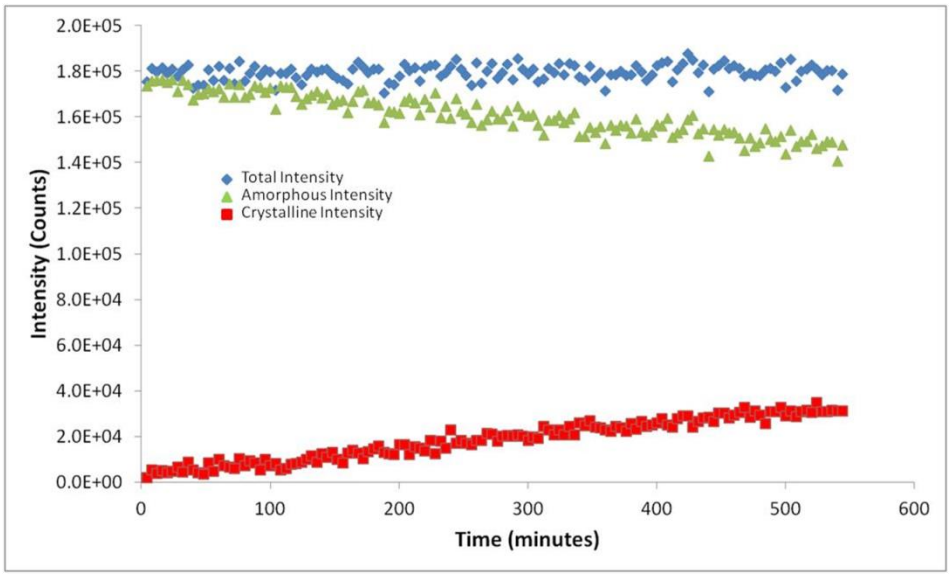
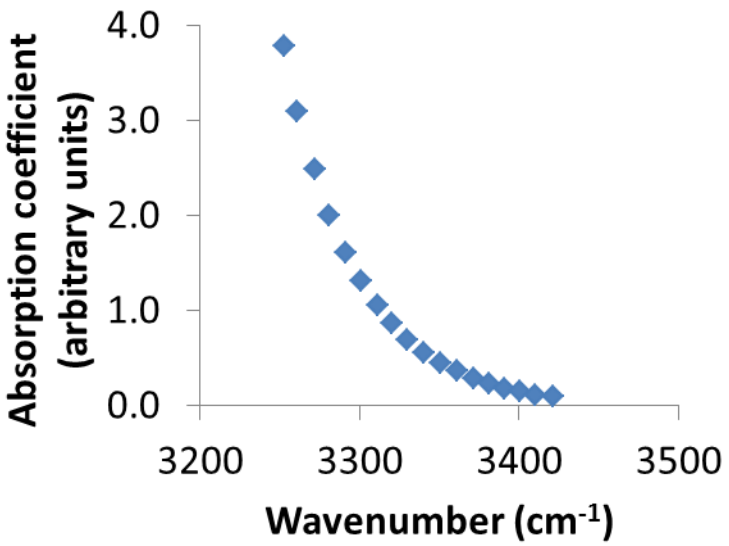
Supporting Information



Supporting Figure 1. A representative plot of the total (crystalline + amorphous), amorphous and crystalline integrated intensity during the isothermal crystallization studies of amorphous NIF-PVP (10% w/w) at 70°C. Initially, the sample was X-ray amorphous (no evidence of crystallinity), and at the end of the experiment, it was ~15% crystalline. This data indicates that the % crystallinity can be expressed as crystallinity index.[1]



Supporting Figure 2. A plot of absorption coefficient versus frequency of NH stretching vibration. The absorption coefficient of the NH stretch vibration is known to be highly wavenumber dependent.[2] From Beer-Lambert's law, the size of any population is proportional to the quotient of peak absorbance and the absorption coefficient. Therefore, to estimate the relative extent of hydrogen bonding the height of drug-polymer peaks, from the subtracted spectra, were divided by the wavenumber specific absorption coefficient.

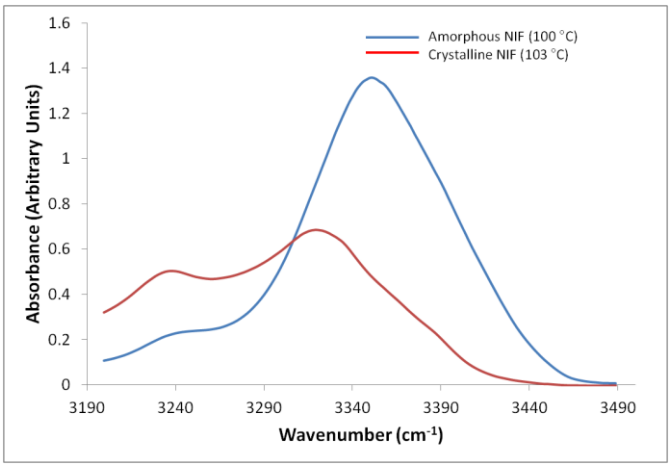
Supporting Information S3

Polymer	Molecular weight	MW of monomer	Solid Dispersions*			
			No. of monomers		Drug to monomer ratio	
			10% w/w	20% w/w	10% w/w	20% w/w
PVP	2,500	111	~$0.054*10^{23}$	~$0.108*10^{23}$	~2.9:1	~1.3:1
HPMC - AS	18,000	252	~$0.0239*10^{23}$	~$0.0478*10^{23}$	~6.5:1	~2.9:1
PAA	1,800	72	~$0.0836*10^{23}$	~$0.167*10^{23}$	~1.9:1	~0.8:1

Supporting Table 1. Calculation of number of drug molecules "available" per monomer unit of the polymer for hydrogen bonding interaction. Calculations (assuming one hydrogen bonding interaction per monomer) suggest the rank ordering of hydrogen bonding: PAA > PVP > HPMCAS. The experimental results are not in agreement with the theoretical calculations. A possible explanation is the strength of drug-monomer interactions. A comparison of the friction coefficient of the PVP SD (10% w/w) and the HPMCAS solid dispersion (20% w/w) suggests that despite a similar number of monomers available for interaction between the drug and the polymer, the much stronger interactions between PVP and NIF result in a higher friction coefficient.

*The calculation assumes 10 g of SD, and the polymer content is either 1 g (10% w/w) or 2 g (20% w/w).

Supporting Information S4



Supporting Figure 3. FTIR spectra revealing an amorphous to crystalline transition of NIF from 100 °C (amorphous form) to 103 °C (crystalline form).

References

1. Nunes, C.; Mahendrasingam, A.; Suryanarayanan, R., Quantification of Crystallinity in Substantially Amorphous Materials by Synchrotron X-Ray Powder Diffractometry. *Pharm Res* **2005,** *22* (11), 1942-1953.

2. Skrovanek, D. J.; Howe, S. E.; Painter, P. C.; Coleman, M. M., Hydrogen Bonding in Polymers: Infrared Temperature Studies of an Amorphous Polyamide. *Macromolecules* **1985,** *18* (9), 1676-1683.