in the storage tank.

Close the RO permeate water outlet valve.

Connect the flexible pipe with RO permeate line and RO reject line and dip in soft water storage tank.

Open the feed valve of solution tank (soft water storage tank outlet valve)

Start RO feed pump and circulate the water for 30minute.

Stop the RO feed pump and open RO reject outlet valve and drain the water.

After fully drain of solution, stop the RO feed pump and collect 500 liter fresh in HDPE soft water storage tank.

Start the RO feed pump and drain the water.

Stop the RO feed pump and open the RO permeate outlet valve and drain the water.

Start the softener and collect the soft water in soft water storage tank

Start the RO system and flush the water from RO permeate and RO reject line till the conductivity comes in limit of RO-II permeate water (Less than 20µs/cm).

If conductivity and pH with in limit then remove the flexible pipe and connect the RO permeate line with Mix Bed.

**7.4 WATER FOR INJECTION**

**SOURCE:**

The water generated by passing purified water through the Multi column distillation Unit is called water for injection.





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**STORAGE:**

WFI STORAGE TANK:T-301	
Description	Specification
Type	Jacketed
Nominal Capacity	3000 Liters
Process Fluid- Shell side	WFI
Process Fluid Density – Shell side	1000 kg/ m <sup>3</sup>
Design Standard	ASME Section VIII, Div-1
Design Pressure – Shell side	1-3kg/sq cm.
Design Temperature	150°C
Max. Operating Pressure	1.5 Kg/sq cm.
Hydro test pressure	3.0 Kg/sq cm
Joint efficiency Shell	0.85
Joint efficiency Dish	1.0
Shell Thickness	5 mm
Dish Thickness	Top Dish 5mm thick Bottom Dish 5mm thick
Jacket Dish Thickness	4 mm
Jacket Shell Thickness	4 mm
Cladding Shell Thickness	2 mm
Cladding Dish Thickness	2 mm
Make	Pharmalab
MOC	All Contact parts: SS316L
Internal Finish	Electro-polished to Ra < 0.4 μm
External Finish	Matt finished up to 180 grit

**OPERATION, CLEANING & SANITIZATION OF PURIFIED WATER DISTRIBUTION LOOP & STORAGE TANK PROCEDURE**

**Pre start up:**

Ensure the electrical supply ‘ON’ position from MLDB.

Ensure the sampling valve is in closed position.

Ensure the compressed air valve is in “ON” position.

Ensure and check the set points as below:

Supply conductivity (CT 101) : 1.29μs/cm

Dumping Delay (FDV 101) : 1Second

Return Flow (FT 101) : 1.2 M<sup>3</sup>/Hrs.

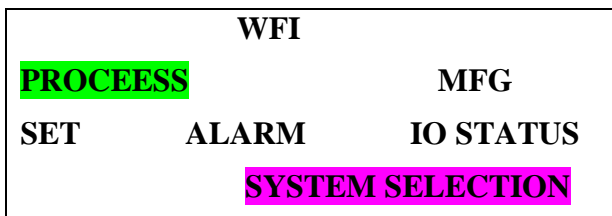


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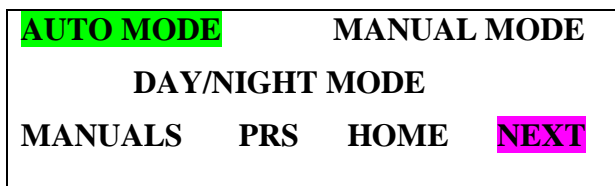
Return Conductivity (CT102) : 1. 29µs/ cm  
 Dumpling delay (FDV 102) : 1 Second  
 Inlet delay (AV 101) : 1 Second  
 Return Temp. (TT101) : 50 Deg. C  
 Temp. Hy. : 00  
 Flow Control (FT 101) : 2.3 M<sup>3</sup>/Hrs.  
 Starting Method (AUTO MODE)  
 Go to login screen of HMI and enter the digital password as 456.



Go to next screen and select the PW SYSTEM.



Select the PROCESS



Select the **AUTO MODE**.

Ensure and check the supply loop pressure is 3-6 Kg/cm<sup>2</sup> and return pressure is between 1-1.5 Kg/cm<sup>2</sup>.

Ensure and check the return flow is between 1.2-2.3 m<sup>3</sup> / Hr.

Ensure and check the conductivity is less than 1.29 µs/cm.

Fill the operation record of PW distribution loop

Inform to all users the PW loop is under sanitization.

Drain the purified water from storage tank of PW along with distribution Loop by opening of all user valves one by one.

Select the Sanitization mode from PW distribution loop control panel.

Allow the Boiler steam in Jacket of PW storage tank to heat the fresh purified water up to 80-90°C temperature.

Circulated the PW water from storage tank to distribution loop for 1 hour and monitor the temperature at return line of loop. It should be 80-90°C.

Open the valves at all user point slowly & one by one to drain the circulated water for one minute of each user point valves.

Fill the tank along with distribution loop with pure steam at 1.5 Kg/cm<sup>2</sup> pressure.

Hold the pure steam in distribution loop along with storage tank for 1 hour.

After one hour, drain the steam from all user points, one by one approximate 1 minute from each of user point's valve.



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After flushing the steam, close all the user points' valve.

Start the Purified Water Generation Plant and fill the tank with PW and informed to Quality Control department for sampling of PW.

**MULTICOLUMN DISTILLATION PLANT :**

S.No.	TITLE	DESIGN PROVISION
1.	Output	1000LPH at 3 Kg./ Cm <sup>2</sup> of plant steam.
2.	Operating	Automatic real time printing.
3.	PLC	Mitsubishi PLC with E-1061 colour touch screen HMI.
4.	Purified water	Pressure sensing.
5.	Identification of control panel	<ul style="list-style-type: none"><li>• HMI</li><li>• Emergency push button.</li></ul>
6.	Packing box size (approximately) LXWXH	Colum 1&2: 129''LX66''WX58''H. Colum 3&5: 129''LX86''WX58''H. Colum 3&5: 129''LX86''WX58''H. Double Cooler:94''LX32''WX18''H Pump: 28''lx 24''Wx 41''H.
7.	Printer	Epson Lx-300, 80 Colum Don't Matrix Printer.

**OPERATION OF MULTILUMN DISTILLATION PLANT:**

**PROCEDURE:**

Check and ensure that the MCDP feed water flow not more than 1000LPH.

Check and ensure that the MCDP feed water pressure in between 10-15kg/cm<sup>2</sup>.

Check and ensure that the MCDP feed water conductivity not more than 1.29µs/cm.

Check and ensure that the RAW steam temperature not less than 143°C.

Check and ensure that the RAW steam pressure not less than 3kg/cm<sup>2</sup>.

Check and ensure that the MCDP cooling water inlet temperature not more than 30 °C.

Check and ensure that the MCDP cooling water flow not less than 1200LPH.

Press the SET PARA key and check the parameters as below:

Preheating time : 060 Sec.

INL Hooter off Time : 060Sec.

Printing Time : 600Sec.

PRA Print time : 015Min.

PRA Print Disable : Yes

Boiler Steam Temp. : 143°C

WFI Temp. Low : 85°C

WFI Temp. High : 95°C

Cool Water Temp : 30°C

WFI Conductivity : 1.00 µs/cm

F.W Conductivity : 1.29 µs/cm

Vent off time : 300 Sec.

Initial Drain Time : 60Sec.

Purging Time : 30Sec.

Purging Fault On Time : 54 Min.

Purging Fault Off Time : 54 Min.

Drain Time : 30Sec.

Shut Down Time : 300Sec.



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Push the 'RUNNING' button on HMI main screen for stop the Multicolumn Distillation Plant.  
Next screen will be display as below.

<b>VIEW</b>	<b>MAIN MENU</b>	<b>SET PARA</b>
P & I	SHUT DOWN CYC. ON	MFG PARA
START		MAINTENANCE
LOG IN	ACK	LOG OUT

After 5 minute Multi column cycle will be stopped and next screen will display as below.

<b>VIEW</b>	<b>MAIN MENU</b>	<b>SET PARA</b>
P & I	PLANT READY TO START	MFG PARA
RUNNING		MAINTENANCE
LOG IN	ACK	LOG OUT

Close the valve of compressed air.  
Switch off the main panel.

Put Off the MCB from MLDB.

**PURE STEAM GENERATION PLANT**

S.No.	TITLE	DESIGN PROVISION
1.	Model	150 PSG
2.	Capacity	150KG/HR.
3.	Feed water supply & sensing	WITH LOOP SYSTEM AND LEVEL SENSING AT NCGR Tank
4.	Operation	Automatic
5.	PLC	Mitsubishi , HMI E-1061
6.	Packing Box Size( Approximately) LXWXH	Main Machine : 128''LX61''WX 53''H NCGR Tank: 56''L x 56''W x 77''H.
7.	Non Condensable Gas Remove Arrangement	Contact Part MOC- SS316L Feed water flow rate-175 LPH. Feed water Inlet Temp.-Ambient. Feed water Inlet Pressure 0 Max.2.0kg/cm <sup>2</sup> . Plant steam -6.0 kg /cm <sup>2</sup> Pressure & 165 °C Temp. Feed water outlet Temp.: 75 to 80°C. Tank – 1 No's Manual Diaphragm Valves- 2 No's Pneumatic Valve – 3 No's Heat Exchanger – 2 No's Steam Trap – 1 No. Level Sensor- 2 No's
8.	Printer for Data Printing	Epson L X 300, 80 Column Dot Matrix Printer.



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**OPERATION OF PURE STEAM GENERATION PLANT PROCEDURE**

**Starting Procedure:**

Open the valve of purified water zero dead leg valve.

Go to Main Screen of HMI of PSG.

<b>VIEW</b>	<b>MAIN MENU</b>	<b>SET PARA</b>
P & I		MFG PARA
MODE		MAINTENANCE
<b>LOG IN</b>	ACK	LOG OUT

Push the LOG IN, keyboard screen will appeared as digit 0 to 9, enter the digital password  
Next screen will display as below.

<b>VIEW</b>	<b>MAIN MENU</b>	<b>SET PARA</b>
P & I		MFG PARA
<b>MODE</b>		MAINTENANCE
LOG IN	ACK	LOG OUT

Push the MODE.  
Next screen will appeared.

NCGR	<b>START</b>
MACHINE	<b>START</b>
MAIN	ACK

Push the NCGR START and after 2 minute push the MACHNIE STARTS  
After starting of PSG and both NCGR and Machine status will display as **RUNNING**.  
Check the set parameter as below:



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Pre Heating Time	: 60Sec.
Inlet Hooter Off time	: 90Sec.
Para Print time	: 015sec.
Printing time	: 030Sec.
Para. Print Disable	: Yes
Boiler steam Temp.	: 120°C
PW Conductivity	: 1.29µS/cm
Pure Steam Conductivity	: 1.00µS/cm
Purging Time	: 50 Sec.
Purge Fault On Time	: 10 Min.
Purge Fault Off Time	: 10 Min.
Pure Steam Pres. High	: 3.5 kg/cm <sup>2</sup>
Pure Steam Pres. High Fault ON Delay	: 10Sec.
Pure Steam Pres. Low	: 3.0 kg/cm <sup>2</sup> .
Pure Steam Pres. Low Fault On Delay	: 10Sec.
Tank Temperature	: 80°C
Feed Water Temp.	: 80°C
Low Level Delay Time	: 30Sec
High Level Delay Time	: 30 Sec

**Precaution:**

- Ensure the conductivity of Purified water is within limit of < 1.29µs/cm.
- Ensure the conductivity of Pure Steam is within the limit of < 1µs/cm.
- Ensure the boiler steam temperature in NLT 143°C
- Ensure the feed water flow is between 300-350LPH.
- Ensure the feed water pressure is between 4-8 kg/cm<sup>2</sup>.
- Ensure the pure steam pressure is between 3.0-3.5 kg/cm<sup>2</sup>.

**Stopping Procedure:**

- Push the **NCGR RUNNING**, after pressing **STOP** screen will display.
- After 5 minute push **MACHINE RUNNING**, after pressing **STOP** screen will display.
- Close the valve of boiler steam line.
- Close the valve of compressed air.



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**9.0 SCHEMATIC DRAWING OF WATER SYSTEM**

Schematic Drawing of Water System attached as per Annexure-I

**10.0 TECHNICAL DETAILS OF WATER SYSTEM & ATTACHMENT DOCUMENT:**

**ATTACHMENTS:**

- 6.1 List of Water system sampling points.
- 6.3 Schematic Diagram for Purified Water System and Water for Injection System.
- 6.4 Standard testing procedure and specification of Raw water ,Treated water, Purified water and Water for Injection As per in-house specification raw water , in-house specification for treated water, USP for purified water & USP for water for injection.

**11.0 SPECIFICATION AND TEST METHODS**

- **RAW WATER (IH)**
- **TREATED WATER(IH)**
- **PURIFIED WATER (USP))**
- **WATER FOR INJECTIUON (USP)**

**12.0 CERTIFICATE OF WATER ANALYSIS**

- **RAW WATER**
- **TREATED WATER**
- **PURIFIED WATER**
- **WATER FOR INJECTIUON**

**Referee the certificate of performance qualification doc.**

**13.0 VALIDATION OF WATER SYTEM**

- **PHASE I**
- **PHASE II**
- **PHASE III**

**13.1.1 Phase -I validation Study:**

Once the water purification and distribution system has been verified, having Installed and operated, the initial phase of water system validation shall be undertaken. In this phase water sampling shall be done from all sampling points i.e. all water treatment points, storage points & point of use for a



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period of 2-4 weeks. In this period worst case simulation conditions should be arised just before the sample which normally occurs during routine manufacturing conditions .A tentative frequency of sanitization of not more than two weeks shall be set before the phase I study and confirmed after the phase II study. If there is any failure with respect to bioburden in between three weeks the phase I study has to be re-initiated with increase in the frequency of sanitization. At the end of this phase draft SOP for operation, cleaning, sanitization and sampling method of water system shall be confirmed.

### 13.1.2 Phase- II Validation Study

This study is to demonstrate that the system shall consistently produce the desired quality of water when operated in conformance with the SOPs. The sampling shall be done from all the sampling points for a period of Three weeks. In this phase worst case conditions need not be simulated.

### 13.1.3 Phase III Validation study:

The third phase of validation is designed to demonstrate that when the water system is operated in accordance with the SOPs over a long period of time (one year) with all seasonal variations, it shall consistently produce water of desired quality attributes. During this period sampling shall be done as per the routine sampling plan. Which include all water treatment points, minimum of one point of use and minimum of one outlet of storage tank in rotation completing in a week.





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**PHASE I VALIDATION**

**13.2 Sampling Considerations:**

**13.2.1 Phase I Sampling**

After successful operation of water distribution system as per Operational Qualification Phase I validation study shall be undertaken. The sampling shall be done from all water treatment points, storage points & point of use for 2-4 weeks between. Following worst case conditions and interventions shall be created (which occurs during routine manufacturing condition) just before the sampling from water treatment points and storage points.

Power off for a period required for the commencement of power through generator set.

The sampling shall be carried out as per the sampling plan (Phase-I & II). All the samples draw in phase-I validation shall be tested as per their respective specifications and test procedures for chemical & microbiological analysis. Attached (Phase-III) with the protocol.

Satisfactory test results of Phase I samples shall establish that Purified Water for primary cleaning of equipment / components and input to pure steam generator, as well as water for injection is suitable for manufacturing of sterile injection .However sampling from water distribution system shall be continued as per requirement of phase II validation study.

**(For details – Refer Sampling point & Sampling plan- Annexure - II)**

**PHASE II VALIDATION**

**13.2.2 Phase II Sampling:**

At the end of phase I validation study following SOPs shall be established.

1. Operation of Purified water generation & Operation of Water for Injection generation.
2. Sanitization of water distribution and generation system of PW & WFI.
3. Sampling of water.

Sampling shall be done daily from all the sampling points as described above for a period of 2-4 weeks between dated without worst case simulation. Successful validation study in phase II shall demonstrate that the system shall consistently produce desired quality of water when operated in conformance with the SOPs.

In case of any failure w.r.t. CFU count, sanitization frequently has to be reviewed. Any leakage or stagnancy of distribution system due to mis-operation or sampling error may result into microbial failure. Hence an extensive investigation is required before revision for the requirement of frequency of sanitization. Any microbial count, (Through within limit), shall be identified and action shall be decided on the basis of type of organism and re-occurrence of the organism in next sample(s) (if any).



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Initial failure in particular content more than standard limit during phase I study can be because of accumulation of particulate and improper cleaning after installation. But during phase II validation failure due to particulate count is not a usual phenomenon. It may be possible due to improper cleaning of sampling aids. Hence re-sampling after proper cleaning of sampling aids and flushing of sampling points for longer periods are recommended. If failure in re-sampling is observed again, investigation should be undertaken, including affect of water circulation on material of construction of pipeline. Rectification or modification in the system should be carried out if investigation demands so. On the basis of investigation result, period of phase II validation study to be extended.

### EVALUATION OF VALIDATION STUDY

The phase I and II validation studies revealed no major deviation from the specifications and all the sampling points were found to be well within the acceptable limit during the entire course of validation.

Thus the routine monitoring (Phase III) was started with the sampling frequency as stated earlier in this manual.

#### 13.2.3 Phase III Sampling:

Sampling schedule during this phase shall be in accordance with the sampling plan. One-year test data shall be compiled. Out of specification data shall be listed separately with complete investigation and action taken reports.

Data shall be compared for different seasons to establish the compatibility of the system due to the seasonal variations.

Satisfactory test data shall reflect the efficacy of the system to give desired quality of the water consistency.

#### 14.0 ABBREVIATIONS:

S.No.	Abbreviated Form	Full Extended Form
1.	CGMP	Current Good Manufacturing Practice
2.	DQ	Design Qualification
3.	P & ID	Piping and Instrument diagrams
4.	PW	Purified Water
5.	SOP	Standard Operating Procedures
6.	TOC	Total Organic Carbon
7.	URS	User Requirement Specification
8.	USP	US Pharmacopoeia



# PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

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S.No.	Abbreviated Form	Full Extended Form
9.	EPDM	Ethylene Propylene Diene Monomer
10.	ERW	Electric Resistance Welding
11.	EU	European Union
12.	FDA	Food and Drug Administration
13.	POU	Point of Use
14.	PTFE	Poly Tetra Fluoro Ethylene
15.	ppb	Parts Per Billion
16.	WFI	Water For Injection
17.	SB	Spray Ball
18.	°C	Degree Celsius
19.	µs/cm	Micro Siemens per Centimeter
20.	LPH	Liter per hours .