

# Pharmaceutical Plant Simplifies REACTOR MONITORING

Bottom outlet valve with built-in sensor obviates new vessel entry point

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**THE NEED** for process analytical technology (PAT) to optimize pharmaceutical and fine chemical production processes has increased steadily in recent years. Such technology enables real-time monitoring of reactions, providing immediate data on critical process-control parameters. If problems arise during the reaction, the parameters can be modified before the batch is completed. This results in energy and material savings and reduces product sampling. In addition, it ensures optimal product quality.

The manufacturing processes can be monitored with sensors that are installed either directly in the vessel or in the pipeline. If effective process analysis requires sensor installation in the vessel, a suitable entry point must be found. However, modification of existing vessels is prohibitively expensive, involves revalidation and, sometimes, is not even permitted. Entry from the top also can be a problem for low volume batches. So, when a large global pharmaceutical manufacturer wanted to add a sensor to some reactors at a plant in Ireland, it opted for an innovative, cost-effective solution — a bottom outlet valve that incorporates a sensor that quickly and accurately monitors concentrations, phase separations and chemical changes in process liquids (Figure 1). This eliminated the need to modify the existing vessels.

The PAT sensor is an integral part of the valve disc and is directly exposed to the liquid in the

vessel. The combination allows an effective inline measurement of relevant parameters without any process connection adapter. It provides a low-cost option for implementing modern PAT in both existing and new vessels.

Because the sensor is located in the bottom part of the vessel, even low-volume batches can be monitored in real time. If necessary, the sensor can be removed quickly between batches without having to extract the valve from the vessel. The valve, made by SchuF of Germany, comes in a wide variety of specifications, including various actuator types, sizes, accessories and materials such as stainless steel, high-nickel alloy, glass or perfluoro-alkoxy polymer lining.

## SUCCESSFUL APPLICATION

During product development of the sensor, its maker, SensoTech of Germany, has been working closely with the large manufacturer of pharmaceuticals in Ireland. The valve/sensor combination now is being used successfully at one

VALVE WITH INTEGRATED SENSOR



Figure 1. Bottom outlet valve incorporates a sensor for measuring concentrations, phase changes and chemical changes in process liquids.

of the pharmaceutical firm's plants. It is installed at the vessel bottom of a dissolving station. The maintenance-free LiquiSonic sensor measures the concentration of voriconazole in the vessel at a temperature of 25°C to 45°C. The solvent is toluene. The sensor meets the process requirement for Zone 1 explosion protection and is coated with a high-nickel alloy that allows it to withstand aggressive chemical environments.

Many process liquids are prepared by dissolving solid or liquid substances in a solvent. For producing a homogeneous solution with a defined concentration, the analyzer is used to adjust the flow rates of the main substance and the solvent. Measuring directly in the vessel provides accurate concentration values also during startup and rundown processes (forerunnings and last runnings).

The combined valve/sensor provides a variety of benefits, including:

- exact dosing, which helps to save resources;
- inline concentration measurement to ensure constant product quality;
- process monitoring for online process documentation and traceability;
- direct control of the set formula, which increases operational reliability;
- inline process analysis without a costly process connection; and
- direct measurement in the vessel, eliminating dead space.

The advantages are best summed up by an engineer at the pharmaceutical company: "This relative[ly] simple but innovative valve installation optimizes our process significantly through reduced batch cycle time, improved quality and increased process reliability."

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## INTEGRATION INTO THE CONTROL SYSTEM

A LiquiSonic controller displays and processes the measured values. At the pharmaceutical firm, a CAN-bus cable connects the sensor to the controller. The controller can handle up to four sensors. Indeed, at the plant, it gets inputs from another LiquiSonic sensor that monitors concentration in the main pipeline. The controller can store characteristics and records of different process liquids. So if there is a product change, the correct concentration is displayed automatically. The measured values can be read out to do further analyses and create protocols. The clear trend

view provides project and technology engineers with a quick overview of the course of the process.

For automatic process control, the measured values can be transmitted to the process control system via fieldbus, analog or digital outputs, serial ports or Ethernet. At the pharmaceutical manufacturer, the data are sent to the process control system via a 4–20-mA signal to enable maintaining constant concentrations during the batch process.

## ANALYZER CAPABILITIES

The sensor provides precise data on concentration and density, for example, in alkalis, acids, solutions, emulsions or suspensions. In addition, its technology detects phase transitions, enabling accurate and automatic control of phase separation processes. In a continuous process, the concentration monitoring is used to control the valve. This can offer a significant advantage, for example, where there are fast and exact separations among product, intermediate and carrier phases.

The sensor can continuously monitor even complex reactions like crystallizations or polymerizations. So, process parameters such as degree of saturation, seeding point or crystal content can be controlled in a targeted manner.

The technology is based on the measurement of sonic velocity. An ultrasonic signal is sent through the liquid from a transmitter to a receiver; the travel time is a substance-specific value from which concentration can be determined. The transmitter and receiver are integrated in the sensor and their robust construction makes the sensor maintenance-free. Because the sonic velocity also depends on temperature, two temperature sensors also are integrated in the sensor. Sonic velocity measurement is possible in process liquids with temperatures between -20°C and 180°C.

Unlike with other measurement methods such as refractometers, sealing of the actual sensor element is not necessary.

The sensor offers a measuring accuracy of 0.05 wt % that is independent of deposits in contrast to other measuring methods. (The rounded sensor edges preclude formation of deposits anyway.) The sensor design includes no moving components and complies with the strict hygiene requirements of the pharmaceutical industry. Because of the sensor's extreme robustness, mechanical vibrations or pressure surges have no influence on the measurement. ●

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