

Pharmaceutical Purified Water

Perspectives in Pure Water Analytics



9 News

THORNTON

Leading Pure Water Analytics

Implementation of the Multiparameter Concept in Pharmaceutical Water Preparation

A German customer successfully employs a 770MAX multiparameter transmitter to measure conductivity, TOC and ozone in the production of purified water, complying with international Pharmacopoeia requirements.



Anton Hübner GmbH & Co. KG, Ehrenkirchen, Germany

Anton Hübner GmbH & Co. KG, is one of Germany's most important manufacturers of products for the health food store market. Over 200 employees are engaged in the manufacture of some 300 different products, including non-prescription drugs, medicinal products, nutritional supplements, and cosmetics. In the course of modernization of the water supply installation in the production area, the entire ultrapure water system, including preparation, storage and distribution was completely renewed. Throughout the production area, only "Purified Water" complying with international Pharmacopoeia requirements is used. Hübner pays special attention to achieving outstanding microbial quality of the water.

Water preparation, Hager+Elsässer GmbH, Stuttgart

"After in-depth comparison between different suppliers and processes as well as an intensive exchange of experience with other purified water producers, we decided to go for the system from Hager+Elsässer in Stuttgart", recalls Peter Rupprecht, head of process engineering at Hübner. Hager+Elsässer GmbH has long been a leader in the field of water preparation in Germany. Each project for the pharmaceutical industry is reliably planned and carried through in accordance with cGMP. All types of water preparation techniques are available, which makes it possible to work out an optimal solution for each individual application requirement.



METTLER TOLEDO

Purified water production and distribution system

Purified water is produced by Anton Hübner using a softening process, reverse osmosis and electro-deionization (EDI). During softening in an ECOSOFT TS unit, regeneration of the ion exchange resin is carried out using hot brine which at the same time effectively provides for sanitization of the softener. "The microbial quality of the softened water is really exceptional", says Peter Rupprecht.

The next stage employs a ROCEDIS™ system combining reverse osmosis and electro-deionization. The unit can be fully sanitized using hot water. The distinctive feature of this system is the electro-deionization step which is operated without any recirculation of concentrate. This rules out microbial problems such as have been reported in connection with other types of EDI equipment "As yet, hot-water sanitization has not been necessary explains Peter Rupprecht. Three loops, 100, 200 and 300m long, as well as a 10 m³ storage vessel complete the ultrapure water equipment. Two loops are operated as cold water loops with ozone and UV disinfection, the third loop is continually held at over

80 °C (176 °F). This ensures a sustained supply of high-quality water to the user.

Multiparameter instrumentation

The quality-relevant parameters, electrical conductivity, ozone and TOC concentrations are monitored in the compact distribution system SANICIRCLE using online measuring equipment. For these measurements, Hager+Elsässer relies fully on Mettler-Toledo Thornton instrumentation due to its integral approach and pharmaceutical-specific concept. The 770MAX transmitter strictly follows the multiparameter analysis concept. Up to four SMART sensors can be connected to and controlled by this transmitter. In the application at Anton Hübner GmbH & Co. KG, this powerful feature has been exploited to the maximum extent, and the transmitter is equipped with a sensor for measurement of TOC, an O₃ sensor, as well as two conductivity sensors.

Conductivity

The two measurement points for monitoring of the electrical conductivity are located directly following the reverse osmosis and electro-deionization stages. The monitoring point downstream of electro-deionization is the quality-relevant measurement point.

TOC measurement

The 5000TOC sensor continuously monitors the TOC value in the return line of the distribution system. The advantage for the user is an immediate alarm signal should the TOC value overshoot the set value, even if only for a very short time. This enables all further distribution and extraction of

water for the production to be stopped in time, avoiding reject production and thus increased costs.

Ozone measurement

After UV destruction, ozone measurement is taken to verify that there is zero ozone in the purified water at the extraction point. Via a switchover, it is also possible to monitor the ozone concentration prior to UV destruction as well as in the return line to the storage vessel.

Advantages of "SMART" technology

"SMART" technology recognizes (digitally) which type of sensor is connected to which input, and all relative sensor identification and calibration data is automatically communicated to the transmitter, greatly simplifying cable installation and startup. The method of operation is the same for all channels. The most important plant analytical parameters can therefore be easily measured using only one single system. The plant operator has access to details of all connected sensors via a multiline display.

The 770MAX multiparameter concept offers the customer the following advantages:

- Universal design for all parameters
- Uniform training
- Uniform documentation
- Simplified spare parts
- 1 instrument, 4 measuring points
- Digital technology supports straightforward sensor maintenance

 www.mt.com/770max



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TOC and Conductivity Measurements for Improved WFI Quality

Mettler-Toledo Thornton optimized a series of WFI processes with the installation of TOC and conductivity measuring systems. The accurate, fast measurements contributed significantly to improved WFI quality.

AstraZeneca, Sweden

AstraZeneca is one of the world's leading pharmaceutical companies, producing a broad range of medicines. It is active in over 100 countries. Sales in 2006 totaled \$26.5 billion, with an operating profit of \$8.2 billion. The 27 manufacturing sites in 19 countries employ over 66,000 people. In Sweden it is, with 12,800 employees, the country's largest pharmaceutical company. Furthermore AstraZeneca in Sweden is the largest tablet plant worldwide.

Water quality

Water for Injection (WFI) is frequently used in numerous applications in the pharmaceutical industry. It is non-sterile, purified water produced from drinking water either by distillation or two-stage (double pass) reverse osmosis. To meet microbial quality requirements, WFI is stored and distributed at about 80 °C. Regarding bacteria limits, endotoxins as components of the cell wall are shed during bacterial cell growth and from dead bacteria. With membrane filtration, the endotoxin concentration can be limited. The chemical purity requirements of WFI are the same as for purified water.

Application

AstraZeneca has installed several systems to produce WFI, and therefore the demand to optimize the processes was obvious. According to USP requirements, analytical measurements for TOC also had to be considered. It was decided to install the measuring systems on the return loops of all 8 systems in operation. Based on experience, Mettler-Toledo Thornton recommended the well-established 5000TOC Sensor together with the 770MAX analyzer, and the 243E223 conductivity sensor in combination with the 200CR transmitter.

The products

The Thornton 5000TOC Sensor with 770MAX Analyzer provides an ideal and economical analytical package. The 770MAX can accept 3 other analytical sensors in addition to TOC, including conductivity, pH, ORP, dissolved oxygen or ozone, plus pressure, tank level or two flow sensors. The 770MAX can also interface with two 5000TOC sensors, leaving two additional smart channels for conductivity, pH, ozone or DO measurement and two pulsed flow channels are also available.

Customer benefits

Accurate, fast and convenient measurements of the organic level in WFI systems can save millions of dollars in lost product, pharmaceutical manufacturing downtime and regulatory investigations. Benefits such as continuous online measurement in a low-maintenance, industrial package with proven Multi-Parameter technology are highly welcome.

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Training and Technical Services

On-site instrument operation and calibration training workshops

THORNTON's Operator Training Courses are tailored to each customer's requirements. The course is conducted in a classroom setting where interaction between instructor and participants is encouraged. Each attendee is supplied with material detailing the course content. Instruments are provided for hands-on participation.

The areas covered in this training program focus on THORNTON instrumentation, calibration, and maintenance specific to your facility. Additional technical topics may be added or substituted as requested.

Traceable instrument calibration

THORNTON offers instrument calibration and validation services traceable to national standards, industry guidelines

and/or regulatory requirements. Services using factory-trained technicians are available at our facilities in Bedford, Massachusetts or on-site at your location. Each calibrated/validated instrument is supplied with the appropriate calibration documents.

Specialized conductivity calibrations

Choose one of seven unique conductivity calibrations to fit your application needs, from standard calibrations to customer-specified temperature and ASTM verification points. System calibrations are also available where the instrument and sensors are calibrated together optimizing system accuracy.

Service and calibration contracts

A THORNTON representative will provide on-site service for items covered under the agreement. These services include, but are not limited to:

- Calibration/validation of instrument and sensor system
- Issuance of appropriate documentation
- Identification and verification of all software revisions
- Minor repairs or adjustment of instruments
- Installation and validation support services
- TOC test services
- On-Site System Suitability Testing

Tradeshows	Location	Dates 2007
Semiconductor		
SEMICON West	San Francisco, CA USA	July 17-19
SEMI - Taiwan	Taipei, Taiwan	Sept 12-14
UPW - USA	Austin, TX USA	November 7-8
SEMI - Japan	Tokyo, Japan	December 5-7

Tradeshows	Location	Dates 2007
Power Generation		
South West Chemical	Page, AZ USA	July 16-19
AEP BRO	Columbus, OH USA	August 14-16
IWC Pittsburgh	Pittsburgh, PA USA	October 21-25
SCIENSTECH (NUS)	Clearwater Beach, FL USA	November 13-15

Tradeshows	Location	Dates 2007
Pharma UPW		
ISPE - Boston	Foxboro, MA USA	October 17
ISPE - Annual USA	Lake Buena Vista, FL USA	November 4-7

Mettler-Toledo Thornton, Inc.

36 Middlesex Turnpike
Bedford, MA 01730, USA

www.mt.com/thornton

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