FlowCam®

Flow Imaging Microscopy for Biopharmaceuticals: Four Important Considerations

FlowCam uses Flow Imaging Microscopy (FIM) to characterize particles in liquid biopharmaceutical formulations. There are several important features of FIM instruments to keep in mind if you are considering adding FIM to your workflow.

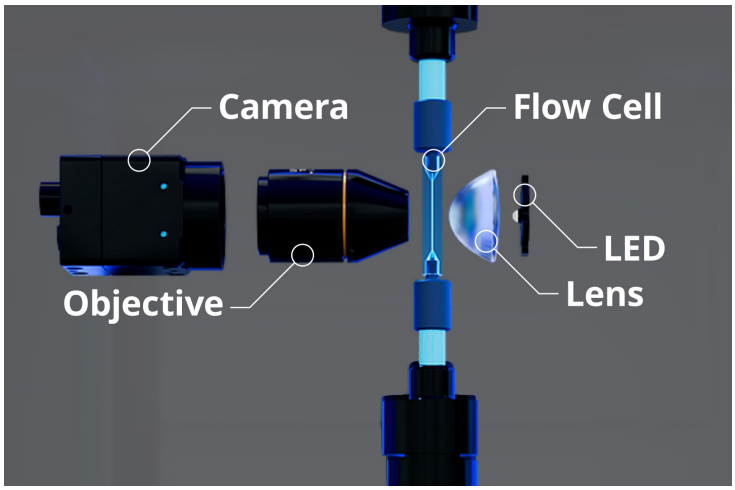

Figure 1. Internal components of a FlowCam flow imaging microscopy system

1. SAMPLE VOLUME

The biopharmaceutical drug development process is expensive, and the biological ingredients are often in short supply. To mitigate long-term costs, it is helpful to be able to detect any particle-based problems early in the process by analyzing the smallest volume sample of the formulation possible. Therefore, it is important to know the minimum sample volume required by a particle analyzer for optimal particle analysis to be achieved without depleting the sample.

2. FLEXIBILITY

Not all drug products are alike – different samples can differ in the types of particles they contain depending on their active pharmaceutical ingredient, formulation, and container closure system. These differences can influence the sizes and optical properties of the particles to be monitored to characterize a sample.

Some FIM instruments are only equipped with a single magnification objective lens, restricting the size range of the particles they can analyze. This greatly limits the research questions the instrument can be used to address. An instrument like FlowCam that offers interchangeable magnification objective lenses can process particles over a broader size range. This flexibility is desirable as it allows a single FIM instrument to monitor multiple relevant particle populations, such as subvisible and visible particles in protein and gene therapies or single cells and cell clusters in cell therapies.

FIM instruments also typically offer users limited ability to adjust how particles are processed to account for differences in the types and appearances of particles in a therapy. This restriction can lead to errors in the reported particle concentrations and sizes. Having the option to adjust instrument parameters that influence particle processing can ensure that even challenging particle types are counted and sized accurately, yielding accurate measurements on a wide range of sample types.

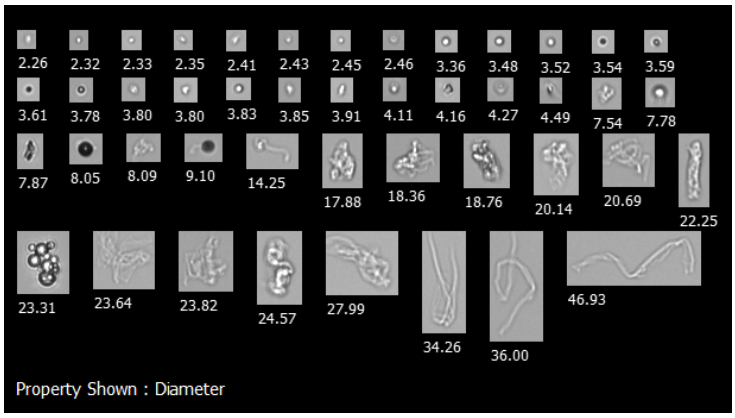

Figure 2. A FlowCam collage of particles present in a biotherapeutic sample, including protein and silicone oil droplet aggregates

3. IMAGE QUALITY

Image quality is paramount to the value of a flow imaging microscopy system. It determines how well FIM instrument software can match patterns and classify particles. The better the overall image quality, the easier it is for the instrument's software to recognize patterns, classify particles, and report accurate particle features in biologic drug products.

The value of FIM in this process is its ability to calculate physical properties and differentiate morphological features of subvisible particles directly from highly-resolved digital images.

Because FIM instruments like FlowCam are designed with fixed optics at known magnifications, distance measurements on the image can be converted to real distance measurements on the object. Thus, unlike other particle imaging modalities like light obscuration, laser diffraction, and dynamic light scattering, calculations are not made based on assumptions. Rather, FIM calculates sample properties directly using individual particle images. Therefore, the precision and accuracy of the data relies on image quality.

Many biopharmaceutical formulations are composed of particles, such as proteins, that are translucent or have refractive indices similar to their suspension environment. Poor image quality could result in low-concentration calculations and increased measurement variation with low statistical confidence.

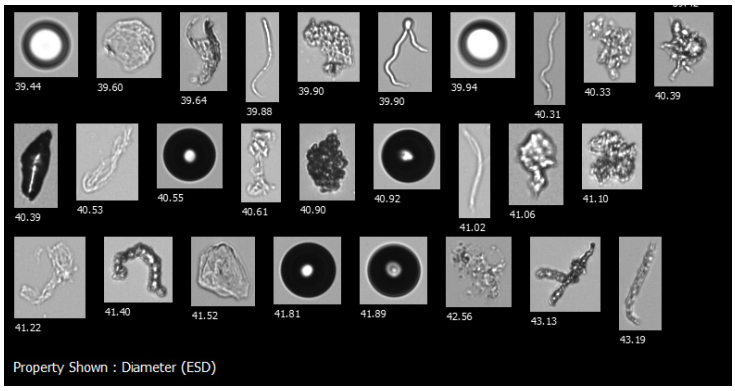

Figure 3. A FlowCam collage showing air bubbles, silicone oil droplets, protein aggregates, and other potential foreign contaminants in a biotherapeutic sample

Images that are not well-resolved can make distinguishing protein aggregates and other sample contaminants difficult. Additionally, not being able to identify morphological differences among aggregated proteins – protein globules versus clusters of rod-shaped particles, for example, could result in missing bacterial contamination in a sample.

When considering FIM systems, one with the highest image quality and software capable of extracting accurate particle data would be preferred when trying to meet rigorous regulatory standards.

4. EASE OF ANALYSIS AND DATA PROCESSING

Once your data and images are captured, it is important to have an easy way to analyze them. Choosing an FIM system with a software platform that allows you to efficiently interact with your data and extract the information you need quickly and easily is an important thing to consider.

Software features to look for include:

- The ability to sort and filter particle images based upon criteria supplied by the user, with immediate visual feedback
- Sophisticated pattern recognition capabilities that immediately find and display all similar-type particles in a heterogeneous sample
- Creation of user-defined particle-type libraries to instantly enumerate concentrations of specific particle types
- Satellite software for post-processing data at a remote location or sharing data with others
- A single system for data acquisition and analysis for tight integration that eliminates lag time and data inconsistencies
- The ability to export to Excel and other databases for added flexibility and additional analysis

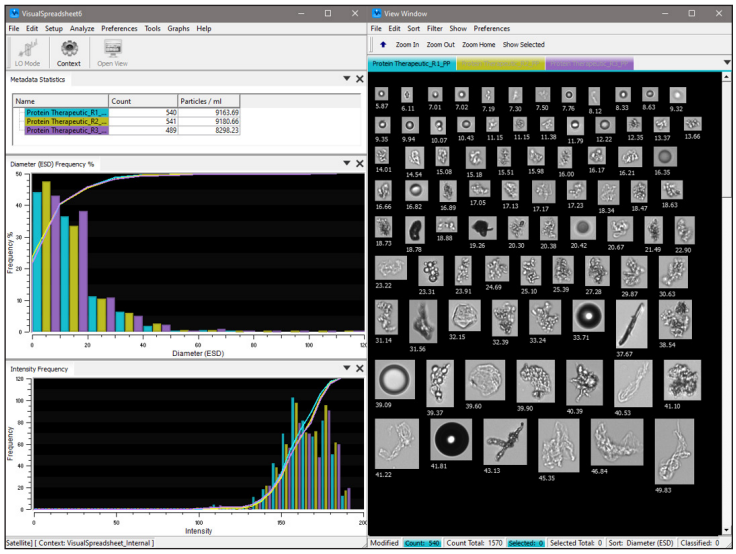

Figure 4. An example of the flexible user interface for FlowCam's integrated software, VisualSpreadsheet®

Learn more about the benefits and specifications for FlowCam and VisualSpreadsheet on our website.