Correlating Anisotropic Nanoindentation Responses with Bulk Powder Tableting on Two Habits of
Famotidine Form B
P. P. Upadhyay¹, M. K. Mishra², U. Ramamurty², A. D. Bond³
¹University of Copenhagen, ²Indian Institute of Science, ³University of Cambridge

Purpose
Polymorphs are well known to have different mechanical properties. Nanoindentation enables mechanical properties to be tested on single crystals, which should provide the best opportunity to establish a correlation with single-crystal X-ray structures. Nanoindentation was performed on the major faces of two habits of famotidine form B, and correlated with the crystal structure using energy-vector models generated by the PIXEL and processPIXEL programs. Bulk powder tableting behavior was tested for the two crystal habits.

Methods
Single crystals and bulk powder of famotidine form B with two different habits were crystallized from various solvent combinations. Polymorph identification and face indexing was carried out on a single-crystal diffractometer, and nanoindentation was performed using a Triboindenter (Hysitron). Energy-vector models were produced using the PIXEL and processPIXEL programs. Bulk powder was crushed prior to tableting and identical sieve fractions were used to minimize the influence of variable particle size. Tablets of weight approx. 100 mg were prepared using a Gamlen Tablet Press (GTP).

Results
Access to different crystal habits of the same polymorph offers the advantage of testing multiple crystal faces to yield a more detailed picture of anisotropic deformation behavior. For famotidine form B, (10–1) and (100) were identified as the major faces of obtained lath and columnar crystals, respectively. Nanoindentation on (100) revealed a higher elastic modulus and hardness value compared to (10–1). The energy-vector model derived from the X-ray crystal structure showed a 2-D network of strong interactions, indicating probable slip between these planar networks. Indentation on the (100) face occurs perpendicular to the 2-D networks, while indentation on the (10–1) face occurs parallel to these networks. This facilitates movement of the slip planes under the applied load for (10–1), consistent with its softer nature. The bulk powders of both habits showed similar tableting behavior, although strain hardening was seen at higher pressure for the columnar crystals. Out-die mean yield pressure (Py) of the columnar crystals showed a good agreement with elastic modulus which was higher compared to the lath one, thus making it difficult to deform at a given pressure.

Conclusion
Nanoindentation responses on the major faces of two habits of famotidine form B demonstrate an anisotropic elastic modulus, which can be effectively correlated with the X-ray crystal structure using an energy-vector model. For the bulk powder tableting behavior, a good correlation was obtained between the nanoindentation elastic modulus and the out-die mean yield pressure though both habits showed similar tableting behaviors. However, a correlation between elastic modulus and mean yield pressure should be used with a caution on account of particle size dependency of Py.