SUPPLEMENTARY INFORMATION

## Application of Resonant Acoustic Mixing in the Synthesis of Vitamin C-Nicotinamide Variable Stoichiometry Cocrystals

Minhthi Bui<sup>a</sup>, Paroma Chakravarty <sup>a</sup> and Karthik Nagapudi \*<sup>a</sup>



Figure S1: (a) TGA and DSC for Form I of 1:1 Nicotinamide-Vitamin C cocrystal. Weight loss up to 100 °C =0.05%. A small endothermic peak (labeled with a "\*") was observed prior to main melting endotherm in the DSC thermogram of Form I. Melting onset of the main endothermic peak = 146.6 °C. The origin of this endothermic peak is unknown. (b) TGA and DSC for Form II of 1:1 Nicotinamide-Vitamin C cocrystal. Weight loss up to 100 °C =1.5%. Melting onset = 146.4 °C.



Figure S2: XRPD patterns of Form I and II before and after drying at 50 °C for 1 hour. XRPD data was collected on the solids obtained from the 20 gram scale up run.



Figure S3: DSC Thermograms of 3:1 Nicotinamide/Vitamin C Cocrystal after LA-RAM using different liquid additives at  $\eta$  of 0.5. LA-RAM was conducted at 60G for 180 minutes.



Figure S4: XRPD patterns of 3:1 cocrystal of Nicotinamide and Vitamin C after 3 and 6 hours of RAM using methanol as the liquid additive shown in comparison to the reference 3:1 powder pattern and Nicotinamide. Peak labeled "\*" is unreacted Nicotinamide.



Figure S5: XRPD patterns of 3:1 cocrystal of Nicotinamide and Vitamin C as a function of the amount of Ethanol used shown in comparison to the reference 3:1 powder pattern, Vitamin C, and Nicotinamide.



Figure S6: DSC thermograms of 3:1 cocrystal of Nicotinamide and Vitamin C made by RAM using methanol and ethanol as the liquid additives. The endotherm labeled "\*" is associated with the unreacted Nicotinamide.



Figure S7. XRPD patterns of (a) Reference Form II and Form II subjected to LA RAM for 3 hours using Ethanol as the liquid additive at a  $\eta$  of 0.5 and (b) Reference Form I and Form I subjected to LA RAM for 3 hours using Methanol as the liquid additive at an  $\eta$  of 0.5.