

VIA ELECTRONIC SUBMISSION

October 30, 2025

Food and Drug Administration
Division of Dockets Management
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

**Re: Onshoring Manufacturing of Drugs and Biological Products; Public Meeting;
Request for Comments (“FDA PreCheck”, FDA-2025-N-2489)**

Dear Sir/Madam:

The United States Pharmacopeia (USP) appreciates the opportunity to comment on FDA’s PreCheck program to advance efficient, science-based facility readiness and support a resilient U.S. medicines supply chain. USP is a private, scientific, non-profit organization founded in 1820 with a mission to improve global health through public quality standards¹ and related programs that help ensure the quality, safety, and benefit of medicines and foods. We work to strengthen the supply chain so that the medicines people rely on for health are available when needed and work as intended. USP is governed by more than 400 organizations, including scientific, healthcare practitioner, consumer, and industry communities, as well as dozens of government agencies, which together comprise the USP Convention.²

General Comments

FDA’s PreCheck program offers a practical mechanism to strengthen domestic manufacturing and improve supply chain resilience by fostering early, consistent alignment on technical expectations for facility design and quality review. In practice, this alignment allows manufacturers to identify and resolve potential compliance or design challenges well before production begins, reducing costly late-stage modifications and inspection delays. By engaging FDA earlier in the facility-readiness process, PreCheck promotes regulatory predictability, supports more efficient CMC development and application review, and ultimately accelerates the availability of high-quality medicines produced within the United States.

USP advances these objectives through three core efforts:

1. Public standards that provide science-based benchmarks for facility design, analytical readiness, and lifecycle management (e.g., <1058>, <1083>, <1224>, <1231>);

¹ USP standards are developed by Expert Bodies comprised of more than 400 organizations and in close collaboration with stakeholders and government agencies, including staff from the U.S. Food and Drug Administration (FDA) who participate as Government Liaisons to USP’s Expert Committees and Expert Panels. These experts collaborate to develop USP standards through an open, transparent process, offering the ability to adjust standards to confront public health emergencies, adapt to new industry practices, and keep up with evolving science and technology. USP’s public quality standards are recognized in the Federal Food, Drug, and Cosmetic Act as official standards for medicines, dietary supplements, and food ingredients.

² USP’s governing bodies in addition to the Council of the Convention include its Board of Trustees and Council of Experts.

2. Applied education and laboratory resources, such as the Advanced Technologies Laboratory, that translate those standards into implementable practices and workforce capability; and
3. Ongoing development or revision of standards for emerging technologies so innovative control strategies can be assessed consistently within PreCheck.

Together, these efforts provide FDA with validated frameworks for regulatory reliance, reducing uncertainty at readiness milestones, and helping to ensure a predictable, efficient transition from facility startup to sustained operations.

Moreover, USP welcomes opportunities to collaborate with FDA and stakeholders to expand standards development for emerging technologies that support PreCheck and to identify additional possibilities where reliance on validated, public standards can facilitate more predictable CMC and facility review.

Standards as Reference Points

Reference to USP public standards within the PreCheck program enables manufacturers to present consistent, science-based information, thereby allowing FDA staff to expedite their reviews. Using these standards, reviewers can streamline assessments, reduce variability, and promote predictable, transparent regulatory decisions. Pertinent USP standards address areas such as pharmaceutical quality systems, sterility assurance, analytical readiness, storage and distribution, and instrument qualification—enhancing predictability from facility design through commercial operations. In practice, existing foundational USP standards that support laboratory systems, supplier qualification, storage and transportation risk-mitigation, monitoring of critical environmental conditions, sterility assurance, analytical procedure transfer, and pharmaceutical water quality are core to PreCheck’s goal of early, consistent alignment on facility expectations. Further, these standards can be cited and aligned with ICH Q12 tools—Established Conditions, Product Lifecycle Management, and Post-Approval Change Management Protocols—so that the specific acceptance criteria, ongoing monitoring requirements, and requalification triggers are defined and tied to risk-based post-approval change pathways. As PreCheck evolves, the program can also clarify avenues for public standards to interface with regulatory review processes and broader quality management initiatives, including deeper integration of ICH Q12 lifecycle elements to support predictable, efficient oversight.

USP documentary standards (monographs and general chapters) are primary compendial sources of CMC information for drug applications, defining identity, strength, quality, purity, performance tests, and the associated analytical procedures and acceptance criteria that underpin their specifications and controls. Within PreCheck’s application submission phase, referencing these public standards allows sponsors to present consistent, reviewable specifications and control strategies for compendial drug products and excipients (e.g., assay/impurities and dissolution; elemental impurities; packaging, storage, and water quality), while demonstrating method readiness through transfer and verification plans aligned to analytical lifecycle principles.

USP’s comprehensive documentary standards provide FDA with authoritative, science-based procedures and system-suitability expectations to anchor method development and verification. This enables FDA to conduct reviews more efficiently and consistently while preserving flexibility for scientifically justified alternatives.



Specific Comments

I. *Advanced Technologies*

Advanced and digital manufacturing technologies may play an important role within the PreCheck program, enabling proactive control strategies and greater transparency between sponsors and regulators. USP notes that incorporating these technologies within PreCheck submissions, supported by reference to relevant public standards, can help manufacturers show validation and lifecycle control using consistent, science-based frameworks. Sponsors can cite these chapters as optional anchors in Type V DMFs and pre-submission materials to present analytics and control strategies in a consistent, reviewable format while preserving flexibility for scientifically justified alternatives.

To operationalize advanced analytics within control strategies, sponsors routinely use relevant USP standards to design, validate, and verify Process Analytical Technology (PAT) and Real-Time Release Testing (RTRT) methods. Related standards for biological assay validation and chemometrics are likewise applied to define model development, maintenance, and requalification exceptions, ensuring that analytical models and PAT methods are managed under reproducible, lifecycle-managed controls.

II. *Sterility and Contamination Control*

Sterile operations and contamination-control strategies are essential for patient safety and operational reliability. Where appropriate, sterility verification may include alternative rapid microbiological methods and integrated sterility-assurance programs aligned to public standards. Manufacturing-applicable USP standards that address sterilization approaches, disinfection practices, environmental monitoring, and contamination control inform zoning, monitoring programs, and risk-control strategies for robust aseptic operations.

For complex modalities where facility design choices carry elevated risk, sponsors can address modality-specific expectations for cell and gene therapies, vaccines, and antibody-drug conjugate facilities—covering containment/segregation, cross-contamination controls, specialized utilities and flows, and scalability—with references to USP chapters pertaining to ancillary materials for cell and gene therapies and chapters on viral safety evaluation. USP standards deliver sterility assurance and aseptic processing guidance, defining sterilization methods, environmental monitoring, and contamination control practices essential for maintaining sterile operations. Early adoption of USP standards for sterility and contamination control enables FDA and sponsors to preempt costly rework and inspection delays, directly streamlining regulatory assessment and deployment of new facilities.

III. *PreCheck Prioritization*

To focus impact where it matters most, PreCheck participation can be prioritized for facilities producing essential and shortage-prone medicines and for projects that materially advance onshoring of key starting materials (KSMs), active pharmaceutical ingredients (APIs), and drug products (DPs). For example, a 2024 USP analysis shows that half of the APIs used in prescription medicines in the United States come from India and the European Union.³ In addition, USP's KSM analysis shows that many medically critical ingredients originate from a small number of producers concentrated in only a few countries, creating systemic points of

³ U.S. Pharmacopeia. USP Quality Matters Blog: Over half of the active pharmaceutical ingredients (API) for prescription medicines in the U.S. come from India and the European Union. 2025. Available at: <https://qualitymatters.usp.org/over-half-active-pharmaceutical-ingredients-api-prescription-medicines-us-come-india-and-european>. Accessed October 24, 2025.

vulnerability and potential for cascading shortages.⁴ These insights can inform FDA's prioritization under PreCheck by identifying where supply risk is highest and where early facility engagement and redundancy planning would have the greatest public-health benefit. Complementing this prioritization, sponsors can utilize USP's Advanced Technologies Laboratory and education programs, with outputs from such pre-competitive training and technical assistance contributing to strengthened shared capability around method transfer, sterility assurance, and PAT readiness.

IV. *Near- and Ally-Shoring Pharmaceutical Manufacturing*

While the PreCheck program advances the Administration's goal of strengthening the supply chain through onshoring, extending PreCheck—or establishing a similar program—for qualified, existing facilities in near- and ally-shore geographies would provide a complementary, near-term resilience boost by diversifying sourcing away from adversary countries. In many cases, production capacity already exists in these countries, and activating these sites can expand the U.S.-aligned supply chain more rapidly than building new plants. Initiatives like PreCheck for these existing facilities could expand the U.S. supply chain, enhancing national security and helping to reduce drug shortages of essential medicines.

Recommendations

To maximize the impact and practicality of the PreCheck program, USP standards and technical capabilities can be leveraged to create predictable, science-based alignment during facility readiness and application review. These recommendations outline how PreCheck can integrate standards, training, and prioritization tools to strengthen regulatory efficiency and supply chain resilience.

- **Encourage the use of USP standards in PreCheck submissions:** Sponsors can reference relevant USP general chapters and reference standards within their PreCheck submission application to demonstrate analytical method readiness, PQS maturity, sterility assurance, and PAT/RTRT capability. This structured, cross-referenced approach helps FDA reviewers to evaluate submissions quickly and systematically, reducing review cycle time and resource strain while supporting risk-based regulatory oversight.
- **Prioritize where risk is highest:** Prioritize PreCheck access for facilities producing essential and shortage-prone medicines and for projects that meaningfully onshore KSMs, APIs, and DPs, using risk insights (e.g., concentration of suppliers and geographic dependencies) to target early engagement where single point failures are most likely.
- **Expand the PreCheck program to near- and ally-shore facilities:** Broadening the scope of the PreCheck program to include qualified near- and ally-shore facilities could complement U.S. onshoring initiatives by expanding supply chain capacity using existing facilities. This approach may help reduce reliance on adversary countries, provide additional flexibility to address supply chain risks, and promote national security while maintaining high standards for regulatory oversight and patient safety.

⁴ U.S. Pharmacopeia. Concentrated Origins, Widespread Risk: New USP Insights on Key Starting Materials. Quality Matters, 2025. Available at: <https://qualitymatters.usp.org/concentrated-origins-widespread-risk-new-usp-insights-key-starting-materials>. Accessed October 21, 2025.

- **Build shared capability via pre-competitive platforms:** Leverage pre-competitive training and technical assistance—such as USP’s Advanced Technologies Laboratory and education programs—to upskill sponsor teams and align expectations on method transfer, sterility assurance, and PAT/RTTR readiness.

USP appreciates FDA’s leadership in launching the PreCheck program and supporting efforts, including the recently announced ANDA Prioritization Pilot. USP values the opportunity to collaborate with the Agency, industry, and other stakeholders to align public standards, technical guidance, and training resources that help support risk-based facility reviews and accelerate safe, high-quality patient access. In support of these objectives, USP is committed to expanding standards development for emerging technologies to support PreCheck and to identify additional opportunities where reliance on validated, public standards can facilitate more predictable CMC and facility review.

Thank you again for the opportunity to provide comments on the FDA’s PreCheck Program. Should you need additional information about USP’s response, please contact Brett Howard, Senior Director, US Regulatory Policy, by phone at 301.692.3296 or via email at brett.howard@usp.org.

Sincerely,

A handwritten signature in black ink, appearing to read 'Fouad Atouf', written in a cursive style.

Fouad Atouf, Ph.D.
Executive Vice President and Chief Science Officer
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