Credibility Assessment of CFD-Based Aerosol Deposition Models for a Pressurized Metered-Dose Inhaler with Valved Holding Chamber

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Abstract

Pressurized metered-dose inhalers (pMDIs) used with valved holding chambers (VHCs) remain a mainstay of inhalation therapy. The physics of device jets, throat passage, and downstream airway transport determine the balance between oropharyngeal losses and delivered lung dose. Computational fluid dynamics (CFD) has matured to the point that it can resolve these coupled processes with transient, polydisperse particle tracking across device and airway scales. However, the credibility of such models must be established and communicated in a structured way. This article reports a model-specific and mechanism-focused credibility assessment, following 7009A intent, for two CFD models: (i) a device–mouth–throat solver that reproduces the propellant jet, spacer flow, and oropharyngeal transport and predicts entry-plane size–velocity–angle (SVA) distributions, and (ii) an airway-scale deposition solver for the oral cavity through segmental bronchi that quantifies regional and lobar deposition fractions, residence time distributions, and delivered lung dose. Two mechanisms of interest anchor the application scope: jet-driven inertial impaction during actuation–inhalation overlap, and sedimentation and diffusion during post-inhalation breath-hold. We define quantities of interest (QOIs) that map directly to these mechanisms and present factor-by-factor gradations on a 0–12 Depositional Credibility Index (DCI) with descriptive anchors at 0, 4, 8, and 12. The factors covered are development technical review, discretization, model form, numerical solver behavior, alignment of the QOIs with decision needs, software assurance, test conditions, and user missteps. Evidence includes grid–time-step refinement data, alternative-closure comparisons, convergence behavior, traceability of inputs, and targeted parameter sweeps for off-nominal use. Across the four model–mechanism pairs, halving the spatial and temporal steps altered regional deposition by less than one percentage point in all cases; replacing hybrid scale-resolving turbulence with unsteady RANS changed oropharyngeal deposition by about one point and modified peak laryngeal wall shear by 12%; and early actuation by 0.3 s increased oropharyngeal deposition from 19.4% to 27.8% through augmented jet momentum at the entrance plane. The device-resolved model delivered a high-fidelity inlet SVA histogram (300 bins) and oropharyngeal loss estimate for the jet mechanism (DCI 12/12 for relevance), whereas the airway-scale model provided lobar shares and dwell times for the breath-hold mechanism (DCI 12/12 for relevance). Two credibility summary tables—one per model—present 32 scored rows, one for every factor × mechanism combination, with one-line bases that restate numeric evidence argued in the prose. The paper closes with an elevation strategy keyed to gaps that most efficiently raise DCI for specific model–mechanism pairs.

Keywords: inhaler CFD, aerosol deposition, credibility assessment

1. Introduction

Pressurized metered-dose inhalers (pMDIs) paired with valved holding chambers (VHCs) have retained clinical importance because they reduce coordination demands and attenuate oropharyngeal impaction relative to actuator-at-mouth use. The deposition performance of a pMDI–VHC system depends on a transient jet discharging liquefied propellant and droplets into a spacer, the delayed uptake of that cloud during inhalation, and the fate of the polydisperse aerosol throughout the mouth, larynx, trachea, and bronchial tree. The two mechanisms that dominate delivered dose are distinct in time and physics: the high-Reynolds-number jet that sets initial trajectories and speeds, and the millisecond-to-second scale drift and diffusion that control distal capture during and after the flow decays.

Computational fluid dynamics (CFD) is used increasingly to quantify these processes. Device-resolved simulations of the nozzle, VHC, and mouth–throat (MT) geometry can capture plume formation, entrainment, and early impaction zones and provide an entry-plane spectrum that seeds downstream models. Airway-scale simulations from the oral cavity to segmental bronchi provide regional deposition fractions, lobar distribution, and residence time distributions across a breath cycle with breath-hold. The attractiveness of these models for product development and mechanistic understanding is tempered by stakeholders' need to understand the level of trust they merit, the ranges over which that trust holds, and the specific kinds of decisions they can inform.

We conduct a structured credibility assessment of two such CFD models against two mechanisms of interest that are both clinically meaningful and physically distinct: jet-driven inertial impaction during the overlap of actuation and inhalation, and

sedimentation plus diffusion during a post-inhalation pause. The assessment separates evidence by model–mechanism pair and reports a Depositional Credibility Index (DCI) on a 0–12 scale with descriptive anchors to summarize the strength of the case. Quantities of interest (QOIs) are nominated based on their direct relevance to the mechanisms and to decisions about device design and use. Numerical evidence includes refinement studies, solver behavior, closure alternatives, and explicit exploration of user missteps. Process evidence covers independent review outcomes and the state of the software toolchain.

The goals of this article are threefold: to present the models and the administration scenario with sufficient detail for technical readers to understand the sources of uncertainty; to map a small set of factors to evidence that is specific to each model–mechanism pair; and to report, clearly and compactly, a graded result that a reader can use to weigh how far and how confidently to extend the models into design or labeling questions.

Depositional Credibility Index (DCI) anchors — gradation.

a.
0: No evidence relevant to the mechanism; model not scoped to the question; no bounds on error.

b.
4: Limited and indirect evidence; partial scoping to the mechanism; some error indicators but no convergence or alternatives explored.

c.
8: Moderate, mechanism-targeted evidence; grid/time-step sensitivity quantified; at least one model alternative exercised; boundary inputs traceable; partial user variability explored.

d.
12: Strong, mechanism-specific evidence; asymptotic behavior demonstrated on mesh and time step; alternative closures bounded; conditions matched to tests; user variability bracketed with quantified impact; independent technical review completed.

2. Device Overview and Administration Scenario

The device under study is a commercially typical pressurized metered-dose inhaler (pMDI) that dispenses a single shot of hydrofluoroalkane (HFA 134a) propellant with a micronized active pharmaceutical ingredient (API) suspension, used in conjunction with a 150 mL valved holding chamber (VHC). The orifice diameter of the actuator nozzle is 0.25 mm; the VHC includes a one-way inspiratory valve and a low-deadspace exhalation path. The mouthpiece and MT geometry follow an adult morphometric mean for oropharyngeal dimensions with a 2.1 cm mouth opening, a 7.5 cm oropharyngeal length to the epiglottic tip, and a 21 mm tracheal diameter downstream of the glottis.

The administration scenario emulates a coached adult use. Inhalation begins at t = 0 s with a linear ramp from zero to 0.5 L/s over 0.5 s, followed by a 2.0 s hold at 0.5 L/s, and a 0.5 s taper to zero, for a total inhaled volume of approximately 1.5 L. The canister is actuated at t = 0.2 s after inhalation onset, and the metering valve remains open for 120 ms with a discharge mass of 12.5 mg, producing an initial two-phase jet that feeds into the VHC. Following inhalation cessation at t = 3.0 s, the subject holds breath for 5.0 s, with no glottic closure in the model, allowing for continued intrathoracic quiescence. Chamber and airway walls are modeled as isothermal at 310 K except for the nozzle and immediate jet core, which cools transiently; the ambient environment is 296 K at sea level pressure.

Two deviations from coached technique are explicitly explored to assess robustness to user missteps: (i) early actuation at t = 0.1 s (100 ms before inhalation begins) and t = 0.3 s (300 ms early), and (ii) late actuation at t = 0.5 s (300 ms late). In addition, a higher inspiratory effort case at 0.8 L/s plateaus for 2.0 s is included to bound the laryngeal shear and residence time effects. These explorations are used strictly to quantify sensitivity of outputs to plausible user behavior and do not form the nominal input set for the credibility scoring.

Test conditions — gradation.

a.
0: Conditions not specified or not traceable to any use scenario.

b.
4: Conditions stated but only loosely related to intended use; key parameters missing or idealized without support.

c.
8: Conditions representative of intended use and reported with tolerances; some off-nominal cases explored.

d.
12: Conditions tightly matched to a verified test rig or clinical protocol; tolerances quantified; off-nominal use bracketed by design; instrumentation or measurements used to set boundary values.

3. Computational Models

Two separate, coupled CFD models are evaluated. The device–mouth–throat jet model resolves the actuator nozzle, the volume of the 150 mL VHC, the inspiratory one-way valve mechanics as a flow-permeable membrane with measured pressure–flow characteristics, the mouthpiece, and an adult mean mouth–throat (MT) passage that includes the oropharynx and laryngeal constriction. The gas phase is a compressible mixture of HFA 134a vapor and air, with heat and mass transfer to evaporating liquid droplets represented by a two-way coupled Lagrangian–Eulerian framework. The droplets are injected according to a time-varying mass flow rate and an initial size distribution characterized in a nozzle test rig. Turbulence is modeled with a hybrid scale-resolving approach (delayed detached-eddy simulation, DDES), which resolves the large unsteady structures of the jet and its interaction with the valve and MT walls. Particle–wall interactions include restitution and sticking criteria dependent on impact Stokes number and film presence; for the jet mechanism, this is a key pathway to oropharyngeal loss.

Figure 1: Schematic of the pMDI with valved holding chamber, mouth–throat geometry, and the two CFD domains used in this study. The device–mouth–throat model resolves the nozzle, VHC, and oral cavity through the larynx; the airway-scale model spans from the incisors to segmental bronchi and accepts an entry-plane size–velocity–angle distribution from the device model.

The airway-scale deposition model spans from the incisors through the glottis, trachea, main carina, and a subject-averaged bronchial tree segmented down to the segmental bronchi (generation 4–6 depending on lobe). The gas phase is treated as incompressible but unsteady; density variations are insignificant beyond the throat for the flow rates studied. Turbulence is represented by a shear-stress-transport k–omega model in attached regions with a wall-adapting local eddy viscosity (WALE) model blended in recirculating pockets to resolve near-wall shear where relevant to deposition. The particle phase is Lagrangian with stochastic turbulent dispersion and includes gravity, Cunningham slip correction for sub-5 μm diameters, and diffusivity computed via the Stokes–Einstein relation. Particle–wall interaction in the conducting airways assumes immediate adhesion upon contact, consistent with mucosal capture; brownian re-entrainment is neglected at this scale. The model accepts an entry-plane SVA histogram at the plane immediately below the glottis from the device–mouth–throat simulation to seed trajectories, thereby linking the two models while maintaining independent numerical settings.

Both models are implemented in the same finite-volume solver framework, but with separate meshes and physics modules. For the device model, the mesh comprises poly-hexcore elements with high-aspect prismatic layers along the nozzle, valve leaflet, mouthpiece, and MT walls. The baseline mesh has 60 million control volumes, with $y+ \leq 1$ over 92% of wetted surfaces during the jet phase to enable near-wall resolution without wall functions. A fine mesh of 110 million volumes and a coarse mesh of 30 million volumes support refinement studies. Time stepping is fully implicit, second-order accurate, with an adaptive time step capped at 10 microseconds during the 0–0.3 s actuation window and relaxed thereafter. For the airway model, the baseline mesh contains 25 million volumes with three-layer prism stacks near walls achieving $y+ < 2$ for most of the oral and laryngeal tract and $y+ < 5$ in larger bronchi. A fine mesh of 50 million and a coarse mesh of 12.5 million volumes are used for sensitivity analyses. The time step is 0.25 ms during inhalation and 0.5 ms during breath-hold, with a refined step of 0.125 ms used in selected runs.

Particle initialization differs by model. In the device model, droplets are released at the nozzle exit over 120 ms with an initial mass median diameter of 14 μm and geometric standard deviation (GSD) 1.9, based on nozzle rig measurements. Evaporation in the VHC and mouthpiece occurs on the 10–100 ms timescale, and diameters shrink to a median of 3.0 μm (GSD 1.7) by the time particles cross the mid-oropharynx under nominal timing. In the airway model, particles are injected at the entry plane beneath the epiglottis using a 300-bin SVA histogram exported from the device simulation; the mass median aerodynamic diameter (MMAD) at that plane is 2.3 μm with GSD 1.8 under nominal actuation–inhalation overlap, and the angle distribution has a mean of 6 degrees from the axial direction with a standard deviation of 4 degrees, and a speed distribution with a 2.1 m/s mean and 0.8 m/s standard deviation.

Model coupling is one-way: the device–mouth–throat simulation writes out the time-resolved SVA histogram at the entry plane for the nominal and off-nominal timing cases, and the airway-scale model consumes that as an inlet condition for particle properties. Gas-phase boundary conditions at the entry plane are specified as time-dependent velocity profiles drawn from the inhalation waveform and are not back-coupled to the device model. This separation allows independent credibility arguments for each model–mechanism pair.

Model form — gradation.

a.
0: Physical phenomena central to the mechanism are omitted or misrepresented; no justification of closures.

b.
4: Primary phenomena represented with standard closures; justification qualitative; no alternatives explored.

c.
8: Phenomena mapped to closures with literature support; at least one alternative closure run demonstrates bounded sensitivity.

d.
12: Phenomena represented by the most appropriate closure for the regime; multiple alternatives bounded; selections traced to validation data or targeted experiments.

4. Deposition Mechanisms of Interest

The first mechanism is jet-driven inertial impaction during the overlap of device actuation and inhalation. In this window,

plume momentum and the geometry of the VHC, valve, and MT govern where particles hit and stick before the cloud equilibrates to the inhalation stream. The competition between evaporation (which reduces particle size and thus Stokes number) and convection (which sets flight time to walls) is especially acute near the constricted larynx. The outputs that inform this mechanism are oropharyngeal deposition fraction, laryngeal hot-spot identification, peak and time-integrated wall shear near the laryngeal inlet, and the detailed SVA distribution at the entry plane into the lower airways.

The second mechanism is sedimentation and diffusion during the breath-hold that follows after the flow decays to near zero. Here, the physics favors small particles moving under gravity and random thermal motion in a slowly changing or quiescent flow. With the trachea and bronchi acting as conduits into which the already size-selected and slowed cloud has penetrated, the residence time distribution and particle size become the main determinants of how much drug reaches smaller conducting airways. The key outputs are lobar deposition fractions, distal (beyond main bronchi) shares, and dwell times computed from particle histories with gravity and Brownian displacement.

Relevance of the quantities of interest — gradation.

a.
0: Outputs bear little relation to the mechanism or intended decision.

b.
4: Outputs indirectly related; mapping to decision requires nontrivial inference.

c.
8: Outputs directly relate to mechanism with clear trace to decision metrics for at least one model–mechanism pair.

d.
12: Outputs are mechanism-specific, complete for the intended decision, and parameterized to feed downstream analysis without re-interpretation.

5. Mesh Generation, Numerics, and Particle Modeling

Mesh generation for both models used a polyhedral core with prismatic boundary layers to balance numerical diffusion and near-wall resolution. The device mesh concentrated resolution in the nozzle throat (minimum cell size 10 μm), around the inspiratory valve (minimum cell size 50 μm), and within 1 mm of the MT walls to capture thin boundary layers affecting impaction. A refinement band followed the jet core from the nozzle through the VHC inlet and across the valve plane to maintain at least 15 cells across the jet diameter during the high-momentum phase. The airway mesh prioritized the laryngeal constriction, main carina, and the first three bronchial generations with local refinements (minimum cell size 75 μm in the larynx and 150 μm in tracheal near-wall layers) to resolve secondary flows that influence deposition.

Temporal discretization in both models is second-order implicit for the gas phase, with sub-cycling for particle updates to preserve accuracy for rapidly evaporating droplets. In the device model, the maximum Courant–Friedrichs–Lewy (CFL) number was held below 1.0 in the nozzle and below 3.0 in the VHC and MT during the actuation window. After 0.3 s, CFL was allowed up to 5.0 as the flow slowed, with additional time steps inserted automatically during valve closure events. In the airway model, the CFL peaked at approximately 2.5 in the laryngeal jet at inhalation onset and remained below 2.0 through the bronchi; during breath-hold, time steps were increased to 0.5 ms as velocities decayed below 0.05 m/s in the segmental bronchi.

Particle modeling in the device simulation included droplet evaporation via a D2-law adjusted for mixed HFA–ethanol shells around API aggregates, with vapor pressure and latent heat drawn from standard correlations. Droplets transitioned to near-dry agglomerates within 80–150 ms depending on local vapor saturation; the code tracked particle temperature and diameter continuously with gas–particle heat and mass transfer computed using Ranz–Marshall correlations modified for high-Schmidt-number conditions. In the airway model, particle diameters were taken as fixed at the entry plane values because further evaporation was negligible at near-saturated conditions and body temperature. Stochastic turbulent dispersion used a continuous random walk with a timescale tied to the local turbulent kinetic energy and dissipation rates. The diffusion coefficient for the smallest particles (0.5–1 μm) was 5.0–1.3 × 1010 m2/s at 310 K; gravity-induced settling was modeled with Cunningham slip correction, yielding terminal velocities from 0.2 to 9 mm/s across the size range considered.

Convergence criteria for the gas phase required iterative residuals to fall at least three orders of magnitude from initial each time step, with a minimum absolute residual of 1 × 105, and mass imbalance per step below 0.2% for the device model and 0.1% for the airway model. Particle statistics were accumulated over at least 1 million trajectories per case for nominal timing, 0.5 million for each off-nominal case, to ensure statistical uncertainty in deposition fractions below 0.3 percentage points for regional bins; binomial standard errors were reported accordingly.

Numerical solver behavior — gradation.

a.
0: No evidence of convergence or stability; solver settings undocumented.

b.
4: Basic convergence claimed; tolerances loose; no time-step study; possible mass imbalance.

c.
8: Convergence monitored with residuals and global balances; at least one time-step sensitivity study; small imbalances quantified.

d.
12: Tight residual and balance criteria; multiple time-step studies across mechanisms; sensitivity shown to be negligible relative to QOI variability.

6. Boundary and Test Conditions

Device actuation parameters were taken from a dedicated nozzle test rig. The mass of propellant discharged per actuation (12.5 mg) was determined by pre/post weighing with a precision of 0.1 mg over 30 shots; the time-resolved discharge profile was inferred from high-speed schlieren imaging and a calibrated piezoelectric transducer at the nozzle, producing a peak discharge at 35 ms and a trailing tail to 120 ms. The nozzle temperature drop during actuation was measured by a micro-thermocouple positioned 1 mm downstream of the orifice, showing a transient decline of 35 °C at 25 ms with recovery by 150 ms; these data informed the evaporation model and boundary heat flux in the nozzle element. Inspiratory valve pressure–flow characteristics for the VHC were measured in a bench rig with step flows from 0.1 to 1.0 L/s; the modeled porous membrane resistance curve reproduced a measured pressure drop of 105 Pa at 0.5 L/s within 3 Pa.

Airflow boundary conditions for the airway model followed the coached adult profile described earlier. The inlet pressure at the mouth was set such that the target volumetric flow rates were achieved; the tracheal outlet split into lobar outlets with resistive elements tuned to match expected lobe flow distributions at steady 0.5 L/s inhalation based on morphometric ratios (right upper 16%, right middle 8%, right lower 26%, left upper 22%, left lower 28%). During breath-hold, a low-level intrathoracic pressure decay of 25 Pa over 5 s was included to emulate glottis-open relaxation; sensitivity to this was negligible for the QOIs reported, with particle velocities below 0.01 m/s in segmental bronchi by 3.5 s.

Environmental and wall temperature conditions were held constant except for the nozzle cooling period, as already described. Wall roughness was set to an equivalent sand-grain roughness of 30 micrometers in the mouth–throat and 15 micrometers in the tracheobronchial model, consistent with literature values for mucosal surfaces. To bound albedo effects, a sensitivity case with half roughness produced a change in tracheal deposition below 0.2 percentage points.
Software quality assurance — gradation.

a.
0: No evidence of version control, testing, or process discipline.

b.
4: Version control in place; some unit tests; limited regression testing; undocumented build steps.

c.
8: Formal version control with change tracking; automated builds; substantial unit and regression tests; documented configuration management.

d.
12: Mature quality system: requirements traceability, hazard analysis, automated verification suites tied to acceptance criteria, and auditable releases.

7. Definition of Quantities of Interest

For the jet-driven impaction mechanism, the device–mouth–throat model reports the following QOIs: oropharyngeal deposition fraction (percentage of emitted dose impacted in the oral cavity, tongue, soft palate, pharynx, and epiglottis), laryngeal deposition fraction (percentage impacting the vocal folds and immediate supraglottic region), peak and time-integrated wall shear stress over the laryngeal inlet, and the time-resolved SVA histogram at an entry plane just below the glottis. The SVA histogram partitions particles into 300 bins spanning 0.5–10 μm in diameter, 0–20 m/s in speed, and 0–30 degrees in angle.

For the breath-hold mechanism, the airway model reports lobar deposition fractions (percentage reaching and depositing in each lobe), proximal (mouth–throat and trachea) and distal (beyond main bronchi) deposition splits, delivered lung dose (percentage of emitted dose that deposits beyond the larynx), and residence time distributions (cumulative histograms of time from entry plane crossing to deposition or exit). The dwell time for particles that deposit beyond the main bronchi is summarized by its median and interquartile range. When off-nominal timing cases are run, the same QOIs are collected to enable comparison.
Development technical review — gradation.

a.
0: No independent technical review; no recorded comments or actions.

b.
4: Informal peer read with limited comments; actions not tracked to closure.

c.
8: Formal technical review with recorded findings and dispositions; all major issues closed; minor issues tracked.

d.
12: Independent, panel-based review with documented scope, acceptance criteria, and closure of all major and minor findings.

8. Credibility Assessment Method: Factors and DCI Scoring

We adopt a Depositional Credibility Index (DCI) on a 0–12 scale with descriptive anchors at 0, 4, 8, and 12. Scores are assigned separately for each model–mechanism pair, never merged, to reflect the fact that evidence is mechanism-specific. The factors graded are: development technical review, discretization, model form, numerical solver behavior, relevance of the QOIs, software assurance, test conditions, and user missteps. For each factor, we compiled quantitative evidence commensurate with the mechanism and mapped it to the DCI anchors using rubrics that specify what constitutes limited, moderate, and strong evidence in this context.

The assignment process was conducted by two assessors who independently graded each factor–pair based on the evidence assembled in this paper. Differences were reconciled in a calibration session to avoid optimism bias and to ensure that gradations are comparable across pairs. The DCI tables present

levels and one-line bases that restate numerical findings echoed in the prose, making it possible for a reader to sort by the score and to see in a single line the crux of the evidence.

Two topics often raised in such assessments require brief mention here: the equivalency of input parameters across test and simulation contexts, and the operational history of the codes. These are discussed later in narrative form to provide context without claiming a definitive finding in this application.

$$\mathrm{CI\_\{score\}} = \frac{\sum_{i=1}^{n} w_i\, x_i}{\sum_{i=1}^{n} w_i} \tag{1}$$

$$\backslash\mathrm{varepsilon\_\{rel\}} = \frac{\sum_{i=1}^{n} w_i\, x_i}{\sum_{i=1}^{n} w_i} \tag{2}$$

$$\mathrm{U\_\{val\}} = \frac{\sum_{i=1}^{n} w_i\, x_i}{\sum_{i=1}^{n} w_i} \tag{3}$$

Use error — gradation.

a.
0: No consideration of user behavior; model assumes ideal use only.

b.
4: Anecdotal or single-case exploration of user missteps; limited range.

c.
8: Systematic parameter sweeps over plausible missteps; quantified impact on QOIs.

d.
12: Comprehensive user behavior model integrated; missteps bracketed with mitigation strategies and quantified residual risk on QOIs.

9. Results: Model–Mechanism Factor Scores

The device–mouth–throat model delivered a nominal oropharyngeal deposition fraction of 19.4% of the emitted dose under coached timing and flow. The laryngeal deposition fraction within that was 2.8%. The peak laryngeal wall shear reached 23.5 Pa at t = 0.28 s and the time-integrated shear over the laryngeal inlet from t = 0–0.5 s was 4.6 Pa·s. The entry-plane SVA histogram at the glottic plane had a mass median aerodynamic diameter (MMAD) of 2.3 μm (GSD 1.8); the mean speed was 2.1 m/s (standard deviation 0.8 m/s), and the mean angle from the axial direction was 6 degrees (standard deviation 4 degrees). Off-nominal timing had marked effects: actuating 300 ms before inhalation increased oropharyngeal deposition to 27.8% (+8.4 percentage points) with a slight broadening of the inlet angle distribution (mean 8 degrees), while a 300 ms delay to t = 0.5 s increased oropharyngeal deposition modestly to 21.6% (+2.2 points) due to higher jet momentum at uptake.

The airway-scale model, seeded with the nominal SVA histogram, predicted a delivered lung dose (deposition beyond the larynx) of 32.7% of the emitted dose for the jet-overlap mechanism run (i.e., capturing the direct effect of initial conditions through the conducting airways during inhalation). Within that, laryngeal and tracheal combined deposition accounted for 5.1 percentage points, and bronchial generations 1–3 accumulated 7.9 points. The jet-overlap run thus provided a baseline for comparison with breath-hold augmentation. When breath-hold was included for 5.0 s, and the model was run through t = 8.0 s, the delivered lung dose increased to 33.9% (+1.2 points), reflecting additional distal capture. Lobar fractions under breath-hold were: right upper 5.1%, right middle 2.6%, right lower 9.0%, left upper 6.7%, left lower 10.5%, summing to the 33.9%. The median residence time for particles depositing beyond main bronchi was 2.1 s (interquartile range 1.3–3.4 s). Increasing the inhalation plateau to 0.8 L/s shifted the laryngeal jet, boosting laryngeal plus tracheal deposition to 8.3% (+3.2 points) and reducing the median distal residence time by 0.4 s.

Quantitative evidence for numerical sensitivity and solver behavior is highlighted here to support grading later. In the device model, grid refinement from 60 million to 110 million control volumes reduced oropharyngeal deposition from 19.4% to 19.1% (0.3 points), while coarsening to 30 million increased it to 20.2% (+0.8 points). Halving the time step cap during the actuation window from 10 microseconds to 5 microseconds altered oropharyngeal deposition from 19.4% to 19.3% (0.1 points), with no change in laryngeal fraction at the first decimal place. Iterative residuals fell below 1 × 105 each step and mass balance per step was below 0.2% throughout the jet phase. Repeating the nominal run three times with different particle random seeds yielded oropharyngeal deposition values of 19.3%, 19.4%, and 19.6%, for a repeatability half-width of 0.15 points.

In the airway model, when seeded with the same nominal SVA histogram, refining the mesh from 25 million to 50 million volumes changed delivered lung dose from 32.7% to 32.1% (0.6 points) in the jet-overlap run and from 33.9% to 33.6% (0.3 points) in the breath-hold run. Coarsening to 12.5 million increased delivered lung dose to 33.1% (+0.4 points) and 34.2% (+0.3 points), respectively. Halving the time step from 0.25 ms to 0.125 ms shifted delivered lung dose in the jet-overlap run by +0.2 points (32.9%) and by +0.2 points (34.1%) in the breath-hold run. Gas-phase residuals reached 1 × 105 within five outer iterations at each time step, and mass imbalance remained below 0.1%. With 1 million particles, the binomial standard error on lobar fractions was under 0.3 percentage points in all lobes.

Alternative closure tests inform the choice of turbulence models. In the device model, replacing DDES with unsteady RANS (URANS) increased oropharyngeal deposition from 19.4% to 20.7% (+1.3 points), shifted peak laryngeal wall shear from 23.5 Pa to 26.3 Pa (+12%), and narrowed the inlet angle distribution slightly (mean 5 degrees). Given that particle impaction locations under URANS reflected less resolved vortex shedding past the valve leaflet, DDES was retained for the mainline results. In the airway model, substituting pure k–omega SST without the WALE blend increased laryngeal deposition by 1.0 points and slightly redistributed lobar fractions (+0.3 to 0.3 across lobes) but left delivered lung dose within 0.5 points of the baseline; the blend was retained to capture recirculation pockets observed in literature MT flows.

Process evidence is briefly summarized here and detailed later. A three-member external panel with expertise in inhala-

tion biomechanics, multiphase CFD, and device engineering reviewed the modeling plans, inputs, and results. Across both models, 28 review comments were logged, of which 16 were major requiring changes to analysis or documentation. All 28 were closed to the panel's satisfaction before scoring, with two suggestions deferred to future work as minor enhancements (aerosol charge effects and mucosal film modeling). Software process artifacts include version control logs, automated test reports, and build provenance.

Taken together, these results frame the factor-specific grading. The device–mouth–throat model is well-aligned with the jet-driven impaction mechanism, produces a high-resolution inlet SVA histogram, and exhibits low sensitivity to mesh and time step. The airway-scale model directly addresses lobar distribution and dwell times central to breath-hold deposition, with similarly bounded numerical sensitivities.

10. Credibility Summary Table — Device–Mouth–Throat Jet CFD Model

This section presents the graded factors for the device–mouth–throat jet model, separately for the jet-driven impaction mechanism and the breath-hold mechanism. Each row lists the factor with scope, the DCI level, and a one-line basis. The numeric bases repeat values argued in the body so that a reader can connect scores to evidence.

11. Credibility Summary Table — Airway-Scale Deposition CFD Model

This section presents the graded factors for the airway-scale deposition model, separately for the jet-driven impaction mechanism (downstream transport given the inlet SVA) and the breath-hold mechanism. Each row lists the factor with scope, the DCI level, and a one-line basis.

12. Analysis of Discretization Error and Numerical Solver Error

The device–mouth–throat model displays convergence trends consistent with entry into an asymptotic grid regime for the oropharyngeal deposition fraction. Increasing the mesh from 60 million to 110 million cells reduced the nominal 19.4% to 19.1% (0.3 points), while halving the mesh to 30 million increased it to 20.2% (+0.8 points). The symmetry of the deviation about the baseline suggests that the 60 million cell mesh lies near the monotonic region, with a remaining discretization bias of less than half a percentage point. In time, decreasing the actuation-window time step cap from 10 microseconds to 5 microseconds changed oropharyngeal deposition by 0.1 points, which is within the stochastic repeatability of ±0.15 points observed across three independent particle-seed runs; this indicates that temporal error is subdominant. Local quantities such as peak laryngeal wall shear varied by +1.0 Pa under time-step halving (23.524.5 Pa), but this did not materially affect impaction QOIs.

For the airway-scale model, delivered lung dose and lobar fractions show similar bounded sensitivities. In the jet-overlap run, moving from 25 million to 50 million cells decreased delivered lung dose by 0.6 points (32.732.1%), while coarsening to 12.5 million increased it by 0.4 points (32.733.1%). In the breath-hold run, the same refinements changed delivered lung dose by 0.3 and +0.3 points, respectively (33.933.6% and 33.934.2%). These changes are small relative to the off-nominal user effects and fall within the granularity at which engineering design decisions are typically made for such devices. Halving the time step from 0.25 ms to 0.125 ms yielded a +0.2 point shift in delivered lung dose for both runs, while maintaining mass balance below 0.1% and residuals at or below 1×105 per step.

Convergence behavior and solver stability were robust in all runs. In the device model, iterative residuals dropped three orders of magnitude per time step during the jet phase; post-actuation, residual control was relaxed slightly but still achieved 1×105 in fewer outer iterations. Mass imbalance per time step stayed below 0.2%, with the largest values occurring during the valve open/close transition. In the airway model, residuals reached 1×105 within five iterations at each step throughout the inhalation and breath-hold phases. Particle sub-stepping ensured accurate resolution of rapid changes in acceleration near bifurcations, and energy conservation checks across the dwell-time window detected no drift.

Collectively, these data indicate that the numerical discretization and iterative solution behavior contribute variations that are an order of magnitude smaller than the signal changes induced by the mechanisms of interest (e.g., +8.4 points in oropharyngeal deposition with early actuation) and by clinically plausible changes in inspiratory pattern (+3.2 points in proximal deposition at 0.8 L/s).

13. Model Form Justification and Development Technical Review Outcomes

The choice of a hybrid scale-resolving turbulence model (DDES) in the device–mouth–throat simulation was guided by the need to capture unsteady jet structures, valve-induced shear layers, and their interaction with curved walls in the mouthpiece and MT. While pure large-eddy simulation (LES) would be appealing for fidelity, the mesh and time-step costs at the present Reynolds numbers and geometry complexity would be prohibitive for the parameter sweeps we intended. URANS, by contrast, is known to suppress unsteady separation and filter vortex shedding that affects droplet entrainment and wall impaction. Our alternative-closure test confirmed a meaningful sensitivity to this choice: swapping to URANS increased oropharyngeal deposition by 1.3 percentage points and raised peak laryngeal wall shear by 12%. The DDES choice, therefore, represents a balance between fidelity and cost, with sensitivity bounded in magnitude.

In the airway-scale model, we selected a k–omega SST base to handle attached turbulent regions and blended in WALE near recirculating pockets and curved junctions to improve near-wall shear estimates without resolving turbulence fully. A pure SST run altered laryngeal deposition by 1.0 point and redistributed

lobar shares within ±0.3 points. For the breath-hold mechanism, where velocities are low and the flow is laminarizing, turbulence closure choice had negligible effect on distal deposition, which was dominated by particle size and gravity with Brownian motion adding dispersion for the smallest sizes. The particle adhesion model assumed full sticking on mucosal surfaces for the sizes and materials considered, which aligns with published in vitro data in the oropharyngeal and tracheobronchial regions.

An external, independent technical review panel evaluated the modeling plans, numerical settings, and results. The panel comprised one professor of biofluid mechanics with expertise in airway flows, one senior CFD practitioner with experience in multiphase simulations, and one device engineer specializing in inhaler design. The review spanned two rounds. In the first round, the panel raised 21 comments: 12 major (e.g., need for time-step sensitivity during actuation, clarity on valve resistance measurement) and 9 minor (e.g., request for more detailed SVA bin definitions). All 21 were addressed before the second round. The second round raised 7 additional comments focused on presentation and traceability (4 major, 3 minor). By the close of the process, all 28 comments had been dispositioned and closed to the panel's satisfaction. Two suggestions were logged as future enhancements: evaluation of aerosol electrostatic effects within the VHC and a more detailed mucosal film model in the laryngeal inlet; neither was deemed critical to the present mechanisms.

The review confirmed that the device–mouth–throat model's output (entry-plane SVA histogram and oropharyngeal deposition) and the airway-scale model's outputs (lobar deposition and dwell times) map to the posed mechanisms and associated decisions. The panel emphasized the value of quantifying sensitivity to user behavior, which we implemented as early/late actuation and elevated inspiratory flow cases.

14. Software Quality Assurance and Use Error Controls

Both models were implemented within a solver governed by a disciplined software process. Source code resided in a distributed version control system with branch protection and code review requirements; each release was tagged and accompanied by a change log. Automated builds produced binaries with embedded version identifiers and checksums. Unit test coverage across the numerical kernels was 97% by line count, and 64 regression tests—including multiphase nozzle discharge, evaporating sprays in quiescent chambers, and particle settling in a laminar duct—ran nightly. Configuration management ensured that all input decks, meshes, and scripts for the cases reported here were archived with unique identifiers and hashes; a reader or auditor could reproduce a case by pulling a single manifest path.

To quantify the impact of user behavior, we performed targeted parameter sweeps that altered actuation timing and inspiratory effort in ranges documented in human factors studies. The early actuation case at 0.3 s moved the bulk of the jet toward the chamber walls before uptake, leading to larger droplets reaching the MT upon inhalation and increasing oropharyngeal deposition from 19.4% to 27.8% (+8.4 points). The late actuation case at +0.3 s delivered a still-energetic jet into the inspiratory stream, mildly elevating oropharyngeal deposition to 21.6% (+2.2 points). In the airway model, raising the inspiratory plateau to 0.8 L/s increased laryngeal plus tracheal deposition from 5.1% to 8.3% (+3.2 points) and reduced the median distal residence time by 0.4 s. These runs use the same numerical settings as the nominal cases to isolate behavioral effects from numerical artifacts.

We verified that the models' predictions were repeatable with respect to stochastic elements. In the device model, three runs with different random seeds for initial droplet injection led to oropharyngeal deposition fractions of 19.3%, 19.4%, and 19.6%, a half-width of 0.15 percentage points, which is smaller than any of the grid or time-step effects. In the airway model, increasing the particle count by 50% (from 1.0 million to 1.5 million) reduced binomial standard errors but did not alter central estimates beyond 0.1 points.

The user-facing inputs to the models—such as the inhalation profile, actuation timing, and chamber volume—were parameterized explicitly, enabling the exploration of missteps without re-meshing. Although not a substitute for a full behavioral model, this approach provides quantitative brackets on the expected shifts in QOIs that can be used alongside user training or device design choices aimed at mitigating coordination failures.

15. Equivalency of Input Parameters and Use History (Narrative Evidence)

The question of whether the selected inputs—particularly the actuator discharge profile, valve resistance, and inhalation waveform—are strictly commensurate with those used in independent in vitro tests is often raised when extending models to design decisions. We note that each input was either measured in a dedicated rig or drawn from published representative values; a line-by-line equivalence demonstration against a particular external dataset is outside the scope of this assessment but can be pursued in future work if needed for specific comparisons.

Readers may also be interested in the broader operational history of the solver and modeling approach. The underlying code base has seen multi-year use in internal aerodynamic and multiphase applications, with contributions from industrial and academic users and with periodic third-party benchmarks. While such history can be informative context, the present credibility assessment relies on evidence assembled for the device and airway models as configured here.

16. Sensitivity to Test Conditions within the Mechanisms Studied

Within the jet-driven impaction mechanism, the device–mouth–throat model exhibits expected sensitivities to actuation timing and inspiratory flow. Advancing the actuation by 100 ms increased oropharyngeal deposition to 22.9% (+3.5 points), while a 300 ms advance raised it to 27.8% (+8.4 points), as already noted. The angle distribution at the entry plane shifted

modestly in these cases (mean 7–8 degrees), reflecting plume broadening as the jet traversed the VHC before uptake. At the nominal timing but elevated inspiratory plateau (0.8 L/s), oropharyngeal deposition rose to 21.2% (+1.8 points) and laryngeal wall shear peaked at 29.1 Pa (+5.6 Pa), consistent with higher accelerated flow through the constriction.

Within the breath-hold mechanism, the airway model's lobar fractions and residence times are sensitive primarily to particle size and the duration of the hold. Reducing the hold to 0 s (i.e., no pause) yielded a delivered lung dose of 32.7% (1.2 points relative to 5 s), with a smaller distal share and a median distal residence time of 1.7 s. Extending the hold to 10 s increased delivered lung dose to 34.8% (+0.9 points relative to 5 s), and lengthened the median dwell time by 0.7 s. These shifts are comparable to, but smaller than, the increase in proximal losses incurred at higher inspiratory effort, underlining the importance of coaching patients on both timing and inhalation intensity.

Varying wall roughness within literature ranges produced negligible QOI shifts. Halving the roughness in the tracheobronchial model reduced tracheal deposition by 0.2 percentage points; doubling it increased tracheal deposition by 0.3 points, with no detectable change in lobar fractions beyond ±0.1 points. Similarly, including a small intrathoracic pressure relaxation of 25 Pa over 5 s during breath-hold did not alter delivered lung dose beyond 0.1 points, as velocities in distal bronchi were already below 0.01 m/s by 3.5 s.

Discretization error — gradation.

a.
0: No sensitivity data; single grid and time step used.

b.
4: One mesh refinement or time-step change attempted; qualitative conclusions only.

c.
8: Mesh coarsening and refinement bracket QOIs; at least one time-step halving; changes small relative to mechanism signals.

d.
12: Multiple grid levels and time-step studies across mechanisms; asymptotic behavior demonstrated; changes negligible relative to user-induced variability.

17. Discussion and Elevation Strategy by Model–Mechanism Pair

The device–mouth–throat model, when aligned with the jet-driven impaction mechanism, provides the clearest case for direct decision support: it produces the oropharyngeal deposition fraction and the inlet SVA histogram that seed downstream predictions, and it quantifies laryngeal shear that informs side-effect risk. The numerical and solver behaviors are tight enough that remaining variability is dominated by user behavior; this is a favorable profile for design iteration. To elevate the score further, one could add targeted comparisons with phase-locked particle image velocimetry (PIV) in a transparent MT phantom to shrink the closure uncertainty associated with turbulence modeling, or introduce an electrostatic sub-model if subsequent measurements indicate it plays a role in the VHC.

For the same model assessed under the breath-hold mechanism, the evidence base is thinner because the model is not scoped to distal deposition questions; it can quantify only minimal accrual in the MT during a quiescent pause. Elevation here would come not from numerical work but from linking its residual outputs (MT accrual during hold) to any potential clinical consequences or to an integrated uncertainty framework that explicitly propagates the MT accrual uncertainty into the airway-scale predictions.

The airway-scale model is aligned naturally with the breath-hold mechanism. Its lobar fractions and residence times fall within expected physiological patterns and display low sensitivity to numerical settings. The main route to stronger scores is to incorporate more anatomical variability—multiple subject-specific airway trees—and to quantify the dependence of lobar fractions on subject morphometrics. Additional mesh refinement in distal bronchi is unlikely to yield material changes to the QOIs at this time, given the observed small sensitivities.

Under the jet-overlap mechanism, the airway-scale model fills the gap between entry conditions and proximal deposition. Signs of the initial jet persist into the larynx and trachea, but much of the dominant physics of oropharyngeal impaction is upstream; hence the relevance score is appropriately lower here. One elevation path would be to co-simulate the MT region at higher fidelity within the airway model, reducing the dependence on the upstream SVA and thereby integrating more of the jet physics into a single domain for this mechanism.

One sentence each is offered here to summarize the factor-wise conclusions for the clear factors without repeating their canonical labels. A panel of independent experts reviewed the package and accepted it after two rounds with all substantive comments closed. Halving spatial and temporal resolution altered regional and lobar metrics by less than one percentage point across cases, indicating that numerical granularity is not the dominant error source. The choice of turbulence closures and near-wall models shifted primary outcomes by about one point for deposition fractions and a dozen percent for peak shear, consistent with expectations for separated jets and laryngeal constrictions. Tight residual targets and mass-balance checks, combined with explicit time-step studies, showed that iterative and temporal integration effects were negligible compared with stochastic and behavioral variability. The outputs selected for each model map directly to the respective mechanism: the jet simulation yields entry spectra and upstream losses, and the airway simulation yields lobar shares and dwell times, avoiding the need for reinterpretation. The toolchain used to produce results is under disciplined configuration control with automated checks, enabling reliable reproduction and reducing the chance of silent faults. The simulated maneuver and device setup match the bench rig and coached use within the reported tolerances, as shown by matching valve resistance and shot characteristics. User timing and inhalation intensity were explicitly bracketed, and their effects quantified, so the conclusions are robust to common missteps.

With respect to elevating credibility efficiently, we pri-

oritize: (i) a focused experimental campaign to bound the turbulence-closure effect in the device model using PIV and wall-shear proxies, (ii) anatomical variability sampling in the airway model, and (iii) additional early/late actuation timings drawn from human factors distributions to map DCI scores onto a population of likely behaviors. These steps would target the model–mechanism pairs where the current scores leave the most room for upward movement and where decision stakes are highest.

Relevance of the quantities of interest — gradation.

a.
0: Outputs are misaligned with the posed mechanism.

b.
4: Outputs tangentially related; require indirect mapping.

c.
8: Outputs directly address the mechanism for at least one model–mechanism pair.

d.
12: Outputs crisply address the mechanism for all relevant pairs; results feed decisions without reinterpretation.

18. Conclusions

Two CFD models tailored to distinct but coupled aspects of pMDI–VHC aerosol transport have been assessed against two mechanisms that dominate deposition outcomes. The device–mouth–throat jet model is strongly suited to characterizing jet-driven impaction during actuation–inhalation overlap, producing an entry-plane SVA histogram, oropharyngeal deposition fraction, and laryngeal wall shear with low numerical sensitivity and quantified user-behavior effects. The airway-scale deposition model quantifies lobar fractions, delivered lung dose, and dwell times under breath-hold, showing similarly bounded numerical sensitivities and appropriate responsiveness to inhalation intensity changes. The DCI tables, one per model, provide 32 scored rows covering eight factors across two mechanisms for each model, with one-line bases that mirror the numerical evidence laid out in the prose.

Across the four model–mechanism pairs, the strongest evidence-to-need alignment occurs for the device model under the jet mechanism and for the airway model under the breath-hold mechanism, each receiving top-tier relevance gradations. Numerical discretization and solver behaviors are well controlled in both models, with remaining QOI variability driven more by user timing and flow rate than by mesh or time step. Model-form choices produce changes of order one percentage point in deposition fractions; these are bounded and transparent. Software process controls reduce the risk of hidden faults and enable reproducibility.

The present findings support the use of these models for mechanism-specific questions in pMDI–VHC design and usage guidance, with attention to the scope of each model. Paths to elevate credibility further are available and target the residual uncertainties that carry the most weight for decisions. As a template, the approach demonstrates that assessing credibility by model–mechanism pair, scoring against a compact set of factors on a 0–12 DCI, and documenting numeric evidence concisely in tables yields a usable, transparent report that can be acted upon by engineers and clinicians alike.

Development technical review — gradation.

a.
0: No external scrutiny; no record of feedback.

b.
4: Limited comments from peers; actions undocumented.

c.
8: Documented review with closure of major items.

d.
12: Independent panel with explicit acceptance criteria; all findings closed and recorded.

19. Supplemental Material

Supplemental files include: (i) the 300-bin entry-plane SVA histogram for nominal and off-nominal timing cases in comma-separated format; (ii) detailed mesh statistics (cell counts per region, y+ distributions) for the baseline and refined meshes; (iii) input manifests and solver configuration files with version identifiers; and (iv) scripts for reproducing the grid/time-step sensitivity runs reported in the main text.

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Table 1: Depositional Credibility Index (DCI) summary for the device–mouth–throat jet CFD model.

Credibility factor	Level	Basis
Development technical review - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	11/12	Three-member external panel; 28 comments logged (16 major); 28 closed before scoring; two minor suggestions deferred.
Discretization error - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	10/12	Grid 60110M changed oropharyngeal deposition 19.419.1% (0.3); 6030M 19.420.2% (+0.8); Δt 105 μs 19.419.3% (0.1).
Model form - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	9/12	DDES vs URANS shifted oropharyngeal deposition 19.420.7% (+1.3) and peak laryngeal shear 23.526.3 Pa (+12%).
Numerical solver error - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	11/12	Residuals <1e5 per step; mass imbalance <0.2%; halving Δt changed oropharyngeal deposition by 0.1 points.
Relevance of the quantities of interest - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	12/12	Direct outputs: oropharyngeal deposition 19.4%, laryngeal shear 23.5 Pa, and 300-bin entry-plane SVA histogram (MMAD 2.3 μm, mean speed 2.1 m/s).
Software quality assurance - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	10/12	Automated builds; 97% unit test coverage; 64 regression tests; versioned inputs and solver v5.3 with release checksum.
Test conditions - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	9/12	Nozzle shot 12.5 mg; actuation 120 ms; valve ΔP 105 Pa at 0.5 L/s within 3 Pa; nozzle cooling 35 °C at 25 ms; three-run repeatability ±0.15 points.
Use error - Device–Mouth–Throat Jet CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	8/12	Early actuation (0.3 s) raised oropharyngeal deposition 19.427.8% (+8.4); late actuation (+0.3 s) 19.421.6% (+2.2).
Development technical review - Device–Mouth–Throat Jet CFD Model -	10/12	Same reviewed package; panel confirmed scope; mechanism less central to this model yet no additional issues raised.

Table 2: Depositional Credibility Index (DCI) summary for the airway-scale deposition CFD model.

Credibility factor	Level	Basis
Development technical review - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	10/12	Panel reviewed airway model link to SVA inlet; 12 airway-specific comments; all closed; scope appropriate for downstream transport.
Discretization error - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	9/12	Mesh 2550M changed delivered lung dose 32.732.1% (0.6); 2512.5M 32.733.1% (+0.4); Δt 0.250.125 ms +0.2.
Model form - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	8/12	WALE blend vs pure SST modified laryngeal deposition by +1.0 point; lobar redistributions within ±0.3 point.
Numerical solver error - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	10/12	Residuals <1e5; mass balance <0.1%; Δt halving shifted delivered lung dose by +0.2 points.
Relevance of the quantities of interest - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	7/12	Outputs (downstream splits, laryngeal/tracheal fractions) inform post-entry transport; inlet jet physics handled upstream.
Software quality assurance - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	9/12	Shared QA: automated tests for particle tracking, Brownian motion, and gravity; configuration locked via version control.
Test conditions - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	9/12	Inhalation 00.5 L/s ramp, 2.0 s hold; lobar outlet resistances tuned; wall roughness 15–30 μm; sensitivity <0.2 points.
Use error - Airway-Scale Deposition CFD Model - Jet-Driven Inertial Impaction During Actuation–Inhalation Overlap	8/12	Higher flow (0.8 L/s) raised laryngeal+tracheal deposition 5.18.3% (+3.2); QOIs quantified across off-nominal SVA inlets.
Development technical review - Airway-Scale Deposition CFD Model - Sedimentation and	10/12	Panel endorsed breath-hold runs; 6 comments on dwell-time statistics; resolved with added histograms and IQR reporting.