



# WHITE PAPER

## OPPORTUNITIES FOR DRUG INFORMATION AND USE STANDARDS

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COUNCIL OF THE CONVENTION SECTION ON QUALITY OF PATIENT CARE

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### INTRODUCTION

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As a standards-setting organization for medicines and other healthcare articles, the United States Pharmacopeial Convention (USP) has contributed broadly and deeply to the provision of information supporting rational therapeutic decision-making and safe medicine use. In this white paper, USP's Council of the Convention Section on the Quality of Patient Care provides a situation analysis of these and allied contributions, focusing on the general topic of drug information and use standards. A separate white paper will consider safe medication use.

Standards generally apply to people, processes/practices, and/or products. USP now provides an extensive array of product standards for drug and food articles in the *United States Pharmacopeia (USP)*, *National Formulary (NF)*, *Food Chemicals Codex (FCC)*, and allied compendia. These product standards support testing to assure identity, strength, quality, and purity of foods and drugs. Beyond these product standards lie others that support rational therapeutic use—process and practice standards—and perhaps clinical practice standards as well that can be associated with education and training. Process/practice standards also might promote improved operations of healthcare teams and systems. This paper uses the term *drug information and use standards* to define collectively the concept of standards to promote rational and cost-effective therapeutic decision-making for medicines. Such standards could be applied in the paradigm that moves from diagnosis to treatment. Once a diagnosis is made, many therapeutic guidelines exist; many are maintained on an Agency for Healthcare Research and Quality (AHRQ) web page at <http://www.ahrq.gov/clinic/>, that speak to multiple treatment interventions ranging from the extremely simple to the highly complex. Use of medicines also ranges from the simple to the complex, and the complexity in an era of biomolecules and molecular medicine is increasing by the year. Typically, information and use standards for medicines begin with Food and Drug Administration (FDA)-approved efficacy and safety information in drug labeling. This information is amplified over time with further studies and clinical usage.



How this further information is generated and applied is a subject of considerable societal interest. It relates not only to rational therapeutic decision-making but also to payor and quality of care needs and decision-making. Such information is needed more critically now than ever before. The cost to provide continuing information and standards about a medicine is borne primarily by the private sector—and increasingly the information itself is a web-based commodity. Multiple compendia provide a basis for reimbursement, and many hundreds, if not thousands, of pharmacy and therapeutic committees provide administrative decisions to support cost-effective treatment for defined populations. USP's foray into drug information and use standards might build on the organization's ongoing responsibility for maintenance of the Medicare Model Guidelines. Many other organizations also are involved in such standards, and USP would necessarily ally with them in its "neutral convener" role in any further standards-setting attempts. Increasingly, as a dominant payor, the United States Federal government is involved, and a public-private model of some sort might be optimal. If such a model is considered, financing, scope, governance, and many other questions and challenges will arise.

With the exception of the every-three-year Medicare Model Guidelines updates, or the most part, USP has exited activities associated with the provision of drug information and use standards. The larger question for the organization now relates to its specific role as a practitioner-based, volunteer-driven, standards-setting organization. USP can do anything it wishes in the way of drug information and use standards, being bound only by resource constraints. The issues for consideration in this white paper might thus be:

- In an era of health care crisis and reform, what are the societal needs for drug information and use standards to support rational therapeutic decision-making?
- If these needs can be defined and USP, by virtue of its structure and history, can uniquely fulfill them—with availability of adequate resources—does it have a responsibility to do so?

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## USP'S HISTORY IN DRUG INFORMATION

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### 1. UNITED STATES DISPENSATORY

When the first *United States Pharmacopeia (USP)* appeared in 1820, it deliberately excluded most explanatory material regarding preparation techniques, which the authors considered to be too rudimentary. However, a need did exist for a Dispensatory—a volume that would not only select official drugs and provide recipes for preparations, but would also give full descriptions and indications of the drugs and explain applicable practitioner techniques. George B. Wood and Franklin Bache, two of USP's founding physicians, produced the first *Dispensatory of the United States of America (USD)* in 1832. They viewed its purpose as both instructional (for poorly trained physicians and pharmacists) and as a means to solidify the national authority of the *USP*, to which the *USD* deferred. The *USD* went on to become one of the most popular American medical reference books of the 19<sup>th</sup> century, overshadowing the *USP* itself in terms of everyday usage. The *USD* continued to be popular well into the 20<sup>th</sup> century, but started to lose its authority with the rise of the Food and Drug Administration and other sources of drug information as they emerged. Its link to the *USP* was formally severed in 1880. The last (27<sup>th</sup>) edition of the *USD* was published in 1973.



## 2. USP DI SERIES

The *USP Drug Information* resource (*USP DI*) was created in 1980 as a complete, unbiased compilation of clinically relevant information about therapeutic products, for the use of practitioners (physicians, nurses, pharmacists) and patients. *USP DI* was recognized in the Social Security Act as an authority for reimbursable off-label use under Medicare and Medicaid. It comprised three volumes—*USP DI Volume I: Drug Information for the Health Care Professional*; *USP DI Volume II: Advice for the Patient*, and *USP DI Volume III: Approved Drug Products and Legal Requirements*. Originally produced in print format only, a *USP DI* product line extension in the form of an interactive laser disk focusing on a single disease (About Your Diabetes) was attempted in the late 1980s. Maintenance proved a costly and time-consuming hurdle, and the disk was discontinued in the mid-1990s.

Another attempt to move the *USP DI* into the increasingly important online delivery mode was attempted in 1994, when USP acquired the Drug Evaluations database from the American Medical Association (AMA-DE). The goal was to integrate the AMA-DE data into the *USP DI* database. Again, technical complexity and the difficulty and expense of maintenance led to the project's termination. A third attempt to develop a *USP DI* relational database was launched in the mid-1990s, this time contracting with Carepoint, a provider of pharmacy management software. Yet again, the program was abandoned due to technical complexity and costs. In 1998, USP sold the *USP DI* database and licensed the *USP DI* trademark to Thomson Healthcare, but retained editorial oversight of the off-label use material in the publication. In 2000, Thomson launched the *USP DI* Desktop Series CD ROM, capturing a "large share" of healthcare web portal and hospital web site segments with *USP DI* branded content. However, changes in some state pharmacy regulatory requirements in 2001 resulted in a sharp decline in the number of pharmacies ordering the product. In addition, the chain pharmacy market was demanding a single vendor for all electronic solutions, which the Thomson *USP DI* could not provide. USP and Thomson explored a variety of strategic options over the next few years, but ultimately it made the most financial and operational sense for USP to exit the business completely. In 2004, the *USP DI Volume I* and *Volume II* became the responsibility of Thomson Healthcare. Under the agreement, Thomson could edit, create content, and publish these texts under the *USP DI* name until the 2007 edition, after which Thomson's right to use the name ceased. *USP DI Volume III* continued to be owned in its entirety by USP. Thomson continues the *USP-DI* product under the name *DrugPoints*.

Many other entities have provided drug information in various compendia to support sound therapeutic decision-making. An analysis of these types of compendia appeared in a series of three articles earlier this year in the *Annals of Internal Medicine*; a summary editorial references the three articles.<sup>1</sup> Overall these articles and summary editorial are generally critical of the various compendia in terms of their currency, consistency, and other factors.

## 3. MODEL GUIDELINES

The Medicare Modernization Act (MMA) of 2003 defines the role of USP (Section 1860D-4(b)(3)(C)):

*(ii) MODEL GUIDELINES – The secretary shall request the United States Pharmacopeia to develop, in consultation with pharmaceutical benefit managers and other interested parties, a list of categories and classes that may be used by prescription drug plans under this paragraph and to revise such classification from time to time to reflect*

<sup>1</sup> Sox, HC. 2009. Editorial: evaluating off-label use of anticancer drugs. *Annals of Internal Medicine*, Volume 150, Number 5



*changes in therapeutic uses of covered part D drugs and the additions of new covered part D drugs.*

In addition, Section 1860D-11(e)(2)(D) creates a “safe harbor:”

*(ii) USE OF CATEGORIES AND CLASSES IN FORMULARIES – The Secretary may not find that the design of categories and classes within a formulary violates clause (i) if such categories and classes are consistent with guidelines (if any) for such categories and classes established by the United States Pharmacopeia.*

With this legislative mandate and on behalf of the Secretary of the Department of Health and Human Services, the Centers for Medicare and Medicaid (CMS) awarded USP a cooperative agreement to develop and revise the Part D Prescription Drug Benefit Model Guidelines. A new Model Guidelines Expert Committee was formed to accomplish the task. While the MMA did not specify the frequency of updates to the Guidelines (“...from time to time...”), the Expert Committee and CMS agreed that an annual update was appropriate given the rapidly evolving nature of pharmaceuticals. Version 1.0 was a large effort, involving a review of how other formularies are categorized and presented.

At its highest usage (2006), 74% of health plans were using the USP Model Guidelines (Version 1.0). The Model Guidelines Categories and Classes provided a formulary structure that helped ensure beneficiary access while preserving needed flexibility for pharmacy benefit managers (PBMs) and health plans. USP developed an additional component to the Model Guidelines: Formulary Key Drug Types (FKDT), which offered additional protection for beneficiaries and a useful tool for CMS in reviewing formularies. Although not mandatory, the FKDT have been utilized by CMS as part of its Formulary Review Guidance, and serve as standards that promote consistency, fairness, and ease of administration. Usage of the Model Guidelines lessened in subsequent years, primarily due to plan consolidation and a broader use of internal classification systems due to plans’ comfort with the CMS process. Nevertheless, the guidelines contributed substantially to the availability of a comprehensive, yet affordable, benefit. As with all its standards, USP actively solicited and welcomed participation and input on Guidelines development from interested stakeholders, including manufacturers, drug plans, practitioners, and patients. USP’s experience with the Model Guidelines was summarized in a report published in *Annals of Internal Medicine* in 2006.<sup>2</sup> Its work on behalf of the Federal government followed a primary activity where USP participated in a consortium of interested organizations to produce a document entitled “Principles of a Sound Drug Formulary System” (2000).<sup>3</sup>

By 2008, CMS decided that the Guidelines had achieved a significant level of success and stability. Based on this, USP and CMS agreed to move from an annual revision timeline to a three-year cycle. CMS continues to use the current Model Guidelines and FKDT through plan year 2011, and USP is maintaining the current versions on its web site. The goal is for USP to start work on Version 5.0 in 2010.

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<sup>2</sup> Narrative review: the US Pharmacopeia and Model Guidelines for Medicare Part D Formularies. USP Model Guidelines Expert Committee, USP Staff [Williams, RL] *Ann Intern Med* 145, 448–453 (2006)

<sup>3</sup> <http://www.usp.org/hqi/patientSafety/resources/soundFormularyPrinciples.html> 2009



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## EXPLORATION OF NEW OPPORTUNITIES

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### 1. DRUG INFORMATION CONSULTATIONS

In 2005 and again in 2006, USP convened special meetings, called Drug Information Consultations, where individuals and organizations gathered to discuss the feasibility and advisability of developing practice standards associated with drug information. In these meetings, USP sought a clear understanding of the current gaps in drug information and where its standards-setting expertise might be used to augment information used by practitioners, plans, and patients in decision-making about rational drug use. At the time of these meetings, USP was engaged in the development of Model Guidelines for the Medicare Prescription Drug Benefit and was considering how that activity might also be supported with additional drug information for the healthcare community. Despite a number of useful suggestions from a broad range of participants, these consultations did not generate any specific activity (notes of meetings are available). A Board Task Force (2005-2010) was formed to monitor USP's interests in the topic.

### 2. APPLIED DRUG INFORMATION RESOURCE

Working with the American Medical Association, the American Nurses Association, and the American Pharmacists Association, USP led a series of meetings that explored the concept of an Applied Drug Information Resource (ADIR). The general idea for the ADIR was to advance “personalized medicine” concepts, in which general information about a medicine would be adjusted by patient-specific characteristics. The product would yield information directed to diverse practitioner and patient constituencies. The opportunity did not progress.

### 3. COMPARATIVE EFFECTIVENESS

Comparative effectiveness (CE) studies of specific treatment approaches—including various pharmacotherapies, lifestyle changes, imaging procedures, and surgical interventions—have great current and potential value. They add to the body of knowledge that helps health care practitioners, as well as patients and their families, make treatment decisions. The infusion of funds (through the American Recovery Reinvestment Act of 2009, also known as the “Economic Stimulus” Legislation) that will support additional research is a welcome development. The bill provides \$1.1 billion for CE research:

- \$300 million to the Agency for Healthcare Research and Quality (AHRQ);
- \$400 million to National Institutes of Health (NIH); and
- \$400 million to the Department of Health and Human Services (DHHS).

Observations about this funding that are relevant to USP include:

- Organizations can make proposals for CE project funding (the process is still being determined by agencies).
- According to the conference report, funding is not to be used to mandate coverage decisions, but instead is for generating useful research comparing clinical outcomes.

- The law also establishes the Federal Coordinating Council for Comparative Effectiveness Research, made up of high-level government officials, for the purpose of coordinating healthcare research across the Federal government.
- IOM has engaged the community in a better understanding of the types of CE studies needed.<sup>4</sup>
- AHRQ has conducted workshops and engaged in other tasks to generate evidence-based information and engage the community in understanding how database analyses can generate useful CE information.<sup>5</sup>

CE studies *per se* will be valuable and must, more frequently, become one of the inputs used by practitioners and patients to guide therapy following diagnosis, despite the fact that CE is sometimes linked in public discourse to rationing of healthcare. Diagnosis and treatment can be aided by development of a treatment model—captured and presented as a generally applicable set of process standards—that addresses key aspects of the decision-making process that are often considered in an ad hoc fashion, if at all. In turn, these process standards support treatment programs (protocols) to guide the practitioner and patient/consumer alike. These treatment programs themselves are also process standards that are frequently lacking for the individual patient when he or she leaves the immediate healthcare provider’s setting.

#### 4. PHARMACOTHERAPY GUIDELINES

Comparative Effectiveness results could be put into action through extended pharmacotherapy treatment standards. USP could serve as a convener of organizations to 1) develop an innovative, multidisciplinary, patient inclusive approach for integrating CE research study outcomes into pharmacotherapy standards/guidelines—treatment program standards—and 2) apply this approach to two separate, established, model standards or guidelines for particular disease treatments.

Aspects/features of the approach include:

- AHRQ-funded evidence-based studies, including CE studies;
- Conferences and Webinar(s); and
- Disease/condition candidates for which a wide range of treatment therapies exist, the cost of therapies varies widely, and which are part of a discrete patient population that would be affected.

In all cases, transparency of work would be emphasized, partners would represent the interdisciplinary health care team (including patients and payors), and USP committees and members would be part of the process.

#### 5. SPECIALTY MEDICINES

Specialty medicines are the product of innovative technologies (often, but not solely, biotechnology engineered molecules) that target unmet medical needs and are expensive because of limited patient populations, high cost of manufacture, and the increased risk and cost of development programs. In

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<sup>4</sup> [www.iom.edu/cepriorities](http://www.iom.edu/cepriorities) (July 2009)

<sup>5</sup> <http://www.ahrq.gov/clinic/outcomix.htm> (July 2009)



addition, the forced evolution of the pharmaceutical industry business model from reliance on historically successful but fading “blockbusters” to larger numbers of innovative specialty medicines requires higher prices to fuel growth.

Exacerbating the cost problem is that, as a consequence of structural and financial realities in the approval process and the costs and risks of development, these medicines are often used for unapproved indications for which evolving data sets are suboptimal when compared with data supporting their use in approved indications. Such use is generally for chronic, inadequately treated diseases with high morbidity and mortality, creating compelling demand for utilization and making it difficult to deny access. Access may seem arbitrary, depending upon the sophistication of the practitioner and patient in confronting the payor, which contributes to a growing sense of unfairness.

The payment for these medicines varies considerably among plans. Medicare covers specialty pharmaceuticals under Parts B and D, depending upon seemingly unrelated factors, including the route and place of administration. Therefore, care may be driven by reimbursement rather than clinical considerations. Both private and public (Medicare) payors use tier structures (essentially a cost shift to patients) to reimburse for these medicines. Since Medicare Part B (and most private plans) lacks out-of-pocket maximums and these medicines can cost tens of thousands of dollars per year, they are simply unaffordable for many under the current system.

To effectively allocate scarce health care resources, standards are needed to support rational therapeutic use of specialty medicines. These standards are now left to individual pharmacy and therapeutics committees, their health plans, and/or individual practitioner and patient decision-making. The question arises whether a national process could lead to standards to better inform these decisions.

The sensitive and inevitably controversial nature of these standards requires that this process be inclusive, transparent, and objective. USP possesses a structure and history that uniquely position it to achieve these objectives.

## 6. INFORMATION STANDARDS

USP’s Information Expert Committee chairs have advocated that USP provide information standards rather than the information itself. Such standards would serve as a framework within which others could create information. This concept relates directly to USP’s standards-setting and practitioner-based character and links the quality of patient care to the quality of the information used by healthcare professionals and patients. Examples of information standards (as distinct from information) could include the adequacy of research study design, methodology, analysis, and communication of results. Other standards could include:

- Linguistic competency for verbal or aural messaging and comprehension targeted at specific audiences, e.g., level of language used, languages available, visual depictions, words presented per minute;
- Cultural sensitivity in messaging: ethnicity, gender, age, etc.;
- Ethics in targeting vulnerable populations: elderly, children, terminally ill;
- Competency in decision-making: use of duress, undue influence, physical and mental capacity, etc.;



- Patient–provider relationships and conflicts of interest;
- Direct to patient advertising: "free" samples; and
- Requirements for post-regulation marketing surveillance.

## 7. NATIONAL AND INTERNATIONAL APPROACHES

Through its Essential Medicines List, the World Health Organization (WHO) has sought to provide a limited list of medicines to decrease inappropriate prescribing and promote rational use.<sup>6</sup> The WHO Essential Medicines List is used by many nations throughout the world to create national formularies that expand and/or contract the WHO list to meet local needs. In principle, USP's Model Guidelines provides a "table of contents" for a U.S. national formulary. Combining the approach with the AMA-DE in evaluating individual medicines within each category and class of the Model Guidelines further supports a U.S. national formulary, which does not now exist. The opportunities and challenges of such an approach are generally well known. An essential medicines list speaks to the best medicines within a country, region, or even the globe. In this context, it speaks to official medicines in the *United States Pharmacopeia*, which were always intended to be the best medicines. The *National Formulary* in the United States provided quality standards for non-official medicines. It was adopted by USP in the 1970s and has evolved into a book of excipient monographs. A seminal paper by T. Donald Rucker, Ph.D., argued that USP should advance a "true" national formulary in the U.S.<sup>7</sup>

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## SUMMARY

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At the outset, this white paper asked the following questions:

- In an era of health care crisis and reform, what are societal needs for drug information and use standards to support rational therapeutic decision-making?
- If these needs can be defined and USP, by virtue of its structure and history, can uniquely fulfill them—with availability of adequate resources—does it have a responsibility to do so?

The U.S. Federal government has turned to USP's standards-setting activities and expertise on many occasions over more than 100 years, not only when it recognized *USP* and *NF* as official compendia of the United States, but also for purposes of reimbursement on two occasions<sup>8</sup> and, more recently, to assure beneficiary access in the Medicare Part D legislation. In these cases, USP was recognized as a trusted, neutral organization that could bring together diverse stakeholders and make objective, science-based decisions through an open and transparent process. In the current state of healthcare reform and crisis, it may be time

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<sup>6</sup> Reidenberg, MM. Can the selection and use of essential medicines decrease inappropriate drug use?. 2009. *Clinical Pharmacology and Therapeutics*, Volume 85, Number 6.

<sup>7</sup> Rucker, TD. November 15, 1999. A public-policy strategy for drug formularies: preparation or procrastination?. *American Journal of Health-System Pharmacists*, Volume 56.

<sup>8</sup> Omnibus Budget Reconciliation Act of 1990 (Public Law 101-508) signed into law November 5, 1990 and The Omnibus Budget Reconciliation Act of 1993 (Public Law 103-66) 107 Stat. 312, enacted August 10, 1993. [http://assembler.law.cornell.edu/us-cgi/get\\_external.cgi?type=publ&target=103-66](http://assembler.law.cornell.edu/us-cgi/get_external.cgi?type=publ&target=103-66) ), ( <http://www.answers.com/topic/united-states-statutes-at-large> )



to call upon USP again. There is a deep logic, expressed in many countries over many years, for governments to seek non-governmental practitioner experts to achieve a public health good, such as drug information and use standards. But even if the U.S. Federal government does not turn to USP at this juncture, this does not mean that USP should not act. While USP has a need for sufficient financial resources to set drug use and information standards, it has access to the greatest resource of all: a cadre of healthcare experts from around the world who have, can, and could set, through activities of the Council of Experts, drug information and use standards in ways that would speak profoundly to patients and practitioners in a time of great need. The Council of the Convention Section on the Quality of Patient Care seeks creative thinking about a strengthened role for USP in setting drug use and information standards.