APPLICATION NOTE A083-FP08

FLOW SOLUTIONS FOR CONTINUOUS PHARMACEUTICAL MANUFACTURING

Traditionally, most human pharmaceuticals are manufactured in a step by step batch process with extensive tests between steps to insure consistent quality and efficacy of the finished medicine. The production of pharmaceuticals is a highly-regulated process with government agencies inspecting and approving both the process and the facilities where medicines are manufactured.

In 2016 the US Food and Drug Administration (FDA) allowed for the first time in its history a manufacturer to switch from the traditional batch manufacturing process to a continuous manufacturing process. Continuous manufacturing is a pioneering technology that has the potential to transform how medicines are made in the future.

Improvements in Process Analytical Technology (PAT) has allowed the automation and streamlining of what were previous laborious step by step manufacturing processes. This together with the trend towards niche drugs designed to treat a smaller number of people with rare diseases has seen the adoption of Continuous Pharmaceutical Manufacturing in various pharmaceutical companies in the recent years.

As the name suggests Continuous Pharmaceutical Manufacturing involves designing a process where the various steps are automated from beginning to end with minimal manual intervention. Continuous manufacturing demands a higher level of accuracy and monitoring of chemical additions. This is best achieved by using mass flow to measure and control liquid additions where ever possible.

Recently Bronkhorst assisted a leading pharmaceutical company by utilising their mini CORI-FLOW range of instruments in complete skid solutions for their new continuous manufacturing processes.

Application requirements

In order to manufacture pharmaceuticals in a continuous way, the chemical reactants need to be added, mixed and transferred in an accurate and repeatable way throughout the entire process. The process was designed to be modular in that it needed to be easy to modify the process by adding and removing process components as required. Process data collection was vital with real time mass flow, densities and temperatures being recorded and archived for regulatory authorities.

Important topics

- Accurate liquid mass flow control
- Repeatability
- Flexibility, plug & play
- Compactness

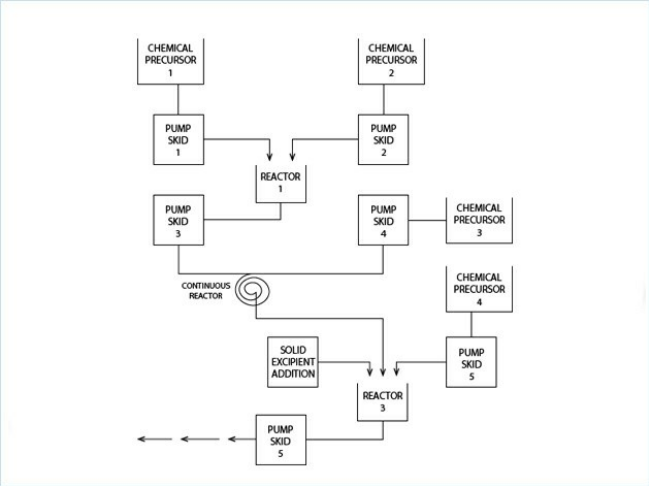
Process solution

For accurate control of liquid flows in continuous pharmaceutical manufacturing applications, Bronkhorst designed and supplied a complete skid solution that combined mini CORI-FLOW mass flow devices with a gear pump, pressure sensor from the IN-PRESS range and a number of liquid filters and valves.

These compact 750 mm sized standardised skids were designed to be stacked somewhat similar to "Lego building bricks", which allows for the flexible assembly and disassembly of the process system. Each medicine to be manufactured requires a different configuration of dosing devices for chemicals, so combining multiple skids results in a bespoke solution. The current application at the pharmaceutical company, typically 11 skids are used to manufacture one product, of which a part is shown in the enclosed process scheme.

By eliminating time-consuming and error-inducing interruptions that can occur in traditional pharmaceutical batch processing, the new continuous manufacturing process is faster, more reliable and more flexible. Communication with the Bronkhorst skid is via the Profibus protocol, the company utilises a DCS (Distributed Control System) which controls the entire process centrally, records data and archives all the data for regulatory and traceability purposes.

Download the flyer 'Continuous Pharmaceutical Manufacturing'.



Flow scheme

Recommended Products

MINI CORI-FLOW™ M12

Min. flow 0,1…5 g/h
Max. flow 2…200 g/h
Pressure rating 200 bar
Independent of fluid properties
High accuracy, fast response

IN-PRESS P-502CI

Min. pressure 2...100 mbar
Max. pressure 1,28...64 bar
Absolute or gauge pressure
Compact IP65 design

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