



# Crystallisation MicroFactory Test Bed

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## Seed generation:

- IKA MagicLab wet mill employs particle size reduction using rotor stator framework (Coarse, medium and fine) which imparts shear rates using different rotational speed.
- Small crystal sizes can be generated which would not be accessible through standard crystallisation approaches.
- DR/DRS module specifications: Speed ranges from 3K to 26K, throughput 50-200 L/hr & circumferential speed 5-40 m/s. Peristaltic pump can be set up in wet mill loop to vary flow rates.
- Generated seeds are added to the MSMPR crystalliser to avoid nucleation and enhance growth in the process.



Figure 1: IKA MagicLab Wet mill

## Crystallisation:

- Mixed Suspension - Mixed Product Removal (MSMPR) is the continuous crystallisation test bed used for crystallisation of different APIs.
- Group of 5 stirred tank jacketed vessels mounted at staggered heights so that the overflow from one vessel feeds autonomously into the next vessel under the effect of gravity.
- Flexible crystallisation cascade unit which allows change in parameters like vessel number, vessel volume, flow rates, residence times, temperature profiles and have potential for adding antisolvent/acid to tailor yield, crystal size distribution (CSD) and polymorphism.
- Operates under steady-state conditions, allowing higher reproducibility and better control of important crystal properties such as the purity and the size distribution. For most drug substances, the crystal size distribution (CSD) is a critical quality attribute (CQA) impacting the drug product performance in the patient.
- With dedicated set-up, 5 vessels of 250 mls volume & 180 mls working volume, flow rates can range from 1 ml/min to 18 ml/min, residence time of 10 mins to 180 mins, and temperature range with dedicated heater chiller with neoprene tubing compatibility is -20 °C to 80 °C.



Figure 2: MSMPR skid crystalliser

- Online PATs (e.g., FBRM, PVM, UV) are used to monitor and control solution concentration, particle size & shape, etc. Assisted by offline measurements (e.g., HPLC, Mastersizer/Morphologi G3) to provide more accurate measurement and validation.
- MSMPR can be operated manually or automated via Perceptive software.
- For MSMPR to be controlled by Perceptive software, tags are published, and the software is modified to allow DCS control.
- PATs like FBRM and UV are connected via virtual machines. Furthermore, they can be connected to SIPAT server which allows real time engine to take control and robust design can be achieved with this.

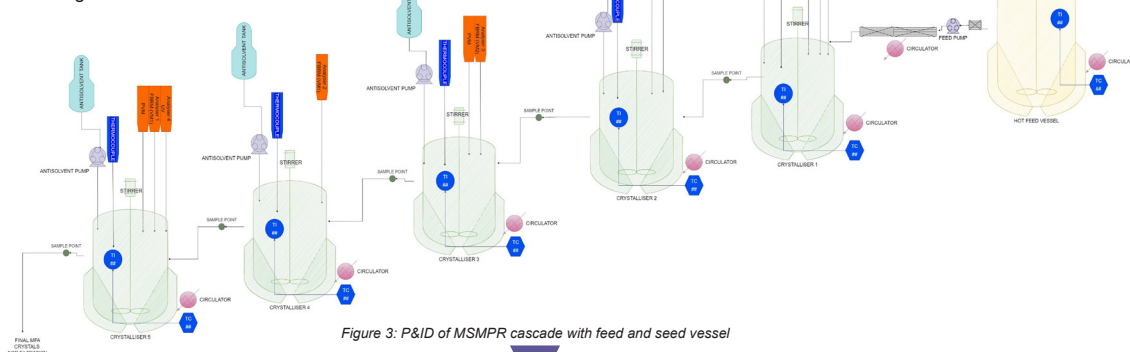


Figure 3: P&ID of MSMPR cascade with feed and seed vessel

## Isolation:

- Coupled with MSMPR to isolate products at laboratory scale automatically in a continuous manner
- Different sintered metal filter medium pore size can be used.
- Carousel consists of 5 ports of 20 mm diameter, 30 ml capacity. Different isolation stages operated in each port.
- Equipment can handle 10-400 microns size particles & capable of processing wide range of solid loading.
- Operating Temperature: -20 °C to 100°C.
- Pressure: -1 bar to 1.5 bar.
- Core technology is based on well established dead end filtration.
- AWL CCF20DD unit can also be automated via Perceptive software.
- AWL CCF20DD unit can be coupled with mass spectrometer (e.g. SIFT-MS) to monitor residual solvent removal during drying.

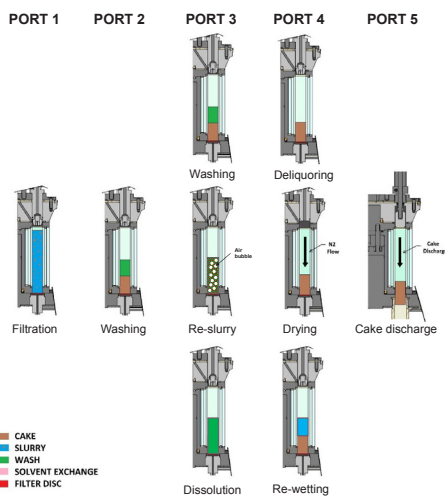


Figure 4: Operations in CCF20DD



Figure 5: CCF20DD Continuous Carousel Filter with Re-slurry, Dissolution and Drying unit