



# Method Optimization and Validation for Particle Size Distribution for Cefixime Trihydrate Using Malvern Mastersizer 3000

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Particle size distribution refers to the quantification of particles based on their respective sizes. Maintaining precise control over the distribution of particle sizes is crucial for pharmaceutical drug development and production. The particle size distribution of powders is extensively used as a significant parameter for assessing both quality and performance.

Given the significance of particle size distribution (PSD), our study focuses on optimizing and validating the PSD method using Malvern Mastersizer 3000 for determining the particle size distribution of cefixime trihydrate, active pharmaceutical ingredient (API) . The method proposed by the API manufacturer employs sunflower oil as a dispersant, which often exhibits inconsistent quality, thereby affecting the final results.

Hereby, additional optimization based on paraffin oil as dispersant is proposed, retaining the application of the initial instrument parameters. Consequently, the measurement of PSD using Malvern Mastersizer 3000 with paraffin oil as a dispersant affords control of the API PSD within the specification limits. The optimized method is validated by assessing the repeatability of the measurements and intermediate precision. The criteria for validation include an RSD of no more than 10% for D50, RSD of no more than 15% for D90, and for particles smaller than 10 microns, the RSD limit is doubled.

**Keywords:** Mastersizer 3000, particle size distribution, paraffin oil, dispersant, validation, optimization

## References

1. ICH Guideline Q2(R1): “Validation of Analytical procedures: Text and Methodology”, November 2005
2. European Pharmacopoeia 9<sup>th</sup> Edition 2017, General Chapter 2.9.31 Particle Size Analysis by laser Diffraction
3. ISO 13320:2009 Particle Size Analysis – Laser Diffraction Methods