Application of Image Analysis extensions to processes of relevance to drug development

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Although the regulator only expects information on aggregates (size and numbers) for large particles (e.g. the United States Pharmacopeia (USP) chapter 'Particulate Matter in Injections' <788> defines concentration limits for particles in parental solutions that are ≥ 10 and 25 mm and the USP chapter 'Subvisible Particulate Matter in Therapeutic Protein Injections' <787> makes the recommendation to monitor particles < 10 µm, the FDA welcomes any information on the presence of smaller particles in the sub-visible size-range (0.1-10 mm), and importantly, this information should be coming from orthogonal techniques. Yet, despite all marketed techniques, aggregate prediction and profiling remains a challenge in the formulation of biopharmaceuticals due to artefacts associated with each analytical method.

On the other hand, a number of image analyses can be used to observe events related to aggregation such as Spatial Intensity Distribution Analysis or Raster imaging correlation spectroscopy (RICS). RICS, an image analysis extension initially developed by the group of E Gratton, enables the assessment of molecular mobility that can occur through exploitation of the time-related information inherent in confocal images acquired from a raster scanning laser beam in a similar manner to FCS with the added capability of spatial correlation analysis. Here the suitability of Raster Image Correlation Spectroscopy (RICS) as a novel particle sizing approach was evaluated against a combination of well-established sizing tools (micro-flow imaging, dynamic light scattering and RMM) for characterisation of sub-visible aggregates in the 0.05-50 µm size range in simple solutions or in pre-filled syringes following stresses.