Report of the Chair of the Council of Experts

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USP AND YOU
Shoulder to Shoulder on the Path to Improve Global Health

2010–2015 and Beyond

- Outstanding Scientific Achievements
  - 2015 Convention Meeting Science Pavilion
  - A Forum for Dialogue
- Impact on Global Public Health
- Our Future Direction

2010–2015 By the Numbers

USP–NF

- 434 new and 1,180 revised monographs
- 92 new and 142 revised general chapters

Food Chemicals Codex

- 135 new and 191 revised monographs
- 10 new and 22 revised general tests and assays

Medicines Compendium and *Herbal Medicines Compendium*

- 351 new monographs
- 2 new general chapters

2010–2015 By the Numbers

Reference Standards

- 560 First time Reference Standards
- 1,626 Replacement Reference Standards

Released the
USP Compounding Compendium

Expanded the
Dietary Supplements Compendium

USP & You: By the Numbers

- Expert Volunteers
  - 1,000+ experts serving on 26 Expert Committees, 72 Expert Panels, and 1 Advisory Group
  - From the United States and 48 other countries
- Collaborators and Stakeholders
  - Government (U.S. FDA and others)
  - Industry
  - Academia
  - Convention Members and Observer Organizations
- 900+ USP Staff in U.S., India, China, Brazil, Switzerland, Ghana, Ethiopia, Nigeria, and Indonesia

Select Examples of USP's Mission Impact Since 2010

- Eradicating Toxic Impurities in OTC Products
- Addressing Heparin Adulteration
- Pharmaceutical Excipient Quality
- Addressing Adulterated Dietary Supplements
- Addressing Adulterated Milk Powder
- Test for Elemental Impurities in Drug Products
- Prescription Container Labels

Eradicating Toxic Impurities in OTC Products

Context

- Acetaminophen impurities: 4-Aminophenol identified as a nephrotoxin in products containing acetaminophen
- Contaminated cough syrup: Dextromethorphan containing the toxic impurity levomethorphan causes deaths

Negative Public Health Impact

CBS/AP, November 26, 2012

At least 13 dead in Pakistan from toxic cough syrup

Drug Alert No. 129, January 2013

Contaminated Dextromethorphan active pharmaceutical ingredient

Opportunity for USP Impact

- Develop standards and methods for monitoring 4-Aminophenol in acetaminophen-containing products
- Develop method for analysis of levomethorphan in dextromethorphan

Eradicating Toxic Impurities in OTC Products

USP Relevance and Contributions

- USP Expert Panel worked with U.S. FDA and industry to evaluate procedures and establish criteria that are acceptable to stakeholders, developing a new General Chapter <227> *4-Aminophenol in Acetaminophen-Containing Drug Products* and revising the necessary monographs
- USP helped ensure the safety of products containing dextromethorphan by developing an HPLC method for monitoring the toxic impurity levomethorphan at 0.1% level

Public Health Impact

- Stronger standards help ensure quality products in the future
- Public confidence in OTC products improved

Addressing Heparin Adulteration

Context

- 2007 FDA Public Health Advisory following reports of adverse events in pediatric dialysis patients
- Followed by similar reports in 2008–2009 and recall of commercial lots of heparin
- Relevant, up-to-date public standards to detect adulteration of heparin products needed but not available

Negative Public Health Impact

- 94 deaths and several hundred reports of adverse events linked to contamination of heparin drug products

Opportunity for USP Impact

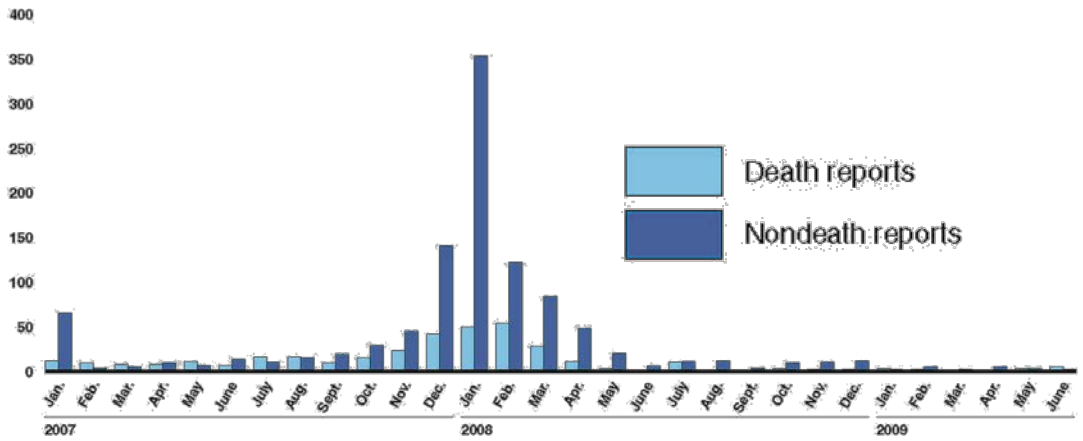
- Test methods needed capable of identifying heparin components and discriminating from adulterants

Addressing Heparin Adulteration

USP Relevance and Contributions

- Introduction of additional methods for identification to include a proton NMR method, with associated Reference Standard
- Development of additional methods for identification and additional References Standards
- The sensitivity of the proton NMR method to OSCS was improved

Public Health Impact
Dramatic reduction in number of reports of adverse events after introduction of standard



Pharmaceutical Excipient Quality

Context

- Expanding global excipient supply chain
- Increased risk of intentional adulteration, substitution, and contamination
- Shortcomings in testing and supply chain controls could be exploited

Negative Public Health Impact


msnbc

Tainted cough syrup kills 21 in Panama

CDC investigation traces mysterious deaths to industrial chemical

Associated Press

updated 5:51 p.m. PT, Fri., Oct. 13, 2006

Most popular


The New York Times

November 26, 2008

WORLD BRIEFING | AFRICA

Nigeria: Contaminated Medicine Blamed for Deaths

By NYT

Opportunity for USP Impact

- Improving specificity of *USP–NF* monograph identification and assay test
- Strengthening acceptance criteria

Pharmaceutical Excipient Quality

USP Relevance and Contributions

- With FDA and Stakeholders, modernized 62 identification tests, 30 assays, and 11 impurity tests
- Developed a general chapter on good distribution practices

Public Health Impact

- Significantly improved testing controls and tools available to qualify an excipient for intended use
- Reduces risk of adulteration and contamination

Addressing Adulterated Dietary Supplements

Context

- Widely used by more than 50% Americans
- More than 50% of GMP inspections lead to warning letters
- Compendial methods that do not detect non-targeted adulterants can be exploited
- Compliance with USP standards only required for products labeled USP

Negative Public Health Impact

- Serious risk to public health when adulterated supplements expose consumers to drugs and drug analogs

Opportunity for USP Impact

- New guidance and analytical tools for the industry and regulators were needed to detect adulteration and to help ensure supply chain integrity

Addressing Adulterated Dietary Supplements

USP Relevance and Contributions

- USP adulteration workshop served as a forum for industry, regulators, and academia to develop solutions
- General Chapter *<2251> Adulteration of Dietary Supplements with Drugs and Drug Analogs*: USP's Expert Panel proposed analytical tools to detect adulteration
- A new USP Dietary Supplement Adulteration Database is in development to detect signals of concern and to prioritize standards development

Public Health Impact

- Ongoing modernization of USP standards to help meet GMP requirements for scientifically valid analytical methods will help reduce risk of serious health issues

Addressing Adulterated Milk Powder

Context

- Adulterated milk powder contained toxic substance in place of essential protein
- Method for protein determination could not differentiate between melamine and protein
- If and when food adulteration occurs, food safety is in the hands of criminals

Negative Public Health Impact

- In 2008, economically-motivated adulteration of milk powder with melamine kills six infants and hospitalizes more than 50,000 babies
- In 2007, adulterated pet foods kills more than 2,000 and harms more than 39,000 pets

Opportunity for USP Impact

- Better methods for protein determination were needed, along with tools to better identify other problem areas

Addressing Adulterated Milk Powder

USP Relevance and Contributions

- USP's Expert Panel and Advisory Group are working with more than 15 organizations (regulators and industry) to help solve the issue
- To date, the Expert Panel and the Advisory Group have produced:
  - The Food Fraud Database
  - Food Fraud Mitigation Tool
  - 7 peer-reviewed scientific manuscripts (more to come)
  - 3 new appendices (more to come)
  - Several reference materials
- Developed better methods to detect the substitution of high-nitrogen materials for protein

Public Health Impact

- Increased consumer confidence in food products
- Stronger standards help ensure food safety in the future

Test for Elemental Impurities in Drug Products

Context

- Contamination with toxic metals controlled in USP using 19th century method
- Heavy metals are not typically present but there is a possibility of contamination with significant negative consequences
- Not all toxic metals are detected, false positives or negatives possible

Negative Public Health Impact

- Potential adverse health effects from contaminated products

Opportunity for USP Impact

- Need for rapid cost-effective screening systems capable of detecting contaminating metals in healthcare products

Test for Elemental Impurities in Drug Products

USP Relevance and Contributions

- USP created a standard to assist with the control of metal contamination from both toxicological and technological perspectives
- Extensive collaboration between USP, regulators (U.S., EU, and Japan), industry stakeholders, and other Pharmacopoeias
- ICH developed the ICH Q3D guidance that follows the USP approach for the testing
- Harmonized approach and implementation timing

Public Health Impact

- Consumers assured of safe medicines
- Stronger standards help ensure quality products in the future

Prescription Container Labels

Context

- In 2008, the Institute of Medicine identified that patient labeling on the amber vials that pharmacists use was a critical root cause of patient misunderstanding
- Non-adherence and medication errors can occur

Negative Public Health Impact

- Medication errors leading to adverse health events

Opportunity for USP Impact

- Lack of universal standards for labeling

Prescription Container Labels

USP Relevance and Contributions

- USP Expert Panel of pharmacists, health literacy experts, and the pharmaceutical industry developed a standard for a patient-centered prescription vial label
- General Chapter <17> *Prescription Container Labeling*
- Supported by USP Convention members, practitioner and patient organizations, as well as NABP (adopted by three state boards of pharmacy to date)

Public Health Impact

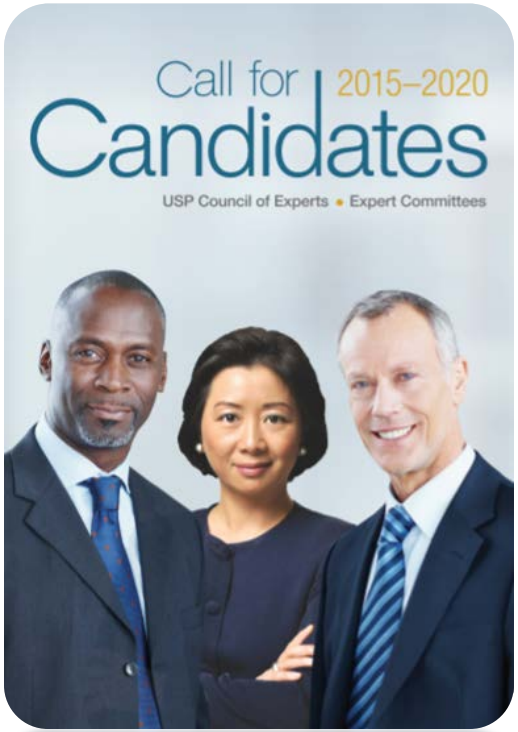
- In 2015, ~1 of 5 Americans are receiving prescriptions in states that cite General Chapter <17> and require patient-centered prescription labels
- Patients have the best opportunity to understand how to safely and appropriately use their medications

Potential High Impact Standards-Setting Topics in 2015–2020

- Recombinant therapeutics and monoclonal antibodies
- Address quality of botanical dietary ingredients
- Be part of *USP–NF* Up to Date
- Help harmonize excipient monographs
- Detect and prevent food fraud
- Modern dosage forms: Nanoparticles, Nanoemulsions
- Revise general chapters for compounding

2015–2020 Future Directions

- How will we impact quality standards together?
- Your collaboration is critical:



  - Today at the 2015 Convention Meeting special luncheon
  - As expert volunteers on the 2015–2020 Council of Experts
  - Convention Membership Fora: Listening Tours, visits to your organization, partnership meetings, and more
  - USP & You: Shoulder to Shoulder, Together, We Will Improve Global Health

2015–2020 Future Directions