

Navigating the USP 601a Update for Nasal Delivered Dose Uniformity

In 2022, the U.S. Pharmacopeia (USP) Chapter <601> introduced a significant change to the testing procedures for nasal spray and aerosol products, causing confusion in the industry. Specifically, the new guidelines recommend using the DUSA (Dosage Unit Sampling Apparatus) tubes for nasal Delivered Dose Uniformity (DDU) testing. However, these updates contradict existing product-specific monographs, creating inconsistencies that could compromise product quality, increase testing costs, and lead to operational inefficiencies.

Navigating Contradictory Guidelines

The update to USP <601> calls for DUSA tubes in nasal spray testing, which contradicts long-established monographs that have used primarily volumetric flasks. According to an informal industry survey, over 90% of professionals continue to use volumetric flasks, citing their ease of use, reliability, and cost-effectiveness. The proposed method in USP <601> introduces unnecessary complexities, such as the requirement to apply vacuum pressure during testing—an illogical step for nasal sprays, which are closed systems.

Risks and Costs of the New USP Guidelines

The updated USP <601> guidelines add several unnecessary steps to the testing process,

increasing both time and costs. These include the use of additional equipment like vacuum pumps, flow meters, and DUSA tubes. These extra steps not only complicate the testing process but also introduce potential sources of human error. As a result, manufacturers face higher operational costs, longer testing times, and the need for more consumables.

In contrast, the existing method for Fluticasone Propionate, which uses volumetric flasks, has been shown to provide accurate and reliable results at a lower cost. A recent case study comparing the USP product specific monograph to the newly proposed USP general <601> method found there was no benefit to testing performance, plus the traditional method resulted in faster testing with fewer complications.

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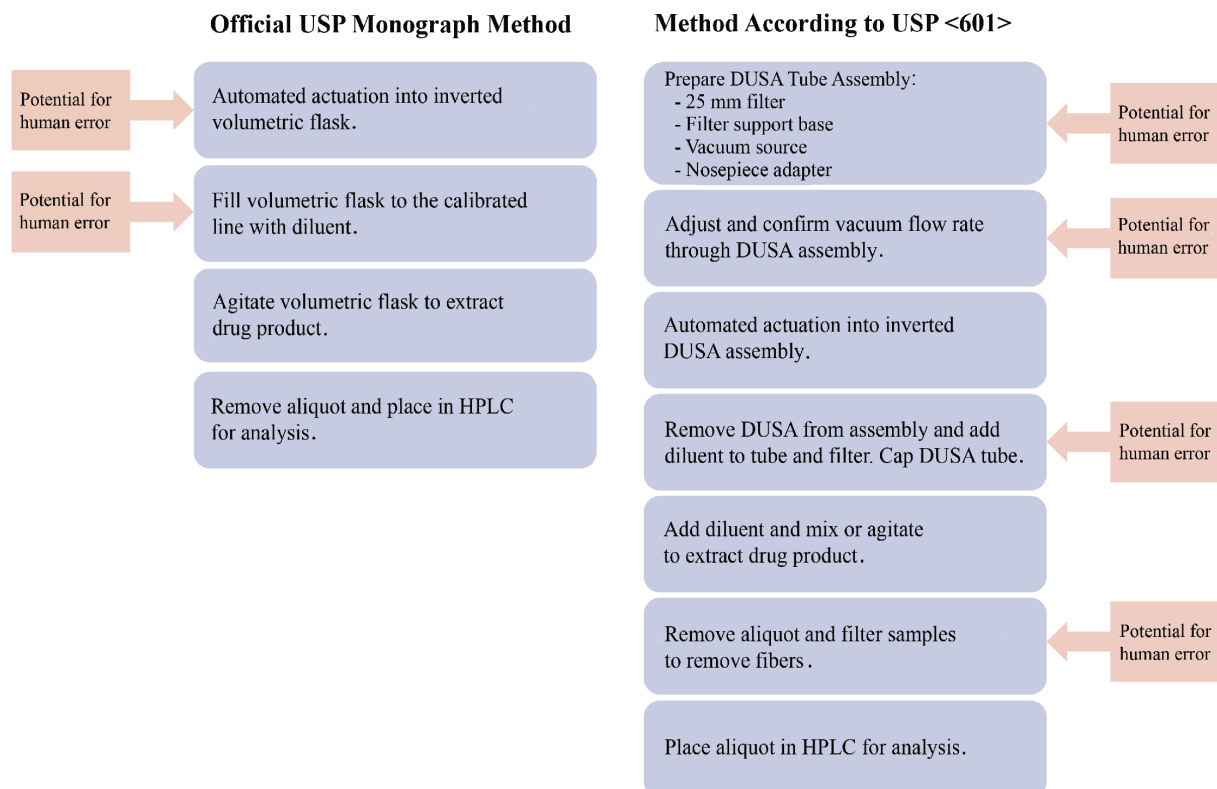


Figure 1. Comparison of number of steps and the potential for human error between official USP Fluticasone Propionate monograph and USP <601>



The Solution: Adherence to Proveris Testing Protocols

Navigating the regulatory landscape of nasal spray testing doesn't have to be difficult. The key is to follow product-specific guidance documents—which continue to use traditional methods like volumetric flasks and conical flasks—and avoid the confusion introduced by USP <601>.

One crucial aspect of navigating the regulatory environment is understanding the hierarchy of guidance documents. Regulatory bodies like the FDA, USP, and IPAC-RS play crucial roles in the Orally Inhaled and Nasal Drug Product (OINDP) development and approval process and have rules on how their guidance documents should be followed. One of these rules is to prioritize product-specific guidance documents over general documents.

The Hierarchy of Regulatory Documents

1. FDA Product-Specific Guidance: These documents are the most specific and authoritative guidelines available. They provide tailored recommendations for individual drug products, including nasal sprays. The FDA's product-specific guidance
2. USP Product-Specific Monographs: Like the FDA guidance, USP product-specific monographs offer detailed, tailored testing methodologies for individual drug products. These monographs take precedence over the general chapters of USP, such as USP <601>, because they are developed with specific drug formulations and device designs in mind. Following the monograph ensures that the testing methodology matches the exact specifications needed for that product, ensuring compliance and product integrity.
3. General Chapters (e.g., USP <601>): These are generalized guidelines meant to provide testing standards across a wide range of products. While important, general chapters should always be considered secondary to product-specific guidance documents. In cases where there is a conflict between a general chapter and a product-specific

is the key document manufacturers must follow, as it reflects the most up-to-date regulatory expectations for that particular product type. If the FDA's guidance does not align with a general USP chapter like USP <601>, manufacturers should adhere to the FDA's product-specific guidance to ensure compliance and smooth approval processes.

monograph or FDA guidance, the more specific document should be followed. This ensures that the unique needs of the product are met, whether in terms of testing procedures, safety, or efficacy.

The 2022 update to USP <601> does not align with product-specific monographs for nasal sprays, which continue to favor traditional methods like volumetric flasks for DDU testing. Manufacturers should prioritize these more specific documents to ensure their products remain in compliance with regulatory standards.

Conclusion

The updated USP <601> general chapter has introduced confusion and unnecessary risk for nasal spray manufacturers. While the industry works to align testing standards, manufacturers can mitigate the impact of these changes by sticking to proven, product-specific guidelines. Understanding the hierarchy of regulatory documents is crucial—always follow the most specific guidance (FDA product-specific guidance or USP product-specific monographs) over general chapters like USP <601>.

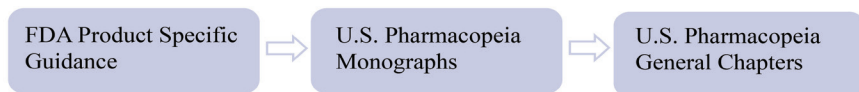


Figure 2. Hierarchy of guidance documents

Optimized Nasal Spray Testing Solutions from Proveris Laboratories

With decades of experience in optimizing testing workflows, Proveris Laboratories provides solutions that streamline DDU testing, reduce human error, and cut down on unnecessary costs. Our industry knowledge and expertise in OINDP testing instrumentation enables us to provide standard and custom testing services that adhere to the most up to date regulatory standards.

Benefits of Partnering with Proveris Laboratories

- Accurate and Reliable Results: Proven methods that ensure precision
- Cost Efficiency: Reduce overhead with simplified testing procedures
- Faster Time to Market: Get to market quickly with streamlined workflows
- Regulatory Compliance: Stay aligned with FDA, EMA, USP, and other global regulatory standards
- Trust in our expertise to help you navigate these challenges and optimize your testing procedures

Contact us to discuss how we can help you maintain product quality, reduce costs, and stay compliant with industry standards.



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