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 a variety of established and developing applications for FlowCam including protein, cell, and gene therapies.

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.

Comparison of Protein-like Model Particles Fabricated by Micro 3D printing to Established Standard Particles

Amara I, Germershaus O, Lentes C, Sass S, Youmto SM, Stracke JO, Clemens-Hemmelmann M, Assfalg A. *Journal of Pharmaceutical Sciences*. 2024; 113(8), 2394-2404. https://doi.org/10.1016/j.xphs.2024.04.011

Protein aggregates are among the most prevalent particle types found in protein therapies, making it essential for researchers to measure them accurately as part of quality control processes. Utilizing particle standards that simulate protein aggregates can be highly beneficial in validating both subvisible and visible particle analysis techniques, which are crucial for studying this significant particle type.

This study introduces an innovative particle standard that employs 3D printing technology to produce particles with morphologies that closely mimic protein aggregates of various sizes. Throughout the research, FlowCam was a critical tool to characterize these particle standards and compare them to conventional protein aggregates. Additionally, the study highlights FlowCam's effectiveness in monitoring subvisible, visible, and "gray zone" protein aggregates within samples. By integrating these standards with advanced technologies like FlowCam, researchers can more accurately measure and mitigate the presence of these potentially harmful particles in biopharmaceutical samples.

Potential risk factors of protein aggregation in syringe handling during antibody drug dilution for intravenous administration

Fukuda M, Nagae S, Takarada T, Noda S, Morita S, Tanaka M. *Journal of Pharmaceutical Sciences*. 2025. https://doi.org/10.1016/j.xphs.2024.12.029

A frequently neglected component of drug product design and particle control is the effect of sample handling on stability within clinical settings. To address this, researchers frequently conduct in-use studies to evaluate how the stresses encountered during administration affect the stability of the therapy.

This manuscript serves as an exemplary case of how FlowCam can support in-use studies. The authors detail their investigation into how the speed of filling and dispensing syringes impacts protein aggregation and particle formation. Their findings indicate that rapid movement of the syringe stopper encourages particle formation while introducing a surfactant mitigates this effect. This knowledge can be instrumental in providing clinicians with guidance on handling therapies to enhance patient safety and designing drug products that are more resilient to typical clinical handling.

Representative training data sets are critical for accurate machine-learning classification of microscopy images of particles formed by lipase-catalyzed polysorbate hydrolysis

Greenblott DN, Calderon CP, Randolph TW. *Journal of Pharmaceutical Sciences*. 2025; 114(2), 1254-1263. https://doi.org/10.1016/j.xphs.2024.12.031

In Polysorbates serve as essential excipients in the formulation of many biological drugs due to their capacity to reduce the drug substance's adsorption onto various interfaces. However, these molecules are susceptible to degradation, which can lead to the formation of free fatty acid particles and potentially exacerbate protein aggregation. Consequently, the task of monitoring free fatty acid particles has become increasingly significant for researchers.

This manuscript illustrates that FlowCam can measure free fatty acid particles and differentiate between those formed under varying conditions. By examining the morphology of different fatty acid particles, researchers can identify methods to develop particles that closely resemble those produced in drug products throughout their shelf life. The ability to distinguish between different fatty acid particles aids researchers in exploring polysorbate degradation and devising effective strategies to monitor the particles that result from this process.

Evaluation of subvisible particles in human immunoglobulin and lipid nanoparticles repackaged from a multi-dose vial using plastic syringes

Hada S, Na KJ, Jeong J, Choi DH, Kim NA, Jeong SH. *International Journal of Biological Macromolecules*. 2023; 232, 123439. https://doi.org/10.1016/j.ijbiomac.2023.123439

Lipid nanoparticles (LNPs) have emerged as a significant delivery system for gene therapies, particularly following the COVID-19 pandemic. However, as a relatively new biotherapeutic approach, the impact of subvisible particles in these therapies is not as thoroughly understood as in more traditional therapies.

This study examined the buildup of subvisible particles in multi-dose vials of an LNP therapy after multiple dose withdrawals. The researchers discovered that, as expected, the number of particles identified by FlowCam increased with each subsequent dose if clinicians did not exercise caution during sample withdrawal. These findings are consistent with those observed in multi-dose protein therapies. This understanding of particles in LNP therapies can assist researchers in comprehending how these particles form and their implications for drug safety.

Optimization of Flow Imaging Microscopy settings using spherical beads with optical properties similar to those of biopharmaceuticals

Kurinomaru T, Takeda K, Onaka M, Kuruma Y, Takahata K, Takahashi K, Sakurai H, Sasaki A, Noda N, Honda S, Shibuya R, Ikeda T, Okada R, Torisu T, Uchiyama S. *Journal of Pharmaceutical Sciences*. 2023; 112(12), 3248-3255. https://doi.org/10.1016/j.xphs.2023.10.007

Adeno-associated virus (AAV), like other pharmaceutical substances, has the potential to aggregate, resulting in larger particle sizes. However, AAV therapies typically comprise smaller particles than other biotherapeutics, likely due to their low viral titers. This characteristic can present challenges in obtaining precise particle measurements.

This manuscript introduces an innovative method for accurately measuring AAV aggregates. The approach involves fine-tuning instrument parameters and settings with small polymethylmethacrylate (PMMA) beads to ensure precise measurements of small bead sizes. These optimizations allow researchers to achieve accurate and consistent particle measurements, even when using different FIM instruments. These measurements are crucial for effectively studying AAV aggregation in these pharmaceutical products.

Osmotic properties of T cells determined by flow imaging microscopy in comparison to electrical sensing zone analysis

Roesch A, Windisch R, Wichmann C, Wolkers WF, Kersten G, Menzen T. *Journal of Pharmaceutical Sciences*. 2023; 113, 104587. https://doi.org/10.1016/j.cryobiol.2023.104587

Assessing the proportion of viable cells within a sample is crucial in developing cell therapies. This assessment serves as a quality control measure for the therapy and aids in capturing additional sample metrics. FlowCam offers researchers a significantly more efficient method for evaluating cell viability than traditional cytometry-based techniques.

In this study, the authors devised a straightforward approach that integrates Trypan blue staining with standard image analysis tools available in instrument software to differentiate between viable and nonviable cells. The viability measurements obtained through this method showed a strong correlation with traditional fluorescence-based viability assays. Within the study's framework, the dependable viability data enabled the authors to formulate more effective strategies for cryopreserving cell therapy samples than those achievable with conventional cell therapy analysis techniques. Regardless of the data's application, obtaining precise viability measurements is essential for researchers to optimize the proportion of viable cells in therapies administered to patients.