FlowCam®

Influential FlowCam Studies for Biopharmaceuticals

Flow Imaging Microscopy (FIM) has emerged as an essential tool and an increasingly common approach in analytical labs for the quantification and characterization of particles in biotherapeutics. The body of scientific research using FlowCam technology to analyze biotherapeutic samples is continuing to grow and expand.

These publications not only demonstrate the utility of FlowCam in biotherapeutic development and manufacturing but highlight exciting new applications for FlowCam such as artificial intelligence-based particle analysis as well as cell and gene therapy development.

As new research is published, we continue to review the literature where FlowCam is utilized for essential and innovative studies in the field. These peer-reviewed journal articles showcase novel FlowCam applications in biotherapeutic development. They also highlight the overall importance of FlowCam-based particle monitoring strategies in the development of safe, effective biotherapeutics. The evidence produced by these authors with FIM technology can demonstrate not only the utility of FlowCam as a particle characterization tool but can also suggest new applications for the technology in your research.

Subvisible Particle Content, Formulation, and Dose of an Erythropoietin Peptide Mimetic Product are Associated with Severe Adverse Postmarketing Events

Kotarek J, Stuart C, de Paoli SH, Simak J, Lin TL, Gao Y, Ovanesov M, Liang Y, Scott D, Brown J, Bai Y, Metcalfe DD, Marszal E, Ragheb JA. *Journal of Pharmaceutical Sciences.* 2016; 105(3), 1023-1027. https://doi.org/10.1016/S0022-3549(15)00180-X

This FDA study compared two formulations of a recalled protein therapeutic that exhibited drastically different adverse responses in patients that resulted in patient fatalities. The researchers used FlowCam to identify elevated particle concentrations in the formulation associated with more severe adverse events.

Deep Convolutional Neural Network Analysis of Flow Imaging Microscopy Data to Classify Subvisible articles in Protein Formulations

Calderon CP, Daniels AL, Randolph TW. *Journal of Pharmaceutical Sciences.* 2018; 107(4), 999-1008. https://doi.org/10.1016/j.xphs.2017.12.008

The researchers behind this study developed AI-based techniques to identify FlowCam images of protein aggregates and other particles generated by different accelerated stability techniques. The trained AI technique could use FlowCam images to accurately predict the accelerated condition that the sample was exposed to.

Forced Degredation of Cell-Based Medicinal Products Guided by Flow Imaging Microscopy: Explorative Studies with Jurkat Cells

Grabarek AD, Jiskoot W, Haw A, Pike-Overzet K, Menzen T. *European Journal of Pharmaceutics and Biopharmaceutics.* 2021; 167, 38-47. https://doi.org/10.1016/j.ejpb.2021.07.004

This study investigated Jurkat cell viability changes following exposure to accelerated stability stresses. The researchers combined FlowCam with AI-based image analysis to develop a fast, label-free method to determine cell viability which was used to investigate cell health following these stress studies.

Coriolis Pharma

Quantitative Evaluation of Insoluble Particulate Matters in Therapeutic Protein Injections Using Light Obscuration and Flow Imaging Methods

Shibata H, Harazono A, Kiyoshi M, Ishii-Watabe A. *Journal of Pharmaceutical Sciences*. 2022; 111(3), 648-654. https://doi.org/10.1016/j.xphs.2021.09.047

In this study, researchers analyzed commercialized protein formulations via FlowCam (i.e. flow imaging microscopy) and light obscuration, a compendial technique for monitoring particle concentrations and sizes. The comparisons revealed that FlowCam detected higher particle concentrations than light obscuration in these samples and particularly those that contained elongated, translucent particles.

Effects of Transportation of IV Bags Containing Protein Formulations via Hospital Pneumatic Tube System: Particle Characterization by Multiple Methods

Linkuviene V, Ross EL, Crawford L, Weiser SE, Man D, Kay S, Kolhe P, Carpenter JF. *Journal of Pharmaceutical Sciences*. 2022; 111(4), 1024-1039. https://doi.org/10.1016/j.xphs.2022.01.016

The researchers in this study investigated particle generation in IV bags with and without protein when transported in a hospital via a pneumatic tube system. FlowCam analysis of these samples revealed that the pneumatic tube system generated additional protein aggregates and plasticizer droplets that would not have been generated had the IV bags been transported by hand.

Protein Aggregation and Particle Formation in Prefilled Glass Syringes

Gerhardt A, Mcgraw NR, Schwartz DK, Bee JS, Carpenter JF, Randolph TW. *Journal of Pharmaceutical Sciences*. 2014; 103(6), 1601-1612. https://doi.org/10.1002/jps.23973

The authors of this study investigated mechanisms of protein aggregation and silicone oil droplet formation in siliconized glass syringes with and without the presence of air-water interfaces. FlowCam was used to investigate both the number and types of particles formed in glass syringes to determine the impact of siliconization and air-water interfaces on particle formation.

Particles in Biopharmaceutical Formulations, Part 2: An Update on Analytical Techniques and Applications for Therapeutic Proteins, Viruses, Vaccines and Cells

Roesch A, Zölls S, Stadler D, Helbig C, Wuchner K, Kersten G, Hawe A. *Journal of Pharmaceutical Sciences*. 2022; 111(4), 933-950. https://doi.org/10.1016/j.xphs.2021.12.011

This research paper reviews recent developments in particle characterization technologies and their applications in upcoming biotherapeutics including cell and gene therapies. The authors discuss submicron FIM (FlowCam Nano) and artificial intelligence-based methods for analyzing FlowCam image data as well as their applications in developing current and novel biotherapeutic modalities.

Automatic Identification of the Stress Sources of Protein Aggregates Using Flow Imaging Microscopy Images

Gambe-Gilbuena A, Shibano Y, Krayukhina E, Torisu T, Uchiyama S. *Journal of Pharmaceutical Sciences*. 2019; 109(1), 614-623. https://doi.org/10.1016/j.xphs.2019.10.034

In this study, the authors developed AI-based approaches for predicting the source of protein aggregates in a sample. This approach accepts sets of FlowCam images from a sample, analyzes each image by multiple texture-based AI classifiers, and uses the output for the entire dataset from each classifier to predict the stress that generated all the particles in the sample.