Spray Pattern and Plume Geometry:
Regulatory Convergence and Technological Innovation in Inhaled and Nasal Drug Products

Spray Pattern (SP) and Plume Geometry (PG) testing have long been incorporated into U.S. regulatory expectations and are now explicitly addressed in the 2026 revision of the European Medicines Agency guideline on inhalation and nasal medicinal products.

Importantly, the revision explicitly incorporates SP and PG as characterisation tests (where appropriate) and notes their use to ensure consistency during development and as a baseline for comparability assessments and lifecycle changes.

This evolution reflects broader international movement toward increasingly data-driven and development-stage *in vitro* performance assessment of orally inhaled and nasal drug products (OINDPs).

Concurrently, advances in high-speed digital imaging and automated image analysis have transformed SP and PG from primarily static geometric descriptors into dynamic, data-rich measurements capable of capturing transient plume behaviour. Modern platforms, including SprayVIEW® measurement system with Viota® software, enable extraction of both conventional metrics and time-resolved parameters such as plume front velocity, supporting deeper mechanistic understanding of aerosol momentum and product performance.

Together, regulatory alignment and technological innovation have elevated SP and PG testing from supportive visualisation tools to central elements of quality assessment, comparability evaluation, and lifecycle management strategies. As OINDP development increasingly emphasises data-driven and mechanistically informed approaches, advanced spray characterisation plays a critical role during product development, where it supports formulation optimisation, device selection, and demonstration of performance consistency.

OINDPs are complex drug–device combination products in which therapeutic performance depends on tightly coupled interactions between formulation properties, device design, and patient use. Unlike conventional oral dosage forms, aerosolised drug delivery involves highly dynamic processes, including atomisation, plume formation, droplet evaporation, and particle transport. Consequently, regulatory authorities require a multifaceted *in vitro* characterisation strategy, incorporating tests such as delivered dose uniformity, aerodynamic particle size distribution (APSD), and spray characterisation to ensure consistent performance and product quality.

Among these tools, SP and PG measurements serve as critical *in vitro* characterisation techniques, providing direct visual and quantitative assessment of aerosol formation at the point of actuation. These tests evaluate the size, shape, and spatial distribution of emitted sprays and plumes and have historically been used as indicators of device performance consistency and formulation–device compatibility. Established for over two decades in U.S. Food and Drug Administration (FDA) guidance, SP and PG testing have supported product development, quality control, and regulatory submissions, while also offering mechanistic insight into formulation–device interactions.[1,2]

More recently, the European Medicines Agency (EMA) has explicitly incorporated SP and PG into the updated guidance for inhalation and nasal medicinal products.[3] This reflects evolving international regulatory expectations and increasing recognition of the value of comprehensive *in vitro* performance assessment in supporting product quality, comparability, and bioequivalence assessments.

Industry groups such as the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS) have also documented the value of SP and PG testing methodologies, reflecting broad scientific consensus on their relevance for capturing product performance characteristics in regulatory and comparability assessments.[4]

In parallel with regulatory developments, advances in high-speed imaging and quantitative image analysis have transformed SP and PG from primarily static or qualitative measurements into highly quantitative tools capable of quantifying aerosol behaviour. Modern imaging platforms enable extraction of parameters such as plume front velocity and evaporation rate, providing deeper insight into aerosol momentum, droplet evolution, and transient plume dynamics.

This article reviews the regulatory evolution of SP and PG testing, highlights recent EMA guidance updates, and discusses how modern imaging technologies are expanding the scientific and regulatory utility of spray characterisation for OINDP development, regulatory submission, and lifecycle management.

Advanced Imaging Platforms for Spray Characterisation

One example is the SprayVIEW system (Proveris Scientific), a high-speed imaging platform designed for quantitative assessment of SP and PG using Viota software. The platform combines high-resolution imaging with advanced analysis to capture plume development over time, extracting both traditional geometric parameters and dynamic metrics. By converting visual plume behavior

Orally Inhaled and Nasal Drug Products,
Left to Right: Dry Powder Inhaler, pMDI Inhalers, Multidose Nasal Spray, Soft Mist Inhaler

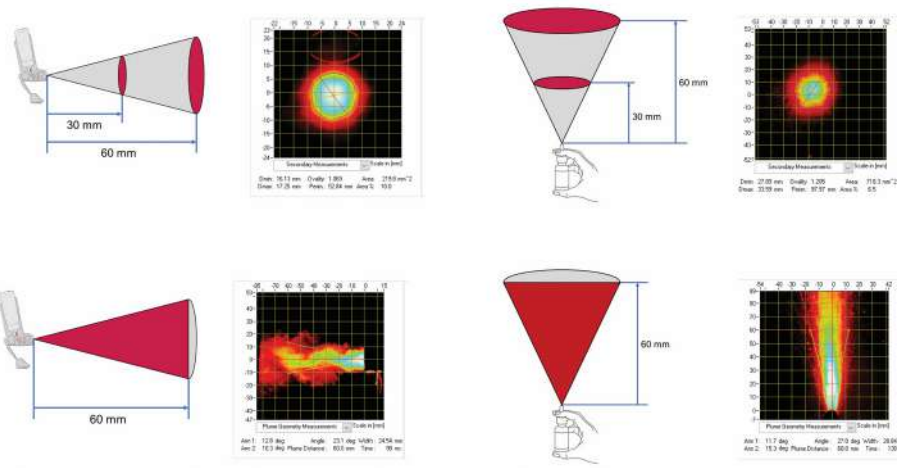
into analysable data, SprayVIEW with Viota supports reproducible measurements when appropriately validated and controlled.

This integrated system allows researchers to correlate droplet evolution with Plume Geometry and velocity, offering a structured quantitative assessment of aerosol performance. Together, the hardware and software enable robust characterisation, supporting formulation optimisation, demonstration of comparability, and regulatory submissions.

Recent EU Guidance and Regulatory Convergence

In 2024–2025, the EMA issued an updated draft guidance on the pharmaceutical quality of inhalation and nasal medicinal products, explicitly incorporating SP and PG into recommended characterisation tests.[3] The guideline specifies that SP and PG should be assessed, where appropriate, to evaluate the performance of the complete finished medicinal product, defined as the formulation in combination with the delivery device.

This represents a major step toward convergence with long-standing U.S. practices, which have included SP and PG in Chemistry, Manufacturing, and Controls (CMC) and bioavailability/bioequivalence (BA/BE) guidance since the early 2000s.[1,2] FDA product-specific guidances have further emphasised SP and PG for certain nasal sprays and inhalation products, reinforcing their role in regulatory submissions.[5] Historically, the EU draft guideline (Oct 2004) did not reference SP and PG, highlighting the evolution of European expectations. The final EMA guidance positions SP and PG as integral components of *in vitro* performance characterisation, alongside APSD, droplet size distribution (DSD), and delivered dose.



Top left and right: Spray Pattern are the cross-sectional views of the spray that is perpendicular to flow direction, usually measured at 2 distances (e.g. 30 mm and 60 mm) from the tip of the mouthpiece or nasal spray edge. Bottom right and left: Plume Geometry is the cross-sectional view of the spray that is parallel to the nominal flow direction, usually measured at 1 distance (e.g. 60 mm) from the tip of the mouthpiece or nasal spray edge.

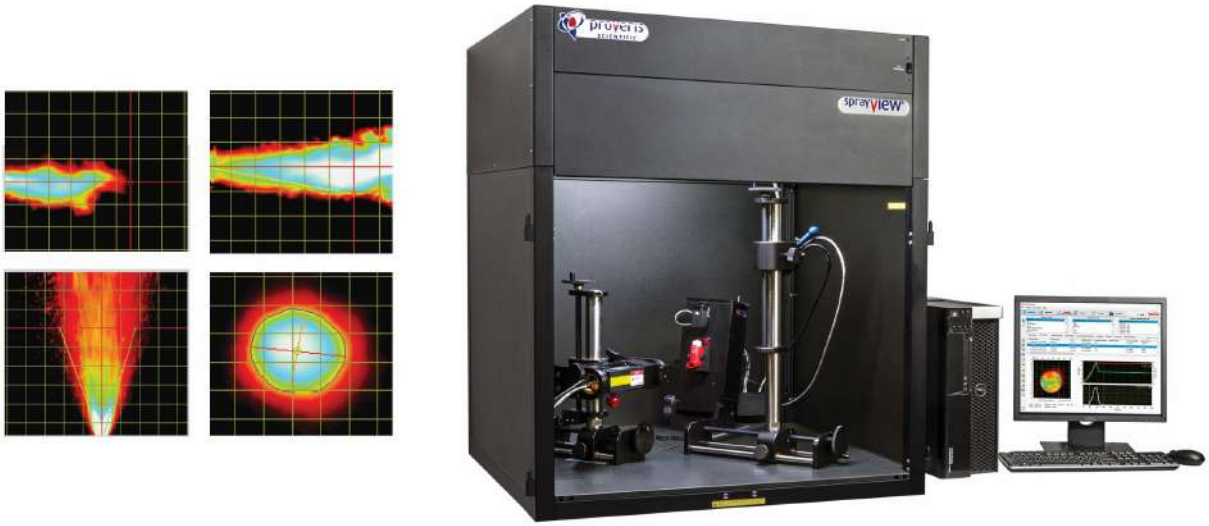
For developers targeting European markets, this encourages earlier integration of spray characterisation into formulation and device programmes, reducing late-stage performance risks and regulatory delays. Globally, regulatory authorities increasingly view SP and PG as essential elements of comprehensive OINDP characterisation, supporting product understanding, comparability, and, where appropriate, reduced reliance *in vivo* studies.

Recent comparative studies have demonstrated that differences in Spray Pattern and Plume Geometry between generic and reference nasal sprays correlate with distinct deposition profiles, underscoring their importance for ensuring pharmaceutical equivalence.[6]

Advances in Aerosol Imaging and Plume Dynamics

Modern spray characterisation has advanced significantly through high-speed digital imaging and sophisticated image analysis. Contemporary systems combine short-duration, high-intensity illumination with high-resolution cameras capturing hundreds of frames per second, enabling detailed visualisation of plume formation from initial actuation through expansion and dissipation.

Image analysis algorithms, including edge detection, intensity thresholding, and spatial measurement routines, allow automated and consistent extraction of geometric parameters with high precision and repeatability. Conventional Plume Geometry metrics such as plume angle, width, and height describe the spatial envelope of the aerosol cloud. High-speed imaging extends these measurements by capturing transient plume behaviour, providing mechanistic insight that static imaging cannot resolve. Plume front velocity, influenced by formulation properties, device design, and actuation mechanics, serves as



Example of spray characterisation using SprayVIEW Measurement System. Top: Plume Geometry (side view) generated from Softmist and pMDI inhalers. Bottom Left: Plume Geometry generated (side view) from a multidose nasal. Bottom Right: Spray Pattern generated from a multidose nasal spray.

a sensitive indicator of aerosol momentum and overall spray performance. (see Table 1 for key definitions)

Analysis of evolving plume morphology and dynamic spray behaviour has been shown to correlate with changes in aerodynamic particle size distribution and related deposition-relevant metrics in metered dose inhaler aerosols, indicating that plume characteristics can offer meaningful insight into aerosol performance beyond traditional static measurements.[7,8]

Advanced Analytical Platforms in Spray Characterisation

Modern platforms provide high-resolution, repeatable, and analysable datasets suitable for both routine quality testing and advanced research applications. Integrated data analytics automate extraction of geometric and dynamic parameters, supporting method validation, system suitability, and trend analysis. Large datasets generated through these platforms support batch release and comparability studies, bridging the gap between *in vitro* measurements and mechanistic understanding.

Although Spray Pattern and Plume Geometry remain *in vitro* measurements, their quantitative nature enables investigation of potential *in vitro-in vivo* relationships. High-speed imaging and plume characterisation provide metrics such as plume front velocity, spray duration, and plume morphology that can be captured in real time and linked to aerosol behaviour. Studies have demonstrated how variations in plume characteristics are accompanied by corresponding changes in droplet dynamics and *in vitro* deposition patterns, supporting the concept that these metrics can inform mechanistic models of regional deposition.[8,9] Aerosol visualisation across inhaler types has shown that plume velocity and spray duration vary substantially with device and flow conditions, indicating that dynamic plume data can serve as meaningful inputs for computational fluid dynamics simulations and deposition predictions.[1,8] Regulatory guidances further recognise Spray Pattern and Plume Geometry characterisation as key *in vitro* attributes in assessing performance and product comparability.[1,10]

Laboratory Test Services and Regulatory Support

Specialised laboratories offer comprehensive spray characterisation services integrating SP, PG, APSD, and additional complementary tests. These services support innovator and generic development, as well as post-approval change management, providing standardised methodologies, controlled test environments, and expert data interpretation.

High-quality, traceable data capture and reporting are essential for regulatory acceptance. Advanced reporting tools allow integration of spray characterisation metrics into broader submission narratives, supporting claims of product consistency, comparability, and robustness. SP and PG data also inform product release decisions and ongoing quality monitoring. Trends can detect subtle changes in device components, formulation properties, or manufacturing processes before performance is impacted, supporting lifecycle management.[11]

Practical Applications and Future Directions

Enhanced spray characterisation has proven valuable in supporting OINDP development and regulatory approval. SP and PG data have informed:

- Differentiation of alternative actuator designs
- Optimisation of formulation viscosity and excipient composition
- Comparability assessments for generic and reformulated products
- Investigation of customer complaints related to spray performance
- Mechanistic insight during root cause analysis of deviations

Beyond product development, metrics such as plume front velocity and evaporation rate provide quantitative evidence for post-approval changes. Continued integration of these dynamic parameters is expected to further enhance scientific understanding and regulatory decision-making. Advanced SP and PG metrics may increasingly guide formulation and device optimisation while supporting regulatory submissions.

Conclusions

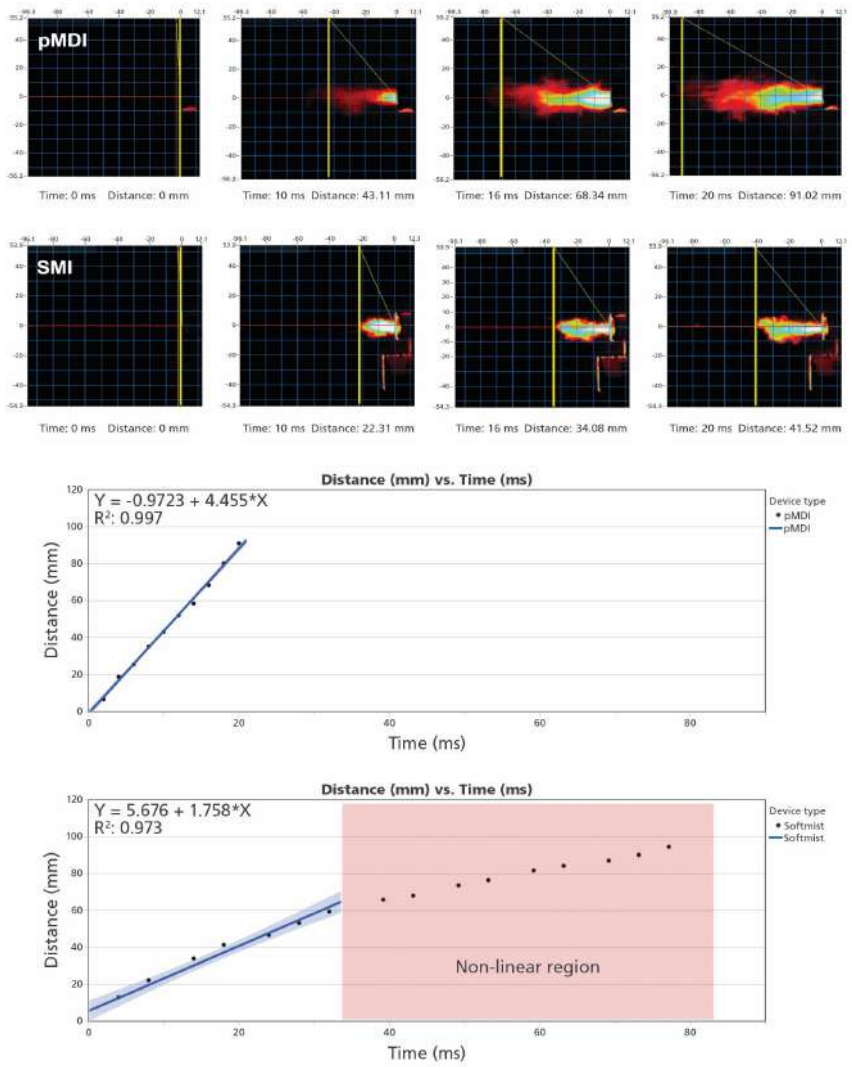
The regulatory and scientific framework for SP and PG testing has evolved substantially over the past decade. Historically emphasised within U.S. regulatory guidance, these measurements are now explicitly addressed in updated EMA guidance, reflecting increasing global harmonisation in expectations for OINDP characterisation. This convergence underscores the growing recognition of SP and PG as meaningful contributors to *in vitro* performance assessment.

Advances in measurement technology have expanded the scope and resolution of SP and PG evaluation. High-speed imaging, integrated data analytics, and platforms such as SprayVIEW and Viota have enabled the transition from static geometric descriptors to quantitative characterisation. Parameters including plume front velocity, evaporation behaviour, and plume evolution over time provide mechanistic insight into aerosol behaviour and performance, supporting regulatory decision-making and product evaluation.

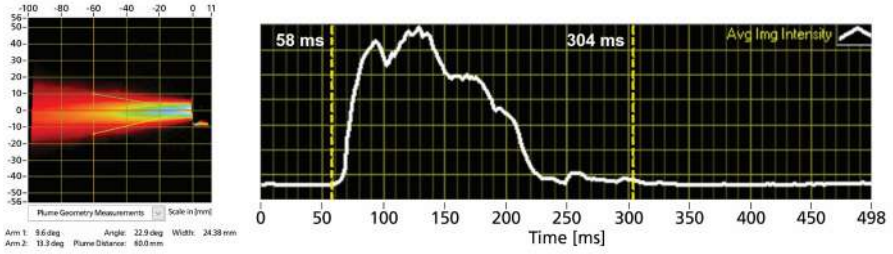
Specialised laboratory testing services continue to play a central role, providing standardised methodologies, controlled test environments, and expert interpretation. As the industry increasingly adopts data-driven and mechanistically informed development strategies, SP and PG characterisation remains

Parameter	Definition	Units	Relevance to Product Performance
Spray Pattern Area	Total area covered by the spray at a defined distance from the nozzle	mm^2	Reflects the overall spatial coverage and dose distribution potential
Spray Pattern Ovality	Ratio of the major axis to the minor axis of the spray ellipse	Dimensionless	Indicates uniformity and symmetry of the spray; high ovality may suggest directional bias
Plume Width	Lateral spread of the plume at a specific distance from the nozzle	mm	Influences deposition area and dose uniformity in the nasal cavity or lungs
Plume Angle	Angle formed by the edges of the expanding plume	Degrees	Affects the coverage pattern and can influence deposition efficiency
Plume Front Velocity	Speed of the leading edge of the aerosol plume immediately after actuation	m/s	Reflects aerosol momentum and transient behaviour; sensitive to formulation/device characteristics

Table 1. Key Spray Pattern and Plume Geometry Metrics



(A) Plume Front Velocity image captures taken with the SprayVIEW system camera produce a series of data points consisting of distance and time components until the plume has left the field of view. (B) Graph plots of the distance versus time data points based on calibrated, time-synchronised plume sequence analysis.



Spray Duration Measurement – an example of time-averaged plume results (left) with time-synchronised intensity profile (right, white curve) indicating the spray duration (58–304 ms).

essential for demonstrating product quality, performance, and consistency in alignment with global regulatory expectations.

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