Real time particle size measurement during high-shear melt granulation

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1. Introduction
The intention of pharmaceutical manufacturers to create more robust and controlled processes in production and development increased since the FDA acheived the implementation of PAT-Tools instead of process validation [11].

2. Aims and objectives
In-line particle measurements are well established in fluid bed granulation to control the progress of the process [2].

3. Experimental method
3.1 Formulation type
Different prototype formulations have been chosen for the experiments.

3.2 In-line sensor
A 4 L bowl with an impeller and chopper was used. The binder was added to the formulation type “B”.

4. Results
4.1 Characterisation of prototype formulation type “A”
Three phases of the granulation process could be seen. First phase – till 50 s – showed the mixing of the powder bed. In the second phase a growth in particle size could be detected. It started after adding the binder until “E”. The binder was added until “E”. In the third phase – beginning at 200 s – no further growth of particle size could be found. The final particle size was about 550 µm.

Further investigations will be necessary, because of an unknown signal shortly after adding the melted binder.

4.2 Influence of binder quantity
Fig. 4 shows a granulation experiment which was monitored by four different channels of the in-line particle size probe. Each channel was set to a different ring buffer size.

4.3 Influence of Microcrystalline cellulose (MCC) quantity
The suitability of Microcrystalline cellulose as component of melt granulates as well as its impact on the particle size should be investigated. These examinations were carried out with a modified formulation type “B”.

5. Conclusion
In this work, the particle size distribution during melt granulation processes could be detected. It was possible to observe different phases of granulate formation during the whole process time. The results were in full accordance with theoretical expectations. The endpoint of the granulation process could be fixed precisely. So it could be shown that the used in-line particle size measurement sensor is in principle able to monitor melt granulation processes in high-shear mixers.

6. References