Chapter 2

Standards for Compounded Sterile Preparations

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Introduction

Poor sterile compounding practice has caused much patient harm and many deaths, but it was the New England Compounding Center tragedy that caused 64 deaths and 753 illnesses in 2012, which changed the world of sterile compounding laws, regulations, and standards (Chapter 1).[1] Such changes included the federal Drug Quality and Safety Act (DQSA) of 2013 and renewed emphasis by accrediting agencies on the compounding and outsourcing of sterile preparations.

The purpose of this chapter is to alert compounding personnel to the agencies that will change their training, practices, and facilities. The chapter covers the major changes wrought by national and state bodies since the previous edition of this textbook. The agencies below are arranged in descending order of the likelihood they will enforce standards for pharmacists and pharmacies that compound sterile preparations. Make no mistake—citations by agencies such as these can lead to revoked licenses, ruined reputations and careers, bankrupted businesses, and even imprisonment for perpetrators.[2-6]

According to a 2015 Survey of Pharmacy Compounding of 349 hospitals, regulators had visited more hospitals asking about sterile compounding in the previous 2 years: 75% of hospitals by state board of pharmacy inspectors, 63% by accrediting surveyors, and 31% by Centers for Medicare & Medicaid Services (CMS) surveyors.[7]

State Boards of Pharmacy

As of April 2015, 27 states require direct compliance with USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations. Another 21 states have compounding regulations although they do not directly refer to USP Chapter <797>. Compliance with this chapter was a strong focus in 70% of the most recent state board inspections. Not surprisingly, in states that require compliance with USP Chapter <797>, more hospitals report being in full compliance.[7]

For those hospitals that were cited for sterile compounding noncompliance, a variety of issues came to light: incomplete or missing logs, timing of training and documentation of competency assessments, inaccurate room pressure monitoring, calibration of automatic compounding devices, improper handwashing technique, and conducting hazardous drug (HD) compounding outside of a negative pressure room.[7]

National Association of Boards of Pharmacy

Founded in 1904, the National Association of Boards of Pharmacy (NABP) is an impartial professional organization that supports the state boards of pharmacy in protecting public health. NABP's member boards of pharmacy are grouped into eight districts that include all 50 United States, the District of Columbia, Guam, Puerto Rico, the Virgin Islands, Australia, eight Canadian provinces, and New Zealand. Because the 50 state boards of pharmacy and the District of Columbia are members of the NABP, the NABP has much influence on the rules and regulations that the respective state boards create. The NABP has long held that prescription compounding is a pharmacist's responsibility and should be regulated by state boards of pharmacy.[8] NABP is recognized as having a consulting role in the DQSA. (See U.S. Food and Drug Administration [FDA] section below.) To distinguish between compounding and manufacturing, NABP defines these terms in its Model State Pharmacy Practice Act:

> *Compounding* means the preparation, mixing, assembling, altering, packaging, and Labeling of a Drug, Drug-Delivery Device, or Device, unless performed in a Food and Drug Administration (FDA)-registered Outsourcing Facility in conformance with Federal law, are in accordance with a licensed Practitioner's prescription, medication order, or initiative based on the Practitioner/patient/Pharmacist/compounder relationship in the course of professional practice. Compounding includes the following:
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> 1. preparation of Drug dosage forms for both human and animal patients;
> 2. preparation of Drugs or Devices in anticipation of Prescription Drug Orders based on routine, regularly observed prescribing patterns; and
> 3. reconstitution or manipulation of commercial Products that may require the addition of one or more ingredients for patient-specific needs.
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> *Manufacturing* means the production, preparation, propagation, conversion, or processing of a Drug or Device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis. Manufacturing includes the packaging or repackaging of a Drug or Device or the Labeling or relabeling of the container of a Drug or Device for resale by pharmacies, Practitioners, or other Persons.[9]

Although NABP strives for uniformity in state board of pharmacy regulations, the boards themselves run the gamut of oversight of sterile compounding. In 2015, Pew Charitable Trusts sponsored a survey to assess the national landscape of state policies on compounding sterile drugs.[10] Authors of the study used public websites and a questionnaire sent to all 50 states and the District of Columbia. Forty-three of the state boards of pharmacy responded to the survey. Alarming inconsistencies surfaced among state policies:

- Only 49% of states require strict adherence to USP Chapter <797> (see discussion below).
- Only 56% track the pharmacies that perform sterile compounding.
- Only 44% track pharmacies that ship or dispense compounded drugs into their state for patients or healthcare providers.
- Only 30% require pharmacies to report serious adverse events and reactions related to sterile compounding.
- Only 24% require pharmacies to report voluntary recalls to either the state or FDA.
- Sixty-five percent allow pharmacies to compound without patient-specific prescriptions.
- Only 21% require pharmacists to have a separate license or registration to perform sterile compounding.