FlowCam®

Flow Imaging Microscopy for Biopharmaceutical Applications

OVERVIEW

As an orthogonal technique recommended by USP <1788>, flow imaging microscopy (FIM) combines high-resolution imaging with the benefits of traditional particle sizers and counters. FIM provides count, size, morphological characterization, and identification of subvisible particles in biopharmaceutical formulations including protein, cell, and gene therapies.

The industry-leading image quality of FlowCam provides insight into the sources of particles in these biological drug products. Flow imaging analysis with FlowCam allows for the optimization of formulations and manufacturing processes to minimize and control particle formation and ensure that USP <787> and <788> particle requirements are met.

HOW FLOWCAM WORKS

The FlowCam imaging analysis system consists of a light microscopy apparatus with a sample flow cell placed in the optics path between the light source and the camera and objective. During flow imaging analysis, a sample is introduced via a syringe pump, and images of particles that pass through the optics are automatically captured and recorded. The resulting microscopic images can then be analyzed to determine the sizes, concentration, morphology, and types of particles in the sample.

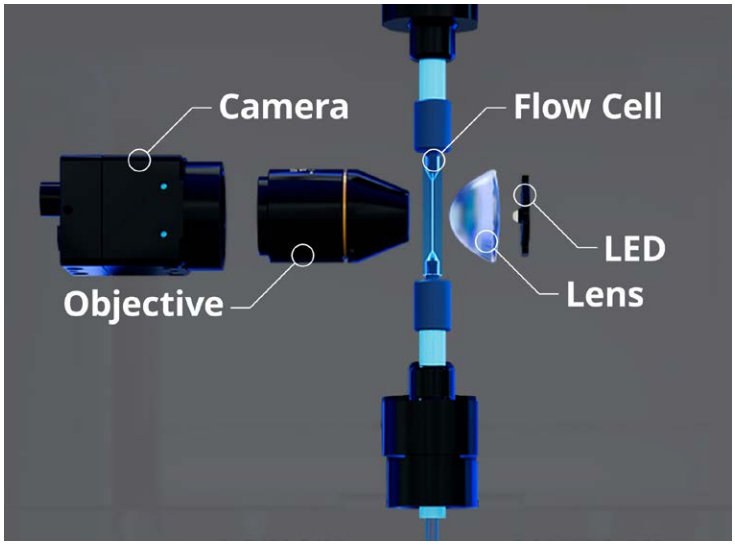


Figure 1. Schematic of the internal components of the FlowCam system

Figure 2. FlowCam 8000 instrument

VISUALSPREADSHEET PARTICLE ANALYSIS SOFTWARE

Turning Data into Insight

VisualSpreadsheet is a powerful and flexible software program for both data acquisition and analysis of images captured with FlowCam. VisualSpreadsheet determines morphological properties including diameter, area, aspect ratio, circularity, intensity, and transparency. Filter and sort particles according to their properties and display results in interactive scattergrams or histograms.

Sophisticated pattern recognition allows users to immediately find and display all particles of similar morphology. Create, define, and save particle type libraries, then compare FlowCam data against existing libraries to instantly determine concentrations of specific particle types.

A 21 CFR Part 11 compliance option is available to meet FDA regulations for data collection and archival.

APPLICATIONS

Protein Therapeutics Development and Manufacturing

FIM provides quality assurance for parenteral drug products by monitoring formulations for problematic particles including protein aggregates, intrinsic particles including silicone oil, degraded polysorbate, and glass flakes, as well as extrinsic contaminants.

FlowCam ensures product quality by characterizing these API aggregates and other particulates in protein, monoclonal antibody, or antibody-drug conjugate formulations.

VisualAI, an add-on artificial intelligence software package available with certain FlowCam models, is a robust and powerful integrated solution for identifying protein aggregate and silicone oil droplet compositions in biotherapeutic samples.

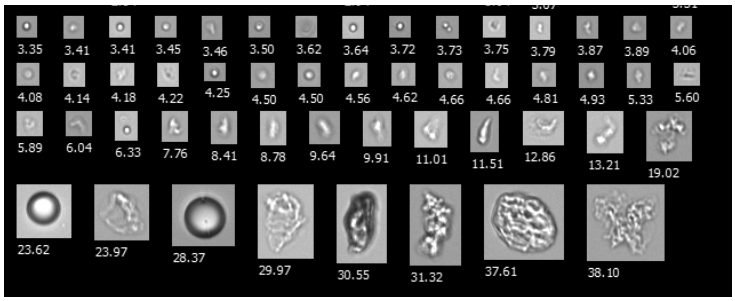


Figure 3. A FlowCam collage of common particles in therapeutic protein formulations, including protein aggregates, silicone oil droplets, and polysorbate particles

Gene Therapy: Formulation Development of Viral and Non-Viral Vectors

Like other parenteral biotherapeutics, injectables in gene therapy are subject to regulations like USP <788> that require particle testing to mitigate safety risks. Flow imaging microscopy, recommended by USP <1788>, can help you assess the stability and quality of the next generation of biotherapeutics designed to treat cancer, immunize against pathogens, and address genetic disorders.

FlowCam detects aggregation in formulations of viral vectors such as AAVs, lentiviruses, and retroviruses as well as non-viral therapies like LNPs or other gene vector carriers, enabling formulation and process improvements during product development.

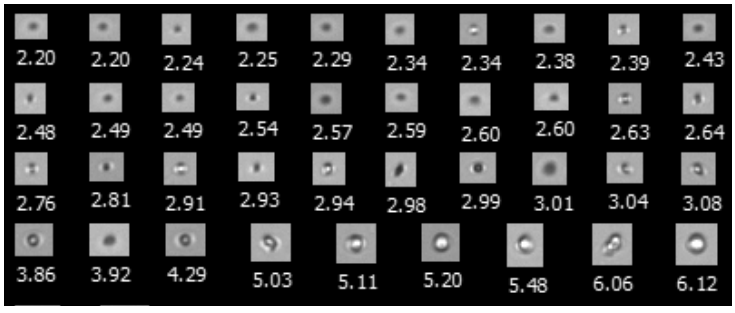


Figure 4. A FlowCam collage of particles in a heat-stressed LNP formulation

CAR-T Cell and Other Cell Therapies

The large size of cells makes it challenging to remove particulate contaminants like cell debris and residual Dynabeads™ from cell therapies without also removing cells. Effective particle monitoring strategies are critical to identifying and controlling particles at the source.

FlowCam enables differentiation between cells, cell-based impurities, and process-based impurities to optimize product manufacturing. The image analysis tools in VisualSpreadsheet measure cell concentrations and viability in samples without the need for fluorescence labeling.

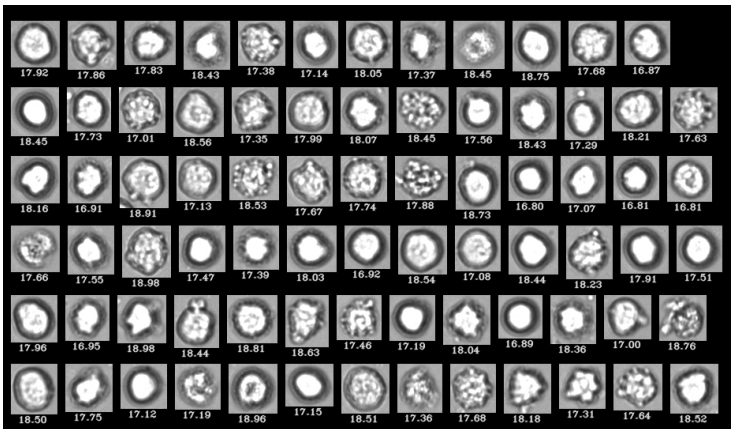


Figure 5. A FlowCam collage of human cells where living cells are distinguishable from dead cells

Other Biotherapeutics

Many large drug delivery vehicles like liposomes, exosomes, and gold nanoparticles have different properties and drug release profiles depending on their size and shape. FlowCam is a non-invasive solution technique for particle count, size, and shape as well as to detect aggregates and contaminant particles.

FlowCam is ideally suited to analyze samples containing larger particles like CHO cells, cell cultures and associated particles like Dynabeads™ and Tentagel™ beads, and hydrogel spheres.

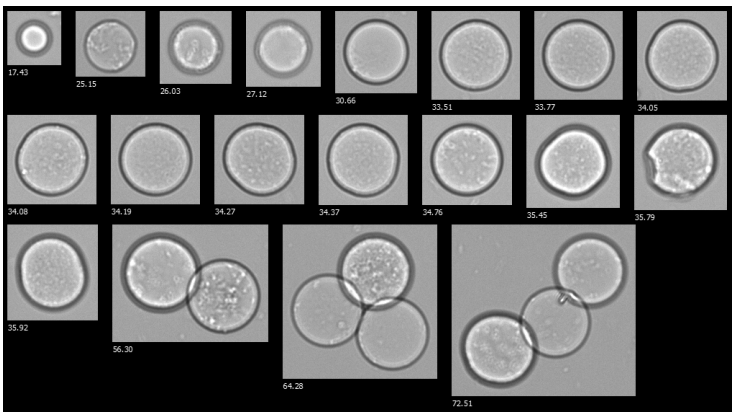


Figure 6. A FlowCam collage of hydrogel microspheres

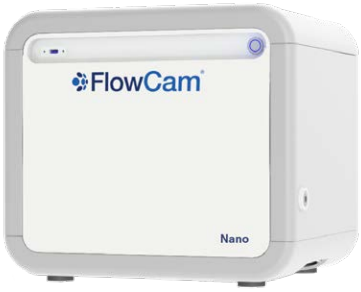
FlowCam® Product Portfolio

FlowCam 8000 Series

Our most versatile instrument for a wide range of applications. Laser excitation available. Particle size range: 2 µm - 1 mm.

FlowCam LO

Flow Imaging Microscopy and Light Obscuration in a single instrument. Particle size range: 2 µm- 70 µm.



FlowCam Nano

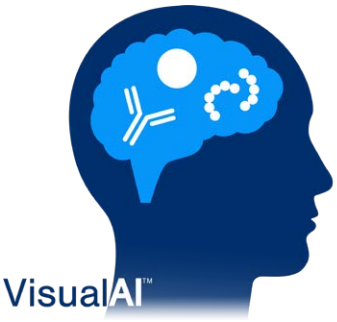
Submicron particle imaging for particles from 300 nm to 2 µm.

ALH for FlowCam™

Optimized Automated liquid handling for unsupervised analysis with FlowCam 8000.

VisualSpreadsheet®

Powerful software to analyze images and visualize your results.



VisualAI™

Artificial Intelligence module to process biotherapeutic particle images captured on FlowCam 8100 and FlowCam LO.

YOKOGAWA