

2006 USP Annual Scientific Meeting
"Impact the Future of Pharmacopeial Standards"

Marriott Denver City Center
September 26–29, 2006

USP Working for You Track

SUMMARY

Track Managers:

- Karen Russo, Ph.D., Director, Small Molecules and Monograph Acquisition, USP
- Beryl Voigt, Director, Executive Secretariat, VOA, USP

Planning Committee:

- Karen Russo, Ph.D., Director, Small Molecules and Monograph Acquisition, USP
- Beryl Voigt, Director, Executive Secretariat, VOA, USP

Overall Track Description

This track provides three main informational sessions on USP: 1) USP Overview and Standards Development Process, 2) USP Education, Verification, and International Sites (repeated), and 3) USP Future Directions and Hot Topics (repeated). The USP Overview and Standards Development Process session provides basic information for the beginner about USP including, history, governance, and compendial processes and requirements. The USP Education, Verification, and International Sites session offers the opportunity to learn about new directions in these three emerging areas for USP. The USP Future Directions and Hot Topics session enables USP to brief our industry colleagues about new and emerging compendial topics. All sessions use a lecture-style format with time allotted for discussion among USP staff, speakers, and attendees.

Session I: Wednesday, September 27, 2006, 1:00–3:00 p.m.

Title: USP Overview and the Standards Development Process

Speakers:

- Angela G. Long, Vice President, Volunteer and Organizational Affairs
- Karen A. Russo, Ph.D., Director, Small Molecules and Monograph Acquisition
- Susan J. Schniepp, Quality Manager, Compendial and Standards, Hospira, Inc

Scope of the session:

- USP Overview
 - USP History and Governance
 - How USP Works (Council of Experts, USP Staff, Stakeholder Forums)
 - USP Resolutions
- The Standards Development Process—USP Perspective
- USP Standards Development Process—Industry Perspective
 - How to Submit Requests for Revision

Highlights

USP Overview

- USP, established in 1820, is the only non-governmental pharmacopeia in the world.
- Organizations that are members of the USP Convention meet every five years to elect the Board of Trustees (BoT) and Council of Experts (CoE), amend the Constitution and Bylaws, and adopt resolutions that help guide the organization during each five-year cycle.
- The Council of the Convention is a communications conduit between the Convention and the BoT and CoE.



- USP has 40 Standards Expert Committees, 16 Information Expert Committees, and one Model Guidelines Expert Committee. The CoE is comprised of the Chairs of the Expert Committees.
- Ad hoc Advisory Panels, formed by Expert Committees or the Chair of the Council of Experts, can include individuals who are not Members of Expert Committees.
- Stakeholder Forums and Project Teams include representatives of trade groups and interests.

Standards Development Process, USP Perspective

- The process is unique in that industry, regulatory agencies, and other have the opportunity to review and comment on proposed revisions.
- Expert Committees decide whether to move revisions forward to be included in the USP/NF.
- Types of revisions include the In-Process Revision (IPF), Preview, Proposed Interim Revision Announcement (IRA), Direct or Immediate IRA, and Revision Bulletin.
- New rules effective September 1, 2006 enable Expert Committees to approve revisions after one cycle of review. A commentary will accompany the official text and explain all changes.
- Flexible monographs allow for differences in synthetic routes and formulations.
- All first-time USP Reference Standard (RS) candidates required in a proposed new/revised monograph or General Chapter need to be received by USP prior to publication in PF.
- New monographs/chapters and revisions that introduce new USP RSs will not become official until the required USP RSs are available for sale.
- Industry is encouraged to submit monographs to USP.
- The Standards for Articles Legally Marketed Outside the United States (SALMOUS) program facilitates the development of monographs for drug substances and drug products intended to treat neglected diseases, but not legally marketed in the US.
- The goal of the Standards for Articles Pending FDA Approval (SAPFA) program is to have a final, official monograph and RS (where appropriate) as soon as possible after FDA approval is granted. SAPFA monographs are published on the USP website until this approval is obtained.

Standards Development – Industry Perspective

- The USP Outreach Program enables industry to participate in setting standards and reduces compliance risks.
- When a company utilizes the Outreach Program, USP liaisons prepare draft monograph submissions at the company's site. Company staff guide the liaisons, define working day hours, conduct daily close-out meetings, and answer questions as needed. All documentation and draft monographs are returned to the company at the end of the visit.
- Less time is needed for a company to gather the data needed to utilize the Outreach Program than the time required for a company to generate a monograph on its own.
- Settling the Confidentiality Agreement is the biggest hurdle for a company utilizing the Outreach Program.

**Sessions II and IV: Wednesday, September 27, 2006, 3:30 p.m. – 5:30 p.m. and
Thursday, September 28, 2006 (1:30 p.m. – 5:00 p.m.)**

Title: USP Education, Verification, and International Locations

Speakers:

- Toby Gouker, USP Pharmacopeial Education Programs
- V. Srinivasan, Vice President, Verification Programs
- Eric Sheinin, Ph.D., USP Fellow, Verification Programs
- Peter Bippus, Director of Sales, Europe, Middle East, Africa
- John Hu, Ph.D., Vice President, International—China
- Kumud Sampath, Ph.D., Vice President, International—India



Scope of the Session:

- New Directions in USP's Pharmacopeial Education Program
- USP's Dietary Supplement, Pharmaceutical Ingredient, and Excipients Verification Programs
- Reports on USP's International Sites and Sales Offices (China, Europe, India)

Highlights

Pharmacopeial Education Program

- As knowledge builders, we are to harvest the Tacit Knowledge of the Pharmacopeial Convention. Explicit Knowledge originates from the USP/NF and other publications and leads to the generation of more Tacit Knowledge.
- The goal is to pull USP resources together and turn them into Pharmacopeial Education (PE) courses.
- Distance learning has evolved from the traditional correspondence course (by mail) to online classes. An expert can impart knowledge in a virtual classroom. A webpage contains content in dropdown boxes. Learning Management Systems enable the construction of these classes.
- Blended learning, i.e. face-to-face courses followed by distance learning, increases the amount that students retain.
- PE classes should expand to other languages.
- Professional certification programs could be developed.

Dietary Supplement and Ingredient Verification Programs

- The Dietary Supplement (DS) Product Verification Program covers vitamins, minerals, amino acids, botanicals, and non-botanical DSs covered by DSHEA and legally marketed in the US. Participating companies go through many months of rigorous tests and reviews to earn the USP-Verified mark.
 - After critical pre-audit documentation has been submitted to USP, a GMP audit is performed of the manufacturing site. When FDA GMPs become official, manufacturers that meet the USP GMPs will be able to meet the FDA GMPs.
 - Auditors will review mandatory criteria as well as product documentation on manufacturing processes and quality control. USP then conducts laboratory testing of product samples.
 - USP must approve all artwork for product labels and promotional materials carrying the USP Verified mark.
 - USP continuously tests and examines selected lots and marketplace samples of approved products. If a product is found not to be compliant, the company would be told to reformulate the product and remove the USP Verified mark from the packaging. In other instances, the company may need to reduce the shelf life of the product. The licensing agreement that a company signs with USP means that USP has legal recourse if the product is found not to be in compliance.
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- Ingredient manufacturers may voluntarily participate in the USP Dietary Ingredient Verification Program (IVP). This program applies to ingredients manufactured and marketed to the DS industry in the US and worldwide.
- The DS Expert Committee establishes guidelines for ingredients to be reviewed under the IVP for which there are no USP-NF monographs. It also ensures that dietary ingredients with known safety concerns are not admitted to the IVP.

Pharmaceutical Ingredient Verification and Qualification Program

- This program is a conformity assessment for drug substances and excipients ensuring that ingredients have been manufactured properly and meet high quality standards.
- USP will audit the manufacturing site after a review of documentation, review the chemistry, manufacturing, and controls (CMC) documentation, test samples for compliance with the USP-NF monograph or, if no monograph exists, the manufacturer's own analytical procedures, review the manufacturer's post-verification/qualification notification of changes, retest items annually, and re-audit the manufacturing site and re-evaluate each article every third year.
- For articles meeting the USP drug substance or excipient verification requirements, the manufacturer may display the USP verified mark on containers and show customers a USP verified Certificate of Standards Compliance.



- For drug product manufacturers whose suppliers have met the USP qualification requirements for an article, USP will provide a report and certificate indicating USP has qualified the supplier of that article.

USP's European Office – Basel, Switzerland

- The office serves customers in Europe, the Middle East, and Africa.
- The office provides a direct link to USP through science support on monographs and RS technical support.
- Products and services provided to customers have lower prices than distributors, faster delivery, and customer service on European time and in the German, Italian, French, Spanish, Arabic, and English languages.

USP China

- USP's office in China, located in Shanghai, opened in February 2006. The laboratory fit-out is underway and is expected to be completed in December 2006. The site will be inaugurated in February, 2007.
- USP-China supports the FDA mission regarding importation of drugs, participates with the Department of Commerce to battle counterfeits, collaborates with regulatory agencies and pharmacopeias to raise awareness of lack of standards and weak enforcement, and serves as a base to provide technical assistance under the USAID grant.
- The global pharmaceutical industry is rapidly investing in China.
- A Memorandum of Understanding (MOU) was signed in 2005 between USP and the Chinese Pharmacopeia Commission and the National Institute for the Control of Pharmaceutical and Biological Products (NICBPB).

USP-India

- In February 2006, the USP India site and dedicated laboratory were inaugurated and the sixth India Stakeholder Forum was held.
- The state-of-the-art analytical laboratory includes HPLC and GC capabilities as well as a dissolution training center.
- USP-India has a Board of Directors comprised of Dr. Darrell Abernethy (President), Mr. John Fowler (Chief Business Officer), and Dr. Srinivasan.
- The objectives of the organization include the establishment of a collaborative laboratory for Reference Standards; collaboration with public research institutions, pharmaceutical companies, and the Indian Pharmacopeial Commission; increasing the availability of USP products and services; promoting USP's PE programs; enlisting Indian pharmaceutical scientists for Council of Experts-related bodies and projects; and the facilitation of the exchange of information on compendial issues.

SESSIONS III & IV: Thursday, September 28, 2006, 8:30 a.m. to 12 noon and Friday, September 29, 2006, 8:30 – 10:30 a.m.

Title: USP Future Directions and Hot Topics

Speakers:

- Todd L. Cecil, Ph.D., Vice President, Standards Development
- Susan de Mars, J.D., Chief Legal Officer

Scope of the Session

- Changes in USP Processes (S. de Mars)
 - Rules and Procedures
 - New Approaches to Monograph Development
- General Notices Update (T. Cecil)
- USP-NF Redesign (T. Cecil)
- Food Chemicals Codex (S. de Mars)
- Hot Topics (T. Cecil)
 - Residual Solvents
 - Harmonization Topics (<905>, <711>)



- Medical Gases
- Protein A
- ISO Approaches/Certified Reference Materials
- Dissolution/Performance Tests/ASTM

Highlights:

Changes to USP Processes

- Revised Rules and Procedures of the Council of Experts became effective on September 1, 2006. A summary of the changes is available on the USP website.
- RS materials must be in-house before related monographs can be published in PF.
- Whole Expert Committees ballot on items proposed for publication in the USP-NF.
- Responses to public comments will be published in the USP-NF in the Commentary section in the front of the book. References in the monographs will refer readers to this section. Confidential information will be excluded from the comments summaries.
- The liaison may be contacted to obtain the status of a revision.
- New approaches to monograph development include Standards for Articles Legally Marketed Outside of the US (SALMOUS) and Standards for Articles Pending FDA Approval (SAPFA).
 - SALMOUS monographs are for neglected diseases (such as malaria). The development of these monographs is being fast-tracked and will not be delayed due to a lack of RS material.
 - The users of SALMOUS monographs are purchasing agents such as UNICEF and the Clinton HIV/AIDS Initiative.
 - SAPFA monographs will be published on the USP website until the articles are approved by the FDA.
 - The FDA has asked for the opportunity to comment on SAPFA monographs before they are posted on the USP website. The FDA-revised text would be incorporated.

USP-NF Redesign

- The USP-NF will be published as a three-volume set in November 2006. Re-designed General Notices, General Chapters, and Monographs will be developed over the next few years.
- In the re-designed monographs, summaries of comments received and responses from the Expert Committees will be listed before the official text, separated from the official text by a rule (line).

Food Chemicals Codex

- USP has acquired the Food Chemicals Codex (FCC). A new Ad hoc Advisory Panel and Expert Committee will oversee the updating and publication of this new USP document.
- USP does not plan to roll the FCC into the USP-NF. Although a monograph could include USP, FCC, and NF standards, the legal recognition of each of these entities is separate.

Future Directions

- Participants preferred that the ability to comment online be limited to one contact per company with one password.
- USP could provide training videos on topic areas about which liaisons receive the most questions. Stakeholders could be asked to help create the videos. Industry could incorporate the videos into their own training programs.

