Inline Monitoring of a Hot Melt Extrusion Process by Near Infrared Spectroscopy
Andreas Gryzcke, Chris Heil, Dirk Leister, Scott Martin
Thermo Fisher Scientific, Karlsruhe, Germany

Overview
A prerequisite for FT-NIR method development for application as an inline sensing technique for quality attributes in extrudates such as drug load homogeneity, dissolution, or content uniformity is well defined calibration models for process monitoring.

Methods
Thermo Fisher Scientific BRABENDER Plastograph 6:1 (BRABENDER, Tarbert, PA, USA) with a feeding rate of 500 g/h into a Pharma 16 HME extruder (Krauss-Maffei, Germany) was used in some experiments as reflective material for the NIR light. Lactose was kindly donated by Dow Wolff, Midland, MI, USA. Sentry® WSR N10, Meggle, Germany was used as model drug and was compounded in 5 different concentrations from 0% to 20% into a syrup of microcrystalline cellulose. Spectra were collected directly in reflection mode only. A first set of FT-NIR spectra was measured for the theophylline-loaded extrudates. For the NIR light through the extrudate the drug is converted into its amorphous form and molecular level interactions. One prominent application is the bioavailability enhancement, where inside the extruder the drug is converted to its amorphous form and molecular level interactions are improved. The NIR light through the extrudate shows the differences in second derivatives from the spectra. The drug loads can be clearly separated and identified.

Results
For the study a goal was to investigate some important pre-requisites to predict a drug load by FT-NIR measurements. It is a total degradation depending on the quality of the FT-NIR model which is a good indicator of a robust model for the extrudate. The NIR model is developed in Thermo Scientific RESULT software for automated in line monitoring technique for quality attributes in an extruder. The spectroscopy of the extrudate, the extruder the drug is converted into its amorphous form and molecular level interactions. One prominent application is the bioavailability enhancement, where inside the extruder the drug is converted to its amorphous form and molecular level interactions are improved. The NIR light through the extrudate shows the differences in second derivatives from the spectra. The drug loads can be clearly separated and identified.

Conclusion
The study presented pre-requisites to allow an accurate prediction of drug load by FT-NIR measurement. By FT-NIR the extruder process can be monitored for several quality attributes. It is required to consider the possible challenges in developing a NIR model for process monitoring and the need to highlight points in process and quality monitoring in the next process iteration. The work also showed that using FT-NIR the real process conditions can be better determined than with the extruder parameters such as torque. The robustness of such an FT-NIR quality attribute in extruders is demonstrated.

References