

THE IMPORTANCE OF USING COMPLEMENTARY PROCESS ANALYZERS FOR THE PROCESS MONITORING, ANALYSIS AND UNDERSTANDING OF FREEZE DRYING

De Beer, T.R.M.^{1*}; Wiggernhorn, M.²; Veillon, R.³; Debacq, C.³; Mayeresse, Y.³; Moreau, B.³;
Burggraeve, A.¹; Quinten, T.⁴; Frieß, W.²; Winter, G.²; Vervaet, C.⁴; Remon, J.P.⁴; Baeyens, W.R.G.¹

SUPPORTING INFORMATION

¹Laboratory of Drug Analysis, Department of Pharmaceutical Analysis, Ghent University,
Harelbekestraat 72, B-9000 Gent, Belgium

²Department Pharmacy, Pharmaceutical Technology and Biopharmaceutics, Ludwig-Maximilians-
University, Butenandtstraße 5 – Building B, D-81377 Munich, Germany

³GSK Biologicals, Freeze drying department, Rue de l'Institut 89, B-1330 Rixensart, Belgium

⁴Laboratory of Pharmaceutical Technology, Department of Pharmaceutics, Ghent University,
Harelbekestraat 72, B-9000 Gent, Belgium

Supporting Information Figures: 6 (figure S-1 to figure S-4)

Figure S-1. The product temperature plateau due to mannitol crystallization during the freezing step can be better monitored using the wireless temperature sensors when higher concentrations are freeze dried.

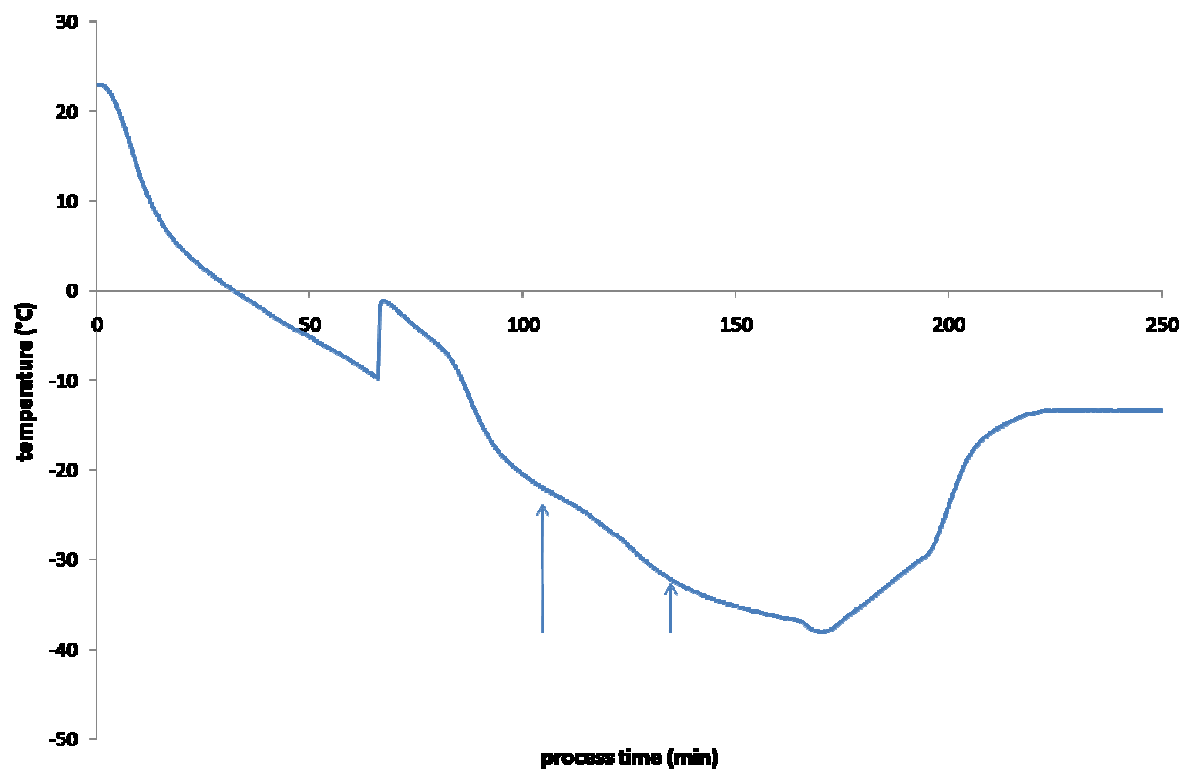


Figure S-2. Peak intensity of Raman ice band (215 cm^{-1}) versus process time during experiment 1.

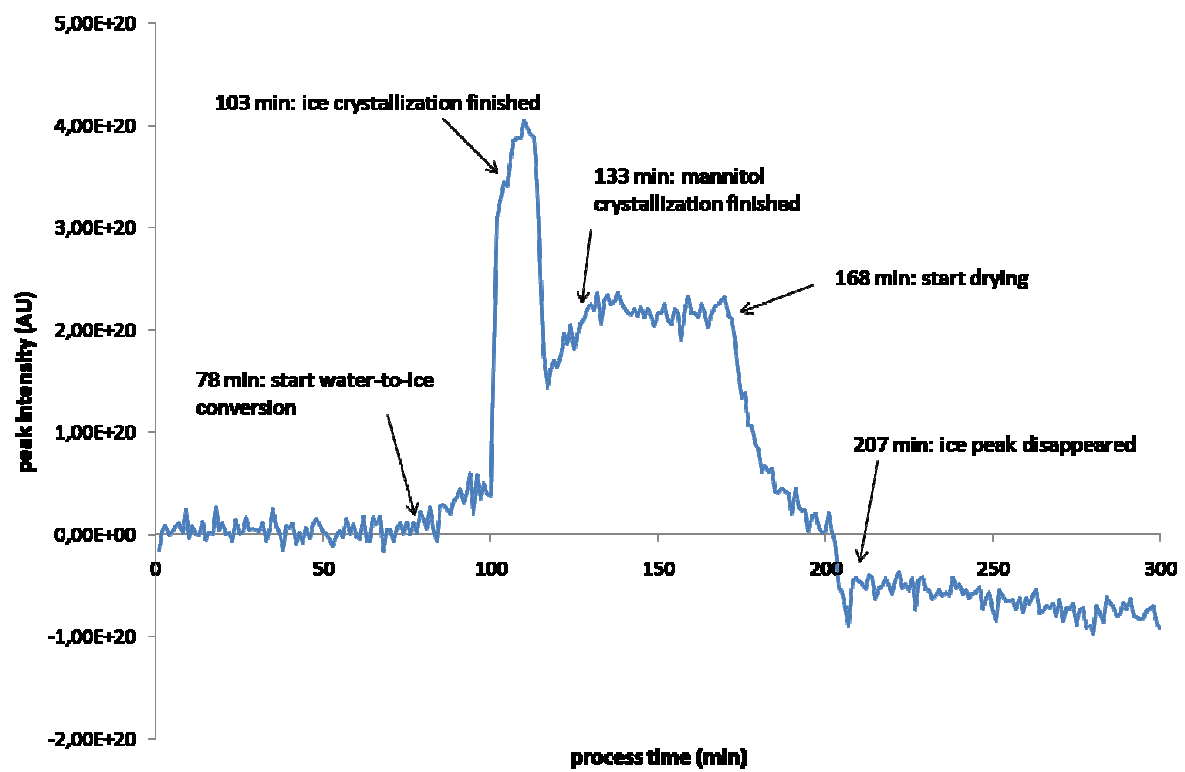


Figure S-3a. PCA result for the NIR data ($4466\text{--}7243\text{ cm}^{-1}$) obtained during the freezing step: scores for PC 1 versus process time plot. PC 1 capture 98.17 % of total spectral variance.

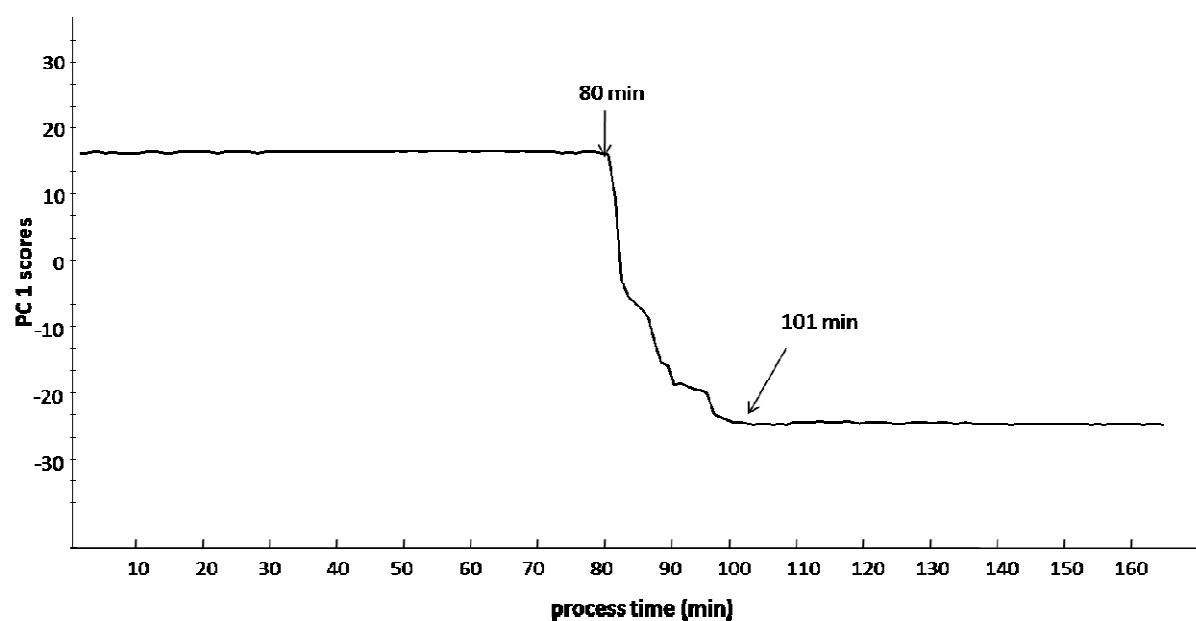


Figure S-3b. Difference between NIR spectra containing ice without crystalline mannitol (spectra collected before 136 min) and NIR spectra containing ice and crystalline mannitol (spectra collected after 136 min).

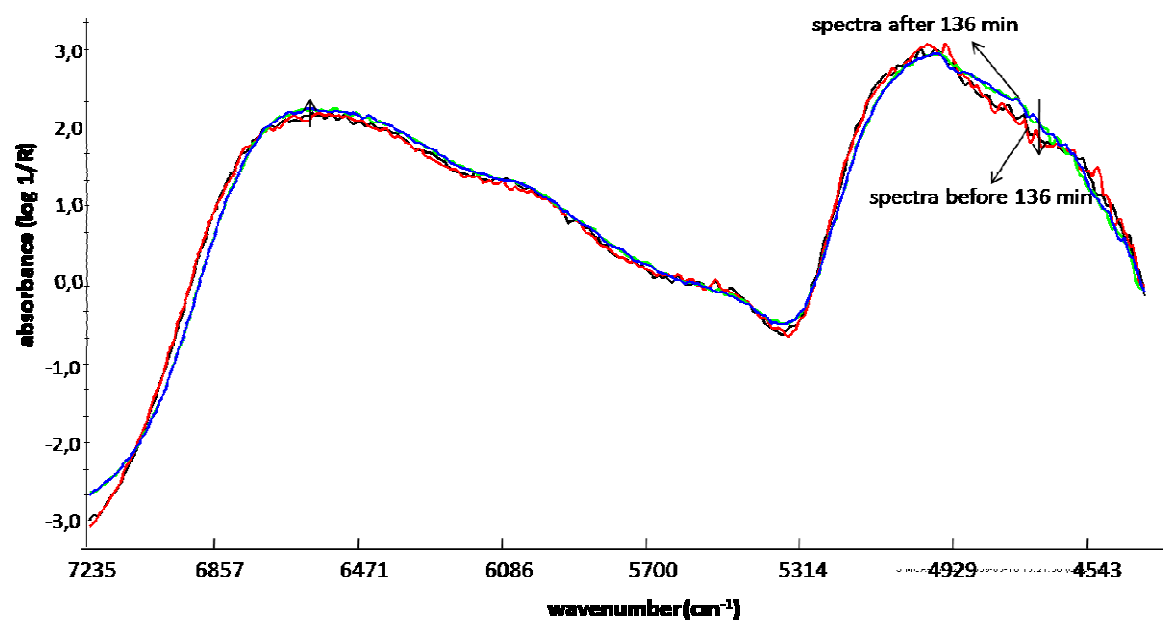


Figure S-4a. Raman spectral changes during secondary drying (1800 – 2300 min, experiment 3): transformation from mannitol hemi-hydrate to α -mannitol.

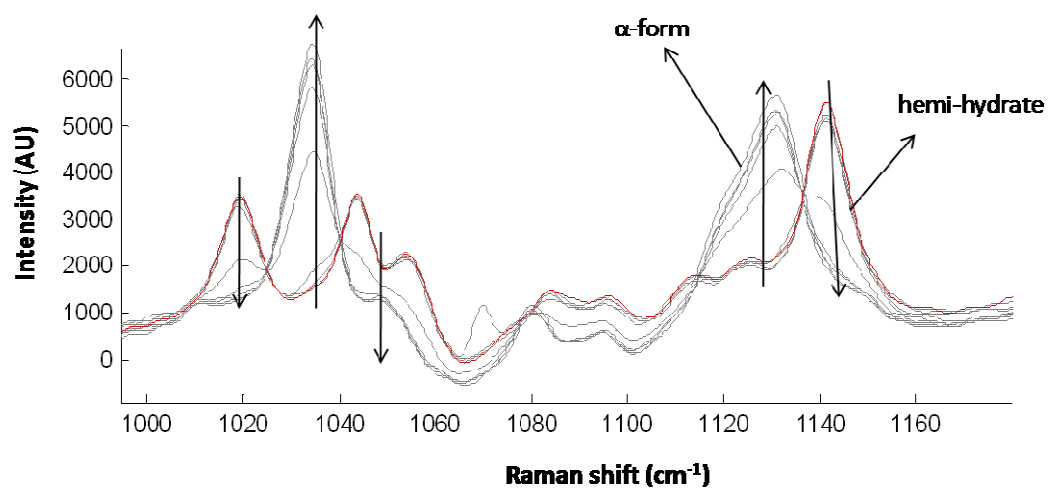


Figure S-4b. NIR spectra (second derivatives) collected during secondary drying of experiment 3 (5319 – 5050 cm^{-1}).

