



**Report of the Chair of the Council of Experts
Roger L. Williams, M.D.**

Introduction by Dr. Williams

In the next 30 minutes or so, my colleagues and I will report on the work of the Council of Experts in this cycle. It is impossible to summarize fully the activities of so many committees working over a five year period. For more detail on these activities, I encourage you to read the written report of the Council's work that was provided in your Convention Member Notebooks. I know you will understand that even this more comprehensive report can scarcely cover adequately the remarkable work of the 62 Expert Committees of the Council of Experts in this cycle.

The 62 chairs of the Council of Experts were elected by you and your predecessors at the March 2000 Convention at this hotel--five short years ago. In the ensuing months, they worked to elect members of their committees, drawing from a large cadre of candidates, who had volunteered to serve on the committees up to the time of the Convention. The total number of volunteers in the Council of Experts at the beginning of the cycle was 651 and at the close now is 619. For the most part, changes in composition were minor--but not necessarily unimportant. Some distinguished chairs of Expert Committees and Committee members unfortunately departed the Council membership--and were replaced by equally distinguished chairs.

As I assumed the Council of Experts chair position at the 2000 Convention, one request I made was to have the Council of Experts organize themselves into four executive divisions--rather than the previous two (Drug Standards Division and Drug Information Division) that had been the case in prior cycles. In the ensuing years, we added a fifth group--termed the Dietary Supplement Multidisciplinary Coordinating Group--to better coordinate the work of four dietary supplement committees and an advisory panel. Based on these decisions, the overall structure of the Council of Experts at the close of the cycle is shown on the slide.

Following USP's rules and procedures, each division executive committee elected a chair. They are Judy Boehlert, Noncomplex Actives and Excipients Division Executive Committee, Sally Seaver, Complex Actives Division Executive Committee, first James Boylan and then Tom Foster, General Policies and Requirements Executive Committee, and Sandy Shepherd, Information Division Executive Committee. All but Dr. Seaver are in the audience today, as are other members of the Council of Experts and Expert Committee chairs.

I acknowledge them now and salute them for their intense and continuing service as volunteers to USP. While I don't regret the structure I imposed on the Council of Experts this cycle, which had both pros and cons, I will certainly acknowledge that it added substantially to the workload of the volunteers and staff. I acknowledge and express my sincere thanks and appreciation for this effort.

In the next few minutes, I have asked senior leadership from USP staff to summarize for you some of the key actions and work of the Council of Experts in the 2000-2005 cycle.

Dr. Eric Sheinin will speak on the standards-setting work of the Council of Expert that results in continuous revision of the *United States Pharmacopeia* and *National Formulary*. Mr. Bill Zeruld will speak on the work of the Information Expert Committees as they moved from providing value-added content for the USP-DI series to the Model Guidelines, working with the Centers for Medicare and Medicaid Services, under the December 2003 Medicare Modernization Act. And, Ms. Diane Cousins will speak to you about the work of the Safe Medication Use Expert Committee, in connection with USP's two reporting programs for medication safety—MEDMARX and the Medication Error Reporting Program.

Dr. Sheinin will begin.

Standards-Setting Activities for USP-NF by Eric B. Sheinin, Chief Science Officer

Thank you, Roger.

In the next few minutes I am going to provide you with a brief report on USP's progress in developing new monographs and in updating existing ones and then briefly discuss some other activities involving the Council of Experts. These efforts are directly related to our mission to promote the public health by disseminating standards and information developed by our volunteers, the Council of Experts and its Expert Committees.

As Roger indicated, at the start of the 2000-2005 cycle he formed four Divisional Executive Committees of the Council of Experts. Three of these Divisions, representing 31 Expert Committees, were intimately involved in the development of the content of *USP-NF*. This slide and the next two list the Expert Committees within each Division and the names of the chairs of each Committee. There were 13 Expert Committees in the Non-complex Actives and Excipients Division with the Executive Committee being chaired by Judy Boehlert. Non-complex actives are generally thought of as small, organic molecules.

The Complex Actives Division consisted of five Expert Committees; Sally Seaver was the chair of the Division Executive Committee. Complex actives are large molecules such as proteins, peptides, blood and blood products, etc.

Finally, the third Division focused on General Policies and Requirements. This Division consisted of thirteen Expert Committees. Jim Boylan chaired the Executive Committee for much of the cycle and Tom Foster, who was vice chair, assumed the chair position in 2004. The Expert Committees in this Division spent the majority of their effort creating and updating general chapters.

In March 2004, USP held the Semi-hemiquinquennial meeting to focus attention on this Convention and the 2005-2010 cycle. Many of the Council of Experts were in attendance at this meeting. Those attendees are shown on this slide along with Roger Williams. The chairs of our Expert Committees, as well as the members of those Committees, are to be commended for their dedication and contributions they made to USP and the public health.

USP-NF is published annually and is available in three formats, print, CD, and internet. Two *Supplements* are issued each year as a mechanism to update the compendia between editions. *USP28* is the 28th revision of the first *USP*, which was published in 1820 while *NF23* is the 23rd edition of the *National Formulary*. The two compendia have been published in a single volume since 1975.

The Ibuprofen tablets monograph is illustrative of a drug product monograph. The monograph consists of a series of tests, the analytical procedures used to monitor the tests, and the acceptance criteria that the article must meet when tested according to those procedures in order to be in compliance with the subject monograph. Drugs marketed in the United States must meet the standards contained in these monographs regardless of whether the manufacture chooses to label the article as USP or not.

As shown in the next slide, *USP28–NF23* contain over 4000 monographs for drug substances, drug products, excipients, dietary supplements, biologicals, and miscellaneous articles along with over 180 general chapters. However, based on products approved for marketing in the United States by the FDA, as well as other articles that are legally marketed, there are approximately 2000 additional monographs that could be included in the compendia. Furthermore, somewhere between 800 and 1200 current monographs are out-of-date in one or more areas and need to be updated. In this cycle we have made considerable progress in developing new monographs as shown in my next slide.

This graphic shows the number of new drug applications approved by FDA annually from 2000 to 2003 versus the number of new monographs that have become official each year from 2000 through the *1st Supplement* to *USP28–NF23*. During this period a total of 493 new monographs have become official. Clearly, USP has made progress toward meeting the goal expressed in our mission statement.

What about our progress toward reducing the backlog of missing monographs? In each year from 2000 to 2002 FDA approved more new drug applications than the number of new monographs that reached official status. In 2003, 139 monographs became official compared to the 72 new drug applications that were approved by FDA. This spike in monographs is attributed to a change in USP policy allowing monographs to move to official status despite the lack of availability of the required reference standards.

According to the General Notices to *USP28–NF23* any tests in these monographs requiring the use of an unavailable USP Reference Standard are not in effect until the specified USP Reference Standard is available. Thus, the tests not requiring the use of a USP reference standard became official two months after *USP26–NF21* or its *Supplements* were published. Some of the other tests have since become official as the missing reference standards have been added to our catalogue.

At this point, we do not have data on the number of new drug approvals in 2004 nor in 2005. However, from 2000 through 2003, FDA approved a total of 314 new applications compared to 315 new monographs becoming official. While it appears that we are at least maintaining the status quo, each new drug application approved for a new molecular entity generally includes at least two potential monographs. A new molecular entity can be considered as an active ingredient that had never been used in approved product in the United States prior to the FDA approval. Further, the new monographs becoming official include dietary supplement ingredients and products, some biological articles, and excipients while the FDA data only represent approvals by the Center for Drug Evaluation and Research. The bottom line is that our backlog of potential new monographs has grown considerably over these past five years.

All proposed new and revised monographs and general chapters are published in USP's bimonthly journal, *Pharmacopeial Forum*. This slide shows the number of proposed new and revised monographs that were published for public comment from 2000 through the first issue of *PF* in 2005. As would be expected, the data show considerable variability from year to year. However, it is obvious that there has been significant activity in this area. Yet, as I indicated, the number of potential new monographs continues to grow and the number of new monographs appearing in *PF* is not sufficient to begin reducing the backlog. In addition, there are still those 800 to 1200 monographs in need of revision. The large majority of the proposed revisions that appear in *PF* do not lead to the type of updating these monographs require.

USP relies mainly on the pharmaceutical industry to provide the information and data to support a proposed new monograph as well as a revision to an existing monograph. We appreciate our industry colleagues and their activities related to the compendia and the development of official USP reference standards. Their contributions allow USP to move forward in regard to the promotion of the public health through the creation of public standards. Despite the cooperation we receive from the industry, there continues to be those 2000 potential monographs and hundreds of monographs in need of updating.

USP has recently initiated an internal project utilizing our Research and Development Laboratory. Scientists in this laboratory are developing chromatographic assays for a number of drug substance monographs where the current procedure is a titration. Such an approach to the drug substance assay is in alignment with the current position of the Center for Drug Evaluation and Research which requires a stability indicating assay for these articles. Depending on the success of this effort, I look for an expansion of the laboratory's role in the coming cycle.

As part of the monograph acquisition and development activity, USP has posted a list of articles on our web site, that currently are without official monographs, but which are either off patent or will come off patent by the end of 2008. As shown on this slide, there are a total of 776 "high priority" monographs that could be developed for such articles. The list of "high priority" monographs is one mechanism for letting interested parties know which monographs are at the top of our list in terms of time remaining until patent expiration.

Working with three Project Teams composed mainly of industry representatives and some Expert Committee members, USP staff developed the Guideline for Submitting Requests for Revision to *USP-NF*. This guideline indicates the type and extent of supporting data and information that should be included in a *Request for Revision* regardless of whether the request involves a new monograph or a change to an existing monograph. This guideline is expected to lead to more complete *Requests for Revision*, which generally will decrease the time from receipt until publication in *PF* and eventual inclusion in the compendia. Currently there are four chapters in the guideline as shown on this slide. A draft chapter on blood and blood products is under development and a chapter on dietary supplement ingredients and products is under consideration.

In closing I would like to say just a few words about some other programs related to the standard setting activities of the Council of Experts. USP plans to release the Spanish translation of *USP29–NF24* in November of this year, in conjunction with the release of the English version. The *Supplements to USP29–NF24* will be translated into Spanish as well. In addition, we are considering translation of the compendia into other languages.

Another addition to our catalogue of publications is the planned release of the USP Pharmacists' Pharmacopeia in June of this year. This new compendium is designed to provide general information and monographs for compounded preparations to the practicing compounding professional. It probably will be available in a soft cover edition as well as electronically. Current plans call for the second edition to be available in January 2007.

In September 2004, working with significant input from the Council of Experts, Expert Committees, and other volunteers, USP held its first Annual Scientific Meeting. Approximately 350 pharmaceutical scientists attended and participated in eight separate tracks. Our volunteers served on planning committees for these tracks and presented many of the talks at the meeting. The second Annual Scientific Meeting will be held the last week of September 2005 in San Diego. Information flyers are available here at the Convention and on the USP website. During the 2000-2005 cycle USP sponsored or co-sponsored five open conferences in the United States as well as international conferences in Argentina, Brazil, China, and India. Several of our Expert Committee members participated in these important meetings.

Finally, I again would like to most sincerely thank all of our dedicated volunteers and USP staff who have worked so diligently to accomplish these achievements over the past five years. I look forward to the 2005-2010 cycle with anticipation and great enthusiasm.

Thank you for your attention. I will now turn the podium over to Mr. Bill Zeruld.

The Model Guidelines Expert Committee by William Zeruld, Vice President, Corporate and International Planning and Development

Thank you Dr. Sheinin.

The 2000-2005 cycle was marked by both the end of an era and the dawn of a new day for USP in the drug information arena. USP exited its involvement in the USP-DI, and yet, may have ended the cycle positioned to play an even more critical role in drug information via the Model Guidelines of the Medicare Prescription Drug Benefit.

For more than 20 years, the cornerstone of USP's contribution to the drug information field had been the USP-DI. When USP sold the DI database to Thomson Healthcare in 1998, the arrangement allowed for USP to continue to develop off-label use and other value-added information, as well as maintain editorial control. Unfortunately, during this past cycle, this arrangement – for a variety of reasons – became untenable. The result was a rapid decrease in the volume of activity for both the Information Expert Committees and USP staff. Therefore, in May 2004, at the direction of the USP Board of Trustees, USP and Thomson Healthcare made significant changes to the original agreement, including:

- 1) USP's exit from contributing content to and providing editorial oversight to the USP DI; and
- 2) Termination of the non-competition clause on December 31, 2006 - many years earlier than originally established.

This latter change reopens a door that had been closed to USP during this past cycle. Before the first half of the 2005-2010 cycle is reached, USP will no longer be restricted in the types of drug information activities it takes on. One activity that USP anticipates expanding is the development of drug information articles for publication in peer-reviewed journals. USP has initiated its venture in this area with a 2004 agreement with the American College of Physicians to develop articles for publication in the *Annals of Internal Medicine*.

Another activity that USP is currently engaged in is the development and testing of algorithms regarding potential drug-drug interactions. This initiative, involving USP's Therapeutic Decision Making Expert Committee, is occurring in collaboration with several organizations, including the Academy of Managed Care Pharmacy.

While these two activities represent important steps for USP in the area of drug information, the naming of USP in the Medicare Modernization Act of 2003 represents a giant leap forward for the organization and its contribution to the public health.

In the Beneficiary Protections section of the law, USP was named to develop Model Guidelines - a list of categories and classes that may be used by prescription drug plans as they develop and design their formularies. To take on this activity, USP's efforts were supported under a \$1.1M cooperative agreement with the Centers for Medicare and Medicaid Services, or CMS. The agreement was for an eight-month period, beginning May 1 and ending December 31, 2004.

Under this agreement, USP was asked to: develop the Model Guidelines; conduct an Outreach Program to solicit input from interested parties; and provide a comprehensive listing of drugs associated with the categories and classes of the Model Guidelines. As part of these deliverables, USP also was asked to perform an environmental scan of existing formulary classification systems and provide CMS with a summary of USP's approach and methodology for creating the Model Guidelines.

At the center of this activity was the newly created Model Guidelines Expert Committee. These volunteers were drawn from USP's existing Expert Committees. USP issued a call for candidates and specified areas of expertise that were of particular interest. Nearly fifty experts responded to the call, facilitating the creation of a highly-qualified committee with 17 volunteers plus the chair of the committee, Roger Williams. This dedicated group of volunteers truly exhibited commitment to the public health, as manifested by their bi-weekly meetings - 14 in all over the eight months; several of which were two-day meetings. In addition to their time, they contributed significant expertise and true passion to fulfilling our mandate.

Of course, they were not alone in taking on this highly visible and at times, highly controversial activity. For example, the Expert Committee was provided with an environmental scan, performed on behalf of USP by Booz Allen Hamilton. This scan included results of secondary research as well as over fifty interviews with stakeholders across the healthcare spectrum. USP also created four Advisory Forums for the purpose of giving these constituencies - beneficiaries, drug plans, manufacturers, and providers - a voice into the process.

The Outreach Program that USP offered included several components: 1) a public meeting held in Baltimore, which drew nearly 750 total participants, 2) a formal public comment period, which resulted in nearly 1,300 submissions to USP, and 3) consultations with 22 organizations. This Outreach Program enabled any interested party the opportunity to participate in the development of the Model Guidelines. USP supplemented this effort by using its website as a means to communicate information about USP's process, updates on the status of USP's efforts, and more.

An extremely valuable resource to the Model Guidelines Expert Committee was the existing body of Information Expert Committees. These committees were able to lend their in-depth knowledge in their specialty areas to the proceedings, supporting critical decisions of the Model Guidelines Expert Committee. In total, the members of the Model Guidelines Expert Committee as well as those of the other Information Expert Committees volunteered nearly 3,000 hours of their time over this eight month period.

At the foundation of this enormous set of activities was the USP staff. Information specialists, meeting planners, legal experts, public relations staff, IT staff, and many others worked very closely and intensely to ensure that the Model Guidelines Expert Committee had what it needed to complete the project on time.

As the project director for this entire set of activities, I was privileged to be in a position to see how all of the components fit together. While there were different points of view and perspectives offered throughout the process, all of the parties who participated were united in their desire to see the creation of Model Guidelines that would be used to the benefit of the public health and that would support the successful implementation of the Medicare Prescription Drug Benefit.

The Model Guidelines signify a renewal for USP in the drug information arena. USP looks forward to working with CMS to revise and maintain the Model Guidelines over time based on, in the words of the law, "changes in therapeutic uses of covered Part D drugs and the additions of new covered Part D drugs." Ideally, this effort will require implementation of a comprehensive drug information service supported by a new slate of Information Expert Committees. Only through continuous vigilance and monitoring of the drug information landscape can USP maintain the currency and relevance of the Model Guidelines and thus support good pharmaceutical care for the Medicare population and beyond.

USP's involvement in the Model Guidelines activity in combination with the ending of the non-competition clause in December 2006, result in great optimism and excitement for USP and the Information Division in the 2005-2010 cycle.

Before we move to this future, however, I would be remiss if I did not take this moment to extend USP's great appreciation to the Information Expert Committees of the 2000-20005 cycle and thank them for their passion, their patience, and their contributions. It has been a challenging cycle in many ways and your dedication and commitment to USP during this time has been an integral part to laying the foundation for this expansive future.

I would like now to turn the podium over to Ms. Diane Cousins.

*The Patient Safety Expert Committee/USP's Reporting Programs by Diane D. Cousins, R.Ph.,
Vice President, Center for the Advancement of Patients Safety*

USP has operated reporting programs for nearly 35 years and more specifically, medication error reporting programs for nearly 15 years. Yet, in the 2000-2005 cycle, for the first time, this activity became a formal part of the USP standards-setting process through the Safe Medication Use (SMU) Expert Committee, chaired by Dr. William Kelly of Mercer College of Pharmacy. The Committee is considered a cross-cutting Expert Committee because the nature of its work contributes to both information and standards development. The charges of the committee are to:

- Review and analyze reports submitted to USP's reporting programs;
- Recommend, develop, and revise standards for *USP-NF*;
- Make recommendations to the National Coordinating Council for Medication Error Reporting and Prevention; and
- Make recommendations for the development and strengthening of USP's reporting programs.

The Safe Medication Use Expert Committee has 18 members from medicine, nursing, and pharmacy, including academicians, researchers, clinicians, and representatives from government and consumer interests. There are 4 major work groups and eight task forces to conduct data analysis and to address findings. The committee also organized and participated in the work of two project teams — one for Standardized Imprint Codes, and the other for Computerized Prescriber Order Entry or CPOE.

To conduct its work, the Safe Medication Use Expert Committee interacts with other expert committees such as Nomenclature and Labeling, Parenteral Products - Industrial, Pharmaceutical Dosage Forms, the Pediatric Expert Committee, and Packaging, Storage, and Distribution. While there are many work products of this committee, among the most significant are recommendations for patients, caregivers, practitioners, and facilities. For example, based on the committee's analysis of medication error reports, recommendations were issued on such topics as the safe use of insulin products, use of patient-controlled analgesia pumps, safe storage and use of neuromuscular blocking agents, and error avoidance recommendations for pediatric and geriatric populations.

In addition, The Safe Medication Use Expert Committee recommended *USP-NF* labeling and packaging changes. Following are three of those:

- First, because of fatal mix-ups of medical gas cylinders in hospitals, for example Nitrous oxide confused with oxygen, an in-process proposal in *Pharmacoepial Forum* suggests that distinguishing colors used for plastic collars of the valve fittings should be extended to the entire cylinder in the event the collar is missing or damaged. This ongoing work involves the Safe Medication Expert Committee, The Aerosols Expert committee, and the Packaging, Storage, and Distribution Expert Committee.
- Second, medication errors resulted when labeling of multi-dose and single-dose vials was misunderstood by practitioners to mean that the vial contained a total of 20mg, as in the case of Camptosar shown here.

The committee proposed that "For multiple-dose and single-dose injectable drug products the strength of the total vial content, here 100mg in 5ml, should be the primary and prominent expression on the principal display panel of the label. This should be followed in close proximity by strength per milli-liters enclosed in parentheses.

- Third, to give prominence to required warning information on injectables, only cautionary statements may be printed on the top surface of the ferrule and cap overseal of a vial containing an injectable drug as shown here.

There are currently two USP requirements for such warnings: Potassium Chloride, which carries the warning "Must be diluted," and Neuromuscular Blocking Agents, as a class, which carry "Warning: Paralyzing agent", the latter accomplished during this cycle.

As the 2005-2010 Safe Medication Use expert committee engages, several works-in-progress will carry over.

These include recommendations for tablet splitting, decision support rules for CPOE systems, and recommendations to avoid medication errors in the home. In the coming cycle, the contributions and accomplishments by the Safe Medications Use Expert Committee will bolster USP's role in medication safety and amplify impact on public health.

Conclusion by Dr. Williams

I would like to thank most sincerely Eric, Bill and Diane for these informative presentations. USP's core activity is standards setting. For this reason, the summaries you have just heard emphasize the primary work of USP over the last five years. These fine and continuing efforts of the Council of Experts not only result in official and authorized text in *USP-NF*, the Model Guidelines, and other publications of USP, they undergird all USP products and services. Specifically, they support the availability of official USP Reference Standards. I would be remiss in this regard if I didn't acknowledge the especially hard work of the Council of Experts' Reference Standard Committee in this cycle

In prior cycles, as well as the current one, this committee functions as an ad hoc committee of the Council of Experts. I will acknowledge Dr. Sheinin's fine chairmanship in this cycle. And, I salute and honor the members of this committee, which work intensely and diligently to review all relevant data sets in advance of a reference standard becoming available in the USP catalogue. This catalogue is large and growing, and each listing usually requires some consideration of data by the USP Reference Standards Committee. Please note that members of this committee in this cycle were drawn from standing Expert Committees, so they accomplished their hard work in addition to all their other volunteer activities. As Convention Members now know, we have changed our approach in this cycle so that the chair of the Reference Standards Committee is elected. You are now in the process of voting for this important chair position.

In the 2000-2005 cycle, USP established a series of Stakeholder Forums and Project Teams to expand our outreach to manufacturers and other stakeholders. These interactions focused on key topics of importance, which were developed by the Stakeholders at the beginning of the cycle. Subsequently, in the cycle, Project Teams were organized around these key topics. Unlike the Council of Experts and Expert Committee members, Stakeholder Forum and Project Team members serve as representatives of a particular interest group or company and add their organizational perspectives to the discussion. Stakeholder Forum and Project Team deliberations are advisory to the Council of Experts, its Expert Committees, and staff.

In closing, I can only say—speaking from the heart and with the most sincere appreciation—sincere thanks to the Council of Experts in the 2000-2005 cycle. Your work will be long-remembered in the years to come, as we advance the standards-setting activities of the USP to meet the needs of patients and practitioners throughout the U.S. and the world.

