U.S. Pharmacopeia
The Standard of Quality℠

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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket Number 2003N-0361 Anti-counterfeit Drug Initiative

Dear Sir or Madam:

USP congratulates FDA and its Counterfeit Drug Task Force for its activities to address this important public health problem. Specifically, USP expresses support for many of the initiatives that were provided in the October 2003 Interim Report of the Task Force.

USP is a unique, volunteer based organization that creates standards for therapeutic articles. These are applicable from the manufacturer to the dispensing level and can apply to all therapeutic products in the marketplace for which a compendial requirement exists. In this regard, they provide support not only to FDA, but other Federal, state, and local authorities. A brief background statement about USP is provided in an attachment.

We believe there are a number of areas in which USP's activities could be allied with those of FDA as it works to prevent and detect counterfeit therapeutic products in the US marketplace.

- As official compendia of the United States, the *United States Pharmacopeia* and *National Formulary* (*USP-NF*) contain approximately 4000 monographs for substances (drug substances and excipients) and preparations (dosage forms). USP is working to transform these monographs so that they control impurities (see Guideline at www.usp.org/standards/revisionguidelines.index.html). This effort will bring *USP-NF* into conformance with ICH approaches. Depending on route of synthesis and manufacture, impurities can form an unimpeachable marker for a dosage form. It is immediately available, complete, and can be updated readily. It is produced without adding to regulatory burden.

  The task of moving to modern control of impurities—one needed for both private application standards at FDA as well as in USP monographs—is a resource intensive effort. The new approach could be facilitated in many ways, particularly if FDA, USP and pharmaceutical manufacturers could work together collaboratively. Development of standards and reference materials to detect counterfeited articles, or articles that otherwise should not be in the US market, could also be explored.

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- A modern pharmacopeial monograph and associated official USP Reference Standards supports good surveillance testing. Current surveillance testing could be amplified through a network of national laboratories involving USP laboratories and academic centers.

- For over 25 years, USP operated a Drug Product Problem Reporting Program, which supplemented FDA's Drug Quality Reporting System (DQRS). USP would be pleased to determine if it could assist FDA to amplify the DQRS by working with its practitioner community. Specifically this could occur perhaps through expansion of its current medication safety reporting programs to include a program specifically directed to detecting counterfeited products.

- USP is working with the United States Agency for International Development (USAID) to train laboratories in developing countries to conduct surveillance testing and provide reports. USP could disaggregate the results of testing when, and if, US-manufactured products are involved and provide reports to FDA. In addition, USP is maintaining a matrix of drug quality problems reported in USAID-presence countries. The information covers the past five years and is updated once each quarter. The matrix is accessible at www.uspdqi.org. USP also works closely with the World Health Organization's efforts to combat substandard and counterfeit drugs, and is collaborating with WHO on an *Operational Guide to Drug Quality Assurance in Low Income Countries*

- The *National Formulary* contains monographs for excipients. These monographs can be expanded to include specifications for dyes, inks, and taggants. If adopted along the lines of the OTC monograph approach, these monographs should be helpful in allowing manufacturers to make rapid changes to dosage forms. The presumption would be that a change could be made to an approved product with notification, providing the change was for a material for which a monograph existed in the *National Formulary*.

- USP has been working in the area of standards for packaging, storage, and distribution for approximately 70 years. The recent effort was amplified based on Convention directives at the 1990, 1995, and 2000 quinquennia. USP's Packaging, Storage, and Distribution Expert Committee has created a number of standards, expressed in required or interpretive General Chapters. These mandatory and voluntary standards could be amplified to promote packaging that reduces the likelihood of counterfeit products entering the US marketplace. Specifically, unit-of-use containers, blister packs, and new technologies could be facilitated through the public standards-setting activities of USP. USP also can reference standards from other standards-setting bodies, e.g., ASTM.

- In the 1970's, USP coordinated under contract with FDA a National Coordinating Committee for Large Volume Parenterals (NCC-LVP). This Committee allowed USP leadership, the professions, pharmaceutical manufacturers, and other stakeholders the opportunity to facilitate numerous changes in the labeling, packaging, and manufacturing of large volume parenterals and in professional practices relating thereto. A similar approach could be developed by forming a National Coordinating Committee to ensure product integrity and to prevent and/or detect the presence of counterfeit products in the US market. In this cycle, USP has formed a Packaging, Storage, and

Distribution Project Team, similar to the past coordinating committee effort, on the general topic to provide advice to the Council of Experts and the USP staff. This Project Team's focus could be expanded to facilitate and coordinate solutions to counterfeit products in the US market. USP is pleased to note that it has welcomed participation of the Consumer Product Safety Commission in both its standards-setting and advisory activities. Many of the efforts of both the Council of Experts and the Project Team culminated in a USP Open Conference on Packaging, Storage, and Distribution, October 12-15, 2003 in Washington, to which FDA was invited.

- With over 400 healthcare member organizations represented in the USP Convention, USP works well at the interface between practitioners and manufacturers. In this regard, USP would be pleased to consider how anti-counterfeit measures could involve participation of physicians, pharmacists, nurses, and allied healthcare professionals. USP also works to include participation of consumers and patients in its activities. Many examples exist where involvement could be positive. These include educational activities, public conferences, development and maintenance of databases. Development of a database containing packaging and labeling of selected drugs for reference by healthcare professionals could also be explored.

USP is pleased to explore with FDA these and other possible areas in which we could be of assistance. Toward that end, we would be pleased to convene the PSD Project Team and members of USP's Council of Experts to facilitate further discussion on this important topic.

Sincerely yours,

Joseph G. Valentino
Sr. Vice President and
General Counsel

JGV/lfl

BACKGROUND

USP's expertise as a standard-setting body has been recognized numerous times by Congress. USP's standards are published in the official compendia, the United States Pharmacopeia-National Formulary (*USP-NF*). Congress recognizes the compendial standards in the Federal Food, Drug and Cosmetic Act (FDCA) and makes them enforceable by the Food and Drug Administration (FDA). USP standards are also recognized by state laws and are used to govern state practices, such as those involving pharmacy practice.

Congress initially recognized only those USP standards for determining the identity, strength, quality, and purity of articles used in medical practice. The FDCA first recognizes the *USP-NF* as the official compendia and then requires in section 501(b) that drugs marketed in the United States which appear in the official compendia meet the *USP-NF* standards for strength, quality, and purity. In 1938, Congress also recognized and made legally enforceable USP packaging and labeling requirements. Section 502(g) requires that drugs be packaged and labeled in accordance with USP requirements. Such recognition was provided because, at the time, USP had packaging and labeling requirements that were not implemented by the industry and this failure to implement them resulted in numerous fatalities related to medication errors.

USP has the expertise and structure to continuously revise its standards to incorporate new technologies, packaging and labeling that promote better quality products. Its compendia can be utilized to provide measurable standards and specifications for safety purposes such as those already provided for containers, which include moisture, light exposure, and types of containers.

USP, established in 1820, is a not-for-profit organization whose mission is to promote the public health by establishing and disseminating officially recognized standards of quality and authoritative information for use of medicines and related articles for professionals, patients, and consumers. The membership body of the USP represents a consortium of health care organizations, pharmacy and medical associations and schools, and government bodies that direct USP's agenda. To implement this agenda, more than 1,200 expert volunteers, who are health care professionals, scientists, academicians, and government officials, develop USP standards.

In addition to its standard-setting activities, USP operates two reporting programs for medication errors: (1) the Medication Error Reporting (MER) Program; and (2) MEDMARX. Medication error data received through the USP reporting systems have effected changes in single hospitals, across health systems, and ultimately changes in *USP-NF* packaging, labeling, and nomenclature standards.

- USP also operates the Dietary Supplement Verification Program, a voluntary certification program for dietary supplement manufactures. This program combines a manufacturing and label review and a GMP inspection with testing for conformity to *USP-NF* standards and can apply to either or both the bulk raw material used in manufacturing and the finished dosage form.