Drug-Polymer Miscibility across a Spray Dryer: A Case Study of Naproxen and Miconazole Solid Dispersions
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Purpose
Spray drying is one of the most commonly used methods of preparation for solid dispersions. The formulation and process variables of spray drying can affect the drying kinetics from solution droplets which play a role in drug-polymer miscibility. During spray drying liquid droplets may also be subjected to a slightly different microenvironment drying conditions. In this study drug-polymer mixing was evaluated across two laboratory spray dryers using two model solid dispersions.

Methods
The solid dispersions of naproxen/PVP-VA and miconazole/PVP-VA were prepared by spray drying. The amorphous-amorphous phase behaviour was assessed based on the glass transition width and the crystallinity was also determined from the melting endotherm of MDSC measurements. The structural changes and the phase behavior were further investigated using ATR-FTIR and PXRD.

Results
Spray dried dispersions with 30% (w/w) naproxen collected from the transport tube of the Pro-C-epT Micro-spray dryer showed the narrowest glass transition width which indicates the highest degree of drug-polymer mixing compared to the other locations. A halo pattern also showed structural changes and variations in solid dispersions collected from different locations. Samples with 50% (w/w) naproxen loading collected from the cyclone and the cyclone steel part of the Buchi mini spray dryer showed a melting endotherm (T_m at 112.2 ± 0.8 °C and H_f between 0.7 and 1.8 J/g) whereas samples from the cyclone tube to the drying chamber were devoid of crystalline material. The variations in drug-polymer mixing extend to miconazole/PVP-VA solid dispersions where 20% drug loading showed location dependent drug-polymer mixing. The variation may extend to a single location of a spray dryer where different particle size range solid dispersions showed variation in glass transition width.

Conclusion
This study showed that variation in drug-polymer miscibility and solid form of the drug in solid dispersions can occur across spray dryers in small scale manufacturing processes. Optimization of formulation and spray drying process parameters is imperative to diminish these variations in order to enhance homogeneity of solid dispersions in the laboratory scale spray dryers.