Topic	Identifying All critical Quality parameter of Purified Water generation and distribution
1	Critical Quality Parameter
2	Fish-Bone on Failure Mode analysis of Purified Water generation and distribution
3	FMEA of Purified water generation and distribution system

Visit : https://pres.net.in

Material	Machine
Chemicals usages	Recirculation Pump with VFD
NaoCl	Distribution Pump
HCl	Sanitary pump
SMBS	Spray Ball 360 deg
Anti scaling	Storage tank
Feed water source/quality	Leakages
Compressed Air	Corrosion
Gasket GMP grade	Ozone generator
Bursting Disc and PLC control	Distribution piping
Contact part MOC 316L	RO membrane replacement
Zero dead leg valve user point	
Dead leg not more than 1.5D	
Silicon tubing/leachablity	
Air filter Maintenance	
Filter jacket temperature	
Integrity	
Replacement	
Damage/rupture	
Integrity	

Failure Mode analys

Man	Method
Training	Roughness verification
Hygiene	Joints/Boroscopy
Testing	Hydro Test
Incident reporting	Slope verification
Breakdown handling	Passivation
Analyst Qualification	Velocity
Handling of sample	Turbulent flow
Chemical testing	Reynolds Number
Microbial testing	Tank coverage study
In adequate training	Dranablity Study
	Hold Time study
	Sample Analysis
	Labelling and identification
	QC Release
	Solution preparation/dilution
	Hold Time study
	Approved Vendor source
	Sample storage
	Analyst error
	Sampling kit preparation
	Testing delay/ storage condition

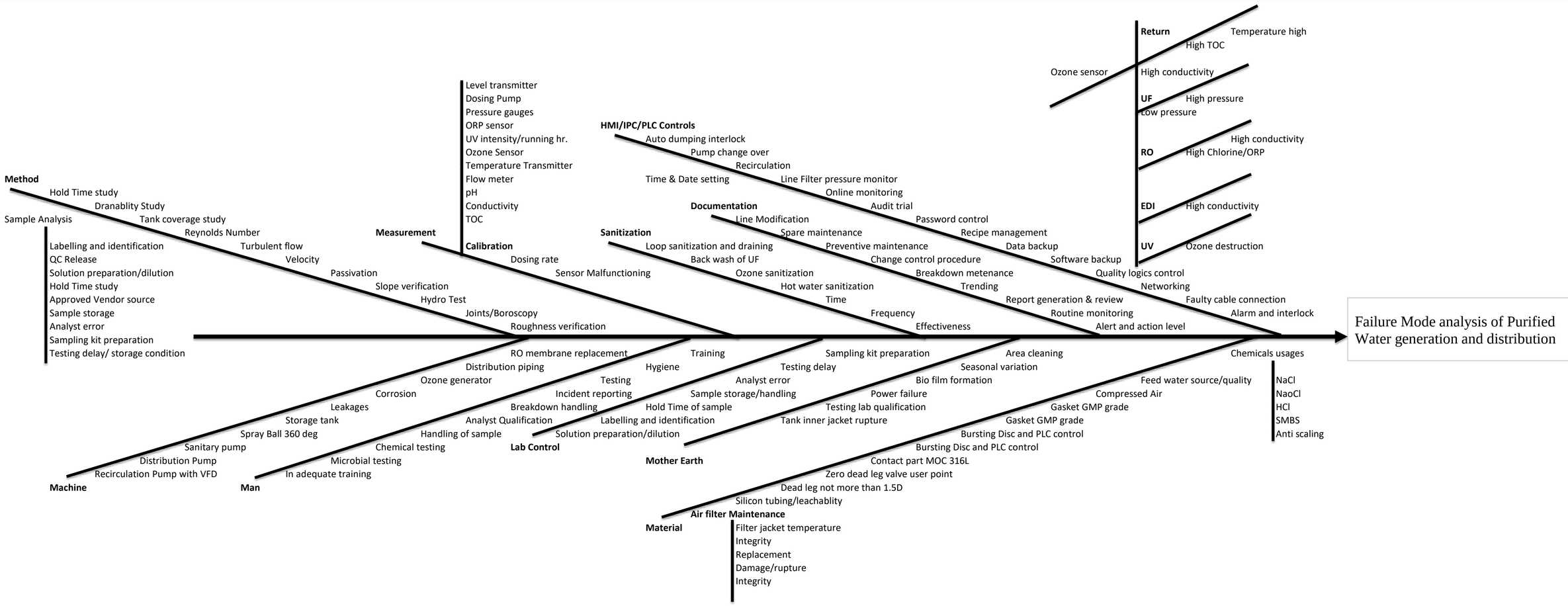
sis of Purified Water generation and distribution

Measurement	Mother Earth	Lab Control
Calibration	Area cleaning	Solution preparation/dilution
TOC	Seasonal variation	Labelling and identification
Conductivity	Bio film formation	Hold Time of sample
pH	Power failure	Sample storage/handling
Flow meter	Testing lab qualification	Analyst error
Temperature Transmitter	Tank inner jacket rupture	Testing delay
Ozone Sensor		Sampling kit preparation
UV intensity/running hr.		
ORP sensor		
Pressure gauges		
Dosing Pump		
Level transmitter		
Dosing rate		
Sensor Malfunctioning		

Sanitization	Documentation
Effectiveness	Line Modification
Frequency	Spare maintenance
Time	Preventive maintenance
Hot water sanitization	Change control procedure
Ozone sanitization	Breakdown metenance
Back wash of UF	Trending
Loop sanitization and draining	Report generation & review
	Routine monitoring
	Alert and action level

HMI/IPC/PLC Controls
Auto dumping interlock
Pump change over
Recirculation
Line Filter pressure monitor
Online monitoring
Audit trial
Password control
Recipe management
Data backup
Software backup
Time & Date setting
Networking
Faulty cable connection
Alarm and interlock
Quality logics control
UF
High pressure
Low pressure
RO
High Chlorine/ORP
High conductivity
EDI
High conductivity
Return
High conductivity
High TOC
Temperature high
Ozone sensor
UV
Ozone destruction

Fish-Bone on Failure Mode analysis of Purified Water generation and distribution



Risk Evaluation

System	Sub system/Item/ stage/Function
NaOH Dosing Unit	NaOH dosing pump NaOH solution tank pH sensor
Filtration	Cartridge Filter
Osmotron	Reverse Osmosis System
Osmotron	EDI (Electro deionisation) Module
Storage tank for Purified water	Level Transmitter
Storage tank for Purified water	Vent filter (0.2 µ hydrophobic)
Storage tank for Purified water	Dynamic Spray Balls
Storage tank for Purified water	Tank drain valve
Storage tank for Purified water	Rupture disc
Storage tank for Purified water	Temperature transmitter
Storage tank for Purified water	Tank does not have sanitary construction

Purified water distribution loop	Two No's of Pump with variable frequency drive (VFD) Flow transmitter
Purified water distribution loop	Online conductivity meter TOC analyser
Purified water distribution loop	Mechanical finish and MOC
Purified water distribution loop	Slope
Purified water distribution loop	Passivation
Sanitization	Purified water storage and distribution
System Controls and operational logics	Online monitoring and control logic

System Controls and operational logics	IPC / HMI/ PLC
System Controls and operational logics	IPC / HMI/ PLC
System Controls and operational logics	IPC / HMI/ PLC
System Controls and operational logics	IPC / HMI/ PLC

System Controls and operational logics	IPC / HMI/ PLC

Failure modes	Potential effects of failure	Severity [S]
Dissolved gases (CO2) not removed through RO membrane	pH and Conductivity will not maintain	Low
Undissolved particle will pass through RO	RO membrane may damage	Low
RO membrane could not be sanitized	permeate may be contaminated with time.	Low
High conductivity	Loss of time and generated water	Low
Water Level will not monitor/maintained	Water level will be low/high	Low
Venting is not available Water may get contamination with viable and non viable particle	Microbial contamination	Low
Tank internal surface not wet with water during normal operation, chemical and/or thermal sanitization.	Proliferation of microbiological organisms	Low
stagnancy of water	Microbial contamination	Low
Tank will be under- and over-pressurization	Vessel can be damage	Low
Temperature probe malfunctioning	During sanitization temperature will not maintained	Low
Direct contact parts are not GMP grade	Chance for getting microbial contamination	Low

Velocity will not maintain Flow rate can not be monitor	Chance of proliferation of microbiological organisms and formation of biofilms	Low
Conductivity and TOC will be high in PW	Chance for getting microbial contamination	Low
1. GMP grade material not used 2. Good engineering practices not followed	Chance for getting microbial contamination	Low
Water stagnant in the loop	Chance for getting microbial contamination	Low
Loops are not cleaned properly after installation	Chance for getting microbial contamination	Low
Improper Sanitization	Chance for getting microbial contamination	Low
Not able to control and monitor online process data	System failure not able to recognize	Low

1. System allows the access to unauthorized user 2. Unauthorized use of the system and application software Wrong user profiles / privileges assignment 3. Wrong use of the system and application software 4. Same username / password assigned to multiple users 5. Wrong use of the system and application software and incorrect workflow traceability 6. Access to the application and to the Operational system without password 7. Unauthorized use of the system and application software 8. The system allows to change the date and time of the workstation The date and time reliability of the system results is compromised	System security failure	Low
1. The system does not allow to obtain correct and complete copies of data 2. Copies of GxP relevant data cannot be submitted in an appropriate format to the authorities 3. Data can be corrupted and falsified, with no trace Original data loss 4. Backup & Restore activities are not in place 5. Data loss	Data Integrity	Low
1. The system audit trail does not record all required information related to performed changes	Data Traceability	Low
The system does not automatically manage system operations according to recipe steps and process parameters, Process not correctly executed	Failure in Process/recipe Management	Low

The monitored process parameters are not correctly displayed Unfeasibility to record/monitor the process parameters values The system does not save monitored process parameters values Loss of monitored data related to process parameters	Failure in Critical Process Parameters Monitoring and Trends	Low

Mechanism of failure	Probability of occurrence [P]
It will pass through RO membrane	Low
If filter damage it will not able to retain the undissolved particles	Low
If not sanitized with defined frequency	Low
System will drain High conductivity water	Low
If system not installed Level transmitter	Low
1. Storage tanks required venting to compensate for the dynamics of changing water levels. 2. If integrity of filter failed or choked	Low
1. If the spray balls are not able to wet entire tank including headspace	Low
If 100% drainage not happened through drain valve	Low
Pressure-relief valves and bursting discs not considered	Low
Temperature probe if not calibrated	Low
If the MOC of contact part are not GMP grade	Low

1. Pump malfunctioning 2. Lower velocity in distribution loop	Low
1. Improper installation 2. Uncalibrated instrument	Low
1. Inadequate internal finish 2. Improper piping joints 3. Inadequate flanges, unions and valves	Low
Improper slope of distribution loop	Low
Passivation not performed	Low
1. If the sanitization is not effective 2. Frequency of sanitization not establish 3. Alternate sanitization procedure not available	Low
1. Improper installation 2. If the system integration not qualified/verified	Low

Unavailability of different level of user privileges Improper assignment of user privileges	Low
1. Unavailability of data protection, back up and restoration procedure	Low
1. Unavailability of Audit Trial	Low
1. Unavailability of recipe management	Low

1. System controls are not establish	Low

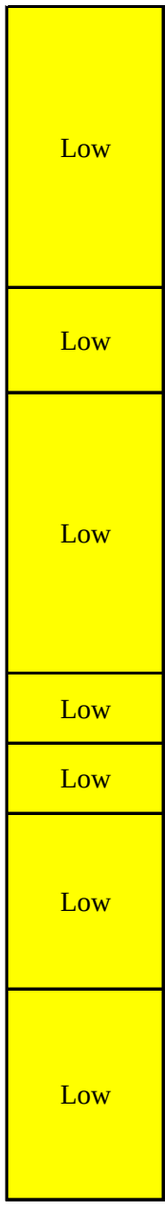
Control	Detection [D]
1. Gaseous CO2 will convert to dissolved ionic form by NaOH and further will removed by RO. 2. PLC control NaOH Dosing Unit is provided.	Medium
1. Pressure gauge provided on the filter and out let to verify the pressure differential .	Medium
1. Hot water sanitization provision considered for RO membrane sanitization	Medium
1. Conductivity shall be monitored and recorded at downstream of EDI.	Medium
1. Level Transmitter considered as part of design to monitor level in the PW tank. 2. Tank will be provided with low level sensor to create alarm and stop supply water. 3. Tank will be provided with control system for sensing high level of water in tank and it will stop the supply of water in the tank.	Medium
1. Sanitary vent filter (0.2 µ hydrophobic) considered with heat tracing housing. 2. Temperature transmitter is considered to monitor the vent filter jacket temperature. 2. Periodic filter integrity to be per formed as per procedure.	Medium
1. Dynamic spray balls considered to ensure that the entire tank surface including headspace is wetted with 360 Deg Rotation 2. Riboflavin tests to be performed to verify the spray coverage inside the vessel.	Medium
1. Slope towards drain considered in vessel design 2. Drainablity study to considered during qualification.	Medium
1. Rupture discs are provided on storage vessels to protect them from under- and over-pressurization 2. Rupture disks equipped with a rupture alarm device to safeguard for the mechanical integrity of the tank. 3. Compound pressure indicator considered for monitoring of tank pressure.	Medium
1. Temperature sensor PT100, RTD Sensor , Range-0 to 150°C considered 2. Periodic calibration to be considered as per the schedule	Medium
1. Tank is made of SS316 L and tank is provided with steam jacket for heating of water required for sanitization. 2. Direct contact surface (tank, pipe, valve, spray ball, sensors) shall be made of SS316 L (surface finish 0.3 □m RA) or suitable elastomer e.g. PTFE, silicone etc. 3. All pipe connection shall be sanitary triclover type.	Medium

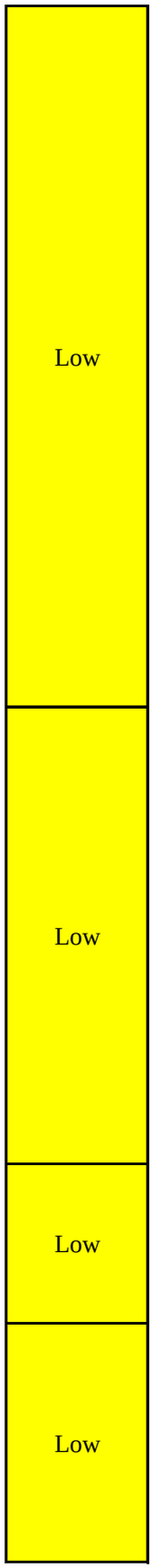
1.Pump will maintenance of continuous turbulent flow circulation within water distribution systems 2. Centrifugal pumps for loop water re-circulation with VFD to maintain velocity in the line. 3. Variable frequency drive (VFD) to maintain return line velocity minimum 1.2 m/sec (4 f/sec). 4. Reynolds number verification to be performed as part of qualification to ensure the tabulate flow	Medium
1. Installation verification to be considered during qualification for conductivity and TOC analyser 2. Periodic calibration to be performed as per procedure	Medium
1. Internal material surface roughness of not greater than 0.8 micrometre (Ra). Electro-polishing improves the resistance of the stainless-steel material to surface corrosion. 2. Automatic Orbital welding consider for piping joints and 10 % joints are considered for quality inspection. 3. Hydro test to be considered for all PW distribution loops to test the for strength and leaks of piping. 4. Where flanges, unions or valves are used they are hygienic or sanitary design. 5. User point are considered with zero dead leg valve.	Medium
1. Slope of the distribution pipe line considered not less than 1:100 , so that the system can be completely drained.	Medium
1. System shall be passivized after initial installation or after significant modification. After passivation system shall be cleaned.	Medium
1. PW loop is integrated with an automatic ozone sanitization & hot water sanitization process with the help of heating tank water by supplying steam to the tank jacket. 2. The temperature of the hot water in the PW tank and the distribution loop shall be monitored during sanitization cycle. 3. Frequency of sanitization to be established during performance qualification.	Medium
1. Online instruments like conductivity, TOC, temperature, flow rate, and pressure will facilitate improved operational control of the attributes and parameters and for process release. 2. Installation verification of all measurable devices to be performed during qualification 3. Control logics and system integration to be verified during operational qualification	Medium

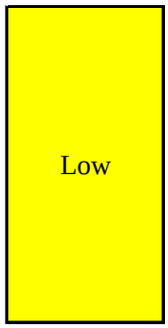
A. Password Management : 1. Password is required to access the system 2. Different level of authorization is provided based on the operation Password length considered more than or equal to 6 character to strengthen the password 2. Password maximum age is consider for expiration of current password 3. Password history will prevent to select previous to select the old system password 4. Inactive time lockout duration will ensure the auto lock out of the system to prevent the unauthorized access in case of system is unattended 5. Unsuccessful attempt of more than 3 time will block the particular user authorization. B. User management : 1. The system shall have minimum 4 Access levels (Operator, Supervisor, Engineer and administrator). 2. Provision to create individual users. 3. Provision to create minimum two numbers of administrators. 4.Date and time change option shall be available only for administrator. 5. Operator shall have the privileges only to operate the equipment.	Medium
1. System data transfer and archival is restricted to admin level 2. Software shall be provided by the OEM (Original Equipment Manufacturer) with current version and date. 3. GMP relevant data shall be available in non editable readable format. E.g. PDF	Medium
1. Audit trial provision available in the system.	Medium
1. System shall be run with configured recipe. 2. Any changes to the qualified recipe shall be performed based on the approved change request by System administrator.	Medium

1. Input output are considered as part of qualification program. 2. Safety interlocks and alarm shall be schemulate as a part of qualification. 3. System was provided with 240 GB hard drive for storage of process data. 4. Online / Offline data back up provision of process data has considered.	Medium

RPN
Low
Low
Low
Low
Low
Low
Low
Low
Low
Low
Low


Low
Low
Low
Low
Low
Low
Low


Low
Low
Low
Low


Low

Palash Chandra Das

M. Pharma

LinkedIn Link

Pharmaceutical Chemistry

Core Technical Area: Qualification & Validation , Sterility Assurance, QMS, Risk Management

Palash Chandra Das is the Technical Writer focuses on technical writing including investigative reports and operating procedures. His passion for writing is displayed in the many writing sessions he hosts via his Blogs at https://pres.net.in.

Mr. Palash Chandra Das is recognized as an expert in the field of aseptic manufacturing of parenteral products, and is a frequent presenter at several web conferences and technical training for Sterile Drug Manufacturing.

He earned his Master's for Pharmaceutical chemistry from the University of West Bengal University of technology in India.

Since 2011 Palash has associated with installation, qualification and operation several production-lines in standard Clean room Technology as well as in Isolator Technology at major regulatory facility across India.