Report and Recommendations to the North Carolina Board of Pharmacy

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Pharmacy Compounding Work Group

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In November 2012, the North Carolina Board of Pharmacy (NCBOP) charged the Pharmacy Compounding Work Group (PCWG) to comprehensively review the existing regulations governing pharmacy compounding, with a specific focus on sterile compounding practices. Additionally, the PCWG was charged with reviewing the NCBOP’s execution of its existing authority. A copy of the charging document is attached to this report as Exhibit 1.

Members of the PCWG met four times (December 20, 2012, January 14, February 18, and March 25, 2013) to discuss the issues posed in the charging document. The PCWG interpreted its charge to assess broad, big-picture sterile compounding regulation issues. Accordingly, the PCWG endeavored to create a framework within which more effective, safe, and sensible sterile compounding regulations might be crafted. If the NCBOP elects to proceed with any recommendation of the PCWG, additional work to complete the regulatory framework may be required of NCBOP staff, the PCWG, external consultants, or other work groups.

The PCWG makes the following recommendations:

1. The NCBOP should require pharmacies engaging in sterile compounding to identify themselves to the NCBOP. Using existing regulatory power, the NCBOP should define sterile compounding by reference to USP standards. Pharmacies engaging in conduct meeting the definition of sterile compounding should be specifically identified so that Board staff can more easily and efficiently focus investigative and inspection resources on them.

The PCWG also recommends that identified sterile compounding pharmacies be further identified by sub-categories keyed to the particular type(s) of compounding the pharmacy performs – i.e., high-, medium-, and low- risk sterile compounding. Additional categories may be needed, also, for non-sterile compounding, and compounding for veterinary patients.

Presently, pharmacies applying for a North Carolina pharmacy permit may identify as a “compounding pharmacy”. The current self-identification measure neither differentiates between sterile compounding and non-sterile compounding, nor compounding risk level. The NCBOP should amend pharmacy permit applications to require those pharmacies engaging in sterile compounding to identify with specificity the types of sterile compunding performed.

2. In order to protect the essential purpose of the “office use” provision of Rule .1810 (21 NCAC 46.1810), the NCBOP is encouraged: (1) to explore ways to explain its interpretation and enforcement of the “office use” clause; and (2) create safeguards against abuse. Current North Carolina law includes an “office use” provision that allows “practitioners [to] obtain compounded drug products to administer to patients within the scope of their professional practice” even though “compounded drug products [may] not be offered to other entities for resale. 21 NCAC 46.1810(1).
The PCWG believes strongly that this provision serves important patient access functions, especially when a particular drug is listed by the FDA or ASHP as being in shortage. But the provision could be misused by unscrupulous compounders to stray into manufacturing. The PCWG believes, for instance, that compounding what are essentially copies of commercially available, non-shortage drugs and compounding products for practices to resell are common abuses of the “office use” provision. The PCWG recommends that the NCBOP clarify the rules relating to these abuses and any other abuses the NCBOP deems necessary.

Ultimately, the PCWG believes the “office use” provision should be preserved in favor of patient access functions over striking the clause because of the dubious actions of the few.

3. The NCBOP should incorporate into its regulations USP 795 and 797 standards and enforce compliance by all compounding pharmacies. The PCWG believes that these standards reflect best practices in the field, and Board staff has consistently advised pharmacies in North Carolina that USP standards reflect best practices. Formally adopting USP 795 and 797 standards will keep North Carolina up to date with the national trend of states specifically incorporating them into regulations.

4. The NCBOP should encourage, but not require, sterile compounding pharmacies to seek accreditation from NCBOP-approved accrediting bodies. The NCBOP should approve accrediting bodies whose standards, at a minimum, comply with the NCBOP’s regulations. Additionally, the accrediting bodies must be able to adequately accredit either or both retail and hospital sterile compounding pharmacies.

The PCWG believes accreditation is an effective means of aiding the NCBOP’s public protection mission. The NCBOP could use a pharmacy’s accreditation status, or lack thereof, as a guide to efficiently allocate its inspection resources. Accreditation, however, will neither diminish nor supplant the NCBOP’s inspection and enforcement authority.

5. The NCBOP should modify existing inspection and investigation policies for compounding pharmacies to comply with appropriate USP standards and any newly promulgated regulations. Additionally, the NCBOP should provide training in the new policies and procedures to NCBOP investigators.

Presently, all NCBOP investigators have baseline training in sterile product preparation, and two NCBOP investigators have extensive training in USP 797 standards. New training should be focused on raising the training level of all NCBOP investigators on USP standards. Furthermore, a subset of investigators will be identified and trained to an expert level in USP standards. The NCBOP is strongly encouraged to seek outside expert advice in drafting the new policies and
procedures, and in training NCBOP investigators. Also, the NCBOP is encouraged to have outside experts assist NCBOP investigators when necessary.

6. The NCBOP should require all out-of-state compounding pharmacies either holding a North Carolina pharmacy permit or seeking a North Carolina pharmacy permit to comply with appropriate USP standards and all North Carolina regulations for sterile compounding. The PCWG believes out-of-state accountability is essential to protect North Carolina patients from sub-standard sterile compounds. The NCBOP is encouraged to determine the most effective method of monitoring out-of-state compliance, such as requiring accreditation or providing the NCBOP, annually, with inspection records evidencing compliance with USP standards.

7. The NCBOP should specifically encourage pharmacists to obtain high-quality, high-level continuing education in all compounding fields, but especially sterile compounding. To the extent that such courses are available, but not “accredited” by typical pharmacy CE accrediting agencies (such as ACPE), the Board should identify them, apply its own accreditation standards and/or work with the North Carolina Association of Pharmacists to apply accreditation standards, and publicize the courses’ availability and content. Assessment of compounding-specific continuing education obtained by pharmacists and technicians practicing in the field should be a standard part of a compounding pharmacy inspection or investigation.
Exhibit 1: PHARMACY COMPOUNDING WORK GROUP

Members

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Introduction

In early October 2012, health care providers in Nashville, Tennessee observed an unusual cluster of fungal meningitis cases traceable to patients who underwent certain spinal procedures at St. Thomas Hospital. Ultimately, public health officials traced the fungal contamination to three lots of preservative-free methylprednisolone acetate provided to pain and surgical clinics by the New England Compounding Center in Framingham, Massachusetts. Meningitis cases came to number in the hundreds, deaths in the dozens, and patients in over 20 states were affected.

On October 3, 2012, the North Carolina Board of Pharmacy summarily suspended NECC’s out-of-state pharmacy permit – the first state or federal agency to take action against NECC.

The NECC contamination case starkly reminds all state boards of pharmacy how critical their role is, and must be, in the protection of the public health and safety. Accordingly, the North Carolina Board of Pharmacy is conducting a comprehensive review of its regulatory power (and execution of that power) over compounding pharmacy, with a specific focus on sterile compounding.
**Charge to the Work Group**

The Compounding Pharmacy Work Group (“CPWG”) is charged to review the Board of Pharmacy’s existing statutory and rules-based framework for regulating compounding pharmacy practices, with a specific focus on regulation of sterile compounding practices. The CPWG shall recommend any changes to that authority deemed necessary or desirable.

The CPWG is also charged to review the Board of Pharmacy’s execution of its existing authority. The CPWG shall recommend any changes to the means by which the Board exercises that authority deemed necessary or desirable.

The CPWG is free, as it deems appropriate, to invite presentations and solicit input from persons or entities who are not members of the CPWG. After consideration of comments from the members and the public, the CPWG shall make a report and recommendations to the Board of Pharmacy.

Specific areas of focus shall include the following and other such issues as the CPWG deems appropriate for consideration in keeping with its overall charge:

1. Neither the North Carolina Pharmacy Practice Act nor Board Rules create “categories” for pharmacy permits.
   
   a. Should there be a special category of pharmacy permit for “compounding pharmacies” codified in the Pharmacy Practice Act? How would such a category be defined? What additional requirements for permitting would a “compounding pharmacy” have to meet? What different/additional fee, if any, would be imposed on a permit application/renewal for a “compounding pharmacy”?

   b. If a special category of “compounding pharmacy” permit were not created by statute, should a definition of “compounding pharmacy” be specifically added to Board rules? What would that definition be? What rules-based requirements would a “compounding pharmacy” have to meet for permitting?

   c. If neither statutory nor rule-based creation of a category is needed, how can the Board better track which pharmacies are specialized compounding pharmacies? Pharmacies are now required to self-identify that they compound, but this means that most pharmacies so identify (i.e., if they compound anything, at any level, they self-identify), making identification of truly compounding-focused pharmacies difficult.
d. Should compounding pharmacies be required to file periodic reports of the compounded products dispensed or otherwise transferred as a means of monitoring potential tipping into manufacturing?

e. Are there certain drugs whose compounding should be prohibited? E.g., NTI drugs?

2. Rule .1810 (21 NCAC 46.1810) sets forth specific “compounding” requirements. Is this rule sufficient? What additions or changes are needed?

a. Subparagraph (1) of that rule provides: “Compounded drug products shall not be offered to other entities for resale; however, practitioners may obtain compounded drug products to administer to patients within the scope of their professional practice.” This type of provision, prevalent in state rules, is often the purported justification used by compounders who drift into full-blown manufacturing.

i. Does the “office use” provision need to be repealed? Modified? Clarified? In what ways? By what means (e.g., interpretive guidance or rule amendment)?

ii. Should this rule set forth more specific standards dividing legitimate patient-specific compounding from manufacturing? If so, what standards are appropriate – e.g., incorporation of FDA CPG standards, incorporation of FD&C Act Section 403A standards?

3. With respect to sterile compounding, should Board rules incorporate USP 797 standards?

a. Existing Board standards for sterile product preparation are found in Section .2800 of the rules. Are they sufficient? If not, what are the deficiencies and how should they be remedied?

i. Specific expectations for quality assurance/quality control/continuous quality improvement?

ii. Specific testing requirements (e.g., sterility potency, pyrogenicity, fungal, facility microbial)?

b. A number of states have incorporated USP 797 into legal standards. A 2008 Board task force charged with looking into this issue made no headway.

c. If USP 797 incorporation is appropriate, at what level? Full incorporation? Partial incorporation? If the latter, on what public health and safety basis would some provisions be incorporated and others not?

d. If USP 797 incorporation is appropriate, which pharmacies should have to meet those requirements? Pharmacies that engage in any sterile compounding? Some “threshold” type/amount? If the latter, what defensible, evidence-based public safety reason would there be to set a threshold?
e. If incorporation is appropriate, what enforcement resources will be necessary to ensure compliance?

3 Should the Board require outside accreditation of some/all “compounding pharmacies” (however that term were to be defined, see #1 above)?

   a. If accreditation is desirable, for whom should it be required? A pharmacy that engaged in any compounding? A pharmacy that engaged in sterile compounding? If sterile compounding only, any quantity/type, or some “threshold”?

   b. What legal issues, if any, could be triggered by requiring accreditation? Delegation doctrine issues? Statutory authority issues?

   c. What public confidence issues are implicated?
      i. What accrediting options exist? Is PCAB the only viable option?
      ii. Should NC law provide a mechanism whereby accreditors can become recognized? If so, what criteria?

4. Are changes to the Board’s methods of inspection/investigation of “compounding pharmacies” needed?

   a. Neither the Pharmacy Practice Act nor Board rules require that any pharmacy be routinely inspected at a specific interval. As a practical matter, most pharmacies in North Carolina are inspected every 2-3 years either as a “routine” matter or as part of a complaint investigation.

      i. Should the law require specific-interval “routine” inspections? If so, for all pharmacies? For “compounding pharmacies” specifically?

      ii. If “routine” inspections at regular intervals are proper, at what interval? Can current Board investigative resources absorb such a change? If not, what additional or different resources are needed?

      iii. Should the law require in all cases a pre-opening inspection for a “compounding pharmacy”? If so, for all compounding pharmacies? For sterile compounding capability only? See (b) below for related questions about inspector/investigator resource and training considerations.

   b. Do Board of Pharmacy inspectors/investigators need additional training to effectively inspect “compounding pharmacies”? If so, what approach(es) are optimum:
i. Train 1-2 inspectors as “compounding/sterile product preparation experts capable of an independent “deep dive” inspection?

ii. Train all inspectors to a “triage” level of “compounding/sterile product preparation” expertise. All capable of identifying red flags that would trigger a “deep dive” inspection. Most inspectors have this baseline knowledge.

iii. If “deep dive” inspections are beyond the reasonably reachable/affordable capabilities of in-house inspectors, what persons or entities should be brought in to do them?

iv. What specific outside training/inspection/investigation resources are available for compounding issues generally and sterile compounding particularly?

5. What special issues with respect to permitting and regulating out-of-state compounding pharmacies require action?

a. See question #1 concerning specific definitional issues to consider with respect to compounding pharmacies.

b. What specific questions should the Board add/change/delete on its out-of-state permit application affidavit concerning compounding? Are there “tripwire” questions that need to be incorporated? What should they be?

c. Should the North Carolina Board conduct inspections of out-of-state compounding pharmacies? As a condition of initial permitting? Periodically? If this is desired, what resources would be necessary to accomplish this end? Does the Board have sufficient existing resources, or should the Board seek statutory authorization to charge special fees for such inspections (see generally question #1 concerning potential regulatory changes).