Report of the 2005-2006 Task Force on Standards for Compounding

Members Present:
Judy Gardner (GA), Chair; Charles L. Haytaian (RI); Dennis M. Jones (SD); Sheila Mitchell (TN); Wallace Nelson (NC); Richard R. Smiga (PA); and Susan L. Warren (CO).

Ex Officio Members:
Roger L. Williams, MD, Vice President & CEO, United States Pharmacopeia (USP); Brenda Uratani, Food and Drug Administration (FDA); and Samia Nasr, FDA.

Others Present:
John R. Dorvee, Jr, Executive Committee liaison; Carmen A. Catizone, Eleni Anagnostiadis, Charisse Johnson, Chris Siwik, Donald Talend, NABP staff; and Tameka Houston, NABP pharmacy student intern.

Introduction:
The Task Force on Standards for Compounding met on November 11, 2005. The appointment of this Task Force came at the direction of the NABP Executive Committee in response to Resolution 101-2-05, Sterile Compounding and the Model State Pharmacy Act and Model Rules (Model Act) of the National Association of Boards of Pharmacy.

During the NABP 100th Annual Meeting in April 2004, held in Chicago, IL, the NABP delegation passed Resolution 100-11-04, Sterile Products, which directed NABP to communicate to its member board’s information concerning United States Pharmacopeia (USP) Test and Assays Chapter 797 (USP Chapter 797), “Pharmaceutical Compounding–Sterile Preparations,” and its integration into the Model Act. Subsequently, during the NABP 101st Annual Meeting in May 2005, held in New Orleans, LA, the NABP delegation passed Resolution 101-2-05, Sterile Compounding and the Model Act, which directed NABP to review and revise, where appropriate, its Model Rules for Sterile Pharmaceuticals to reflect applicable standards set forth in USP Chapter 797 in all practice settings that will protect the public health, as well as the safety of the pharmacist and pharmacy technician involved in the compounding of sterile pharmaceuticals.

Review of the Task Force Charge:
Task force members reviewed their charge and accepted it as follows:

This Task Force is charged with reviewing standards set forth in USP Chapter 795, “Pharmaceutical Compounding–Nonsterile Preparations,” and USP Chapter 797, “Pharmaceutical Compounding–Sterile Preparations,” to recommend revisions and provide comments to USP on the respective standards.

USP Presentation:
Roger Williams, MD, vice president and CEO, USP, provided an overview of USP Chapters 795 and 797 and discussed the proposed revisions to USP Chapter 797 per the USP Sterile Compounding Committee. Dr Williams began by reviewing the role of the state boards of
pharmacy and Food and Drug Administration (FDA) in enforcing various USP standards. In addition, he provided a list of USP chapters that are applicable to pharmacy compounding in both community and health system practice settings. During his presentation he addressed USP Chapter 1075, “Good Compounding Practices,” which outlines the general practices to adhere to when compounding non-sterile or sterile preparations. Dr Williams also reviewed the major components of USP Chapter 795 including the responsibility of the compounder, selection and sources of ingredients, quality control, and the stability of non-sterile compounded preparations. Dr Williams reiterated to the Task Force members that USP Chapter 797 addresses the procedures and requirements for compounding sterile preparations including the facilities for such preparations; the training and assessment of personnel regarding the principles and practices of aseptic manipulations; air quality evaluation and maintenance; and principles and practices of sterilization and solution stability. He also addressed the organization and components of USP Chapter 797, emphasizing the risk-based approach in applying the standards based upon the risk level of the sterile preparation being compounded. Dr Williams concluded his presentation by reviewing the proposed revisions to USP Chapter 797 and informed the Task Force members of an upcoming USP Expert Committee Meeting to discuss public comments received regarding USP Chapter 797.

**Recommendations**

**Recommendation 1:** The Task Force agreed that the practice of compounding is a complex area of growing concern. The Task Force recommends to the Executive Committee that NABP communicate to the state boards of pharmacy that increased scrutiny should be directed to compounding activities with equal emphasis on sterile and non-sterile compounded preparations.

**Background:**

Although the Task Force members recognized the inherent risks that incorrectly prepared contaminated intravenous compounded medications pose to patients, they also acknowledged that non-sterile compounded medications (such as topical creams, gels, and ointments) may pose significant risks as well, and therefore require the state boards of pharmacy to be equally vigilant and proactive concerning the regulation of non-sterile compounding. The Task Force members discussed recent cases in which two women died due to lidocaine toxicity after applying a pharmacy-compounded combination of lidocaine and tetracaine topical gel for a medical spa related procedure.

The Task Force members also agreed that the state boards of pharmacy continue to encounter pharmacies that “manufacture” bulk preparations under the guise of compounding. The Task Force reiterated that the state boards of pharmacy should consider such factors as the compounded prescription volume, existence of a practitioner/patient/pharmacist relationship, the use of commercial scale manufacturing or testing equipment for compounding drug products, and whether or not the compounded product is a copy, or essentially a copy, of a commercially available FDA-approved drug product in the market place in distinguishing legitimate compounding from manufacturing.
**Recommendation 2:** The Task Force recommends to the Executive Committee that NABP continue to work with USP and FDA to clarify the application of USP compounding chapters to the pharmacy profession based upon risk-based assessments of compounding practices.

**Background:**

USP Chapter 797 recognizes three risk levels (low, medium, and high risk) of compounded sterile preparations based upon the probability of microbial, chemical, and physical contamination. Based upon the risk level, USP Chapter 797 provides general guidance on the compounding manipulations, equipment requirements, and specification of the compounding environment. Generally, high risk compounded sterile preparations require the most stringent and comprehensive quality assurance procedures that compounding personnel must adhere to including suitable compounding environments. According to a survey NABP administered in March of 2005, approximately nine states require compliance with USP Chapter 797; and information collected since the March 2005 survey indicates that additional states have begun to realign regulations with USP Chapter 797.

The Task Force members and FDA expressed concern that some pharmacies may not recognize the risk-based assessment approach of USP Chapter 797, which often results in the excessive and costly reconstruction of sterile compounding areas and purchasing of unnecessary equipment. Although extensive upgrades to compounding areas and procedures may be warranted and justified, pharmacies should investigate more cost efficient means to meet USP Chapter 797 compliance based upon the risk level(s) of compounding performed. Therefore, the Task Force recommended that NABP collaborate with USP and FDA to communicate to the pharmacy profession that a blanket implementation of the most stringent standards contained within USP Chapter 797 may be onerous.

**Recommendation 3:** The Task Force recommends to the Executive Committee that NABP continue to work with USP to ensure that USP Chapters 795 and 797 provide standards and guidance that are valid, justifiable, and reasonable to achieve integrity of the compounded preparation in consideration of patient safety.

**Background:**

The Task Force members expressed concern that some standards identified in the USP compounding chapters, particularly USP Chapter 797, may require a level of care that is beyond the level of care needed to ensure the safety of the patient. The Task Force agreed that the standards should be based primarily upon sound scientific research that corresponds with the level of rigor necessary to achieve the accepted level of quality for the compounded sterile preparation. Conversely, the Task Force members cautioned that standards within USP Chapter 797 should also meet existing practice guidelines to ensure patient safety.
Recommendation 4: The Task Force recommends to the Executive Committee that NABP endorse the adoption of USP compounding chapters within the Model Act.

Background:
The Model Act’s Good Compounding Practices Applicable to State Licensed Pharmacies currently recognizes and mandates that pharmacists and pharmacies practice in accordance with the current USP-NF Chapters on compounding and sterile product preparation. This addition to the Model Act was pursuant to the recommendation of the 2002-2003 NABP Committee on Law Enforcement/Legislation. Subsequently, the 2004-2005 Committee on Law Enforcement/Legislation amended the Model Rules for Sterile Pharmaceuticals to be consistent with USP Chapter 797, which considers the risk level of sterile products being compounded.

Although agreeing that the state boards of pharmacy incorporate USP chapters on compounding into state rules and regulations, Task Force members cautioned that NABP and the state boards of pharmacy recognize that USP is working to revise USP Chapter 797 in consideration of comments, revisions, and suggestions received from the health care professional community.

Recommendation 5: The Task Force recommends to the Executive Committee that NABP and the state boards of pharmacy continue to engage in collaborative efforts with the FDA, USP, Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and other stakeholders to define and address compounding activities in a cohesive and unified manner.

Background:
The Task Force members agreed that uniformity among conforming assessment bodies, such as the state boards of pharmacy and JCAHO, could ensure consistency and recognition of one standard in pharmacy compounding. In July of 2004, JCAHO began to survey for compliance with USP Chapter 797. The Task Force members also recommended that the state boards of pharmacy work cooperatively with the FDA with respect to investigations and enforcement activities in consideration of the existing NABP/FDA Memorandum of Understanding.

Recommendation 6: The Task Force recommends to the Executive Committee that NABP work with USP and FDA to develop training workshops and educational programming for the state board of pharmacy inspectors/compliance investigators and other NABP members on USP compounding chapters and compounding practices.

Background:
As more states begin to incorporate regulations and rules mandating compliance with USP Chapter 797 and other USP compounding chapters, the Task Force members agreed that state board of pharmacy inspectors/compliance investigators could benefit from training and educational programming. The Task Force recommended that NABP collaborate with USP and FDA to develop educational opportunities. USP volunteered to participate in this effort and indicated it was necessary and beneficial.