

Characterization of visible and sub-visible particulates at Fujifilm Diosynth Biotechnologies

Laboratory Specifics

The biophysical characterization lab at Fujifilm Diosynth Biotechnologies- North Carolina site (FDBU), is operated in a development manner using non-qualified systems. System preventative maintenance and daily performance checks of each system are monitored closely. The lab offers several techniques to monitor visible and sub-visible particulates, as well as non-soluble and soluble aggregates. The description of the Micro-Flow Imaging (MFI) assay is provided below. Other methods are available in the development lab for particulate and aggregate analysis (listed below). Details regarding these methods can be provided by FDBU upon request.

Deliverables

FDBU will document receipt and storage of samples prior to testing, a summary of the specifics of sample testing, pdf reports of the testing results containing required information and a brief summary of results based upon our experience with the MFI techniques.

Sub-visible particulate analysis

Micro-flow imaging (MFI), Bot1 auto-sampler equipped: For this analysis, the sample (**1 mL per measurement**) is introduced into a flow cell as a camera captures images of the particulates passing the camera.

Software outputs (reports) customization

ECD (equivalent circular diameter); this value ranges from **1 to 100 μm** and the number of particulates are categorized into size bins (can be customized to report values comparable to USP <788>, i.e. $\geq 10 \mu\text{m}$ and $\geq 25 \mu\text{m}$).

Circularity parameter (ratio of \sim length to width of particulate, where 1=circular as would be seen with air bubbles, silicon oil, etc).

Aspect ratio; a measure of the denseness of the particulates where dense/dark particulates are typically foreign matter (i.e. plastic) and protein particulates are translucent and usually elongated/fibrous.

Images: the report will contain representative images of the particulates contained in the pre-set size bins. The number of images reported can be set by the operator. All images are captured in the *raw* data file, however the pictures contain a wider camera view and can only be viewed with the instrument software.

Additional FDBU particulate analysis capabilities

1. Visual appearance testing (similar to USP monograph)
2. Dynamic Light Scattering (DLS): particulates/aggregates in the range from 1 to $\leq 1000 \text{ nm}$
3. Multi-angle Light Scattering (MALS): absolute molecular weight, size distribution/heterogeneity, molecular interactions, conjugate analysis
4. HIAC: particulate testing in the μm range