

# High-Precision Conductivity Measurement at Extreme Temperature Differences



Image 1: EVER Pharma Jena with a new high-bay warehouse

**Conductivity sensors used in hygienic applications have to withstand regular CIP (Cleaning in Place) and SIP (Sterilization in Place) processes as well as related strong temperature differences. Therefore, EVER Pharma Jena uses the extremely robust conductivity sensors SE 605 H and SE 680 with Memosens technology from Knick Elektronische Messgeräte.**

EVER Pharma Jena GmbH, which was founded in 1950 as VEB Jenapharm and had operated under the name Jenahexal until their acquisition by the Austrian pharmaceutical manufacturer EVER Pharma in 2011, has specialized in the production of aseptic and sterilized preparations in pharmaceutical phials, vials and pre-filled syringes. Today, the annual production capacities of the company amount to 130 million units. The product range includes neurological products, analgesics and hormones mainly for clinic supplies. The EVER Pharma Jena specializes on crystal suspensions as well as on hormone preparations which are produced in strictly separate plants due to the risk of contamination.

## Efficient CIP/SIP plant

Because of their wide range of products including different active substances, EVER Pharma Jena decided for a process design where the preparation tanks in the production aren't connected with the filling via a static pipe system. Instead, the plant sections are decoupled through the use of mobile sterile filtrate tanks. "This allows us to have a significantly more flexible production at a higher product variant", Martin Reuther, Project Manager at EVER Pharma Jena, says.

In order to establish this process, the company put a new CIP/SIP plant into operation in 2013. This cleaning plant is capable of separately cleaning two sterile filtrate tanks at the same time. If needed, a third cleaning station can be activated. The design results in large time savings with 54 tanks temporarily in alternating use and requiring regular cleaning and sterilization.

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### Process flow

In the preparation plant, EVER Pharma Jena operates three preparation tanks with a capacity of up to 1,000 l. Prior to further processing, the solution prepared in the preparation tanks must be freed from of any existing microorganism through filtration. For this, the tanks are pressurized resulting in the content accumulating the mobile sterile filtrate tanks through corresponding inlet lines and sterile filters. They are located in a plant section of zone A for which, according to the Typical Air Quality Classification (WHO TRS No. 823 Annex 1), strictest antiseptic conditions are required including a room temperature that is almost 100 % particle-free. Then, the mobile sterile filtrate tanks with the filtered solutions are transferred to the filling systems where they are filled in primary tanks. To avoid any external contamination during this process, the sterile filtrate tanks are pressurized.

### Hourly CIP and SIP process, 24 times a day

The cleaning plant is in operation up to seven days a week, around the clock. As EVER Pharma Jena produces different substances even in small batches, the process-wetted plant sections are cleaned and sterilized every hour. First, the sterile filtrate tanks are connected to the cleaning plant and the entire process circuit including the emptied tanks is rinsed with demineralized water and cleaning agents.

Two installed spray balls in the tanks provide for a constant and reliable cleaning of the inside. A toroidal conductivity sensor integrated in the rinsing cycle is used to control the CIP procedure.

### Use of conductive and inductive conductivity sensors from Knick

For this application, the EVER Pharma Jena engineers decided for the hygienic, toroidal conductivity sensor SE 680 with Memosens protocol from Knick Elektronische Messgeräte. Due to its design without any seals, joints and gaps as well as a dirt-repellent surface made of FDA-approved Virgin PEEK, the compact SE 680 is highly durable. The inductive technology isn't influenced by the polarization and doesn't require sensor surfaces that may be subject to corrosion. The SE 680 sensor with an extremely wide measuring range of 0 to 2000 mS/cm at a resolution of 2  $\mu$ S/cm monitors the entire cleaning process and must ensure that, regardless of the derivative, the primary product and residuals of the cleaning agent have completely been removed from the tank. Afterwards, the final rinse with WFI (Water for Injection) will be executed. Based on the requirements of EVER Pharma Jena, the ultrapure water in WFI quality must show a non-temperature compensated conductivity value of < 2.7  $\mu$ S/cm. Higher values indicate that there are still undesirable substances or cleaning agents in the water that require additional rinsing.



Image 2: One of the mobile sterile filtrate tanks that EVER Pharma Jena uses to filter out solid content from active substances. The tanks are cleaned and sterilized every hour.

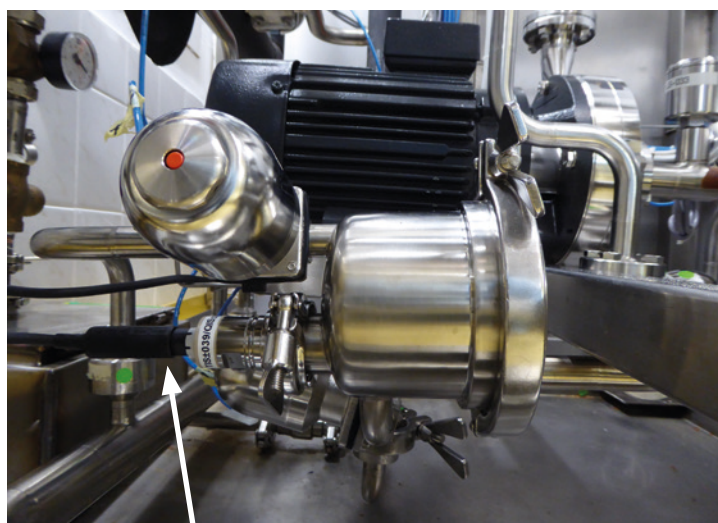


Image 3: Point of measurement of the SE 605 H. In the lower left corner of the picture you see the Memosens sensor connection.



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### No more contaminants

To monitor the final rinse with WFI, the SE 605 H Memosens 2-electrode conductivity sensor is used. This sensor was developed by Knick for measuring ultrapure water in the range of 0.001 to 600  $\mu\text{S}/\text{cm}$ . The SE 605 H has a hygienic design with two coaxially arranged electrodes of electro-polished stainless steel 1.4435 that shows a surface roughness of  $< 0.4 \mu\text{m}$  or  $< 0.8 \mu\text{m}$ . The insulator consists of PEEK, all used materials are FDA compliant. The wet and hot environmental conditions in the plant are no problem for sensors with Memosens technology. A particular feature of this digital sensor technology is that the processing of the measured values based on inductive, contactless data transmission and energy supply takes place in the sensor head. This way, also sensor relevant data can be directly saved and analyzed in the sensor enabling the pre-calibration of the sensors in the laboratory. Thanks to a bayonet coupling, the sensor can be easily connected and disconnected without any cable twisting. Furthermore, it allows inductive transmission of the digitized measured values between sensor and process device. The contactless coupling of the plug connection can neither be affected by moisture, corrosion nor by deposits and it ensures a perfect galvanic separation as well as a trouble-free data transmission.

As soon as the SE 605 H measures the required value of  $< 2.7 \mu\text{S}/\text{cm}$  using the WFI in the last rinsing process, the cleaning process is completed and the SIP process can be started. Here, ultrapure steam, which is heated to  $126^\circ\text{C}$ , is led through the system for 15 minutes in order to reliably sterilize all process-wetted parts of the plant.

### Signal transmission in a compact design

The measured values from the sensors are transmitted to the control system via slim MemoRail analyzers in just 12.5 mm wide DIN rail housings. These analyzers transform the sensor and temperature values into 4 to 20 mA signals and directly transmit them to the control system via two standard-signal current outputs. DIP switches on the front of the housing enable quick and easy configuration of the analyzers, which are suitable for all Memosens sensors (pH glass, ISFET, oxygen, conductivity with two/four electrodes or toroidal sensors).

### Why Knick?

The key criteria for EVER Pharma Jena for selecting the suitable sensors was their robustness against frequent, extreme temperature changes since the hourly cleaning and pure steam sterilization of a plant isn't a day-to-day challenge in the pharmaceutical industry. "Of course, the sensors are also heated by the SIP processes 24 times a day from ambient temperatures to approximately  $127^\circ\text{C}$  and cooled down again", Reuther says. "Conventional conductivity sensors won't withstand this for long. Therefore, our plant manufacturer recommended us to choose sensors from Knick".

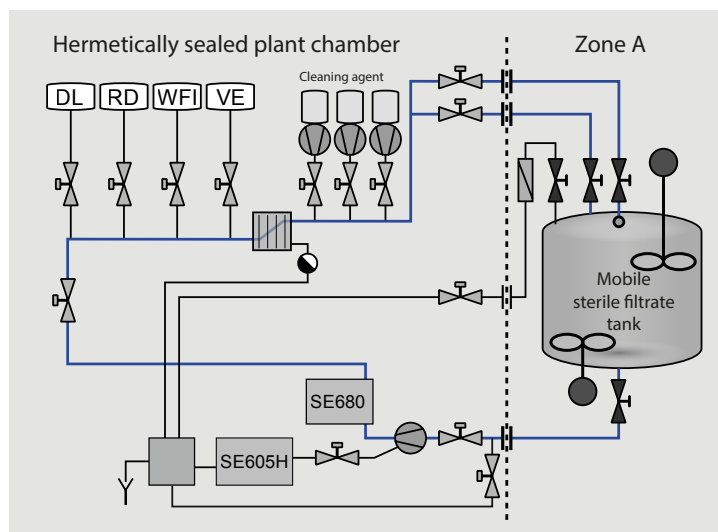


Image 4: Diagram of a new CIP/SIP plant with the conductivity sensors from Knick

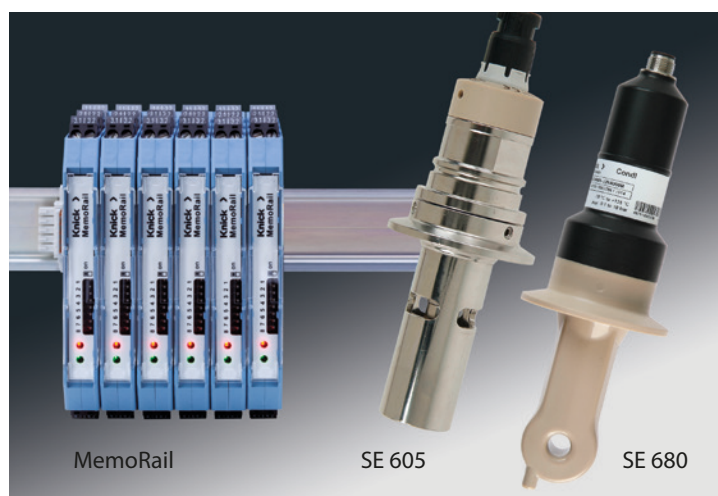


Image 5: EVER Pharma uses SE 605 H Memosens2-electrode conductivity sensor, SE 680 toroidal conductivity sensor with Memosens protocol and the compact analyzers of the MemoRail series for DIN rail mounting.

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