PURIFIED WATER SYSEM

1) SYSTEM REQUIREMENTS

In pharmaceutical plants where high quality water is required for granulation, compounding or other manufacturing processes, a feed water and distribution system should be provided which will meet the United States Pharmacopoeia / European Pharmacopoeias (USP/EP) specifications for purified water. The system resistively of 0.8 megohm per cm (maxim of 1.25 mircrosiemens conductivity) at a water bacteria contamination level of 100 cfu per millimeter. Table IV lists the quantitative interpretation of USP/EP Purified Water.

The periodic monitoring and analysis for content of individual elements and particle counts will be replaced under the proposed specification with an "on line" conductivity meter. Likewise, Total Organic Carbon (TOC) Values have, historically not been part of a periodic intercomponent - monitoring program. But, consideration should still be given to the future provision of a TOC analyzer, selected for determining, Purified Water and Feedwater TOC levels. Upon successful commissioning of the system, testing procedures must be established to confirm compliance with the USP/EP Purified Water (or Water for Injection) requirements.

2) RECOMMENDED SYSTEM

The Potable Water System (s) will be fed from the facility's Water Chlorination and Filtration System, typically consisting of a water storage tank, constant pressure booster pumps, clarifies, multi-media filters, activated charcoal filters and two chlorine injection systems (refer to sketch PP - 1).

The USP/EP Purified Water System shall consists of parallel water softeners, chemical feed system with break tank, 5.0 micron filters and parallel two pass reverse osmosis (RO) units. The chemical feed system will be utilized to render the residual chlorine harmless to extend the contact time required to facilitate the reaction between the sodium bisulfate and chlorine. On smaller systems (designed to produce 50 liters per minute or less provided, the type of semipermeable membrane used in the RO units will depend on the results of the site water analysis. As an alternate to the two pass RO units, a mixed 0bed, twin-bed or continuous Deionization (CDI) Unit, followed by an Ultraviolet sanitisation lamp with 0.22 micron filter may be provided. Refer to sketch PP-2.

A for system diagrams. This system shall have the following features.

All piping and wetted surfaces downstream of the storage tank shall be 316L, stainless steel with 240 grit electropolish finish. Piping shall be equivalent to schedule 10, seamless pipe connected by a system of orbital welded and Tri-Clover clamped joints.

A conductivity controller with in-line probe shall divert water from filling the storage tank to the break tank, via 2-position control valves (diaphragm valves with solenoid actuators) whenever the conductivity of the feed water is too high.

The RO units will operate simultaneously. Whenever the RO units are indexed "ON" the conductivity controller shall be over ridden and the fill water shall be predetermined period (15 minutes, adjustable) to insure adequate system flushing and water quality.

Clean-in-place (CIP) connections shall be provided in the break tank, adjacent to the isolation valves at each RO unit, adjacent to the isolation valve at the storage tank inlet and adjacent to the storage tank in the Purified water return line directly above the spray ball. Chemical sanitisation will be by use of portable CIP equipment.

The storage tank will be maintained at a slightly positive pressure. The tank will be equipped with both an aseptic vent filter and rupture or nitrogen blanket and automatic pressure relief vent. The distribution system shall be insulated.

The distribution system shall consists of two recirculated piping loops. The first loop shall consist of a full size main passing within six pipe diameters of each individual valve service outlet. A back pressure-sustaining valve (adjustable) shall maintain a minimum pressure of 0.3 bar at the highest point in the system. The second loop shall contain the steam / heating hot water and chilled water heat exchangers, circulating pump, and tank mounted spray ball. Periodical (minimum once yearly) chemicals sanitisation of the recirculated piping loops and storage tank is required to remove bio-films which may form on the interior wetted surfaces when the system is operating at an ambient temperature. The spray ball is intended to wet all interior tank surfaces during sanitisation and therefor, it shall be located above the maximum operating water level.

The hot water exchanger shall be supplied with either medium pressure steam or medium temperature hot water to maintain the system at between 65 and 85°C for a minimum of six hours during the sanitisation cycle.

The optional shilled water exchanger should be designed to lower the system temperature to below 20°C within 30 minutes at the end of the sanitisation cycle. sanitisation of the system shall occur during non-production hours. An ozonator may be substituted in place of the two heat exchangers shown, but it would operate continuously to aid in sanitisation of the recirculating system.

Notes

As an alternative to heat sanitisation, an ozonator (ozone generator) may be provided. The ozonator shall be selected to maintain a minimum of 10 ppm of ozone in all parts of the distribution system, ahead of the back-pressure sustaining valve. The return line should then be connected to the tank mounted spray ball. In this alternate system the second recirculating loop containing the heat exchangers, and the insulation of the storage tank and distribution system are not required.The ozonator should operate for a minimum period of 6 hours daily. The ozone will dissipate from the water in approximately 20 minutes, and unless a residual

Level of ozone in the water at the service outlets will adversely affect the intended process or finished products, the ozonator can be operated continuously. Ozone detectors should be used for monitoring and/or controlling the levels in the system.

System shall include a blowdown cycle. This will be either an intermittent blowdown (i.e. 25% of system volume per day) or continuous blowdown (i.e. 1% system volume per hour) cycle.

A replaceable fixed orifice should be used to established the desired rate of blowdown. The blowdown cycle should not operate during either the chemical or heating sanitisation cycles.

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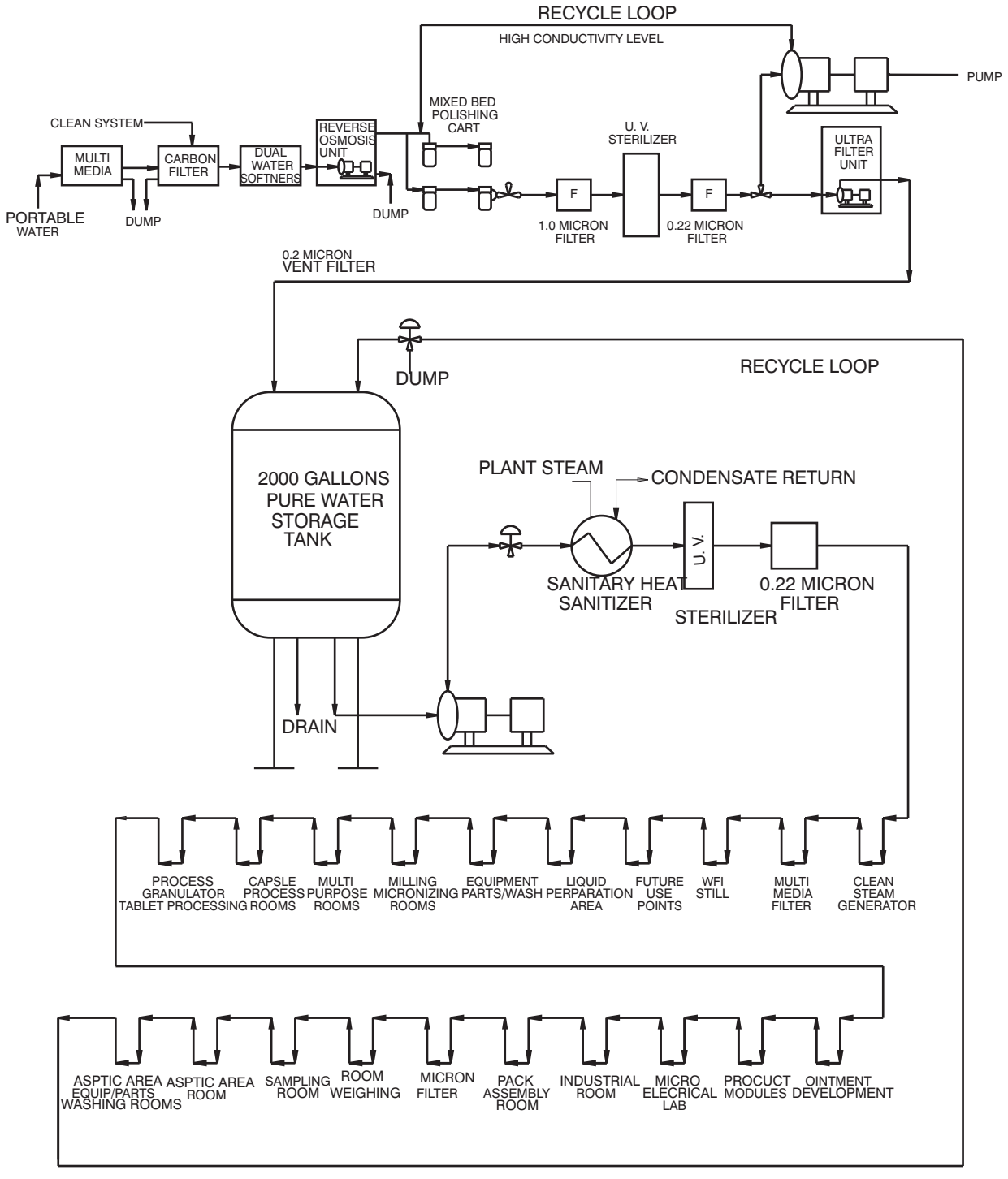
The blow down cycle will help to reduce the concentration of pyrogens in the recirculated portion of the water system.



USP WATER PURIFICATION LOOPING SYSTEM