



Nebulizer Performance – In Vitro Test Study Plan for 510(k) Submissions

Next Breath is a full service cGMP compliant laboratory for analytical testing of nebulizers for pre-market 510(k) approval. We have extensive experience with air-jet, ultrasonic and small volume/high output nebulizers. Next Breath has also worked with nebulizers intended for use with ventilators and oxygen/helium compressed air sources. Using the study design as described below for a model air-jet nebulizer, Next Breath will customize a program to meet your requirements, help select a predicate device, conduct the relevant experiments, interpret the test results and generate a report suitable for inclusion in your regulatory submission. We also offer cleaning validation experiments and a full range of biocompatibility testing such as volatile organic components.

Next Breath also has expertise testing add-on devices such as spacers and holding chambers. In addition, Next Breath provides formulation development services of active pharmaceutical ingredients (API) for nebulized platforms.

In Vitro Test	Test Parameters	Test Metric(s)	Equipment	Objective(s)
<i>Aerosol Performance: Particle Size Distribution by Cascade Impaction</i>	Quantify the particle size distribution from three nebulized drug products	Fine Particle Dose MMAD/GSD Emitted Dose Amount of Drug Remaining in Nebulizer Cup	Andersen Cascade Impactor USP Induction Port Next Generation Impactor Mass Flow Meter Vacuum Pump HPLC Marple Miller Impactor (alternate)	1. Compare nebulizer performance between the test and predicate device
<i>Gas Flow Range Study</i>	For nebulizers that use a range of flow rates to deliver the drug product, quantify the particle size distribution	Fine Particle Dose MMAD/GSD Emitted Dose Amount of Drug Remaining in Nebulizer Cup	Compressed Air Source Dry Gas Meter Andersen Cascade Impactor USP Induction Port Mass Flow Meter Vacuum Pump HPLC Marple Miller Impactor (alternate)	1. Establish in vitro aerosol performance at varying flow rates (e.g. 4 lpm and 9 lpm.) 2. Compare nebulizer performance between the test and predicate device
<i>Cleaning Validation</i>	Quantify the particle size distribution from one to three nebulized drug products	Fine Particle Dose MMAD/GSD Emitted Dose Amount of Drug Remaining in Nebulizer Cup	Andersen Cascade Impactor USP Induction Port Mass Flow Meter Vacuum Pump HPLC Marple Miller Impactor (alternate)	1. Confirm that cleaning procedure does not alter aerosol performance - test device only
<i>Droplet Sizing by Laser Diffraction</i>	A secondary method used to characterize the particle size distribution from three nebulized drug products	DV10, DV50, DV90 Emitted Dose by Weight Amount of Drug Remaining in Nebulizer Cup by Weight	Malvern Spraytec	1. Compare nebulizer performance between the test and predicate device

Three of the four following nebulized drug products should be evaluated for Particle Size Distribution by Cascade Impaction, Gas Flow Rate Range Studies and Secondary Particle Size Determinations: albuterol sulfate inhalation solution, ipratropium bromide inhalation solution, cromolyn sodium inhalation solution and/or budesonide inhalation suspension.