## Preparation of Theophylline-Benzoic Acid Cocrystal and On-Line Monitoring of Cocrystallization Process in Solution by Raman Spectroscopy

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## SUPPLEMENTARY MATERIAL

Appendix A:

**Figure S1.** (a) The variation of Raman spectra at 1270-1360 cm<sup>-1</sup>; (b) The change of relative peak intensity of 1323/1331 cm<sup>-1</sup> in TP-BA cocrystal formation in slurry crystallization at 298.15 K.

Figure S2. (a) The variation of Raman spectra at 1120-1200 cm<sup>-1</sup>; (b) The change of relative peak intensity

of 1161/1171 cm<sup>-1</sup> in TP-BA cocrystal formation in slurry crystallization at 298.15 K

**Figure S3.** (a) The variation of Raman spectra at 890-940 cm<sup>-1</sup>; (b) The change of relative peak intensity of 918/925 cm<sup>-1</sup> in TP-BA cocrystal formation in slurry crystallization at 298.15 K

**Figure S4.** HPLC chromatograms of slurry crystallization products in Table 3: exp 1 (a); exp 2 (b); exp 3 (c); exp 4 (d) and cooling crystallization product (e)

Appendix B:

Table S1Information about Raman spectra in the range of 1640-1720 cm<sup>-1</sup> in Figure 5aTable S2Information about Raman spectra in the range of 1270-1360 cm<sup>-1</sup> in Figure S1aTable S3Information about Raman spectra in the range of 1120-1200 cm<sup>-1</sup> in Figure S2aTable S4Information about Raman spectra in the range of 890-940 cm<sup>-1</sup> in Figure S3a

## Appendix A:



**Figure S1.** (a) The variation of Raman spectra at 1270-1360 cm<sup>-1</sup>; (b) The change of relative peak intensity of 1323/1331 cm<sup>-1</sup> in TP-BA cocrystal formation in slurry crystallization at 298.15 K. The information about time interval of Raman spectra are listed in Table S2.



**Figure S2.** (a) The variation of Raman spectra at 1120-1200 cm<sup>-1</sup>; (b) The change of relative peak intensity of 1161/1171 cm<sup>-1</sup> in TP-BA cocrystal formation in slurry crystallization at 298.15 K. The information about time interval of Raman spectra are listed in Table S3.



**Figure S3.** (a) The variation of Raman spectra at 890-940 cm<sup>-1</sup>; (b) The change of relative peak intensity of 918/925 cm<sup>-1</sup> in TP-BA cocrystal formation in slurry crystallization at 298.15 K. The information about time interval of Raman spectra are listed in Table S4.



Figure S4. HPLC chromatograms of slurry crystallization products in Table 3: exp 1 (a); exp 2 (b); exp 3

(c); exp 4 (d) and cooling crystallization product (e)

## Appendix B:

Total spectra	Total recording time	Time point of first	Time interval
number	/ min	spectra / min	/ min
90	90	1	1

Table S1 Information about Raman spectra in the range of 1640-1720 cm<sup>-1</sup> in Figure 5a

Table S2 Information about Raman spectra in the range of 1270-1360 cm<sup>-1</sup> in Figure S1a

Total spectra	Total recording time	Time point of first	Time interval
number	/ min	spectra / min	/ min
90	90	1	1

Table S3 Information about Raman spectra in the range of 1120-1200 cm<sup>-1</sup> in Figure S2a

Total spectra	Total recording time	Time point of first	Time interval
number	/ min	spectra / min	/ min
90	90	1	1

Table S4 Information about Raman spectra in the range of 890-940 cm<sup>-1</sup> in Figure S3a

Total spectra	Total recording time	Time point of first	Time interval
number	/ min	spectra / min	/ min
90	90	1	1