

# USP-CHINA

Quarterly Update



in this issue

From the **Vice President, International-China**

## USP, China Grow Efforts to Improve Medicines Quality during Eventful End to 2008



John Hu, Ph.D.

I am pleased to share with you this latest edition of the *USP-China Quarterly Update*, highlighting news of the USP-China site as well as USP's headquarters as it relates to China. This quarter has been a whirlwind of cooperative activities between

USP and China, with the fourth USP-Chinese Pharmacopoeia Commission's (ChP) Joint Scientific Symposium in November; a USP-China Advisory Group Meeting in November; and three prominent Chinese delegations visiting USP's headquarters in the United States throughout the fall and winter. Such activities are a manifestation of the thriving relationship that USP and China share, with the common goal of improving the health of citizens in both nations—and worldwide—through quality medicines and foods.

I'll start with the USP-ChP Symposium, a two-day event in Tianjin that brought together more than 400 representatives from government institutions, academia, and industry to discuss the latest advances in pharmaceutical and food science, with a particular emphasis on Traditional Chinese Medicine (TCM). We were honored to have Mr. Wu Zhen, deputy commissioner of the State Food and Drug Administration (SFDA) and secretary-general of the ChP, open the meeting along with Dr. Roger L. Williams, chief executive officer of USP. The conference was truly an in-

ternational one, with representatives not only from China and the United States, but also from the World Health Organization (WHO) and the European Directorate for the Quality of Medicines and HealthCare (EDQM) offering their perspectives on drug quality control, which was a major focus of the conference along with quality control of herbal and TCM products. Understanding the varying viewpoints on TCM, drug, and supplement products—and the different regulatory structures governing such products by country—is

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From the **CEO**

## Annual Scientific Meetings Offer a Home for Important and High-Caliber Scientific Deliberations

Roger L. Williams, M.D.

USP hosted its fifth Annual Scientific Meeting (ASM) this past September in Kansas City, Mo. The first North American ASM was held in Iselin, New Jersey, at the close of the 2000–2005 cycle and continued in San Diego (2005), Denver (2006), Tampa (2007), and just now in Kansas City (2008). The last in the cycle is planned for Toronto, September 23–25, 2009. These are remarkable events for USP, and in this CEO Column I'd like to give you some background and insight into how they come about. I also want to show how the North American ASMs lead into an equally remarkable series of ASMs around the world.

Over the years I have been especially delighted at the caliber of the scientific deliberations of our ASMs, not only in the United States but around the world. These are proceeding at the highest level, with strong input from our manufacturer stakeholders and many others.

These ASMs replace the USP open conferences of the past, which were dedicated to one or more topics and designed to achieve some degree of consensus. I was privileged to attend these conferences when I was with the U.S. Food and Drug Administration (FDA) and then again when I came to USP in 2000. They were always exciting and well-organized meetings. The ASMs of today, however, are very different from the open conferences of yesterday. They cover a broad variety of topics and are designed not so much to achieve consensus as to let stakeholders know what USP's most urgent science and policy priorities are and, of course, to gain

input, just as did the open conferences of the past.

Let's look first at the recent Kansas City ASM. Planning for such a meeting occurs far in advance of the meeting itself, as meeting planners well know. The hotel was booked in August of 2006, and a planning committee composed of USP Council of Experts members, industry stakeholders, and USP staff began to discuss proposed meeting content. This is an arduous process, with many iterations before the agenda begins to settle down. USP works carefully to build multiple tracks into the ASM, so more topics can be covered, yet repeats some of these tracks so attendees won't miss key sessions. Great care is also taken with logistics and services, ensuring that attendees will have a pleasant time and can focus on the issues at hand. The big days finally do arrive and, from my perspective, they are a joyous time, when hundreds of members of the USP family—volunteers, staff, stakeholders, national and international visitors, and the press—arrive to engage in deliberations on compendial science. And the sidebar and impromptu meetings at an ASM can be as important as the sessions themselves. USP sponsors many outings and special events at ASMs for family and friends,

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key as the markets for these products continue to become globalized. Both USP and China reiterated their commitment to collaborating in setting standards for TCM and other products during the symposium.

The symposium was preceded by a meeting in Shanghai of the USP-China Advisory Group on November 4, during which USP's senior management, advisory group members, and invited guests listened to views on the state of China's pharmaceutical sector and the challenges it faces from representatives of the Shanghai Institute for Food and Drug Control and a number of different Chinese manufacturers. USP seeks to learn about the market in China from Chinese experts—which will allow it to better work with the country—through these types of meetings and was very grateful for opportunity to gain insights from both the advisory group members and meeting guests.



USP-China Advisory Group meeting attendees.

Reversing locations, USP hosted a number of Chinese delegations at its headquarters in the United States during the past quarter. A group of almost 20 from the SFDA visited USP in December to meet with USP's senior management to further explore the differences in regulatory requirements in the United States and China, and to discuss progress on joint activities between the two countries—particularly in the context of the USP-ChP Memorandum of Understanding (MOU) that was signed in 2008. One of the MOU's areas of focus—expansion of working relationships—was on full display at the meeting with the attendance of three Chinese scientists who are currently in residence at USP: Dr. Mingzhe Xu, visiting scientist from the National Institute for the Control of Pharmaceutical and Biological Products (NICPBP), Ms. Zhou Yi, visiting scientist from the ChP, and Ms. Shi Shangmei, visiting scientist from the ChP. Earlier in December, USP also hosted a Chinese delegation of six representatives from the Zhejiang Institute for Food and Drug Control, led by Ms. Tao Qiaofeng, deputy director, also a past USP visiting scientist. During that meeting, possibilities for cooperative activities were discussed—including standards development, collaborative testing of reference standards, and a potential MOU. Finally, USP hosted members of the Board of Directors of Huahai Pharma in mid-November. During this visit, USP presented a Certificate of Appreciation to Huahai for its donations of reference materials and continued support of USP.

As you can see, this is an exciting time for USP's and China's shared pharmacopeial endeavors, with many activities already in progress and a number of prospective activities on the horizon. USP and China can truly raise the quality of medicines, supplements, and foods for its citizens through cooperative activities related to setting and promoting the use of public standards. I will keep you updated on the progress of such activities through this newsletter. As always, please contact me with any questions or comments at [jh@usp.org](mailto:jh@usp.org).

# Introducing USP's Certified Reference Materials Program

Next Generation of Quality Standards to Provide a Higher Degree of Confidence in Measurements

In September 2008, USP released its first Certified Reference Material (CRM), Dextromethorphan Hydrobromide. That was about a month after becoming the first global pharmacopeia to receive International Organization for Standardization (ISO) accreditation as a producer of chemical CRMs. The release represented the next generation of exceptional, quality reference standards from USP that pharmaceutical manufacturers could begin utilizing to help ensure improved information for measurements of their products when meeting requirements set forth in the *United States Pharmacopeia–National Formulary (USP–NF)*. Each CRM comes with a Certificate of Analysis containing data on certified property value, uncertainty value, and for the first time an expiration date (period of validity), all of which aim to produce a higher level of trueness and traceability in measurement.

Additional CRM features and applications include:

- Metrologically based testing and statistical analysis;
- Traceability to an accurate realization of the unit in which the property value is expressed;
- Trueness and traceability of CRM measurement system helps with consistency and comparability of measurement data among labs and over time;
- Data for calibration, validating processes, comparison and value assignment;
- Values meet ISO 17025 documentation requirement for testing labs; and
- CRM program meets the requirements of ISO 17025 and ISO Guide 34 for Reference Materials Producers (RMPs).

To learn more about this program, USP Chief Metrology Officer William Koch, Ph.D., explains some of the key aspects of CRMs:

## When did the CRM initiative at USP begin?

Planning for the CRM program started in 2005. Analytical testing using collaborating laboratories began in 2006. Since then, I'm proud to say USP has become the first global pharmacopeia to produce CRMs, and in doing so, is meeting the demanding measurement needs of the industry, which are always increasing. Along the way, USP has published two *Stimuli* articles on the topic—including one from *Pharmacoepial Forum 33 (6)* that just received an award from the Cooperation on International Traceability in Analytical Chemistry (CITAC), an international group dedicated to metrology in analytical chemistry, for having high impact. The CITAC award was for publishing a "Most Interesting/Important Paper on Metrology in Chemistry" in 2008, which I think speaks to the value and recognition of USP's CRM program.

## Why is USP pursuing the production of CRMs?

Recognizing the need to advance state-of-the-art pharmaceutical testing to be consistent with ISO guidelines used by nearly all industries, CRMs seemed to be a necessity. USP has always produced quality reference materials and the CRMs are a further improvement in the final product by advancing the metrological science of our reference standards; the purpose of the CRMs is to provide a higher degree of confidence in the analytical measurement. This increased level of confidence then leads to more accurate decisions regarding product specification and acceptance limits.

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and this year in Kansas City was no exception.

Moving beyond the Kansas City meeting, USP's ASMs are designed to springboard into other science meetings in different regions of the world. The remaining scientific meetings in 2008 were in China, then in Jordan and Cairo. In 2009 they will take place in India, Europe, and Central America before starting the cycle again in September 2009 in Toronto. ASMs held outside North America are adjusted carefully to meet national and regional needs. For example, the recent meeting in China emphasized Traditional Chinese Medicines (TCM) because that is a particularly important topic for our Chinese hosts. USP always tries to work with a hosting organization to make the meeting a success. For example, in Jordan we work with the Jordan Association of Pharmaceutical Manufacturers, and in Central America we partner with our friends in the Mexican Pharmacopeia (FEUM). Each meeting is a little different—and that, of course, is what makes the follow-on meetings as exciting as the primary one in North America.

Next year, we hope to make the final ASM of the 2005–2010 cycle a huge success by partnering with our friends to the North. Canada is not just a neighbor—it is a close partner in USP's standards-setting activities, with 23 representatives

participating as Expert Committee or Advisory Panel members. Canadian scientists and other stakeholders help USP in many other ways as well, so I'm especially delighted that we will leave the United States for the beautiful city of Toronto.

As I close, I have to emphasize something very important to USP and to its Board of Trustees. The new Board of Trustees' Strategic Plan, recently finalized, was presented to attendees at the Kansas City ASM by Dr. Duane Kirking, speaking on behalf of the Board. That Strategic Plan emphasizes that USP is a science-based standards-setting organization, and it is the compendial science undergirding our standards in USP's five compendia that is the core of our ASMs. Over the years I have been especially delighted at the caliber of the scientific deliberations of our ASMs, not only in the United States but around the world. These are proceeding at the highest level, with strong input from our manufacturer stakeholders and many others. It is a true joy to listen to these discussions and to see thorny scientific issues move from debate to resolution. For this, I express my deep thanks and appreciation to all involved—those who plan, those who speak, and those who attend. 🍷

## USP Hosts First International Food Ingredients Issues Workshop




Attendees of the USP workshop heard experts from around the world speak on food ingredient standards and practices.

China, Australia and Japan. Scientific topics that were discussed over multiple presentations included biotechnology, genetically modified organisms (GMOs), allergens, supplements, and active packaging.

The food-related issues found in current international headlines, such as contamination and adulteration, were also frequently addressed throughout the workshop.

“Melamine is an issue of adulteration, not an illegal use,” said Junshi Chen, M.D., from the National Institute of Nutrition and Food Safety with the Chinese Center for Disease Control and Prevention. He spoke on food ingredient regulations in China, saying that current practices in general are acceptable and in compliance with international practices. Chen did say there was a lack of specification for almost half of the food additives approved for use and that few specifications for flavors and a list for packaging materials have not been updated in about 10 years. He ended by saying that there are food safety problems in China because of the rapid development of China’s economy.

Vincent Hegarty, founding director of Michigan State University’s Institute for Food Laws and Regulations and an expert in setting up food standards and agencies in the Middle East, summed up the meeting by noting that, “A majority of countries still have overly fragmented, less developed, or outdated systems for food control.”

USP will host another Food Ingredients Issues Workshop in 2009. Presentations from the 2008 meeting are available at [www.usp.org/meetings/agendas/foodIngredientsWorkshop2008-10-15.html](http://www.usp.org/meetings/agendas/foodIngredientsWorkshop2008-10-15.html). 

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### Why is a stated level of uncertainty so important?

All measurements are comparisons, and there is always some uncertainty when making such comparisons. Knowledge of this uncertainty (or variability) helps one decide if the measurement is adequate to meet the needs. With the stated level of uncertainty, the user has the ability to propagate uncertainty to the final result, and is able to make meaningful comparisons of measurement results. If it is assumed that the variability of a standard is zero, this assumption will underestimate the total measurement uncertainty and could lead to a wrong decision. A CRM becomes very helpful here because it includes an uncertainty value, as well as a statement of traceability (that is, a declaration of how the measurement was made and which standards were used to support the measurement). Hence, the three components

inherent in a CRM and provided either explicitly or implicitly in a Certificate of Analysis for a CRM are: 1) the property value, tested and certified to be true, 2) the uncertainty of this property value, and 3) the path of metrological traceability. These three components, taken together, add confidence in and assurance to the subsequent measurements using the CRM.

### Are there plans for additional CRMs to be released?

USP is committed to producing CRMs, and you can expect to find more available to purchase each year. USP has developed criteria for the selection of future CRMs, and is working to identify a list of candidates.

For additional information about USP Reference Standards and CRMs, visit: [www.usp.org/referenceStandards](http://www.usp.org/referenceStandards). 

## upcoming events

### TRADE SHOWS

#### API CHINA

Xi’an: May 12-14, 2009  
Booth No.234-236 (Hall B2)

#### CPHI CHINA

Shanghai: June 23-25, 2009  
Booth No. E1B22

### PHARMACOPEIAL EDUCATION

#### cGMP: A QUALITY SYSTEMS APPROACH FOR APIS

Shenyang: March 24, 2009  
Chengdu: March 26, 2009

#### COURSES ESSENTIALS OF MICROBIOLOGICAL TESTING

Taiwan: April 9-10, 2009  
Tianjin: April 13-14, 2009  
Hangzhou: April 16-17, 2009

#### DEVELOPING COMPENDIAL HPLC PRACTICES

Shenzhen: April 21, 2009  
Shanghai: April 22, 2009  
Qingdao: April 24, 2009

#### VALIDATION OF COMPENDIAL PROCEDURES/EFFECTIVELY USING USP-NF

Guangzhou: May 19-20, 2009

Dates and location of courses are subject to change. Please check the USP Web site at [www.usp.org](http://www.usp.org) for updated information.