

Leading Water Treatment Solution Provider Chooses Mettler-Toledo Thornton

THORNTON

Leading Pure Water Analytics

When Leo Pharma and Veolia Water Solutions & Technologies developed a cutting-edge water system and needed fast, accurate and reliable water sensors, they turned to Mettler-Toledo Thornton.

Plant expansion

Leo Pharma (Vernouillet, France) is a producer of anti-thrombotics in pre-filled syringes, blister packed tablets of diuretics, and several leading antibiotics. Leo Pharma invested nearly \$20m in a new syringe filling line to increase syringe production capacity to 18,000 syringes/hour. The new line carries out cleaning, siliconization and sterilization of syringes in situ. This requires the use of Water for Injection (WFI) at different rinse stages on the syringe manufacturing line and clean steam for steaming-in-place. WFI and clean steam are supplied from a water purification plant designed and installed by Veolia Water Solutions & Technologies – using Mettler-Toledo Thornton pure water instrumentation – which is housed in a new, purpose-built Clean Utilities Building.

The pre-filled syringes produced in the Vernouillet, France facility are destined for the international market including the USA, so the manufacturing facility is inspected by the US Food & Drug Administration (FDA). This means that both WFI and clean steam have to be produced from purified water and all three of these substances have to comply with the United States Pharmacopoeia (USP). Clean steam, used in the filling machine and for sterilization in situ, has to meet the same specifications as the WFI.

Advanced pure water production

The Clean Utilities water purification system consists of two sections: production, storage and distribution of purified water, and production, storage and distribution of WFI and clean steam. Veolia uses Mettler-Toledo Thornton in both sections to ensure accurate and precise measurements of the water being used, and also to ensure that the purification equipment is working at each stage.

The purified water production system is designed to produce a continuous output of 4,000L/h of USP purified water without any chemical additions. Town water is first filtered, using a 10 µm cartridge filter, to remove any particulate material and then softened in duplex softeners.

The next stage of purified water treatment is reverse osmosis. Permeate from the reverse osmosis unit is further purified by continuous electrodeionization (CEDI) which combines ion exchange and membranes to produce a continuous output of purified water with conductivity typically less than 0.2 µS/cm and silica less than 50 µg/L. Mettler-Toledo Thornton's cutting-edge line of conductivity sensors assures optimal conductivity is being monitored in this stage.

Dissolved carbon dioxide gas, which is poorly removed by both reverse osmosis and CEDI, is removed from the reverse osmosis permeate by membrane degassing using a hydrophobic membrane which allows gas to pass through it. Membrane



degassing completely eliminates the need to dose caustic soda (the usual means of carbon dioxide removal in RO membrane systems). For ultimate security, the reverse osmosis and CEDI streams are duplicated and, when there is no demand for make-up from the purified water tank, the system runs in recirculation mode to prevent stagnation and minimize bacterial growth.

Benefits of the THORNTON solution

“For the purified water production skids we have chosen the THORNTON 770MAX which enables us to simplify our electrical cabinet design. The 770MAX is a compact and multi-channel transmitter designed to ensure process efficiency with minimal effort on our part,” said Hervé Caron, Project Manager at Veolia Water STI.

Water for Injection

WFI is produced by distillation, as required by the European Pharmacopoeia. In order to minimize both the operating costs and the environmental impact, Veolia Water Solutions and Technologies carried out a study which showed an 8-column multiple effect still to be the most energy efficient option. The still delivers 2,800 L/h of WFI at 85 °C and atmospheric pressure, into an insulated 7,000 L vertical tank from which it is continuously circulated around a 250 m long distribution loop supplying six points of use. The complete system is designed to meet all the requirements of cGMP and the ISPE Baseline Guide and is fabricated from 316L stainless steel electropolished to 0.6 µm Ra.

The WFI water system is sterilized by pressurized hot water at about 1.5 barg in a fully automatic sequence. The sequence is automatically logged for

validation purposes. The conductivities are monitored on WFI loops by multiple Mettler-Toledo Thornton transmitters including the 770MAX. The 770MAX is coupled with the 5000TOC analyzer which measures a USP critical parameter: Total Organic Carbon. “Mettler-Toledo Thornton’s ‘Smart’ sensors give us peace of mind for the commissioning phase; particularly the automatic ‘plug-and-play’ sensor setting recognition,” emphasizes Hervé Caron.

The second point on the purified water loop is used to feed the clean steam generator, which is identical in principle to a distillation plant except that there is only one column and the steam is not condensed. The generator produces 660 kg/h of clean steam at a pressure of 2 barg which is used for in situ sterilization of vent filters, purified water and WFI tanks, feeding the autoclave and for the steaming in place of process equipment. Each WFI generator is fitted with Mettler-Toledo Thornton transmitters for design consistency.

Automatic control of the clean utilities plant is by six independent programmable logic controllers linked via a PROFIBUS DP network. The operator interface complies with 21 CFR Part 11. The design, construction and start-up phases of the clean utilities plant were managed under GAMP (Good Automated Manufacturing Practice), allowing the project to be executed in an orderly, standardized form recognized by the pharmaceutical industry.

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Transmitter 770MAX