

## Solid dispersion – an industrial scale one step process for poorly soluble drugs

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### **Purpose.**

The oral bioavailability enhancement of poorly soluble drugs remains one of the most challenging aspects of drug development. Incorporating the poorly soluble drug substance into a solid dispersion is known to be effective in enhancing the oral bioavailability. The primary limitations in commercializing this technology have been the lack of efficient manufacturing process and chemical-physical instability. The MeltDose proprietary technology overcomes these limitations as based on incorporating the drug substance in a meltable vehicle and subsequently spraying the mixture on a particulate carrier (e.g. lactose) using a fluid bed equipment. Most importantly this is a one step process in contrast to other approaches.

### **Methods.**

Fenofibrate (aqueous solubility <0.3 µg/ml) was dissolved in a mixture of melted PEG 6000 and Poloxamer 188 in a heated pressure tank and sprayed on lactose 200 mesh in a fluid bed using a specialised heated binary nozzle. The particle size distribution of fenofibrate as precipitated in the solid dispersion was determined by laser diffraction (Malvern Mastersizer 2000) in aqueous suspension dissolving the remaining excipients of the granulate. The appearance of the fenofibrate crystals was examined by SEM by filtering off the crystals from an aqueous suspension on a 0.22 micron filter.

### **Results.**

Fenofibrate recrystallizes in a solid dispersion as crystalline particles with a median volume particle size of approx. 1 µm. The granular product was tableted by direct compression. The dissolution profile of the tablets and the particle size of fenofibrate was stable during storage. PK studies revealed increased bioavailability and elimination of the food effect as compared to 35% increased bioavailability with food observed for plain tablet formulations. The product is FDA approved and marketed in the USA.

### **Conclusion.**

The MeltDose® technology has the following main process advantages:

Gentle process: No water or organic solvents, controlled atmosphere, etc.;

Flexibility in choice of excipients and processing;

Flexibility in choice of vehicle;

Direct tablet compression;

High drug load;

Easy scalability; and

One step process

Conventional equipment and low production cost.