Importance of Up-To-Date USP Standards

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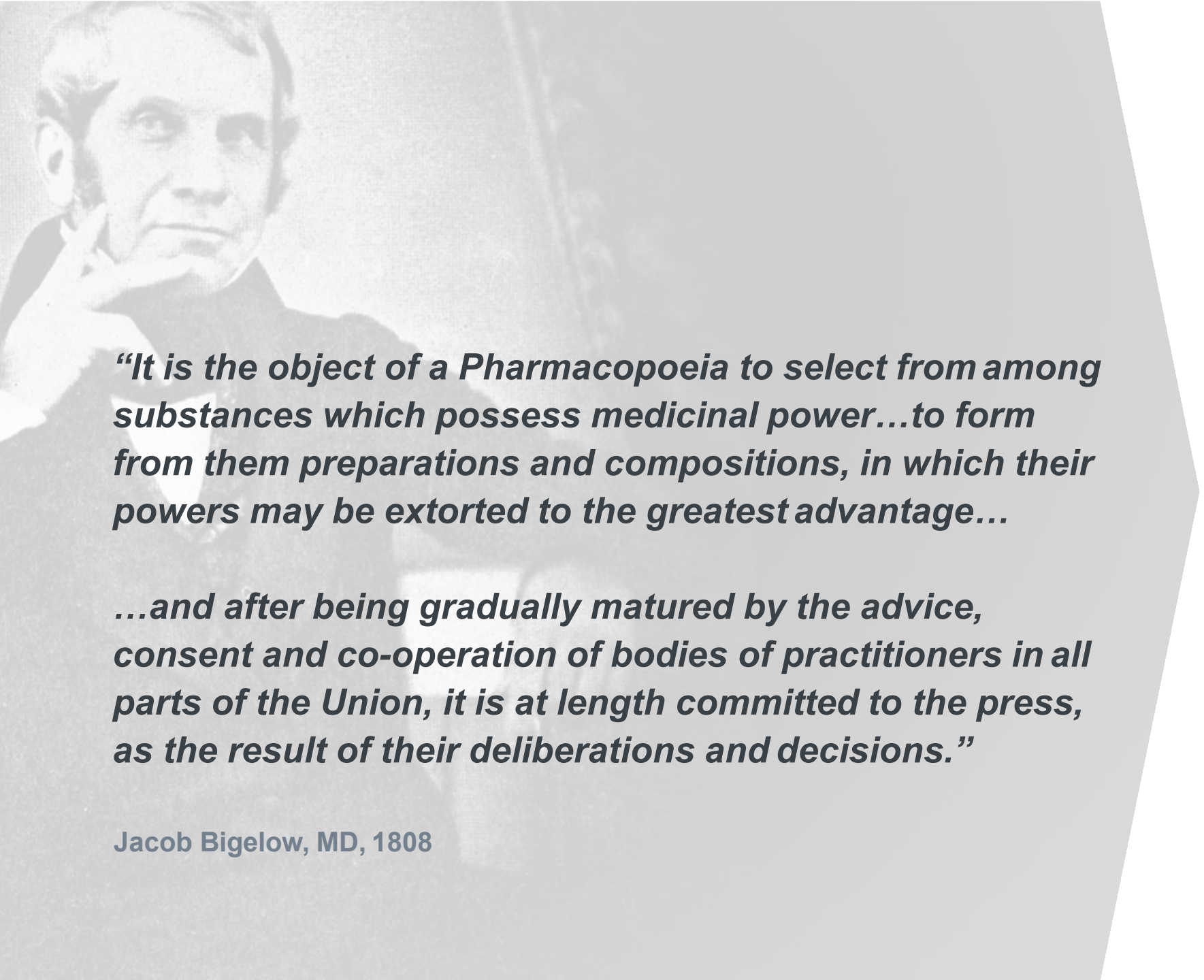
Overview

- USP mission and people
- Ensuring access to quality medicines
  - Looking back: How USP committed to update our standards (monograph modernizations)
  - What we have learned
  - Looking ahead: Partnering to ensure access to quality medicines

USP mission and people



"It is the object of a Pharmacopoeia to select from among substances which possess medicinal power…to form from them preparations and compositions, in which their powers may be extorted to the greatest advantage…

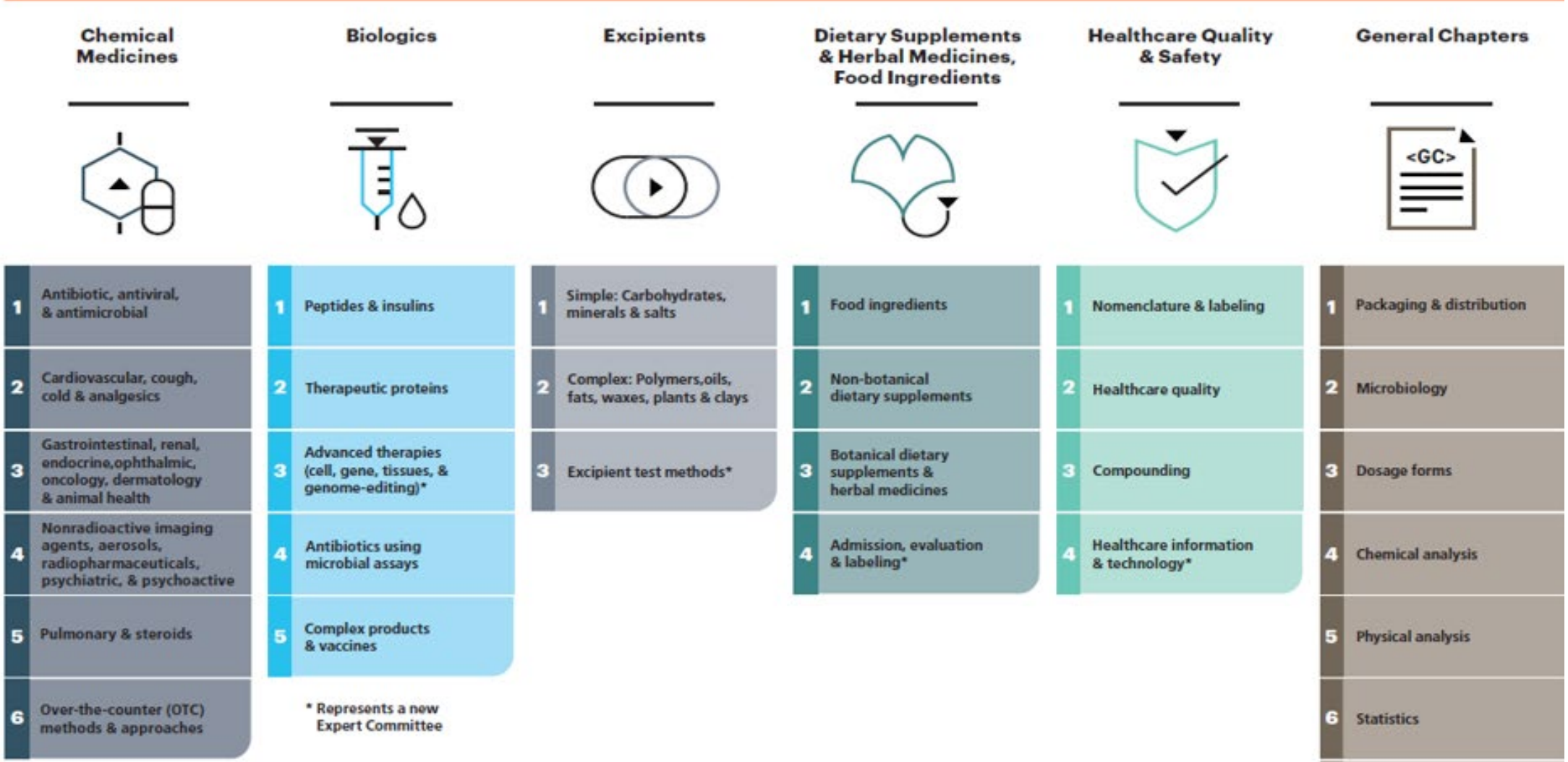
…and after being gradually matured by the advice, consent and co-operation of bodies of practitioners in all parts of the Union, it is at length committed to the press, as the result of their deliberations and decisions."

Jacob Bigelow, MD, 1808

Our enduring mission

To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.

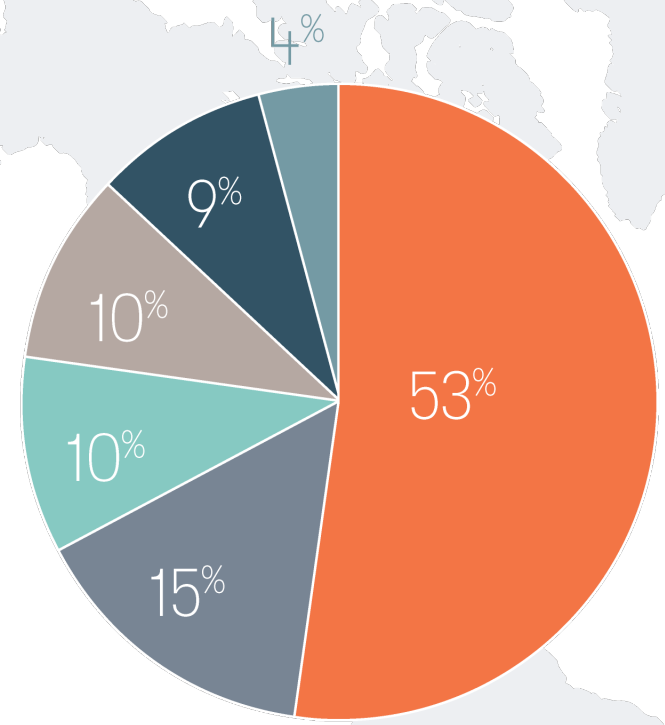
The breadth of USP's work can be seen through the scope of our expert committees



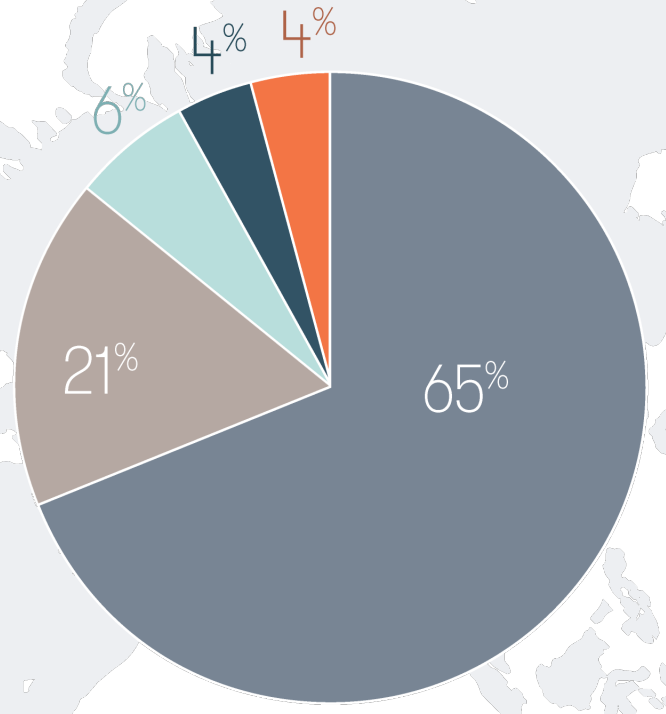
2020-2025 Council of Experts-Expert Committees

Our staff is located where medicines are made

1200+ Staff



- Laboratory/Science
- Development, Mrkt & Program Ops
- Administration
- Global Public Health
- External Affairs
- Global Information Services

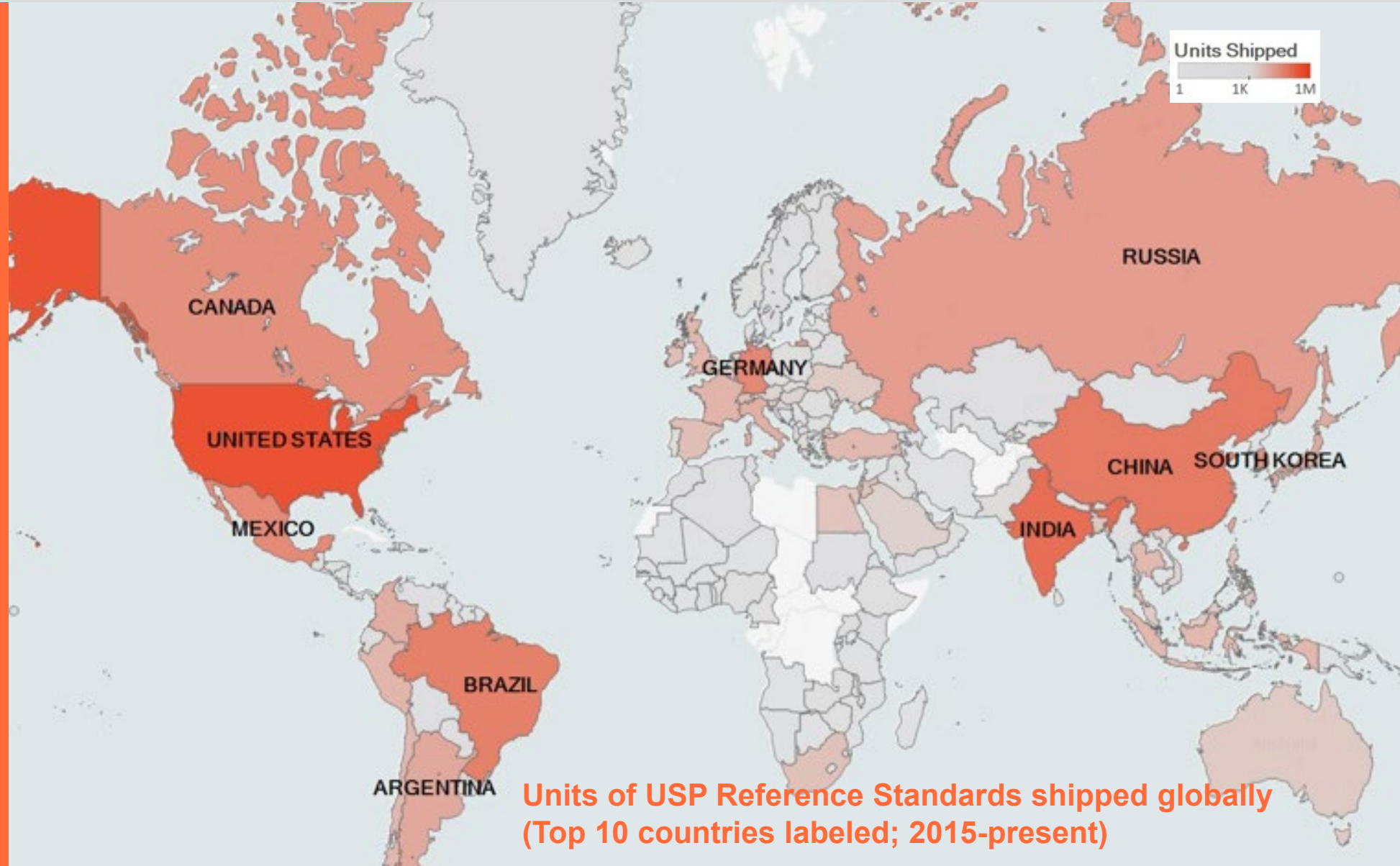


- United States
- Brazil
- India
- Other global sites: Ethiopia, Europe, Ghana, Indonesia, Nigeria, Singapore
- China

Standards usage drives our global staff presence

~80% of medicine API manufacturers are located outside the United States[1]

USP Standards were shipped to over 22,000 manufacturers in FY19



Units of USP Reference Standards shipped globally (Top 10 countries labeled; 2015-present)

[1] FDA https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance

2 Looking back: How USP committed to update our standards (monograph modernizations)

Responding to the needs of our stakeholders

- Meetings in 2014 with stakeholders, including industry and the FDA, emphasized importance of USP standards keeping Up-To-Date
- We asked:
  - Have we established standards for the most important products?
  - Are our 4,700 standards current, relevant, and suitable for intended use?

Our public facing commitment in 2015 for “monograph modernization”

Why invest in Up-To-Date standards?

- To facilitate common quality targets across manufacturers
- To eliminate outdated techniques
- To provide a foundation for innovation by leveraging new standards
- To ensure identification and removal of complex chemicals, including impurities, from processes

2015-2020 Resolution II:

“USP Monograph Modernization”

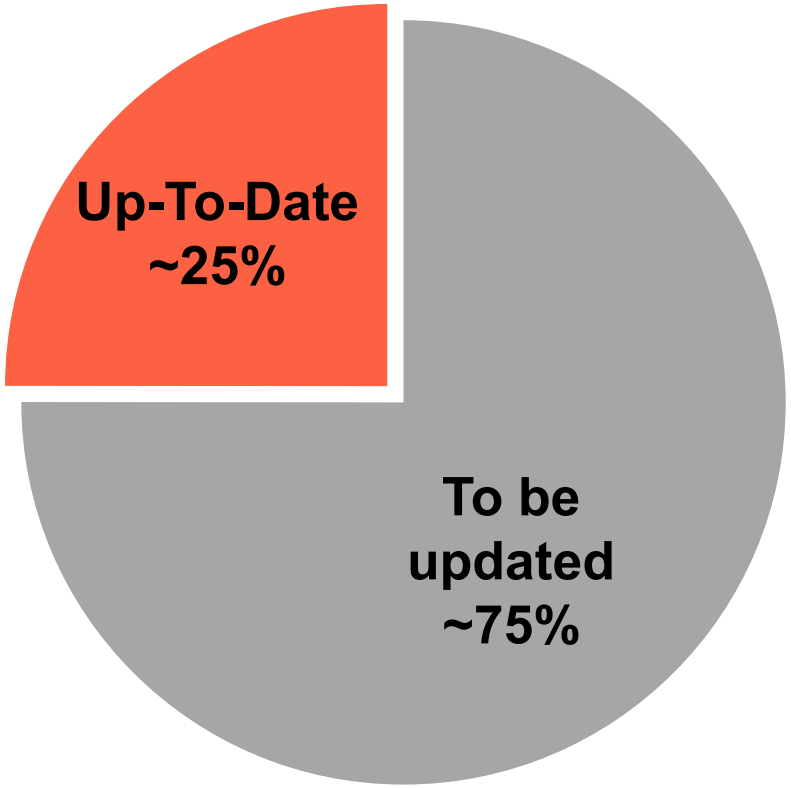
USP will meet the needs of U.S. Food and Drug Administration (FDA), industry, and other stakeholders for modern monographs within *USP–NF*. (Now referred to as Up-To-Date)

3

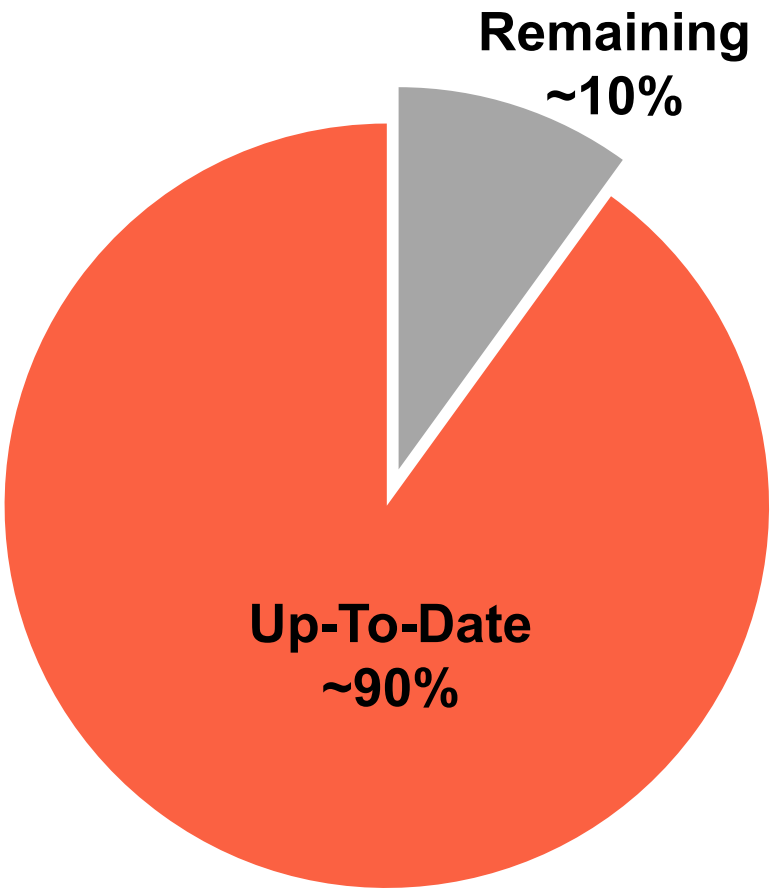
What we have learned from Up-To-Date

Our progress since 2015 – Status of USP's 4,700 Monographs

2015



June 2020 (est)



Up-To-Date challenges

To ensure the quality of medicines, we are committed to Up-To-Date standards … but we still face challenges

Partner resources/priority challenges

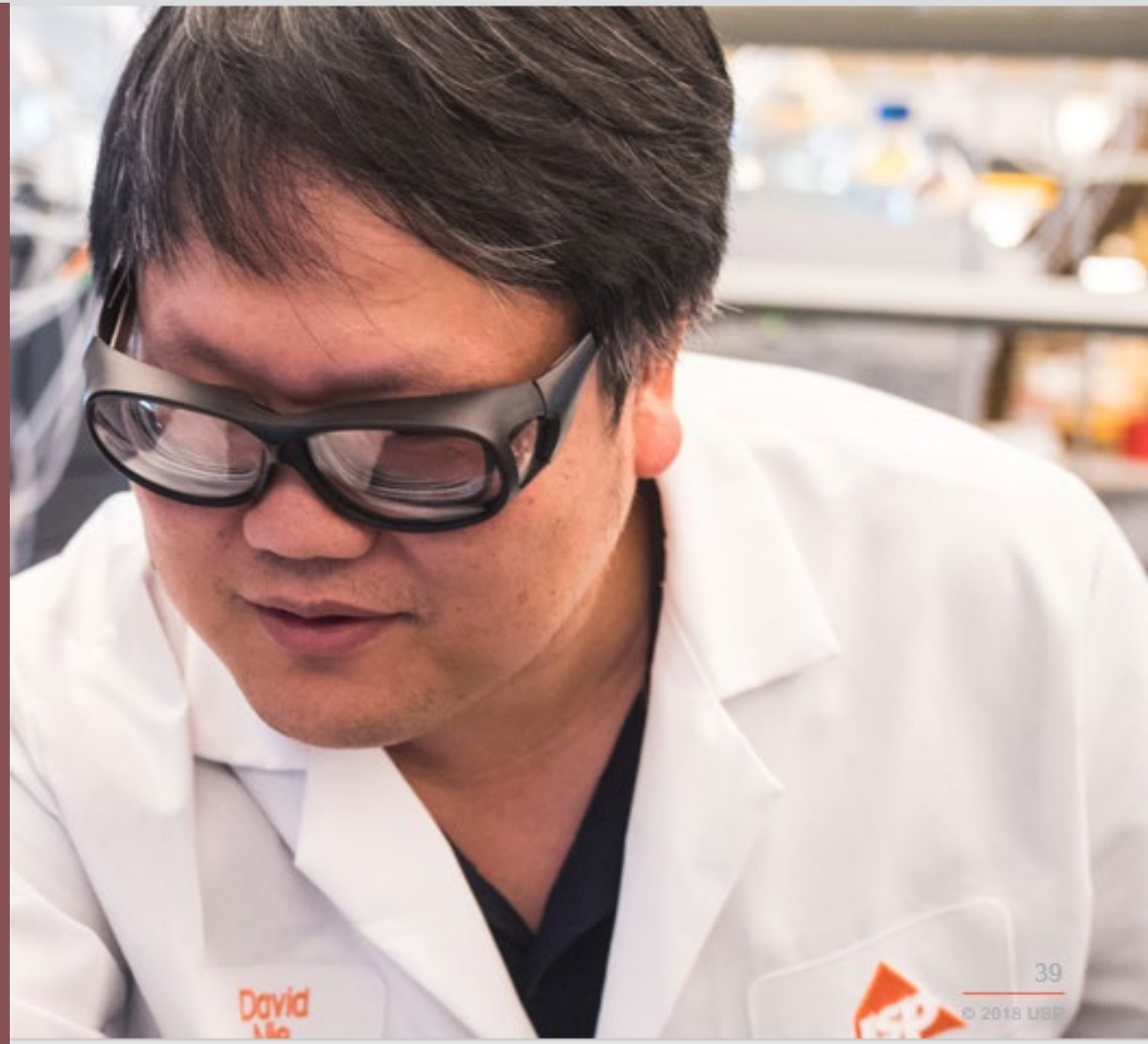
Information sharing

Monograph donations

1. Partner resources/priority challenges

- **Pace of innovation** is faster than ever through new molecules, dosage forms, combination products, and drive to digital
- **Changes in pharmaceutical market** drive need for efficiencies while challenging traditional approaches to ensuring quality
- **Growth and complexity of the global supply chain** require renewed shared vigilance to ensure medicine quality

We believe these are shared challenges (industry, regulators, USP)



New USP tools to help adapt to the pace of change

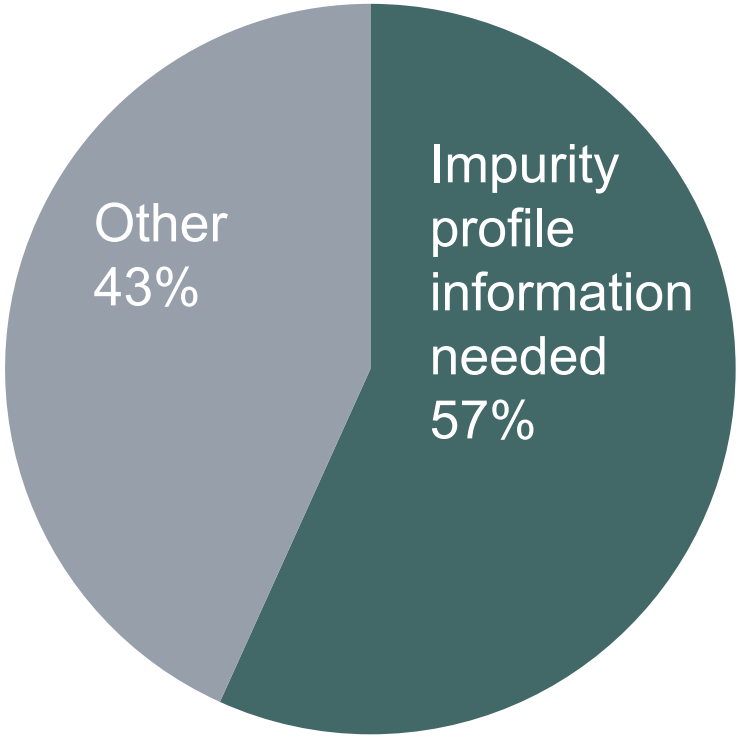
- USP must keep pace with industry change
- Examples of new tools we are deploying to increase our stakeholders' USP-related work efficiency
  - **Digital USP-NF**
  - **Impurities for Development**
  - **New Pending Monograph Process** (Scientific Expo, booth #16, Tues Nov 5, 3:30-5:30pm)
  - **Education and training programs**
  - **Excipient and API verification** (Scientific Expo, booth #13, Tues Nov 5, 3:30-5:30pm)

Digital USP-NF with personalized dashboard, real-time search and filter, personalized bookmarks, and ability to sign up for specific document notifications with over 1.5 million monthly page views

2. Information sharing challenges

- Regulations governing confidential commercial information limit ability of regulators and USP to exchange critical information
- Over half of all cancelled or deferred USP monographs are due to inconsistencies with FDA approved drug application impurity profile
- Current processes are inefficient, labor intensive, and time-consuming for all

Reason for cumulative deferrals of a monograph (USP 41 1S)



n = 148

Information sharing challenges can impact public health

- Good public quality standards cannot be created without critical quality attributes
- Absence of core quality attributes, like impurity limits, compromise critical supply chain protections

We are working to clearly communicate the most necessary attributes of our quality standards…

Sample USP drug monograph; organic impurity profile

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ciprofloxacin ethylenediamine analog	0.68	0.5
Ciprofloxacin	1.0	—
7-Chloro-6-piperazinyl analog[a]	1.2	0.3
Chlorociprofloxacin[b]	2.0	0.3
Any individual unspecified impurity	—	0.2
Total impurities	—	1.0

[a] 7-Chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

[b] 6-Chloro-1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

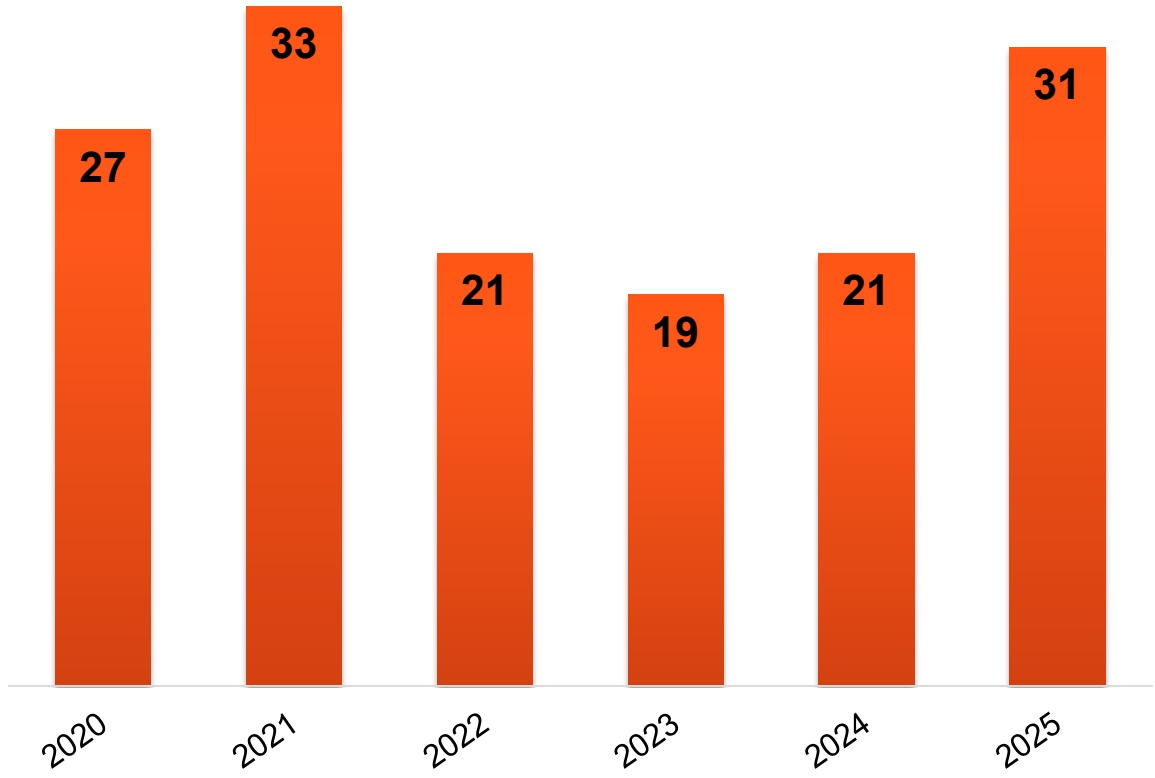
Impurity name

Critically needed information

…in turn, our industry partners can more readily provide to USP impurity specifications from the most recent FDA approved application.

3. Mismatch between capacity of industry to provide methods and materials and the number of public standards needed

- Donation of materials and methods by manufacturers enables volunteer experts to partner with USP staff in creating a public quality standard
- Current need for over 400 standards for off-patent, off-exclusivity medicines that are critical to public health
- At least another 150 medicines are anticipated to be multisource by 2025



Number of medicines with anticipated loss of exclusivity by year

A proposed solution

USP tools to increase industry capacity to donate methods and materials:

- Having a single point of contact
- Temporarily embedding USP scientists to work with your team to facilitate document procurement
- Providing custom lists of public standard needs mapped to your portfolio of ANDAs
- Supplying compendial resources, including documents, spreadsheets, and databases

Ways in which industry can help deliver high priority public standards of greatest patient need:

- Submit your current analytical procedure and supporting validation data
- Provide methods for a new or revised documentary standard
- Provide bulk material to be evaluated as candidates for USP Reference Standards

4 Looking ahead: Partnering to ensure access to quality medicines

Partnerships through our shared challenges

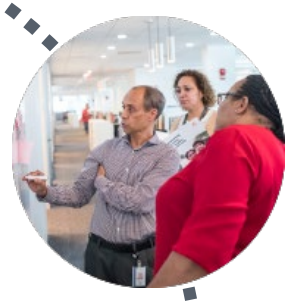
Partnering with our expert volunteers

USP's public quality standards, developed by volunteer experts, including government liaisons, enable transparent processes that ensure quality methods, APIs, and education

Partnering with industry

Manufacturers must be able to bring quality pharmaceuticals to market and depend on quality-assured methods, materials, and resources to reduce risk to market entry

Access to quality medicines

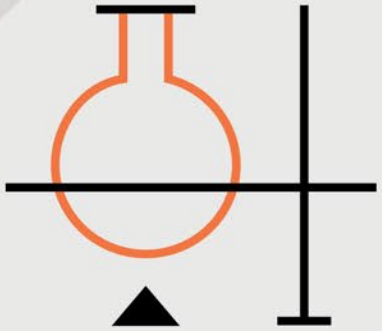


Partnering with regulators, including the FDA

Regulators must be able to ensure pharmaceuticals are approved for market regardless of technology used. They depend on a quality-assured scientific basis for decision-making in regulatory review, manufacturing practices, and enforcement

Do USP's public quality standards help manufacturers bring quality medicines to market?

Our 2018 perception survey findings reaffirm our important mission to develop public quality standards that support critical access to quality medicines



Average time for formulation reduced by

26%

Method development time reduced by

31%

Validation time reduced by

29%

Total product development time reduced by

19%

The study's margin of error was >5% at 95% confidence interval, n=92

Source: *J Pharm Sci* "Commentary on the Benefits of US Pharmacopeial Standards: A Generic Pharmaceutical Industry Survey"

n = 92 respondents from at least 44 generic pharmaceutical manufacturers

USP/FDA collaboration on pending monograph process

- The new Pending Monograph Process (PMP) is used to revise existing, or create new, USP-NF monographs to accommodate products under review by FDA
- Provides an efficient mechanism for industry, FDA, and USP alignment in the drug approval and monograph development processes
- Program was designed in close collaboration between USP and FDA, and based on feedback from industry
- USP and FDA co-hosting a booth on this program-please stop by for more information

How can we work together to build trust in medicine quality?

- Collaborate to create public quality standards
  - Industry donations of materials and methods as candidates for public standards
  - New program in response to global medicine supply challenges: USP will provide USP-NF Online access free-of-charge to manufacturers not currently subscribed
- Dialogue to exchange learnings
  - How can we help you build capabilities or efficiencies?
  - What efficiencies can we continue to build into our processes?
- Bring collaborative expertise to bear
  - Delivery of USP-Education courses to industry
  - Become a USP volunteer expert

Call for Candidates

2020–2025

Central to USP's achievements are the contributions of countless professionals, who volunteer their time and knowledge in USP's Council of Experts and Expert Committees and Panels.

Our Call for Candidates is now open.

Join other motivated colleagues to help us set the standards that make it possible for 2 billion people around the world to have access to quality medicines, foods and dietary supplements.

Contact us at USPVolunteers@usp.org

Stay Connected

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Empowering a healthy tomorrow