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PUBLICATION SPOTLIGHT

LEARN MORE ABOUT CONTAMINANTS IN YOUR THERAPEUTICS WITH MFI

Flow-imaging techniques are known to provide more data and sensitivity with subvisible particle detection in therapeutics compared to compendial methods like light obscuration and manual microscopy. To validate this notion, the National Institutes for Food and Drug Control in China conducted a first-of-its-kind, recently published study in which light obscuration and micro-flow imaging (MFI) methods were both used to analyze particulate matter in 17 commercial therapeutic monoclonal antibodies (mAbs)[1]. In this study, researchers found that detection with MFI provided a higher particle count than light obscuration overall, a crucial indication that certain contaminants can otherwise go undetected with compendial methods, thereby increasing the risk of adverse side-effects in patients. Contributing factors of higher particle counts with MFI were also discussed in this paper.

The study analyzed multiple lots of 17 different commercial mAbs, resulting in a total of 205 samples that were each evaluated with light obscuration and MFI. All the mAbs tested were in different physical forms – lyophilized powders, syringes, and liquid-in-vials. With both detection methods, particles in the following size ranges were evaluated: ≥2 µm, ≥5 µm, 2-10 µm, ≥10 µm, and ≥25 µm. Higher particle counts were detected with MFI for most samples, and interestingly, for all the size ranges, samples that were in syringes or as lyophilized powders revealed higher particle counts than liquid-in-vials. Possible causes of these observations were thought to be silicone oil droplets in syringes and introduction of air bubbles during sample reconstitution (for powders).

The contribution of proteinaceous particles in high particle counts was also investigated. Such an evaluation was made possible with MFI Image Analysis software that provided filters based on 10 different morphological parameters. Two filters—aspect ratio (AR) and Intensity STD—were applied to distinguish translucent proteinaceous particles from other contaminants across different samples in the study. The first filter provided information on particle circularity, while the other filter revealed the degree of light observed across the particle. The combination of these filters enabled particles to be classified according to these morphological parameters, and particle counts per group were provided.

Applying both filters, multiple analyses of samples were conducted, and MFI consistently showed a higher particle count than light obscuration for several samples. Notably, the particle counts were repeatable between runs, indicating that the MFI method is also very reproducible.

The number of non-proteinaceous particles detected after applying the above MFI Image Analysis filters were found to be comparable to particle counts from light obscuration. This observation led to the conclusion that proteinaceous particles were the cause of higher counts in MFI. To test this, two sets of data analysis were conducted. First, the total particle count with MFI was correlated with the total particle count from light obscuration, resulting in a poor R^2 value of 0.781. Then, the non-proteinaceous particles detected with MFI were plotted against the total count, indicating a much stronger correlation between the two methods (R^2=0.933). This indicated that the translucent protein aggregates indeed played a role in increasing the particle count with MFI detection.

This study demonstrated that advanced imaging tools like MFI relay information on subvisible particles that are often not captured by compendial methods. Such a finding is critical, as such tools can be used to significantly improve drug formulations, thus reducing the risk of immunogenicity in patients. Whether you want to be sure of the number of particles in your drug or distinguish between different particulate types, MFI offers the data and ease-of-use that you're looking for. Read the paper for more details on this study or visit bio-techne.com/instruments/micro-flow-imaging to learn more about advancing your subvisible particle detection.

REFERENCES

1. Guo, S., Yu, C., Guo, X., Jia, Z., Yu, X., Yang, Y., Guo, L., & Wang, L. (2021). Subvisible Particle Analysis of 17 Monoclonal Antibodies Approved in China Using Flow Imaging and Light Obscuration. *Journal of pharmaceutical sciences,* S0022-3549(21)00491-3. Advance online publication. https://doi.org/10.1016/j.xphs.2021.09.021

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