Stability in pharmaceutical process

Application note A059-FP08-0716A

◆ Pharmaceutical drugs

A leading healthcare company asked Bronkhorst Switzerland for assistance in optimizing a novel production route for API - which are biologically active ingredients in pharmaceutical drugs. This production route is rather unique, and may lead in the future to a procedure that is yet unprecedented within this line of business.

A critical part of the production route is the accurate and smooth dosing of a reaction mixture that contains hard, solid particles with a variable content. The healthcare company started developing this route with a mini-plant, equipped with a single diaphragm pump for dosing chemical compounds. However, this setup could not deliver the required high flow rates, and the pump produced a high level of pulsation, which led to serious problems in process handling. Furthermore, there was no flow control - only some flow monitoring - and the dosing accuracy was not sufficient enough, so they asked Bronkhorst to get involved in the project.

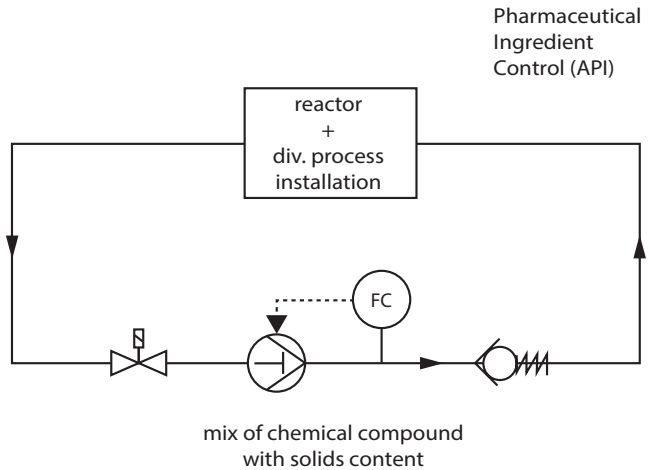
Bronkhorst's mini CORI-FLOW M15 Coriolis Mass Flow Meter in combination with LEWA's PID-controlled LDB3 three head pump.

Application requirements

As the production route is relatively new, and the process fluids are critical to handle, process reproducibility and stability are key requirements. Furthermore, the required high flow rates have to be met, as well as a high dosing accuracy. For this purpose, but also to be able to vary the dosing range, a good control of the dosing process is necessary. Moreover, in order not to disrupt the reaction which is part of the production route, the dosing equipment should not give too much pulsation.

Important topics
- ◆ Stable process and better monitoring
- ◆ Accurate dosing, leading to:
- ◆ Cost reduction of dosed chemicals
- ◆ Improved process flexibility

Process solution



Flow scheme

A combination of LEWA's PID-controlled LDB3 three head diaphragm pump and Bronkhorst's mini CORI-FLOW M15 Coriolis Mass Flow Meter did the trick. The mini CORI-FLOW comprises a PID controlled keyboard that is used here to control the pump. The controlled three pump heads are working smoothly together, leading to an optimal dosing behaviour in which pulsation is strongly reduced, with a stable and accurate flow.

Lower consumption of chemical compounds will lead to lower costs. Since the process fluids and their raw materials are expensive, and the chemical reaction involved in the process is critical to handle, accurate dosing and better monitoring of the used fluids will positively affect the production costs.

As the healthcare company wants to produce a broad range of active pharmaceutical ingredients, the current setup with three pump heads and control equipment is flexible enough to make this possible.

This setup of pump and mini CORI-FLOW can be remotely controlled and monitored with a software tool from other computer systems within the healthcare company. Besides controlling every process parameter, measurement data can be ... ▶

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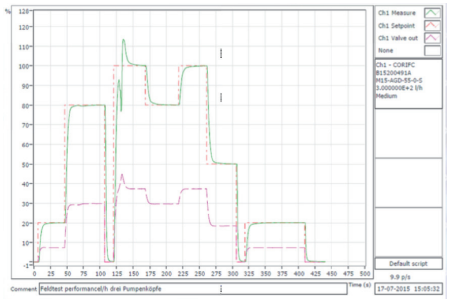
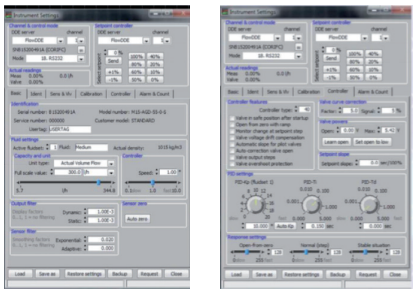
... logged and documented as part of the data management facilities within the software tool.



Field test performance of the setup with three pump heads



Configuration settings of the mini CORI-FLOW M15

Recommended Products

mini CORI-FLOW M15

In addition to the previously developed mini CORI-FLOW series M12-M14 for ranges from 0,1 g/h up to 30 kg/h, Bronkhorst developed the new model M15 for mass flow rates between 0,2 and 300 kg/h. Similar to the models for lower flow rates, M15 contains a uniquely shaped, single loop sensor tube, forming part of an oscillating system.

- Direct mass flow measurement
- High accuracy, excellent repeatability
- Cost-effective design
- Compact design, with integrated PID controller
- Additional density and temperature outputs
- No dead volume (single, uninterrupted tube)
- Analog I/O-signals, RS232-connection, optional on-board fieldbus interface
- IP65 design, optional ATEX approval Cat.3, Zone 2

mini CORI-FLOW Series M12-M14

The unique design of the miniature Coriolis sensor features unsurpassed performance, even with changing operating conditions in pressure, temperature, density, conductivity and viscosity. Contrary to many other Coriolis flow meters on the market, mini CORI-FLOW offers integrated PID control and close-coupled control valves or pumps.

- Direct mass flow measurement, for liquids and gases
- High accuracy, excellent repeatability
- Cost-effective design
- Compact design, with integrated PID controller for fast and stable control
- Now suitable for (very) low flow ranges
- Digital technology allows fieldbus communication

FlowPlot

FlowPlot is a software application for monitoring and service purposes on Bronkhorst digital instruments. It gives good insight in the dynamic behaviour of meters and controllers and allows adjustment of controller, alarm and counter settings. While plotting, the software tool can store the measured data in a CSV file, thus serving as a data logger.

- FLOW-BUS signal monitoring program
- Setpoint for 1 channel (5 programmable values)
- Plots up to 8 parameter values versus time
- Parameters selectable from one or more channels
- Suitable for controller response check
- Trigger facilities for fast step responses
- Scaleable X-axis in time and Y-axis in percent from nominal calibrated value

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FP: Food, Pharma & Beverage
08: Pharmaceutical