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# Applications of Imaging and Microscopy over the Life-cycle of Lipid Multiparticulates

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Lipid multiparticulates (LMPs) offer a flexible dosage form that can be given as sachets, incorporated into capsules and tablets, or used as injectables. The solvent-free melt-spray-congeal (MSC) process results in LMPs with controlled and narrow particle size distributions. The wide variety of available matrices and formulation approaches make LMPs amenable to a broad range of targeted release kinetics (e.g. immediate, modified, or extended release), and further release modifications can be acheived by application of coatings. Particle size, matrix identity, and physical state of both lipid and drug are all critical-to-quality attributes (CQAs) when targeting a desired release. This work presents case studies where microscopy offered an invaluable means to provide scientific insight into each of these CQAs and their relation to *in-vitro* release mechanisms.

The impact of critical process parameters (CPPs) in conjunction with LMP formulation were evaluated by high-speed photography to understand and optimize the process for controlling particle size distribution.

Thermal light microscopy is applied for formulation screening to identify API-lipid miscibility and resultant particle architectures. Physical mixtures of API and lipid excipients are analyzed with a heat-cool cycle across relevant processing temperatures. Semi-quantitative information about API solubility as a function of temperature aids in manufacturing decisions. Upon fast cooling, the microscopy of the molten solution gives a picture of the expected particle architechture with respect to API-excipient miscibility. Additional insights that can be gleaned from this test include, impacts of API on lipid congealing temperature and subsequent manufacturability, API polymorph changes, and stability insight.

Finally, a variety of microscopy techniques can be employed to help understand the relationship of CQAs on biorelevant *in-vitro* performance to provide mechanistic understanding of drug release from the LMP. In this regards, microscopy is especially insightful when unanticipated release behavior is observed.

References

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