

PHYSICAL STABILITY OF AMORPHOUS SOLID DISPERSIONS: XRPD AND COMPUTATIONAL STUDIES OF 'MISCIBILITY'

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The standard method of assessing miscibility of an amorphous API-polymer dispersion is based on the number of glass transition temperatures (T_g) measured using differential scanning calorimetry (DSC). It has been our experience that this method has predictive limitations, particularly when phase separation in the mixture produces amorphous domains with sizes less than approximately 30 nm, below the resolution of DSC. Therefore, we have developed a complimentary x-ray powder diffraction (XRPD) method coupled with novel computational techniques to assess the physical state in such systems. Results from the application of these new techniques to the assessment of miscibility in five model dispersion systems (felodipine:PVP, nifedipine:PVP, ketoconazole:PVP, pimozone:PVP and felodipine:polyacrylic acid) will be presented and compared to a DSC-based approach. In addition, long-term (approximately 1 year) results of a physical stability study of these dispersion systems will be presented and compared to predictions made from the XRPD/computational analysis. Lastly, the effects of humidity stress on the miscibility of amorphous dispersions will be discussed using the example of felodipine:PVP, with implications on accelerated aging studies.