



WHITE PAPER

USP'S ROLE IN PATIENT SAFETY

SEPTEMBER 23, 2009

COUNCIL OF THE CONVENTION SECTION ON QUALITY OF PATIENT CARE

INTRODUCTION

For the last four decades, the United States Pharmacopeial Convention (USP) has relied on spontaneous reporting information to support creation of safe medication use and quality of care standards in the *United States Pharmacopeia (USP)* and allied reports. For the most part, these are standards and supporting information that speak to how practitioners within healthcare systems should adjust their processes and practices to promote safe medication use. At times, USP product standards call for the adjustment of labels and labeling to reduce the likelihood of error.¹

As a volunteer-driven, practitioner-based, standards-setting organization, USP provides an important and unique pathway for practitioners to set standards they use in daily life. USP is not itself a regulatory body and does not enforce its standards; however, conformity assessment bodies may recognize USP standards in ways that enhance their value, impact, and at times make them mandatory. Irrespective of their voluntary or mandatory character, standards provide a safe harbor for practitioners and support optimum health care outcomes.

While beyond the scope of this white paper, USP acknowledges—and has always supported—the remarkable work of academia, the Institute of Medicine (IOM), highly involved standards- and conformity-assessment organizations (many of whom are Convention members), and many others who have worked tirelessly to develop information and provide evidence-based approaches to promote patient safety, safe medication use, and optimal quality care. Much of this effort culminated in the seminal reports of the IOM beginning in 1999 and follow-on activities in the IOM and elsewhere.

The Council of the Convention Section on the Quality of Patient Care presents this white paper as a means of reviewing USP's prior efforts in this area and to encourage the Convention to consider future patient safety opportunities for USP.

¹ For the most part, USP does not provide clinical practice standards, which are the responsibility of practitioner associations, state practice boards, and other certifying bodies.



USP'S LABELING AND NOMENCLATURE RESPONSIBILITIES IN LAW

In the United States, under the Federal Food, Drug, and Cosmetic Act (FDCA), the *United States Pharmacopeia (USP)* and *National Formulary (NF)* are recognized as official compendia. A drug with a name recognized in *USP-NF* must comply with compendial identity standards or risk being deemed adulterated, misbranded, or both. Drugs must also comply with compendial standards for strength, quality, and purity, unless they are labeled to show all respects in which the drug differs. These Federal requirements arise under the adulterated drugs provision of the FDCA at §501(b) as well as the misbranding provisions at §502. The role of nomenclature is particularly important, since the link to drugs “recognized in an official compendium” at §501(b) arises in the statutory provision that addresses the designation of drugs by “established names” at §502(e).

As explained in 21 CFR §299.4, the Food and Drug Administration (FDA) has statutory authority to designate “official” or “established names,” yet it rarely does so. Instead, while continuing to review *proprietary* (brand) names as part of the drug approval process, FDA defers to USP’s Nomenclature Expert Committee in the Council of Experts and to the U.S. Adopted Names (USAN) Council, in which USP plays a key role, to provide *established/nonproprietary* drug product and drug substance names. Accordingly, the term “established name” means an article recognized in *USP-NF* (see FDCA §502(e)(3)), and drugs with such names must meet *USP-NF* standards for identity as well as (unless labeled otherwise) strength, quality, and purity.

The FDA has extensive authority regarding the labeling of drugs, ranging from the package insert, dispensing, and containers, to advertising and promotional materials. The FDCA provides that a drug with a name recognized in an official compendium—including *USP* or *NF*—will be considered misbranded unless it is packaged and labeled as prescribed therein (FDCA §502(g)). Monograph requirements for packaging and labeling are noted in the *USP-NF* General Notices at 4.10 and are reflected in various monographs and General Chapters.

CURRENT ACTIVITIES

1. THE USP NOMENCLATURE EXPERT COMMITTEE

USP’s Nomenclature Expert Committee establishes nonproprietary names for drug substances, drug products, excipients, biologics, dietary supplements, and medical devices for humans and animals. It also promotes uniformity and consistency among the official titles in the *USP* and *NF*. The Committee is concerned with nomenclature for dosage form monographs and other aspects of the language used in the prescription, dispensing, sale, or manufacture of drugs. The Committee works in a collaborative fashion with the USAN Council, and USP has committed to using the USAN as the title of a drug monograph for that substance. The Committee’s authority to develop official nonproprietary names is identified in section 502(e) of the FDCA. The section indicates that a drug is misbranded if its label does not include the “established name” of the drug and each ingredient. It further specifies that the established name of a drug or ingredient is the official title used for the drug or ingredient in an official compendium such as *USP* or *NF*, as long as the FDA has not designated an official name in accordance with section 508 of the FDCA. In early 2006, a federal appeals court decision confirmed that the nonproprietary names



assigned by the USP Nomenclature Expert Committee take precedence over the names informally approved by the FDA during regulatory review. Taken together, the public-private partnerships created through Congressional authority have provided U.S. practitioners with coherent non-proprietary drug substance and product names, and these good naming conventions promote safe medication use and quality of care.

2. SAFE MEDICATION USE EXPERT COMMITTEE

The Safe Medication Use Expert Committee (SMU EC) began its work in the 2000-2005 cycle and continued in the 2005-2010 cycle. The nineteen members of the 2005-2010 SMU EC were drawn from the professions of medicine, nursing, and pharmacy, and include representatives from academia, research, government, and consumer interest. In this cycle, the SMU EC has reviewed and analyzed medication error reports submitted to USP, and from those, the Committee established recommendations for revision and development of standards in *USP-NF* and made recommendations to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) discussed later in this white paper. It also developed guidelines, recommendations, a General Chapter, and publications related to safe medication practices and patient safety. The SMU EC's members provided support to USP's two reporting programs—MEDMARX® and the Medication Error Reporting (MER) Program. The SMU EC's focus has been on policy-level priorities for the safe use of medications and patient safety initiatives. Examples of initiatives appear below:

- Total Dose per Total Volume — The SMU EC developed crosscutting support for a requirement to change labeling to indicate total dose per total volume for parenteral packages of 100mL or less. The recommendation was based on errors in which health professionals mistakenly administered the entire vial content in error—published in *Pharmaceutical Forum (PF)* 31(4) [July-Aug 2005]: Strength and Total Volume for Single – and Multiple-Dose Injectable Drug Products.
- Neuromuscular Blocking Agents — An article, “Improving the safety of neuromuscular blocking agents: A statement from the USP Safe Medication Use Expert Committee” was published in the *American Journal of Health-System Pharmacists*, Vol 63, Jan 15, 2006. The work stimulated a new policy statement from the American Society of Health-System Pharmacists (ASHP) on the use of neuromuscular blocking agents. The publication of this article followed the standard instituted by USP that required the warning, “Warning – Paralyzing Agent,” on the closures of neuromuscular blocking agents.
- Patient Safety Stakeholder Forum — A cross-disciplinary Patient Safety Stakeholder Forum was convened on October 11, 2006 to discern the need for the creation of a new USP publication: “Safe Medication Practices Compendium.” This forum was followed by a USP white paper, “Exploring a Strategic Proposal for the Concept of a Compendium of Safe Medication Practices.” It was eventually concluded that additional exploration was needed to develop such a compendium.
- “Error Avoidance Recommendations for Tubing Misconnections When Using a Luer-Tip Connector: A Statement by the USP Safe Medication Use Expert Committee” was published in the *Joint Commission Journal on Quality and Patient Safety*. May 2008. Volume 34, Number 5: pp. 293-296.

- Physical Environments that Promote Safe Medication Use — General Chapter <1066> *Physical Environments that Promote Safe Medication Use* was created to provide safe medication use standards for all health care settings.
- Guidelines or Standards for Computerized Prescription Order Entry and Other Technologies — The SMU EC is working with Dr. Andrew C. Seger and Dr. Gordon Schiff from Brigham and Women's Hospital on an analysis of computerized prescription order entry (CPOE) errors from the MEDMARX® database to develop guidelines/standards.
- "High Alert Drugs by Location" is being drafted by the Medication Error Data Analysis Advisory Panel of the SMU EC.
- Health Literacy and Prescription Container Labeling — The Health Literacy and Prescription Container Labeling Advisory Panel of the SMU EC is working on recommendations for the development of standards regarding simplifying language; using explicit text to describe dosage/intervals, including purpose for use; organizing the label in a patient centered manner; improving readability; and including supplemental information.
- Standardized Intravenous Concentrations — The SMU EC completed analysis of a Standard Intravenous (IV) Concentrations survey of health system pharmacy directors in order to determine the standard drip and flush concentrations being used in their respective facilities for the treatment of neonates, pediatrics, and adults. The goal is to standardize product concentrations to help decrease medication errors. The SMU EC will recommend standard concentrations for ten High Alert Drugs as a follow-up to an IV SMU survey (and an IV Summit held at USP) and publish an article identifying standard IV concentrations for ten High Alert Drugs by patient type.
- Tall-Man Lettering — The SMU EC will publish an article based, in part, on a research survey titled "Tall Man"/ Enhanced Lettering for Medication Name Differentiation. The survey on Tall Man Lettering was conducted in an effort to better understand the current landscape regarding use of and experience with enhanced lettering as a safety tool. Based on the survey results, the USP Nomenclature Expert Committee will consider the advisability of developing standards. A significant number of responses (1,788) were received from pharmacists (60%), nurses (16%), and physicians (16%), with the remainder coming from pharmacy technicians, nurse practitioners, and other healthcare providers. Cooperation in disseminating the survey was obtained primarily from the American Society of Consultant Pharmacists, the ASHP, the Institute for Safe Medication Practices (ISMP), the Joint Commission, and the National Alliance of State Pharmacy Associations.
- Harmonization with WHO Label Standards for Vincristine and Other Vinca Alkaloids — Three component changes were recommended to reduce the chance of vincristine (and other vinca alkaloids) being administered by the intrathecal route (which is universally fatal). Through a reworded cautionary statement, the recommendation would change to overwrap alert labeling and add a cautionary statement on the cap and



ferrule of the vial. (This proposal is currently under consideration by the Nomenclature Expert Committee.)

3. THE NATIONAL COORDINATING COUNCIL FOR MEDICATION ERROR REPORTING AND PREVENTION

USP serves as the Secretariat for the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP/The Council), an independent body comprised of numerous national organizations. The Council was formed in 1995 through the efforts of its member associations and agencies to focus on ways to enhance patient safety through a coordinated approach and a systems-based perspective.

An interdisciplinary group of 15 organizations and agencies held its first meeting in July 1995. In the past 14 years, the Council has grown to 26 member organizations and two individual members. The five goals that continue to direct the Council's activities are:

- Stimulate the development and use of reporting and evaluation systems by individual health care organizations;
- Stimulate reporting to a national system for review, analysis, and development of recommendations to reduce and ultimately prevent medication errors;
- Examine and evaluate the causes of medication errors;
- Increase awareness of medication errors and methods of prevention throughout the health care system; and
- Recommend strategies for system modifications, practice standards and guidelines, and changes in packaging and labeling.

Council Accomplishments—1995 to Present:

- Defined a “medication error” and encouraged all stakeholders to use this definition to provide a uniform basis for medication error reporting and analysis.
- Developed a medication error taxonomy, index and algorithm for categorizing medication errors
- Issued a statement on calculating medication error rates
- Promulgated recommendations for:
 - Prescribing
 - Labeling and packaging
 - Dispensing
 - Administration



- Verbal medication orders
- Standard bar codes on medication packages and containers
- Reducing medication errors in non-health care settings
- Reducing at-risk behaviors
- Bar coding labels to reduce medication errors
- Promoting safe use of drug suffixes
- Avoiding medication errors with drug samples

The Council has had national and international impact through its multidisciplinary conferences on bar coding, drug nomenclature, and suffix use. Continuing activities and other accomplishments include:

- 1) Developing and disseminating standardized definitions for terms such as *adverse drug event, adverse drug reaction, harm, preventable event*;
- 2) Establishing a dedicated Web site for organizations, government, and practitioners to reference The Council's recommendations and other information;
- 3) Developing a solid oral dosage forms article for broad dissemination;
- 4) Endorsing the ISMP *Safety Self-Assessment for Community/ Ambulatory Pharmacy*;
- 5) Establishing consumer information links to The Council's Web site;
- 6) Developing and disseminating a white paper on the use of bar codes;
- 7) Signing on to a set of *General Principles* supporting legislation to uphold, as privileged, information submitted to error reporting programs (These *General Principles* were incorporated into the Patient Safety and Quality Improvement Act of 2005 that was signed into law on July 29, 2005.);
- 8) Recognition with the 2007 American Pharmacists Association Foundation Pinnacle Award; and
- 9) Receipt of the 2008 Eisenberg Award.

In the coming years, The Council will continue to focus on key issues impacting the safe use of medications. With the help of new and enthusiastic member associations and agencies, The Council will address medication reconciliation as well as geriatric and long-term care issues. The members of The Council are recognized at www.nccmerp.org.



PRIOR ACTIVITIES: USP'S REPORTING PROGRAMS TO SUPPORT STANDARDS

1. DRUG PRODUCT PROBLEM REPORTING PROGRAM

Because of concern with the quality of drug products on the market, in 1971, the USP and the FDA co-founded the Drug Product Problem Reporting Program (DPPR). This was a national program in which health professionals voluntarily reported problems and defects experienced with drug products marketed in the United States. Often, product problems or defects had to do with inadequate packaging or labeling that could lead to errors or confusion on the part of health professionals. Other problems such as inclusion of foreign matter, suspected contamination, questionable potency, and "bioinequivalence" based on observed therapeutic response were also reported among the more than 100,000 observations gathered in DPPR. USP terminated the DPPR contract with the FDA in 1987, but continued a USP Drug Reporting Program until August 2000.

2. MEDICAL DEVICE AND LABORATORY PRODUCT PROBLEM REPORTING PROGRAM

Together with the DPPR Program, USP operated the Medical Device and Laboratory Product Problem Reporting Program (PRP) under contract with the FDA Center for Devices and Radiological Health (CDRH). In this program, USP collected reports on defective medical devices and shared that information with both CDRH and the manufacturers involved in incidents. This program had a major impact on the use of breast implants, dental implants, and marijuana testing kits. It was the precursor to the FDA's MedWatch program. This contract with the FDA was terminated in September 1995.

3. VETERINARY REPORTING PROGRAM

In 1994, USP established a Veterinary Reporting Program (VRP) to assist the FDA's Center for Veterinary Medicine (CVM), the Environmental Protection Agency, and the Department of Agriculture in obtaining information about adverse events with veterinary products. Reports were shared with the appropriate government agency and with the manufacturers of the products involved in the reports. The program was terminated in April 2003.

4. MEDICATION ERROR REPORTING PROGRAM

In 1991, USP established its first Medication Error Reporting Program (MER) in conjunction with the ISMP. MER was designed to obtain spontaneous reports both for the medicine itself and the system in which the medicine was prescribed, dispensed, administered, and used. Between 1991 and 2008, MER received more than 6,000 voluntary reports of actual and potential medication errors. MER identified errors in various health care delivery environments, including hospitals, nursing homes, physicians' offices, pharmacies, emergency response vehicles, and home care. The reports documented that errors are multi-disciplinary and multi-factorial and that they may be made by experienced as well as inexperienced health professionals, support personnel, interns, students, and even patients and their caregivers. Medication errors can and regularly do occur anywhere along the continuum from prescribing to transcribing to dispensing and administration. The causes of errors may be attributed to human error, to product names or designs, and to the medication handling and delivery systems in which the products are used and in which individuals operate and interact. USP submitted MER reports to the FDA as a



MedWatch partner, including adverse drug reactions that came to MER but were not evaluated. MER reports were also shared with the relevant manufacturers.

Examples of important changes USP made to its standards as a result of MER reports appear below:

- Potassium Chloride — Reported deaths due to the accidental misadministration of concentrated Potassium Chloride Injection led to: 1) changing the official USP name to Potassium Chloride for Injection Concentrate to give more prominence to the need to dilute the product prior to use; 2) requiring that labels bear a boxed warning with the words "Concentrate: Must be Diluted Before Use;" 3) requiring that the cap must be black in color (the use of black caps is restricted to this drug product only); and 4) requiring that the cap must be imprinted in a contrasting color with the words "Must be Diluted."
- Vincristine Sulfate — Reported deaths due to confusion and the resultant injection of the anticancer drug, Vincristine Sulfate for Injection, directly into the spine instead of the vein resulted in changes in the requirements for packaging by pharmacies and manufacturers preparing ready-to-use doses. Each dose, whether prepared by the manufacturer or the pharmacist, must now be wrapped in a covering labeled "FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES" and that covering may not be removed until the moment of injection.
- Amrinone/Amiodarone — Reported deaths due to the confusion of similar names Amrinone and Amiodarone led USP and the USAN Council to change the nonproprietary name and official title of Amrinone to Inamrinone.
- Neuromuscular Blocking Agents — Reported deaths due to the inadvertent mix-up of neuromuscular blocking agents (which paralyze the respiratory system) with other drugs led to recommended changes in standards for labeling and packaging of the therapeutic class of neuromuscular blocking agent products.

5. MEDMARX®

MEDMARX® was developed by USP in 1998 as an Internet-accessible, anonymous reporting program that enables hospitals to voluntarily report, track, and trend data, incorporating nationally standardized data elements (i.e., definitions and taxonomy). These standardized elements were drawn from the work of the MER Program, the FDA, NCC MERP, and the ASHP. MEDMARX® is structured to support an interdisciplinary, systems-approach to medication error reduction and fosters a non-punitive environment for reporting. USP created MEDMARX® with the intent to broaden the model to include other health care settings, e.g. long-term and ambulatory care settings, and to include other types of reporting such as medical error and adverse drug reactions.

Hospitals are encouraged to use MEDMARX® as part of their internal quality improvement processes, thereby extending their "peer-review" to other hospitals in the program. Hospitals can review errors entered by other institutions in "real time" and also see any reported action taken by another institution in response to an error in an effort to avoid similar errors in the future.



This feature affords institutions the opportunity to examine errors in a proactive manner. For example, the institution can review the error profile of a drug or class of drugs to determine if certain risk prevention measures or training programs should be established within the institution before a product is added to the institution's formulary. If the error profile is significantly serious, a determination may be made not to stock the drug. MEDMARX® supports the performance improvement standards of the Joint Commission, which requires institutions to look outward at the experiences of others in order to reduce risk.

USP transferred its reporting programs, MEDMARX® and MER, to Quantros and ISMP, respectively, in 2008. USP will continue to use data from these and other programs to enhance its standards-setting activities to promote patient safety and safe medication use. In the interest of public health and to assist practitioners and patients, USP has posted eight annual reports on its Web site free of charge, ensuring full access to this clinically important information.

FUTURE OPPORTUNITIES

1. NOMENCLATURE, SAFETY, AND LABELING EXPERT COMMITTEE FOR THE 2010-2015 CYCLE

In the next cycle, a new expert committee—Nomenclature, Safety, and Labeling Expert Committee— will combine the work of the Nomenclature and Safe Medication Use Expert Committees from the 2005-2010 cycle. This new Expert Committee will build on the work of its predecessors by continuing to develop guidelines, recommendations, General Chapters, and publications related to safe medication practices and patient safety, as well as by linking these efforts to drug naming and the labeling of medications. Via Expert Panels, specific standards-setting activities can be addressed on a broad range of safe medication use and quality of care standards.

2. INSTITUTE OF MEDICINE

In 2007, the IOM published *Preventing Medication Errors*, a report by its Committee on Identifying and Preventing Medication Errors. The report called on USP to work with the FDA and others in several areas related to drug naming, labeling, and packaging. The IOM posited that there are many ways that basic information about a specific drug is communicated to providers and patients and identified some of the more obvious problems:

- Brand names and generic names that look or sound alike
- Different formulations of the same brand or generic drug
- Multiple abbreviations to represent the same concept
- Confusing word derivatives, abbreviations, and symbols
- Unclear dose concentration/strength designations



- Cluttered labeling—small fonts, poor typefaces, no background contrast, overemphasis on company logos
- Inadequate prominence of warnings and reminders
- Lack of standardized terminology

The proposed IOM action plan focused on two overarching principles: 1) product naming, labeling, and packaging should be designed for the end user—the provider in the clinical environment and/or the consumer; and 2) safety should always take precedence over commercial interests. In addition, Recommendation #4 of the IOM report included USP in a list of organizations that should work together to address labeling, packaging, and the distribution of free samples.

CONCLUSION

Based on its nomenclature and labeling recognition in the FDCA and exhortations from the community, the need for USP's involvement in standards to promote safe medication use and quality care is as strong as ever—and may increase in an era of health care crisis and reform. One of USP's greatest strengths lies in its ability to convene a broad and diverse group of stakeholders around issues common to all, and USP can leverage this role by helping to advance standards related to medication safety that are beyond the scope of a single health profession or professional organization. For many years, USP has devoted substantial resources and energy to its safe medication use and quality of care standards-setting activities, but has struggled to find a sustainable financial and public health model for these activities. Convention Delegates must now ask: What is the appropriate role for USP in setting standards related to medication/patient safety, and how will this role be financially supported? The Council of the Convention Section on the Quality of Patient Care calls on the Convention membership to articulate ways in which a standards-setting body such as USP can continue its work based on USP's historical contributions, unique capabilities, and current and possible future positions in law.