

# When Standards Outpace Practice: The Compliance Risks of the Proposed USP <31> Revisions

Jim Menoutis, PhD, FAIC  
Chief Science & Technology Officer  
Quantum Analytics Group

## Abstract

In May 2025 the United States Pharmacopeia (USP) published proposed revisions to General Chapter <31>, Volumetric Apparatus, in Pharmacopeial Forum 51(3), accompanied by a new informational chapter <1331>, Use and Calibration of Volumetric Apparatus. These proposals represent an important modernization of volumetric measurement practices by aligning compendial terminology and calibration expectations with internationally recognized metrology frameworks including ISO 8655, ASTM volumetric glassware standards, and the International Vocabulary of Metrology (VIM).

While scientifically justified, the proposed revisions introduce expectations regarding traceability, device identification, and risk-based calibration management that differ significantly from long-standing laboratory practices. Most analytical laboratories rely on unserialized Class A volumetric glassware manufactured to ASTM or ISO tolerances. In many cases manufacturers do not provide explicit batch calibration certificates, leaving laboratories to rely primarily on manufacturer conformance statements.

If interpreted as requiring apparatus-level traceability and calibration, the proposed revisions could impose substantial operational, manpower, and financial burdens on analytical laboratories worldwide. This manuscript examines the proposed revisions in detail, evaluates their scientific and regulatory rationale, and analyzes their potential impact on laboratories operating under historically accepted volumetric practices.

## Keywords

USP <31>, volumetric apparatus, analytical laboratories, traceability, metrology, GMP compliance, ISO 8655, ASTM volumetric glassware

## 1. Introduction

Volumetric measurement is foundational to analytical chemistry. The preparation of analytical standards, dilution schemes, titration reagents, and reference solutions depends on volumetric apparatus capable of delivering or containing precise volumes. In pharmaceutical quality control laboratories, volumetric accuracy directly influences analytical reliability, method validation, and ultimately the quality of finished pharmaceutical products.

USP General Chapter <31>, Volumetric Apparatus, has historically provided the compendial framework governing volumetric measurement within regulated laboratories. The

currently official version of the chapter, effective November 1, 2020, establishes tolerances and performance expectations for volumetric glassware used in analytical procedures.

In practice, laboratories demonstrate compliance with these expectations primarily through the use of Class A volumetric glassware manufactured according to ASTM and ISO tolerances. Manufacturers supply documentation indicating that the glassware conforms to Class A specifications. Individual pieces of glassware are generally not serialized and laboratories do not typically maintain device-specific calibration histories.

This long-standing approach has been broadly accepted by both industry and regulatory authorities because manufacturing tolerances for Class A glassware are tightly controlled and volumetric deviations are generally small relative to the analytical uncertainty associated with most laboratory methods.

However, the proposed revisions published in Pharmacopeial Forum 51(3) in May 2025 introduce a metrological framework that may significantly alter these historical practices. The revisions incorporate terminology and concepts derived from modern metrology systems, emphasizing traceability, calibration management, and risk-based quality system integration.

## **2. Overview of the Proposed Revisions**

The proposed revision to USP <31> introduces several important conceptual and operational changes to the management of volumetric apparatus.

Key elements of the revision include harmonization of terminology with the International Vocabulary of Metrology (VIM), alignment with ISO and ASTM volumetric accuracy standards, inclusion of piston-operated volumetric apparatus (POVA) such as micropipettes, and greater emphasis on temperature considerations affecting volumetric measurements.

Another important aspect of the proposal is the integration of risk-based calibration management within laboratory Quality Management Systems. This approach is conceptually consistent with broader regulatory trends toward risk-based quality systems, as reflected in ICH Q9 Quality Risk Management and ISO/IEC 17025 calibration laboratory standards.

Collectively, these changes represent a shift toward a metrological framework in which volumetric apparatus are treated as calibrated measurement instruments requiring documented traceability and performance verification.

## **3. Historical Industry Practice**

A critical factor in evaluating the proposed revisions is the recognition of historical laboratory practices involving volumetric glassware.

For decades, most analytical laboratories have relied on volumetric flasks, pipettes, and burettes manufactured according to ASTM or ISO specifications and labeled as Class A. These devices are designed to meet strict volumetric tolerances established through internationally recognized standards.

In routine laboratory operations these devices are not individually serialized. Laboratories typically do not maintain device-specific calibration certificates or calibration histories. Instead,

they rely on manufacturer documentation confirming that the glassware meets applicable Class A tolerances.

This approach has historically been considered sufficient because the manufacturing tolerances for Class A glassware are extremely tight. Furthermore, analytical reliability is typically verified through validated methods, system suitability testing, and quality control procedures rather than through apparatus-level calibration programs.

#### **4. Industry Supply Practices for Class A Glassware**

An additional practical consideration is the way volumetric glassware is supplied by manufacturers. Although glassware may be labeled and marketed as Class A, many manufacturers do not provide explicit batch calibration certificates with each shipment.

Laboratories often receive only catalog documentation or manufacturer conformance statements indicating that the product meets ASTM or ISO Class A tolerances. Consequently, laboratories frequently do not possess device-specific or batch-specific calibration documentation.

This supply practice has historically been accepted because manufacturing processes for volumetric glassware are tightly controlled and subject to internationally recognized standards.

#### **5. Industry Reality vs Proposed Metrological Model**

The proposed revisions introduce a metrological framework that implicitly assumes apparatus-level traceability and calibration management. However routine laboratory practice differs substantially from this model.

Three structural gaps illustrate the disconnect between the proposed framework and existing laboratory operations: the widespread use of unserialized glassware, the absence of manufacturer batch calibration certificates, and the lack of device-level calibration infrastructure in most routine analytical laboratories.

These structural differences create what may be described as a traceability gap between current industry practice and the metrological model implied by the proposed revisions.

#### **6. Operational and Manpower Impact**

Transitioning to serialized and individually calibrated volumetric apparatus would introduce substantial operational demands. Typical pharmaceutical quality control laboratories maintain between 500 and 1500 volumetric devices.

Implementing apparatus-level traceability would require inventory systems, unique device identifiers, calibration documentation infrastructure, and ongoing calibration scheduling.

Estimated manpower requirements include inventorying and labeling equipment, development of SOPs and calibration procedures, analyst training, and ongoing documentation review. For many laboratories these activities could represent approximately 140 to 240 labor hours annually.

## **7. Economic Impact**

In addition to manpower requirements, the financial implications of apparatus-level calibration programs could be significant.

A typical pharmaceutical QC laboratory may maintain approximately 1000 volumetric devices. If ISO-traceable calibration services average approximately \$40 per device, calibration costs alone could reach approximately \$40,000 per cycle.

Indirect costs may include calibration management software, asset tracking systems, administrative oversight, equipment downtime, and replacement of damaged serialized glassware. Total annual costs could reasonably reach between \$60,000 and \$120,000 per laboratory.

## **8. Regulatory Considerations**

Historically, regulatory inspections conducted by agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have not required individual calibration of Class A volumetric glassware when manufacturer certification is available.

However regulatory expectations continue to evolve toward increased emphasis on measurement traceability and data integrity. Inspectors may increasingly request documentation regarding apparatus suitability, calibration strategies, and justification for reliance on manufacturer certification.

## **9. Conclusion**

The proposed revisions to USP <31> represent a meaningful effort to modernize volumetric measurement practices and harmonize compendial guidance with internationally recognized metrology standards.

However, successful implementation of these revisions requires careful consideration of the operational realities of analytical laboratories. The widespread use of unserialized Class A glassware, the absence of manufacturer calibration certificates, and the limited calibration infrastructure in routine QC laboratories highlight the challenges of implementing device-level traceability frameworks.

A balanced approach will therefore be necessary. Such an approach should recognize the value of improved measurement traceability while preserving practical laboratory operations that have historically proven effective in ensuring analytical reliability.

## **References**

1. United States Pharmacopeia (USP). General Chapter <31> Volumetric Apparatus. USP–NF, 2020.
2. United States Pharmacopeia (USP). Proposed Revision to General Chapter <31>. Pharmacopeial Forum 51(3), 2025.
3. USP General Chapter <1331>. Use and Calibration of Volumetric Apparatus.
4. ISO 8655. Piston-Operated Volumetric Apparatus.
5. ASTM E287. Standard Specification for Laboratory Glass Volumetric Ware.
6. ASTM E288. Standard Specification for Laboratory Glass Volumetric Flasks.

7. ASTM E969. Standard Specification for Volumetric Glassware.
8. JCGM 200:2012. International Vocabulary of Metrology (VIM).
9. ICH Q9(R1). Quality Risk Management.

## **ABOUT QUANTUM ANALYTICS GROUP**

### ***WE BRING CLARITY TO COMPLEX ANALYTICAL CHALLENGES***

At Quantum Analytics Group, we combine advanced analytical instrumentation with deep scientific expertise to solve complex problems, not just measure them. As a full-service analytical testing and research partner, we provide chemical and material analysis for regulated and quality-driven industries, supporting product development, quality control, regulatory compliance, method development, contamination investigations, elemental analysis, and failure analysis with clear, defensible results.