Prescription/Non-Prescription Stakeholder Forum

EXECUTIVE SUMMARY

April 11–12, 2022

The U.S. Pharmacopeia (USP) hosted the Prescription/Non-Prescription Stakeholder Forum on April 11–12, 2022. USP provided information designed to support stakeholders, including Industry, regulators, academia, and patient advocacy groups. USP is a non-profit, science-based organization that develops quality standards for medicines, dietary supplements, and foods.

- USP's mission has remained essentially the same since its founding in 1820 to improve the health of people around the world through public quality standards and solutions. – . Meanwhile, major changes in technology, digitization, and the global supply chain are happening worldwide, and USP is adapting and evolving to meet these challenges.
- One way USP helps stakeholders adapt to these changes is by making sense of the amount of scientific information currently being generated. Information isn't valuable unless we distill it down to something useful.
- USP is committed to advocating for quality and ensuring our standards are relevant and utilized.
- Capability building – to be a leading provider of services that advance the supply of quality medicines – is a critical goal and helps support USP's standard-setting work and public health mission.
- Increasingly, USP is collaborating with and convening stakeholders to promote medicine quality and publishing our preliminary work to engage partners earlier in the standard development process.
- Another important area of input is through the USP Convention, as one of USP's governing bodies. In addition to collaborating on critical healthcare and science matters, every five years, Convention Members (more than 500 organizations) adopt USP Resolutions and elect USP's Board of Trustees and the Council of Experts, who lead USP's standards-setting Expert Committees.

<u>Stakeholder Engagement</u>

- Stakeholder engagement is essential, core, and critical to USP's responsibility as a standard setter. USP works in partnership with more than 1,000 expert volunteers, 400 convention members, and numerous regulators worldwide.
- USP strives to develop relevant, impactful standards in accordance with our public health mission, but we are now doing so in a more targeted, agile way.
- Working collaboratively is the key to USP's success. We strive to be responsive to stakeholder input, working together to identify and solve problems.
- Standards development does not follow a straight line – we can tailor our approach to the issue at hand. Not all potential solutions are appropriate for becoming an official standard utilizing the traditional compendial route.
- In response to stakeholder feedback, USP strives to engage stakeholders during the exploratory stage before a standard is even deemed necessary and before a decision on the solution is determined.

- USP's Stakeholder Engagement Model facilitates communications and maximizes our responsiveness to stakeholder feedback, questions, and concerns.
- The Stakeholder Engagement Planning Committee is now more inclusive, representing a wider range of stakeholders to amplify the stakeholder's voices.
- USP recognizes that other organizations are doing great work. As a result, USP does not always have to take the lead or solve the problem; other groups can drive the effort, and USP will continue to support those efforts.
- USP is using innovative ways to engage and leverage the different approaches we learned in a virtual environment, such as asynchronous roundtables, open forums, and knowledge hubs. We continue to learn how best to engage in a virtual/hybrid environment.

Innovative Engagement Tools

The formation of online communities offers a novel way for USP to engage with stakeholders around a particular scientific topic. Last year USP launched its first online community, the Nitrosamine Exchange Knowledge Community, which is a global online community where scientists and others can share best practices, challenges, and solutions in our new virtual world. As a professional network tool, this knowledge community quickly became a forum for all things nitrosamines. Although USP hosts the knowledge community, USP is not in the driver's seat and is not pushing its own agenda; instead, the community of members guides the discussions. In less than 12 months, the nitrosamine Exchange Knowledge Community has over 800 members from 70 countries, with 80,000 page views (to learn more about joining, go to http://nitrosamines.usp.org).

Breakout Sessions on Stakeholder Engagement

During the breakout sessions, USP posed several key questions to participants and gathered their input. USP will use this information to strengthen its ongoing stakeholder engagement efforts.

What has been an effective way that you engaged with USP and/or another organization?

- Engaging one-on-one with the USP Documentary Standards Scientist (DSS, formerly Scientific Liaison) has been highly effective. A Centralized approach will need to ensure the same level of engagement and response.
- Virtual conference tables and small focus groups have worked well.
- Identifying clear action items before the end of each meeting is very important.
- In-person stakeholder meetings allow for more direct engagement, but virtual/hybrid meetings allow broader engagement. Any meeting needs to work at enhancing the experience

What are your goals of engagement, and what does success look like for you?

- Summary: Exchanging information, moving science forward, learning from other experts, engaging regulators, and having transparency throughout the process.
- Having accountability and knowing that something is being done about a problem.
- Timeliness with prompt follow-up, even if the plan did not work out as expected.

- Maintaining ongoing, open communication from all sides. Recognizing that there are different perspectives, it is essential that stakeholders feel heard regardless of the outcome.
- Completing the task, such as developing a monograph and making it available.

Updates from USP

USP–NF Online: A new integrated platform that includes both *USP–NF Online* and *Pharmacopeial Forum* will launch soon; this platform will be more efficient and easier to use. USP has streamlined and enhanced navigation and functionality throughout *USP–NF.* DOIs will be added for monographs and general chapters, making these documents easier to find and cite. A new and improved version of the USAN Dictionary has just launched as well.

Public Commenting: USP's first-ever Public Comment Form is in development, and USP recently held a successful Public Commenting Open Forum. In addition, USP will soon provide a single combined email address to reach all DSSs (formerly Scientific Liaisons). Users will not need to identify and contact the individual DSS who would handle their inquiry.

Prioritization of Standards

Overview: USP is proud of our standards-setting accomplishments, with a total of 9,000 USP standards developed so far in support of our public health mission. However, many challenges are involved in creating public standards with multiple stakeholders across various health care sectors. The global landscape is becoming more complex over time, partly because quality paradigm shifts directly impact standards.

Some of these quality-related concepts and issues include advanced manufacturing, integrated risk-based approaches, and quality by design. Despite the challenges, USP standards have impacted 2 billion people worldwide, thereby helping to empower a healthier tomorrow. However, standards must evolve to respond to public health needs and keep pace with technology in the Industry.

Transition to a new approach: USP is changing its approach to standards development to improve efficiency. In our old way of working, each scientist in Small Molecules was responsible for a portfolio of monographs and had to decide which standard to work on out of their portfolio. This system had limitations; it was difficult to ensure that all donations got processed promptly and consistently. Another problem was that each scientist had to be proficient at every step in many processes, which meant re-learning steps they had not done recently. A time-critical request might mean that the scientist had to suddenly drop all their other work.

In response to these problems, the Small Molecules group is eliminating portfolios for the scientists and switching to a centralized distribution of work. This way, the scientists can focus more effectively on standards with the greatest impact and most important outcomes. The work will now be assigned based on four factors: case prioritization, case requirements, staff capacity, and staff capability. As always, collaboration with USP's stakeholders is critical, and it drives standard development.

Selecting the standards that should be at the top of the list is not simple, and we are constantly learning and evolving. Overall, these are changes to the way USP staff works internally, but the basics of developing monographs have not changed. With the new approach, we can be more efficient and have a greater positive impact on public health.

However, it is important to note that the priorities of one specific manufacturer may be different from the cross-cutting needs that USP is addressing. FDA and other regulators also have priorities that should be considered. Overall, the global landscape for monograph development is becoming more complex. In response, USP will continue to evolve and adapt and will consider all stakeholder concerns and feedback.

Donations Program: Donations are critical to USP's enduring mission because everyone deserves quality medicines. USP needs contributions to draft monographs, bulk materials, and supporting data so we can develop new monographs and revise existing ones. We also welcome proposals for monograph revisions. The benefits of making a donation include contributing to a large community of health and science experts, reducing adulterated and substandard ingredients and products, and maintaining regulatory compliance.

The Donations Program is not new, but we are continually trying to improve the process; it's an evolutionary journey. Our Donor Submission Portal is being enhanced with greater visibility into the real-time status of donations. We will resume face-to-face engagement and recognition as soon as possible. We want to show you how much we appreciate your donations. If you have any questions, please contact us at donations@usp.org.

Feedback from industry speakers: In this session, two speakers shared their feedback and perspectives on USP's process for prioritization of standards for development. They described their experiences interacting with USP while they were working as consultants to companies (sponsors) developing monographs. The consultants said that in some cases, USP was slow in responding or did not respond to their inquiries. Staffing changes led to hand-offs of proposed standards between USP staff members. There were delays in moving a potential monograph forward and understanding the priority of the monographs. A panel discussion followed. USP noted that they were transitioning to the new prioritization approach that is more transparent regarding prioritization. Also, USP must prioritize monographs with the most impact on public health, namely the monographs that will be most needed. The presenter noted that it would have been helpful to know that USP's prioritization system was changing at that time. Greater transparency could have helped the consultant understand the delays and consider changing course if needed. To access the most recent priority list of the Small Molecules monograph, please click here.
An industry attendee asked if USP is interested in learning more about the drivers that lead Industry to make donations for monograph development; USP is very interested in learning more about these drivers.

Industry also noted that in some cases, USP did not tell sponsors/consultants when a monograph submission would be reviewed, which was problematic. If the monograph is not a high enough priority, Industry may decide to utilize a different strategy; therefore, it is very important that USP and Industry communicate about the priority level for the specific monograph early in the process. Industry noted that there are specific reasons for wanting the monograph developed and that it would be important for USP to understand the public health

need. USP is hoping to have a dialogue to enhance their understanding as to the public health need across Industry and regulators.

"Ask Me Anything" Sessions – A Post Day One Event

In these innovative sessions, stakeholders had the opportunity to ask questions of USP subject matter experts. Two sessions were offered, and both generated interest:
1. Guidance on Aspects of Method Validation for Companies
2. Nitrosamines – Knowledge Sharing

DAY 2

Requested Cases for Monograph Modernization
In this session, USP scientists and Industry presented examples of USP general chapters that needed modernization and showed attendees how this was accomplished. Modernization typically involves replacing subjective, outdated, and/or inaccurate tests with reliable, objective, modern methods. One type of subjective test is the organoleptic test, which relies on sensory perception such as vision or smell. These methods are typically unreliable, and their use may also exclude laboratory personnel with visual impairment or reduced sense of smell.

When general chapters such as <191> *Identification Tests – General* are modernized, the improvements affect the monographs that reference the chapters. Public comments and stakeholder feedback play a key role if changes are proposed for general chapters that impact monographs. USP encourages stakeholders to submit requests for revision of USP standards as appropriate. USP continues to identify and pursue opportunities to incorporate modern, updated methods in our standards. Test results should always be accurate and precise, so the modernization process is very beneficial for all stakeholders.

USP's Quality Commitment
USP has a strong, ongoing commitment to quality that encompasses the USP Verification Program, the Promoting the Quality of Medicines Plus (PQM+) Program, our Reference Standards, and our compendia, namely *USP–NF, Food Chemicals Codex, Compounding Compendium,* and *Dietary Supplements Compendium*.

USP has a quality culture – we do everything with quality in mind. This is a leadership commitment. With this approach, we seek diverse viewpoints and act upon them. We have robust independent standards and also strong relationships with our stakeholders. Each staff person has a mission to uphold quality; as an organization, we value having a passion for quality.

USP has a Quality Manual, which is a comprehensive overview document, and we have quality objectives on both the individual and enterprise levels. Our quality management system is certified to ISO 9001 and ISO 17025, and it reflects a systems-based approach. USP also has a CAPA program, and we are moving forward into a digital transformation.

USP Errata Process

The term "errata" refers to "an accelerated revision vehicle used to correct published content in a USP compendium that does not accurately reflect the intended requirements of a standard as approved by the responsible Expert Committee." The errata process is used to correct errors or provide clarifications or missing information, and most errata are minor changes that do not have a broad impact. Information on the exact number and type of errata published since 2018 was shared.

Errors that could have a broad impact are corrected by another revision process on a case-by-case basis. When changes to chemical information are needed (name, structure, or molecular weight), they will no longer be addressed via errata as of July 2022. Instead, chemical information will be updated using Compendial Notices.

Introduction to the New General Chapter <1220>, *Analytical Procedure Life Cycle*

General Chapter <1220> Analytical Procedure Life Cycle was described in this session, followed by a Panel Discussion. The concept of analytical procedure life cycle can be understood as a framework for analytical procedures that holistically incorporates all the events taking place over the procedure life cycle that show that the procedure is fit for the intended purpose. This concept is related to Analytical Quality by Design, which emphasizes sound scientific approaches and quality risk management.

This chapter is not mandatory but provides an alternative approach for selecting methods that are fit for the purpose. GC <1220> also discusses the analytical target profile and method operable design region. In the Panel Discussion, an attendee noted that most legacy products have been validated for GC <1225> *Validation of Compendial Procedures*, and they asked if FDA will expect validation per GC <1220>. A panelist from FDA responded that people could use either approach and do not have to revalidate according to GC <1220>.

CEO Conversations — A Fireside Chat with Dr. Ron Piervincenzi

In this session, USP's Chief Executive Officer answered questions submitted by Industry.

- Could you speak to USP's engagement with regulators such as the FDA?
  - Engaging with regulators is extremely important, and USP stays connected with regulatory bodies worldwide. USP standards are used in more than 140 countries to ensure the quality of medicines being sent to the U.S. and those being used locally. FDA is one of our most important stakeholders; USP has many ongoing interactions with FDA, including our quarterly meetings.

- Some long-time stakeholders may be concerned that USP is reaching out more broadly. Will USP have less time or attention for the long-standing stakeholders?
  - To ensure quality medicines, USP must address the needs of all stakeholders, and going broader doesn't mean that there is less input from our long-standing stakeholders. When it's done right, we can add new voices effectively. Our long-time stakeholders will continue to receive close attention, even as new stakeholders are brought into the fold. It may even help our long-time stakeholders expand their voices and communicate their needs.

- Can you provide some information about USP's expansion, such as the addition of Pharmatech?
  - Pharmatech is a small part of our work/organization, but we are learning a lot by working directly with these colleagues. This has helped us better understand the challenges industry faces. This work is about capability building and advocacy. Most of the world doesn't know how to use the new advanced manufacturing technologies, but at USP, we have a continuous improvement mindset, and we are learning directly. It's not standard-setting work, but it is necessary.

- What do you mean by USP's "expansion"?
  - Actually, it's not an expansion, and I don't think in that term; I think of USP evolving. Over 90% of the standards we have ever created are still in the compendium today. We're still taking care of our monographs to date. Our single biggest effort was our Up-to-Date initiative – a huge undertaking in our prior 2015 to 2020 cycle. Now we're starting to do new work again. It's so much better to start early with a new standard, which can be revised later.

- As you see the disruptors, how are you aligning staff and resources to keep your basic essential work going?
  - We set our 5-year plan and annual priorities. So much of our work is keeping up with our essential, base work. We are also focusing on new analytical processes and complex generics, two challenging new areas.

- What is USP's biggest challenge?
  - There is a whole new level of complexity; new analytical technologies are being utilized more. We are hiring scientists and dedicated teams for this important work. In parallel, we are exploring how best to partner with stakeholders to get the work done effectively; there are many promising collaboration opportunities.
  - As always, no USP standards are created by USP alone, and our standard-setting process seeks input from many sources, including industry stakeholders and the public. The inclusion of these different voices makes USP standards stronger and more effective at protecting public health.

USP appreciates the time and interest of all attendees at the PNP Stakeholder Forum. Additional feedback from stakeholders is always welcome. Send your questions and comments to Jacqueline Starkes at jws@usp.org.