Solid-State Form Analysis in Drug Product by FT-Raman Spectroscopy

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Fourier transform (FT) Raman spectroscopy has become an important tool utilized in multi-disciplinary approachs to the characterization of different solid-state forms of drug molecules. In this particular example of FT-Raman spectroscopy, a quantitative method has been developed for quantifying the amount of crystalline drug in an amorphous drug within a constituted drug product formulation. A Step-and-Repeat™ sampling accessory, which allows the sample to be spun during data acquisition, was used to minimize sample inhomogeneity errors. Utilizing a traditional data processing approach, a linear correlation curve (R^2 = 0.998) was obtained over the working range of 5% to 80% crystalline in amorphous drug substance. The residual standard deviation was 4% and the percent recoveries for the validation samples were between 95% and 102%. The minimum quantifiable limit for the assay is 14% crystalline in amorphous drug, which corresponds to a concentration of 0.8% w/w crystalline in amorphous drug in the overall formulation. Extending data processing to non-traditional approaches, namely chemometrics, lower detection limits were obtained as well as better accuracy and precision. A novel chemometrics approach to quantitative characterization will also be outlined in the presentation.