A Critical Evaluation of Emerging High Resolution Imaging Technologies for the Characterization of Complex Formulations

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The US Food and Drug Administration evaluates emerging technologies, including instrumentation, in order to keep up-to-date with the latest advances and maintain technical agility to address challenging scientific questions. Co-localization of instrumented analytical techniques allows for high throughput multi-analytical capabilities which may offer advantages over the individual techniques used separately. For example, higher contrast or superior spatial resolution may be realized from co-location of analytical techniques.

In this poster, we evaluate two co-located instrumental techniques; atomic force microscopy (AFM) co-located with Raman spectroscopy and hyperspectral imaging co-located with darkfield microscopy as applied to complex pharmaceutical formulations. AFM, when used with a plasmonic tip, enhances Raman signal at a local level, allowing interrogation of chemical identities through Raman spectroscopy with resolution in the 10s of nm, while simultaneously acquiring physical topographic data. Coupling hyperspectral (visible near infrared and shortwave infrared) detectors to a darkfield microscope allows the user to take advantage of the high contrast inherent to darkfield microscopy, while providing hyperspectral characterization of formulation components. Each of these techniques has their own pros and cons, for example, while darkfield-hyperspectral offers advantages of speed and sample preparation, it lacks discrimination for true chemical identification, while TERS offers advantages of superior resolution and true chemical identification, although suffers from slow acquisition times and difficulty in mapping in complex media. The evaluation and understanding of these emerging technologies increases the Agency's capacity to address the challenges associated with the physicochemical characterization of increasingly complex formulations.