A-0501
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§482.25(b)(1) - All compounding, packaging, and dispensing of drugs and biologicals must be under the supervision of a pharmacist and performed consistent with State and Federal laws.

Interpretive Guidelines §482.25(b)(1)

All pharmaceutical services involving compounding, packaging, or dispensing of drugs and biologicals, must be conducted by or under the supervision of a pharmacist and performed consistent with State and Federal laws. The hospital must adopt and implement written policies and procedures to ensure all medications are prepared by authorized personnel.

Compounded Preparations

Hospitals use many medications that need to be reconstituted, mixed or which otherwise may be considered "compounded" preparations. Some may be compounded in the hospital pharmacy and/or the hospital may obtain some or all from external sources. The external sources could include:

(1) Manufacturers;
(2) registered outsourcing facilities, and/or compounding pharmacies.

Regardless of the source, if accepted standards for safe compounding are not met, compounded medications may contain less or more than the intended dose and/or may be chemically or microbiologically contaminated, with potentially devastating or even lethal consequences for the patients who receive them.

Use of Registered Outsourcing Facilities

The Drug Quality and Security Act (DQSA), signed into law on November 27, 2013, contains provisions relating to the oversight of compounding of human drugs. The DQSA created a new section 503B in the FDCA under which a compounder may elect to become an "outsourcing facility." The law defines an "outsourcing facility" as a facility at one geographic location or address that is engaged in the compounding of sterile drugs; has elected to register as an outsourcing facility; and complies with all of the requirements of section 503B of the FDCA. Facilities that elect to register as outsourcing facilities, per section 503B:

- Must comply with the FDA's Current Good Manufacturing Practice (CGMP) requirements, which contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product. The CGMP requirements make sure that a product is safe for use, and that it has the ingredients and strength it claims to have. The FDA's publishes the most current versions of its draft and final regulations and guidance related to compounding on its website: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm ;

- Will be inspected by FDA according to a risk-based schedule; and

- Must meet certain other conditions, such as reporting adverse events and providing FDA with certain information about the products they compound.

In a January 2014 letter to purchasers of compounded medications (available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm380596.htm), the Commissioner of the FDA encouraged the use of registered outsourcing facilities and noted that,"[a]s a purchaser of compounded drugs, you can play an important role in improving the quality of compounded drugs by requiring compounding pharmacies that supply drugs to your facility to register as outsourcing facilities. Once they register, you and the patients you serve can be assured that FDA will inspect these facilities on a risk-based schedule, hold them to CGMP requirements, monitor the adverse event reports they are required to submit to the agency, and require appropriate labeling."

FDA has posted a list of Registered Human Drug Compounding Outsourcing Facilities, including the end date of the last FDA inspection related to compounding, whether investigators observed any significant objectionable conditions, and whether other FDA actions were taken based on the last inspection, at: http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompoun ding/ucm378645.htm

Note that these registered outsourcing facilities are also popularly referred to as "503B pharmacies."

Use of Compounding Pharmacies

Compounding pharmacies, not registered as an outsourcing facility with the FDA, are popularly referred to as "503A pharmacies" and generally are subject to oversight only by their State pharmacy board. If a hospital obtains compounded medications from a compounding pharmacy rather than a manufacturer or a registered outsourcing facility, then the hospital must demonstrate how it assures that the compounded medications it receives under this arrangement have been prepared in accordance with accepted professional principles for compounded drugs as well as applicable State or Federal laws or regulations. For example, does the contract with the vendor include provisions:

- Ensuring that the hospital has access to quality assurance data verifying that the vendor is adhering to current standards of practice for compounding medications and can the hospital document that it obtains and reviews such data?

- Requiring the vendor to meet the requirements of Section 503A of the FDCA concerning pharmacy compounding of human drug products?

For Information – Not Required/Not to be Cited
ASHP Research and Education Foundation™ "Outsourcing Sterile Products Preparation: Contractor Assessment Tool"

The ASHP Research and Education Foundation™ offers a tool that hospitals may find useful for assessing vendors that provide compounded sterile preparations. The tool can be found at:

http://www.ashpfoundation.org/MainMenuCategories/PracticeTools/SterileProductsTool.aspx and click on "Start using Sterile Products Outsourcing Tool now."

Medications Compounded by the Hospital's Pharmacy

Only the pharmacy compounds or admixes all sterile medications, intravenous admixtures, or other drugs except in emergencies or when not feasible (for example, when there is a need for emergency or immediate patient administration of a compounded sterile preparation). In addition, all compounding of medications used or dispensed by the hospital must be performed consistent with standards of safe practice applicable to both sterile and non-sterile compounding.

Compounded medications, whether non-sterile or sterile, may be subject to physical and chemical contamination and unintended variations in strength. Microbial contamination and bacterial endotoxins are particularly hazardous with respect to compounded medications that are intended to be sterile.

Packaging and Labeling of Medications

Safe medication use includes proper packaging and labeling to reduce the risk of error. For individual drug containers: each floor stock drug container is expected to be labeled with the name and strength of the drug, lot and control number equivalent, and expiration date. Appropriate accessory and cautionary statements are included as well as the expiration date and/or, if applicable, a beyond-use date (BUD). In addition, where applicable, each patient's individual drug container is expected to be labeled with the patient's full name and quantity of the drug dispensed.

If the unit dose system is utilized, each single unit dose package is expected to be labeled with the name and strength of the drug, lot and control number equivalent, expiration date and/or, if applicable, a BUD.

For Information Only

Certain provisions of the FDCA address the labeling of prescription drugs generally (e.g., section 503(b)(2) of the FDCA). Section 503B of the FDCA includes labeling requirements for drugs compounded by registered outsourcing facilities (see section 503B(a)(10)). Although hospitals are expected to comply with these requirements, surveyors conducting a Medicare survey do not assess compliance with other Federal laws.

Dispensing of Medications

Medications must be dispensed by the hospital in a manner that is safe and meets the needs of the patient:

- Quantities of medications are dispensed which minimize diversion and potential adverse events while meeting the needs of the patient;
- Medications are dispensed in a timely manner. The hospital must have a system that ensures that medication orders get to the pharmacy and medications get back to patients promptly;
- Whenever possible, medications are dispensed in the most ready to administer form available from the manufacturer or, if feasible, in unit dose that have been repackaged by the pharmacy;
- The hospital consistently uses the same dose packaging system, or, if a different system is used, provides education about the use of the dose packaging system;
- All concerns, issues or questions are clarified with the individual prescriber before dispensing; and
- Medications dispensed by the hospital are retrieved when recalled or discontinued by the manufacturer or the Food and Drug Administration (FDA) for safety reasons.

Medications must be available for administration to patients when needed, including when the pharmacy is not open. Methods to accomplish this when the pharmacy is not open could include, but are not limited to, one or more of the following: automated dispensing units outside the pharmacy, night cabinets, contracted services after hours via telepharmacy contracting, on-call pharmacists, etc.

- Automated Dispensing Cabinets (ADCs) for medications are a secure option for medication storage since they ensure locked storage of medications and allow for electronic tracking of controlled substances and other drugs. These cabinets often have embedded security features, such as login and password or biometric identification so that they can only by accessed by authorized personnel.
- Policies and procedures must address who can access medications during after-hours.

Survey Procedures §482.25(b)(1)

- Determine that only pharmacists or pharmacist-supervised personnel compound, package and dispense drugs or biologicals in accordance with State and Federal laws and regulations and accepted standards of practice by:

- Interviewing pharmacy and hospital staff to determine who prepares and dispenses drugs and biologicals;
- Observing on site preparation and dispensing operations;
- Inspecting drug storage areas.

- Can the hospital demonstrate that compounded medications used and/or dispensed by the hospital are being compounded consistent with standard operating procedures and quality assurance practices? Can the pharmacy director provide evidence that compounded medications used and/or dispensed by the hospital are being compounded consistent with standard operating procedures and quality assurance practices?

- If the hospital obtains compounded products from external compounding sources, are the external source(s) registered with the FDA as outsourcing facilities? If not, can the hospital demonstrate that it systematically evaluates and monitors whether the outside compounding pharmacy adheres to accepted standards for safe compounding?

- Can the pharmacy director explain the risk level(s) of the CSPs being produced in-house and/or obtained from external sources?

- If any CSPs are produced in the hospital:
  - Ask for one or more examples of situations in which a BUD had to be determined for a compounded sterile medication (CSP) based on the policy. Interview pharmacy personnel assigned to carry out this function within the hospital and/or to assess how this is done by external source(s) of CSPs. Is there evidence that the BUDs are determined consistent with the hospital's policies and procedures?
  - Interview staff who engage in sterile and non-sterile compounding. Are they knowledgeable about applicable levels of aseptic practices?
  - Ask the pharmacy director to demonstrate how the following are accomplished to ensure that sterile compounding practices are consistent with standards for the risk level(s) of CSPs being produced for/dispensed to hospital patients:
    - Verification of compounding accuracy and sterility;
    - Environmental quality and controls, including environmental sampling; testing and monitoring; and cleaning and disinfection;
    - Personnel training and competency assessment, including but not limited to accuracy/precision in identifying and measuring ingredients; cleansing and garbing; aseptic manipulation skills; environmental quality and disinfection; appropriate work practices within and adjacent to the direct compounding area; verification/calibration of equipment; sterilization; and post-production quality checks.

- Review the hospital's procedures for maintaining the quality of CSPs during storage, transport and dispensing. Are CSPs packaged in a manner to protect package integrity and sterility? How are CSP-specific requirements with respect

to motion, light exposure, temperature and potentially hazardous contents addressed? How does the hospital ensure that such information is effectively conveyed to non-pharmacy health care personnel and/or to patients/caregivers, if applicable?

- Can the hospital document that it is systematically monitoring and tracking adherence to all of the quality assurance and personnel training and competency standards described above? Have any problems or risks been identified? If so, did the hospital take effective action to protect patients, if relevant, and to effectively remedy the problem/risk?