

Multicomponent Chemical Imaging of Pharmaceutical Solid Dosage Forms with Broadband CARS Microscopy

*Christopher M. Hartshorn¹, Young Jong Lee¹, Charles H. Camp Jr.¹, Zhen Liu³, John
Heddleston¹, Nicole Canfield², Timothy A. Rhodes², Angela R. Hight Walker¹, Patrick J. Marsac³
and Marcus T. Cicerone^{1*}*

¹Materials Measurement Laboratory, National Institute of Standards and Technology,
Gaithersburg, Maryland, 20899 United States

²Merck, Analytical Sciences, Rahway, New Jersey, 07065 United States

³Merck, Molecular & Materials Characterization, West Point, Pennsylvania, 19486 United States

Abstract for Supporting Information

The supplementary material presented here (Figures S-1 to S-4) represents the analysis of the active pharmaceutical ingredient used in this work, indomethacin, prior to being tableted. Also, the final figure S-5 represents the analysis of a single particle of the gamma polymorph after tableting of the solid dosage form. The purpose of including this data is to verify the initial purity of the API polymorphs and to substantiate claims made within the primary manuscript with respect to the crystalline API's impurity discovered by BCARS in the solid dosage form.

SUPPORTING FIGURES

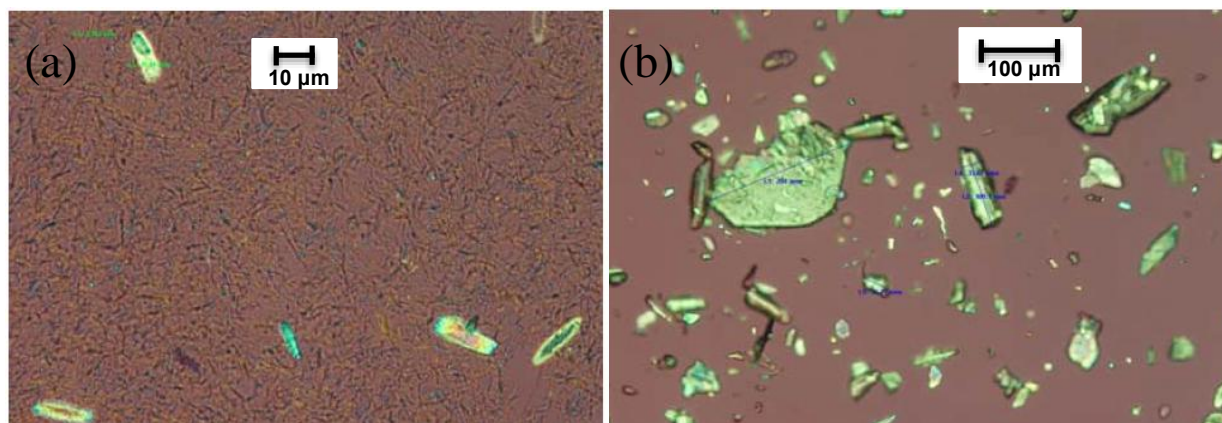


Figure S-1. Optical micrographs of α -indomethacin (a) and γ -indomethacin (b) crystals before tableting on filter paper (α -IMC) and in Petri dish (γ -IMC), respectively.

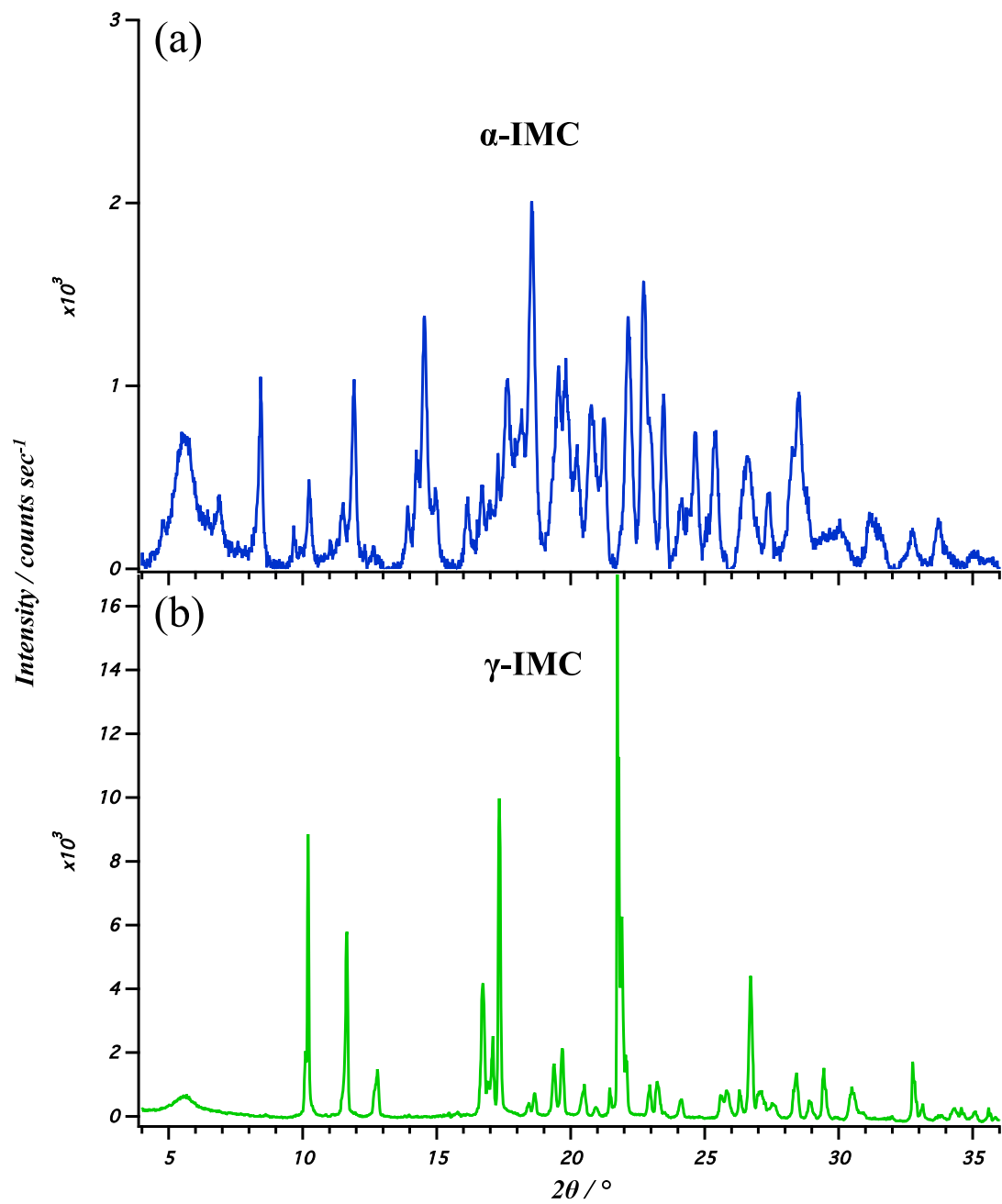


Figure S-2. X-ray diffraction patterns of α -indomethacin (a) and γ -indomethacin (b)

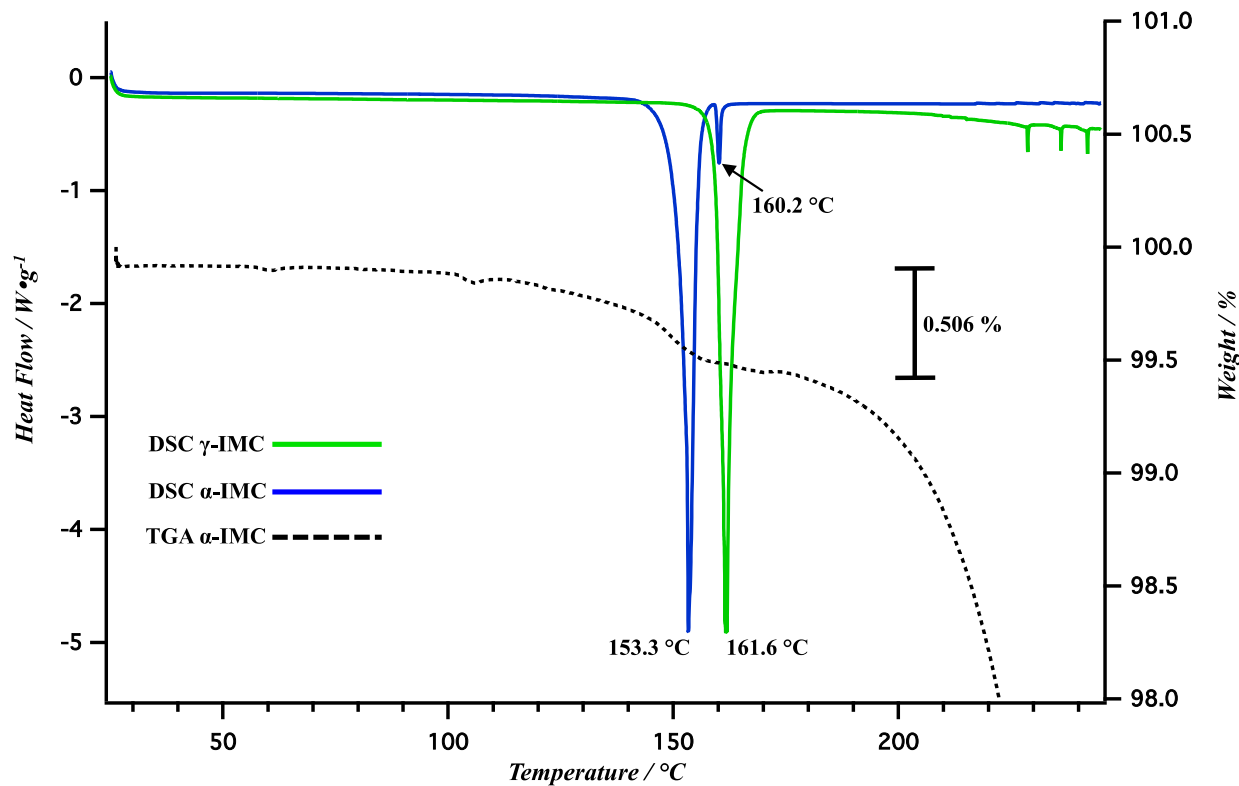


Figure S-3. Thermograms of α -indomethacin (solid blue) and γ -indomethacin (solid green) versus heat flow (left axis). Thermogravimetric data of α -indomethacin (dashed black) prepared with EtOH / H₂O crash, displaying a $\sim 0.5\%$ loss at its melting point from volatiles trapped in solid crystal.

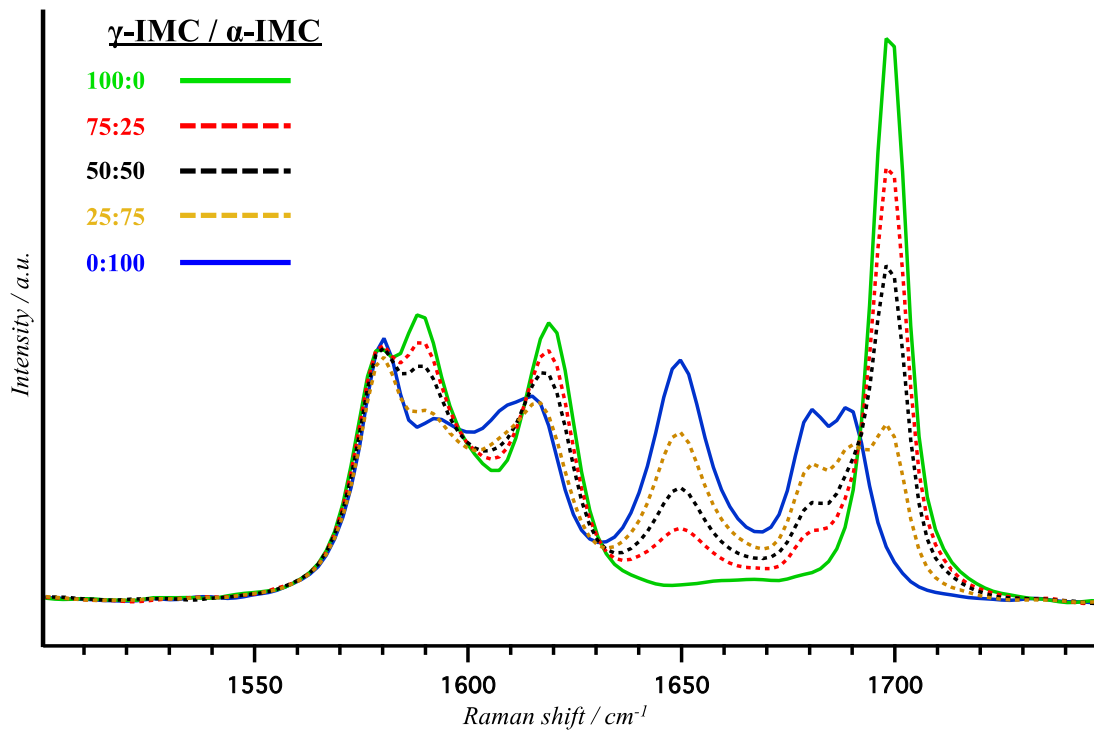


Figure S-4. Spontaneous Raman spectra of 100 % γ -IMC (solid green), 75:25 γ/α -IMC (dashed red), 50:50 γ/α -IMC (dashed black), 25:75 γ/α -IMC (dashed yellow) and 100 % α -IMC (solid blue) tablet surface between 1500-1800 cm^{-1} from while being rotated at 100 RPM for 10 minutes each.

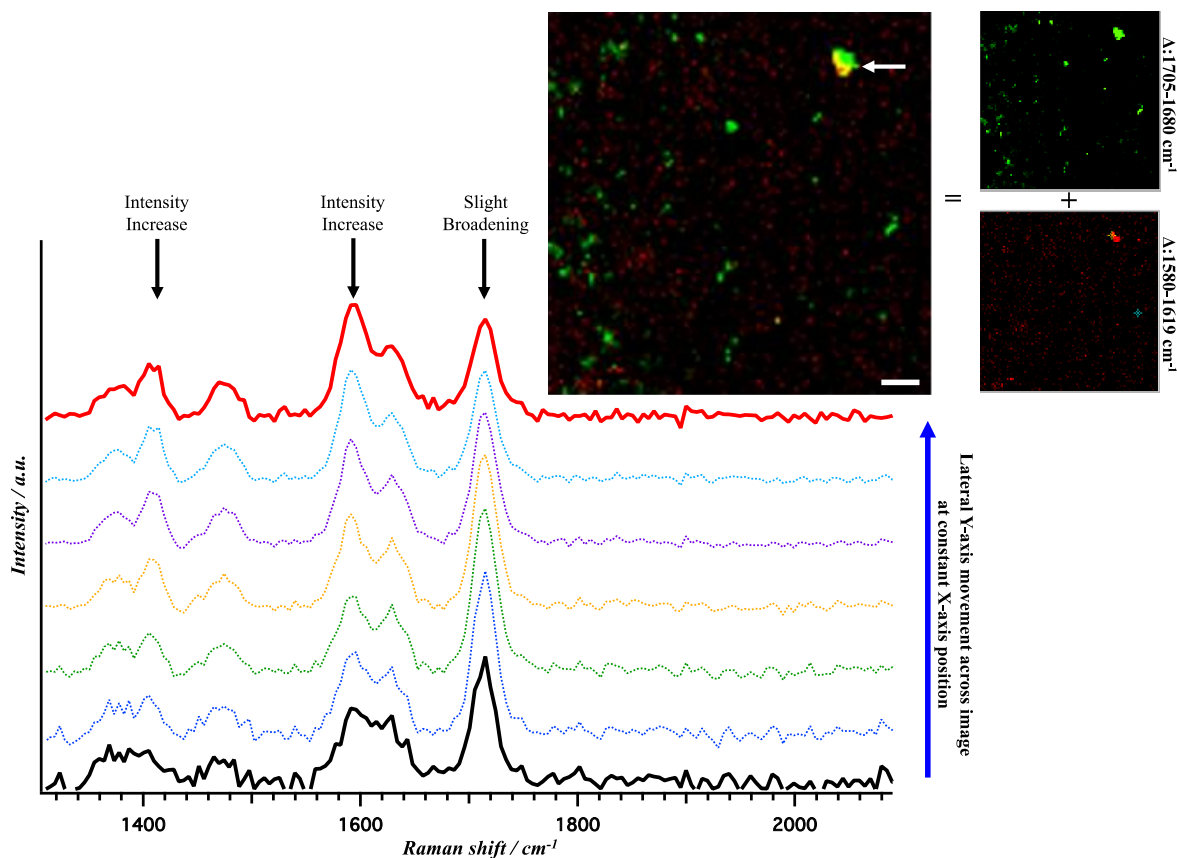


Figure S-5. BCARS spectra of 100 % γ -IMC cryoground tablet surface from separate pixels from the large inset 100 x 100 pixel image from right to left (black to red spectra) beginning at the tip of the white arrow. Images to the right of the large inset image are contrasted to the two spectral signatures and combined are what account for the pseudocolored image to their left.