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INFORMATIONAL LETTER #2015-16

DATE: November 20, 2015

TO: ALL IDAHO HOSPITALS

FROM: DEBBY RANSOM, R.N., R.H.I.T., Chief
Bureau of Facility Standards

SUBJECT: **S&C: 16-01-HOSPITAL:**
REVISED HOSPITAL GUIDANCE FOR PHARMACEUTICAL SERVICES
AND EXPANDED GUIDANCE RELATED TO COMPOUNDING OF
MEDICATIONS

The CMS Survey & Certification Letter #16-01, Revised Hospital Guidance for Pharmaceutical Services and Expanded Guidance Related to Compounding of Medications is being distributed to all Idaho Hospitals.

If you have any questions, please contact our office at 208/334-6626, Option 4.

DEBBY RANSOM, R.N., R.H.I.T., Chief
Bureau of Facility Standards

DR/nm
c: Idaho Hospital Association



Center for Clinical Standards and Quality/Survey & Certification Group

Ref: S&C: 16-01-Hospital

DATE: October 30, 2015

TO: State Survey Agency Directors

FROM: Director
Survey and Certification Group

SUBJECT: Revised Hospital Guidance for Pharmaceutical Services and Expanded Guidance
Related to Compounding of Medications

Memorandum Summary

Hospital Appendix A Updated: The Centers for Medicare & Medicaid Services (CMS) has updated the State Operations Manual (SOM) Appendix A with respect to both the hospital survey process and the interpretive guidelines for the pharmaceutical services Condition of Participation (CoP). The update includes the following features:

- ***Pharmaceutical Services:*** Revisions were made to portions of the pharmaceutical services CoP to bring them into alignment with current accepted standards of practice. To improve clarity, the revised guidance addresses: accepted professional pharmacy principles, including United States Pharmacopeia (USP) standards; compounding of medications, particularly compounded sterile preparations (CSPs); determining beyond-use dates (BUDs); safe and appropriate storage and use of medications; and, policies and procedures related to high-alert medications and minimizing drug errors.
- ***Additional Tag:*** We added a new standard-level tag to allow surveyors to cite to the regulatory language found in the condition stem statement at either the standard- or condition-level, as appropriate, in the Automated Survey Processing Environment (ASPEN).
- ***Preparing CSPs Outside of the Pharmacy:*** We are updating our guidance for the nursing service regulatory requirements concerning medication administration to clarify that hospitals must ensure staff adherence to accepted standards of practice in those limited instances when CSPs may be prepared outside of the pharmacy.

Background

Injections of contaminated compounded medications produced by a compounding pharmacy caused a nationwide meningitis outbreak in 2012. In addition to the compounding pharmacy-related outbreak of meningitis, a recent Institute for Safe Medication Practices (ISMP) article suggests that there are widespread problems with sterile compounding practices in acute care facility pharmacies: <http://www.ismp.org/newsletters/acutecare/issues/20150115.pdf>

The meningitis outbreak raised concerns about compounding pharmacies in general and prompted an investigation by the Office of Inspector General (OIG) regarding the use of compounding pharmacies by hospitals, as well as a follow-up report on oversight of hospital compounding by CMS and accrediting organizations. The latter OIG report (OEI-01-13-00400), released in January 2015, recommended that CMS should:

- Ensure that hospital surveyors receive training on standards from nationally recognized organizations related to safe compounding practices; and,
- Amend its interpretive guidelines to address hospitals' contracts with standalone compounding pharmacies.

The CMS concurred with both recommendations. Previously we issued revised guidance for critical access hospitals (CAHs), including expanded information on compounding. (See S&C policy memorandum 15-19, January 16, 2015). With this policy memorandum we are making similar revisions in Appendix A to the guidance for the Hospital Pharmaceutical Services CoP at 42 CFR 482.25, as well as for portions of the Nursing Services CoP at 42 CFR 482.23, related to medication administration. At a future date, we will also be providing targeted surveyor training related to compounding.

Additionally, in the course of revising and expanding our guidance concerning compounding, we have also reorganized and updated guidance for other parts of the Pharmaceutical Services CoP as well as the Nursing Services CoP.

Highlights of the revisions to Appendix A include:

Pharmaceutical Services:

- We reorganized the guidance by renumbering the condition-level tag as A-0489, creating a standard-level tag at A-0490 for a portion of the condition “stem” statement of the regulation, and including another portion of the condition stem statement in the tag at A-0491, Governing Pharmacy Management and Administration. We also updated and moved much of the guidance currently found in the condition-level tag to these or other standard-level tags, to reduce the potential for confusion about whether the guidance applies only in the case of condition-level citations.

The guidance is now placed to more clearly indicate what must be evaluated when assessing compliance with the condition and standards. Following normal survey procedure, citations issued at the standard-level may, depending on the manner and degree of noncompliance identified, also result in a condition-level citation.

- We have clarified that a hospital must have pharmaceutical services administered in accordance with accepted professional principles, such as those found in the U.S. Pharmacopeia/National Formulary (USP/NF), and have provided additional information about USP standards.

- Similar to the CAH guidance released in January 2015, we have expanded our hospital guidance on the requirements for compounding of medications, particular for CSPs. We have also included discussion of U.S. Food and Drug Administration (FDA)-registered outsourcing facilities, and the implications for assessing compliance when hospitals use these facilities versus using other outside compounding pharmacies as a source for their CSPs. Under the current CoP, hospitals cannot be required to use only registered outsourcing facilities when obtaining compounded medications from an external source. However, if they do so, they will find it easier to demonstrate compliance than would be the case if they use a compounding pharmacy that is not registered with the FDA.
- We also are providing additional guidance on recommended best practice resources, summaries and assessment tools from organizations such as, the American Society of Health System Pharmacists (ASHP), ISMP, and USP in “blue boxes.” Information in blue boxes does not represent regulatory requirements and surveyors must not cite hospitals solely because they do not adhere to practices described in a “blue box.”

Nursing Services: We have updated our guidance for §§482.23(c)(1), (c)(1)(i) & (c)(2), concerning preparation and administration of drugs, to clarify accepted standards of practice required to prevent healthcare-associated infections in those limited circumstances when CSPs may be prepared outside of the pharmacy. We have also included discussion regarding medication beyond-use-dates (BUD).

An advance copy of revised SOM Appendix A is attached. It may differ slightly from the final version that will be published at a later date.

Contact: Questions concerning this memorandum may be addressed to hospitalscg@cms.hhs.gov

Training: The information contained in this letter should be shared with all survey and certification staff, their managers, and the State/RO training coordinators.

Effective Date: Immediately. This policy should be communicated with all survey and certification staff, their managers and the State/Regional Office training coordinators within 30 days of this memorandum.

/s/

Thomas E. Hamilton

Attachment – Advanced Copy SOM Appendix A

cc: Survey and Certification Regional Office Management

CMS Manual System

Pub. 100-07 State Operations Provider Certification

Department of Health &
Human Services (DHHS)
Centers for Medicare &
Medicaid Services (CMS)

Transmittal- ADVANCE
COPY

Date: XXXX

SUBJECT: Revisions to State Operations Manual (SOM), Appendix A -Survey Protocol, Regulations and Interpretive Guidelines for Hospitals

I. SUMMARY OF CHANGES: We are clarifying our interpretive guidance in Appendix A for existing regulations in 42 CFR Part 482, concerning preparation and administration of drugs as well as pharmacy requirements and accepted standards of practice for drug compounding. We are taking this opportunity to make clarifications and updates to existing guidance.

**NEW/REVISED MATERIAL - EFFECTIVE DATE*: Upon Issuance
IMPLEMENTATION DATE: Upon Issuance**

The revision date and transmittal number apply to the red italicized material only. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.

**II. CHANGES IN MANUAL INSTRUCTIONS: (N/A if manual not updated.)
(R = REVISED, N = NEW, D = DELETED) – (Only One Per Row.)**

R/N/D	CHAPTER/SECTION/SUBSECTION/TITLE
R	Appendix A/A-0405/§482.23(c) Standard: Preparation and Administration of Drugs
R	Appendix A/A-0489/§482.25 Condition of Participation: Pharmaceutical Services
N	Appendix A/A-0490/§482.25 Standard level tag for Condition for Coverage: Pharmaceutical Services
R	Appendix A/A-0491/§482.25(a) Standard: Pharmacy Management and Administration
R	Appendix A/A-0492/§482.25...The institution must have a pharmacy directed by a registered pharmacist or a drug storage area under competent supervision...& §482.25(a)(1)- A full-time, part-time, or consulting pharmacist must be responsible for developing, supervising, and coordinating all the activities of the pharmacy services.
R	Appendix A/A-0500/§482.25(b) Standard: Delivery of Services

R	Appendix A/A-0501/§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.
R	Appendix A/A-0502/§482.25(b)(2)(i)- All drugs and biologicals must be kept in a secure area, and locked when appropriate.
R	Appendix A/A-0505/§482.25(b)(3) - Outdated, mislabeled, or otherwise unusable drugs and biologicals must not be available for patient use.
R	Appendix A/A0507/§482.25(b)(5) - Drugs and biologicals not specifically prescribed as to time or number of doses must automatically be stopped after a reasonable time that is predetermined by the medical staff.
R	Appendix A/A0510/§482.25(b)(8) - Information relating to drug interactions and information of drug therapy, side effects, toxicology, dosage, indications for use, and routes of administration must be available to the professional staff.

III. FUNDING: No additional funding will be provided by CMS; contractor activities are to be carried out within their FY 2015 operating budgets.

IV. ATTACHMENTS:

	Business Requirements
X	Manual Instruction
	Confidential Requirements
	One-Time Notification
	Recurring Update Notification

A-0405

(Rev.)

§482.23(c) Standard: Preparation and Administration of Drugs.

(1) Drugs and biologicals must be prepared and administered in accordance with Federal and State laws, the orders of the practitioner or practitioners responsible for the patient's care as specified under §482.12(c), and accepted standards of practice.

(i) Drugs and biologicals may be prepared and administered on the orders of other practitioners not specified under §482.12(c) only if such practitioners are acting in accordance with State law, including scope of practice laws, hospital policies, and medical staff bylaws, rules, and regulations....

(2) All drugs and biologicals must be administered by, or under supervision of, nursing or other personnel in accordance with Federal and State laws and regulations, including applicable licensing requirements, and in accordance with the approved medical staff policies and procedures.

Interpretive Guidelines §§482.23(c)(1), (c)(1)(i) and (c)(2)

According to the Institute of Medicine of the National Academies, medication errors are among the most common medical errors, harming at least 1.5 million people each year.¹ It has been estimated that drug-related adverse outcomes were noted in nearly 1.9 million inpatient hospital stays (4.7 percent of all stays), and 838,000 treat-and-release ED visits (0.8 percent of all visits).² Although technological advances in electronic order entry, medication administration, and electronic medical records hold a great deal of promise for decreasing medication errors, there are a multitude of human and environmental factors that will impact their success. The increasing complexity of medical care and patient acuity present significant challenges that require an approach to medication administration that takes advantage of available technology while recognizing that it must be integrated into the medication administration work processes in a manner that meets the needs of patients and promotes their safety.

The regulations at §482.23(c) and §482.23(c)(1) promote safety in the preparation and administration of drugs and biologicals to hospital patients by requiring preparation and administration in accordance with:

- Federal and State law;
- Accepted standards of practice;

¹Institute of Medicine. Preventing Medication Errors. Washington DC: The National Academies Press, 2007.

²Lucado, Jennifer, et al, *Medication-Related Adverse Outcomes in U.S. Hospitals and Emergency Departments*. Statistical Brief #109, April, 2011. Healthcare Cost and Utilization Project, Agency For Healthcare Research and Quality, Rockville, MD.

- Orders of the practitioner(s) responsible for the patient's care, as specified under §482.12(c) or of another practitioner as permitted under State law, hospital policy and medical staff bylaws, rules and regulations; and
- Medical staff-approved policies and procedures.

Federal and State Law

Federal law regulates the approval and classification of drugs and biologicals. Individual States establish laws and regulations which specify the scope of practice for various types of licensed healthcare professionals, including which medications they may prescribe and administer, including controlled substances.

Accepted Standards of Practice

Hospital policies and procedures for the preparation and administration of all drugs and biologicals must not only comply with all applicable Federal and State laws, but also must be consistent with accepted standards of practice based on guidelines or recommendations issued by nationally recognized organizations with expertise in medication preparation and administration. Examples of such organizations include, but are not limited to:

- *American Society of Health-System Pharmacists* (<http://www.ashp.org/default.aspx>)
- Infusion Nurses Society (<http://www.insl.org>)
- Institute for Safe Medication Practices (www.ismp.org)
- National Coordinating Council for Medication Error Reporting and Prevention (www.nccmerp.org)
- U.S Pharmacopeia (www.usp.org)

Orders of an authorized practitioner

Drugs must be administered in response to an order from a practitioner, or on the basis of a standing order which is appropriately authenticated subsequently by a practitioner. (See §482.23(c)(1) (ii) concerning standing orders.) Generally, the ordering practitioner is the practitioner(s) responsible for the care of the patient in accordance with §482.12(c). However, other practitioners not specified under §482.12(c) may write orders for the preparation and administration of drugs and biologicals, if they are acting in accordance with State law, including scope of practice laws, hospital policies and procedures, and medical staff bylaws, rules and regulations. This includes practitioners ordering outpatient services who do not have privileges in the hospital but who are permitted under their State scope of practice and authorized by hospital and medical staff policy to order outpatient services.

In accordance with standard practice, all practitioner orders for the administration of drugs and biologicals must include at least the following:

- Name of the patient;

- Age and weight of the patient, to facilitate dose calculation when applicable. Policies and procedures must address weight-based dosing for pediatric patients as well as in other circumstances identified in the hospital's policies. (Note that dose calculations are based on metric weight (kg, or g for newborns). If a hospital permits practitioners to record weight in either pounds or using metric weight, the opportunity for error increases, since some orders would require conversion while others would not. Accordingly, hospitals must specify a uniform approach to be used by prescribing practitioners. For example, a hospital could require all prescribers to use pounds or ounces and have the electronic ordering system or the pharmacy convert to metric);
- Date and time of the order;
- Drug name;
- Dose, frequency, and route;
- Dose calculation requirements, when applicable
- Exact strength or concentration, when applicable;
- Quantity and/or duration, when applicable;
- Specific instructions for use, when applicable; and
- Name of the prescriber.

Medical Staff Approved Policies and Procedures

The hospital's medical staff must approve policies and procedures for medication administration, consistent with the requirements of Federal and State law and accepted standards of practice. It is recommended that the medical staff consult with nurses, pharmacists, Quality Assessment and Performance Improvement program staff, and others in developing these policies and procedures. The adopted policies and procedures must address key issues related to medication administration, which include but are not limited to:

Personnel authorized to administer medication

§482.23(c)(2) requires that all drugs and biologicals are administered by, or under the supervision of, nursing or other personnel, in accordance with Federal or State law and approved medical staff policies and procedures. State law requirements include licensure requirements. Policies and procedures must identify categories of licensed personnel and the types of medications they are permitted to administer, in accordance with state laws. The policies and procedures must also address education and training for all personnel administering drugs and biologicals.

Medication administration education and training is typically included in hospital orientation or other continuing education for nursing staff and other authorized healthcare personnel. Training or continuing education topics regarding medication administration may include but are not limited to the following:

- Safe handling and preparation of authorized medications;
- Knowledge of the indications, side effects, drug interactions, compatibility, and dose limits of administered medications;

- Equipment, devices, special procedures, and/or techniques required for medication administration;

Policies and procedures must address the required components of the training and if the training provided during hospital orientation imparts sufficient education or whether ongoing in-services or continuing education will be required to demonstrate competence.

Basic safe practices for medication administration

The hospital’s policies and procedures must reflect accepted standards of practice that require the following be confirmed prior to each administration of medication (often referred to as the “five rights” of medication administration practice):

- Right patient: the patient’s identity— acceptable patient identifiers include, but are not limited to: the patient’s full name; an identification number assigned by the hospital; or date of birth. Identifiers must be confirmed by patient wrist band, patient identification card, patient statement (when possible) or other means outlined in the hospital’s policy. The patient’s identification must be confirmed to be in agreement with the medication administration record and medication labeling prior to medication administration to ensure that the medication is being given to the correct patient.
- Right medication: the correct medication, to ensure that the medication being given to the patient matches that prescribed for the patient and that the patient does not have a documented allergy to it;
- Right dose: the correct dose, to ensure that the dosage of the medication matches the prescribed dose, and that the prescription itself does not reflect an unsafe dosage level (i.e., a dose that is too high or too low);
- Right route: the correct route, to ensure that the method of administration – orally, intramuscular, intravenous, etc., is the appropriate one for that particular medication and patient; and
- Right time: the appropriate time, to ensure adherence to the prescribed frequency and time of administration.

Note: the “5 rights” focus specifically on the process of administering medications. The medication process is generally recognized as consisting of five stages: ordering/prescribing; transcribing and verifying; dispensing and delivering; administering; and monitoring/reporting. Errors may occur in other components of the process, even when there is strict adherence to the “5 rights” of medication administration, for example when there has been a prescribing or a dispensing error. Hospitals are also expected to comply with requirements under the Pharmaceutical Services CoP at §482.25 and the patient safety requirements under the Quality Assessment and Performance Improvement CoP at §482.21, using a comprehensive systems approach to all components of the medication process.

For Information – Not Required/Not to be Cited

Recent literature* identifies up to nine “rights” of medication administration including:

- Right patient
- Right drug
- Right route
- Right time
- Right dose
- Right documentation
- Right action (appropriate reason)
- Right form
- Right response

However, other sources refer to 8 or 10 “rights, and some of these topics, such as right action, appear to involve prescribing and/or dispensing. Accordingly, there does not (yet) appear to be consensus about expanding beyond the 5 “rights.”

*Reference: Elliott, M. and Lis, Y. (2010). The Nine Rights of Medication Administration: An Overview. British Journal of Nursing, Vol. 19, 5, 300-305.

Hospitals are encouraged to promote a culture in which it is not only acceptable, but also strongly encouraged, for staff to bring to the attention of the prescribing practitioner questions or concerns they have regarding medication orders. Any questions about orders for drugs or biologicals are expected to be resolved promptly, whether they arise prior to the preparation, dispensing, or administration of the medication.

Hospitals must also ensure staff adherence to accepted standards of practice required to prevent healthcare-associated infections related to medication preparation and/or administration. Adherence to these standards is assessed under the infection control CoP at 42 CFR 482.42, and details about the required practices are found in the Hospital Infection Control Worksheet.

Compounded sterile preparations (CSPs) may also be a source of healthcare-associated infection if proper precautions are not followed. The applicable standards of practice for safe sterile compounding are, at a minimum, the standards published in The United States Pharmacopeia National Formulary Chapter <797> (“Pharmaceutical Compounding – Sterile Preparations”) and other relevant USP/NF Chapters (USP <797>). (See the guidance for §482.25(b)(1) for more information on the role of USP/NF standards and for discussion of the term “compounding.”) Hospitals must ensure that they meet all currently accepted standards for safe preparation and administration for CSPs, whether they are the type of CSP that must be compounded in an aseptic pharmacy location that meets USP <797> standards for low, medium or high-level risk CSPs or are “immediate-use CSPs” prepared outside of the pharmacy.

Nurses commonly prepare sterile medications that are categorized by USP <797> as “immediate-use CSPs,” which are needed for immediate or emergency use for a particular

patient and are not to be stored for anticipated needs. The following USP <797> standards apply when preparing an immediate-use CSP:

- Preparation of an immediate-use CSP must only involve “simple transfer of not more than three commercially manufactured...sterile nonhazardous products from the manufacturer’s original containers and not more than two entries into any one container or package (e.g. bag, vial) of sterile infusion solution or administration container/device;”*
- “Administration begins not later than one hour following the start of the preparation of the CSP (if not, the CSP must be appropriately discarded);”*
- Meticulous aseptic technique must be followed during all phases of preparation. If the CSP is not administered to the patient as soon as it is ready, “the finished CSP is under continuous supervision to minimize the potential for contact with non-sterile surfaces...,” contamination and/or confusion with other CSPs; and*
- “Unless immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer...,” the CSP must be labeled with at least:*
 - Patient identification information;*
 - The names and amounts of all ingredients;*
 - The name or initials of the person who prepared it; and*
 - The exact one hour “beyond use date” (see below).*

A drug or biological is outdated after its expiration date, which is set by the manufacturer based on stability testing under specified conditions as part of the U.S. Food and Drug Administration’s (FDA) approval process. It should be noted that a drug or biological may become unusable prior to its expiration date if it has been subjected to conditions that are inconsistent with the manufacturer’s approved labeling.

A drug or biological is also outdated after its “beyond-use date” (BUD), which may be reached before the expiration date, but never later. The BUD is the date and time after which the medication must not be used, stored or transported. The BUD takes into account the specific conditions and potential for deterioration and microbial growth that may occur during or after the original container is opened, while preparing the medication for dispensing and administration, and/or during the compounding process if it is a compounded medication.

The BUD is to be based on information provided by the manufacturer, whenever such information is available. The hospital must maintain and implement policies and procedures that provide clear and consistent direction to pharmacy staff regarding how to determine a BUD when complete BUD information is not available from the manufacturer. The policies and

procedures must be based on accepted professional principles which are equivalent to, or more stringent than, those described in the USP/NF (USP).³

According to Chapters <795> and <797> of the USP, the BUD must be safe for patients, and determined conservatively. The section in USP <797> entitled “Determining Beyond-Use Dates,” which addresses sterile compounding, notes that “the truly valid evidence for predicting beyond-use dating can be obtained only through product-specific experimental studies.” It provides an example of testing considered more appropriate for certain types of CSPs such as “CSPs with a narrow therapeutic index, where close monitoring or dose titration is required to ensure therapeutic effectiveness and to avoid toxicity....” It also provides examples of important issues that a pharmacist must be able to critically interpret and evaluate when consulting literature sources in the process of determining a BUD; and distinguishes between reviewing literature specific to a particular drug, composition, concentration of ingredients, fill volume, container, storage conditions and duration of use, etc., versus merely reviewing available publications or tables. The former is the preferred approach, while the latter results in a “theoretical BUD,” which has an inherent likelihood of inaccuracy or error.

Timing of Medication Administration

Appropriate timing of medication administration must take into account the complex nature and variability among medications; the indications for which they are prescribed; the clinical situations in which they are administered; and the needs of the patients receiving them. The chemical properties, mechanism of action, or therapeutic goals of some medications require administration at the exact time prescribed, or within a narrow window of its prescribed scheduled time, to avoid compromising patient safety or achievement of the intended therapeutic effect. However, the therapeutic effect of many other medications is uncompromised by a much broader window of time for administration. Consequently, the application of a uniform required window of time before or after the scheduled time for the administration of all medications, without regard to their differences, could undermine the ability of nursing staff to prioritize nursing care activities appropriately. This could also result in staff work-arounds that jeopardize patient safety due to the imposition of unrealistic or unnecessary time constraints for medication administration. Instead, hospital policies and procedures must specifically address the timing of medication administration, based on the nature of the medication and its clinical application, to ensure safe and timely administration. The policies and procedures must address at least the following:

- Medications **not eligible** for scheduled dosing times;
- Medications **eligible for** scheduled dosing times;
- Administration of eligible medications outside of their scheduled dosing times and windows; and
- Evaluation of medication administration timing policies, including adherence to them.

Medications or categories of medication not eligible for scheduled dosing times

³ All references to “USP” herein are from: *United States Pharmacopeial Convention. USP on Compounding: A Guide for the Compounding Practitioner. Current with USP 37-NF32 through First Supplement. Rockville, MD: United States Pharmacopeial Convention, 2014.*

The policies and procedures must identify medications or categories of medication which are not eligible for scheduled dosing times, either in general or in specific clinical applications. These are medications that require exact or precise timing of administration, based on diagnosis type, treatment requirements, or therapeutic goals. The policies and procedures must reflect consideration of factors including, but not limited to, the pharmacokinetics of the prescribed medication; specific clinical applications; and patient risk factors. Examples of medications that hospitals may choose to identify as not eligible for scheduled dosing times may include, but are not limited to:

- Stat doses (immediate);
- First time or loading doses (initial large dose of a drug given to bring blood, tissue or fluid levels to an effective concentration quickly);
- One-time doses; doses specifically timed for procedures;
- Time-sequenced doses; doses timed for serum drug levels;
- Investigational drugs; or
- Drugs prescribed on an as needed basis (prn doses).

The policies and procedures must ensure timely administration of such medications. In addition they must specify if the policy for the administration of these medications will be applied hospital-wide or only for specific diagnosis types, hospital units or clinical situations.

Medications eligible for scheduled dosing times

Medications eligible for scheduled dosing times are those prescribed on a repeated cycle of frequency, such as once a day, BID (twice a day), TID (three times a day), hourly intervals (every 1, 2, 3 or more hours), etc. The goal of this scheduling is to achieve and maintain therapeutic blood levels of the prescribed medication over a period of time.

Medication administration policies and procedures typically establish standardized dosing times for the administration of all 'scheduled' medications. For example, medications prescribed for BID (twice a day) administration might, under a given hospital's policies and procedures, be scheduled to be administered at 8am and 8pm. Another hospital might choose to schedule BID medications at 7:30 am and 7:30 pm. Use of these standardized times facilitates the medication administration process, e.g., by providing to the hospital's pharmacy that morning doses of all BID drugs must be dispensed and delivered to patient units in time for the scheduled administration. For the nursing staff, the scheduled administration time might prompt prioritization of additional activities that may be required, in the case of particular drugs, such as vital sign assessment or the collection and review of blood work, to ensure safe and timely medication administration.

Policies and procedures for medications eligible for scheduled dosing times must also address: first dose medications, including parameters within which nursing staff are allowed to use their own judgment regarding the timing of the first and subsequent doses, which may fall between scheduled dosing times; retiming of missed or omitted doses; medications that will not follow scheduled dosing times; and patient units that are not subject to following the scheduled dosing times.

Time-critical scheduled medications

Time-critical scheduled medications are those for which an early or late administration of greater than thirty minutes might cause harm or have significant, negative impact on the intended therapeutic or pharmacological effect. Accordingly, scheduled medications identified under the hospital's policies and procedures as time-critical must be administered within thirty minutes before or after their scheduled dosing time, for a total window of 1 hour.

It is possible for a given medication to be time-critical for some patients, due to diagnosis, clinical situation, various risk factors, or therapeutic intent, but not time-critical for other patients. Therefore, hospital policies and procedures must address the process for determining whether specific scheduled medications are always time-critical, or only under certain circumstances, and how staff involved in medication administration will know when a scheduled medication is time-critical. Examples of time-critical scheduled medications/medication types may include, but are not limited to:

- Antibiotics;
- Anticoagulants;
- Insulin;
- Anticonvulsants;
- Immunosuppressive agents;
- Pain medication (non-IV);
- Medications prescribed for administration within a specified period of time of the medication order;
- Medications that must be administered apart from other medications for optimal therapeutic effect; or
- Medications prescribed more frequently than every 4 hours.

Non-time-critical scheduled medications

Non-time critical scheduled medications are those for which a longer or shorter interval of time since the prior dose does not significantly change the medication's therapeutic effect or otherwise cause harm. For such medications greater flexibility in the timing of their administration is permissible. Specifically:

- Medications prescribed for daily, weekly or monthly administration may be within 2 hours before or after the scheduled dosing time, for a total window that does not exceed 4 hours.
- Medications prescribed more frequently than daily but no more frequently than every 4 hours may be administered within 1 hour before or after the scheduled dosing time, for a total window that does not exceed 2 hours.

Missed or late administration of medications

The hospital's policies and procedures must address the actions to be taken when medications eligible for scheduled dosing times are not administered within their permitted window of time. This includes doses which may have been missed due to the patient being temporarily away from the nursing unit, for example, for tests or procedures; patient refusal; patient inability to take the medication; problems related to medication availability; or other reasons that result in missed or late dose administration. Likewise, policies and procedures must also outline guidelines for the administration and timing of new medications which are initiated between standardized dosing times.

These policies and procedures must identify parameters within which nursing staff are allowed to use their own judgment regarding the rescheduling of missed or late doses and when notification of the physician or other practitioner responsible for the care of the patient is required prior doing so. In either case, the reporting of medication errors that are the result of missed or late dose administration must be reported to the attending physician in accordance with requirements at §482.25(b)(6). See interpretive guidance at §482.25(b)(6) for more details on internal reporting requirements

Evaluation of medication administration timing policies

Hospitals must periodically evaluate their medication administration timing policies, including staff adherence to the policies, to determine whether they assure safe and effective medication administration. Consistent with the QAPI requirements at 42 CFR 482.21(c)(2), medication errors related to the timing of medication administration must be tracked and analyzed to determine their causes. Based on the results of the evaluations of the policies and the medication administration errors, the medical staff must consider whether there is a need to revise the policies and procedures governing medication administration timing.

Assessment/Monitoring of Patients Receiving Medications

Observing the effects medications have on the patient is part of the multi-faceted medication administration process. Patients must be carefully monitored to determine whether the medication results in the therapeutically intended benefit, and to allow for early identification of adverse effects and timely initiation of appropriate corrective action. Depending on the medication and route/delivery mode, monitoring may need to include assessment of:

- Clinical and laboratory data to evaluate the efficacy of medication therapy, to anticipate or evaluate toxicity and adverse effects. For some medications, including opioids, this may include clinical data such as respiratory status, blood pressure, and oxygenation and carbon dioxide levels;
- Physical signs and clinical symptoms relevant to the patient's medication therapy, including but not limited to, somnolence, confusion, agitation, unsteady gait, pruritus, etc.

Certain types of medications are considered inherently high risk for adverse drug events. Although mistakes may or may not be more common with these drugs, the consequences of

errors are often harmful, sometimes fatal, to patients. (See also the discussion of high-risk medications (typically referred to as “high-alert” medications) in the guidance for §482.25(a)(1))

For Information – Not Required/Not to be Cited

The Institute for Safe Medication Practices (ISMP) makes available a list of high alert medications, which it defines as those medications that bear a heightened risk of causing significant patient harm when they are used in error. The current list may be found at: <http://www.ismp.org/Tools/highAlertMedicationLists.asp>

In addition, certain factors place some patients at greater risk for adverse effects of medication. Factors including, but not limited to, age, altered liver and kidney function, a history of sleep apnea, patient weight (obesity may increase apnea or smaller patients may be more sensitive to dose levels of medications), asthma, history of smoking, drug-drug interactions, and first-time medication use may contribute to increased risk.

Consideration of patient risk factors as well as the risks inherent in a medication must be taken into account when determining the type and frequency of monitoring. Further, to enhance continuity of care/safe medication administration, it is essential to communicate all relevant information regarding patients’ medication risk factors and monitoring requirements during hand-offs of the patient to other clinical staff, such as when patients are transferred internally from one unit to another, during shift report at change of shift, etc. This would apply to hand-offs involving not only to nursing staff, but also to any other types of staff who administer medications, e.g., respiratory therapists.

Adverse patient reactions, such as anaphylaxis or opioid-induced respiratory depression, require timely and appropriate intervention, per established hospital protocols, and must also be reported immediately to the practitioner responsible for the care of the patient. (See the guidance for §482.23(c)(5) and §482.25(b)(6), concerning reporting of adverse medication-related events.)

An example of vigilant post-medication administration monitoring in the case of a high-alert medication where patient factors may increase risk would be regularly checking vital signs, oxygen level via pulse oximetry, and sedation levels of a post-surgical patient who is receiving pain medication via a patient controlled analgesia (PCA) pump. Narcotic medications, such as opioids, are often used to control pain but also have a sedating effect. Patients can become overly sedated and suffer respiratory depression or arrest, which can be fatal. Timely assessment and appropriate monitoring is essential in all hospital settings in which opioids are administered, to permit intervention to counteract respiratory depression should it occur. (See also the discussion of the requirements for intravenous medications at §482.23(c)(4)).

As part of the monitoring process, staff are expected to include the patient’s reports of his/her experience of the medication’s effects. Further, when monitoring requires awakening the patient in order to assess effects of the medications, the patient and/or the patient’s representative must

be educated about this aspect of the monitoring process. In addition, hospitals are encouraged to educate the patient and his/her representative and/or family members about notifying nursing staff promptly when there is difficulty breathing or other changes that might be a reaction to medication.

Hospital policies and procedures are expected to address how the manner and frequency of monitoring, considering patient and drug risk factors, are determined, as well as the information to be communicated at shift changes, including the hospital's requirements for the method(s) of communication.

Documentation

Note that documentation of medication administration is addressed in the Medical Records CoP, at §482.24(c), which specifies the required content of the medical record. Within this regulation §482.24(c)(vi) requires that the record contain: "All practitioners' orders, nursing notes, reports of treatment, medication records, radiology, and laboratory reports, and vital signs and other information necessary to monitor the patient's condition." Documentation is expected to occur after actual administration of the medication to the patient; advance documentation is not only inappropriate, but may result in medication errors. Proper documentation of medication administration actions taken and their outcomes is essential for planning and delivering future care of the patient. See the guidance for the various parts of §482.24(c) concerning documentation in the medical record. Deficiencies in documentation would be cited under the applicable Medical Records regulation.

Survey Procedures §§482.23(c)(1), (c)(1)(i), and (c)(2)

Verify that there is an effective method for the administration of drugs. Use the following indicators for assessing drug administration:

- Verify that there are policies and procedures approved by the medical staff and governing body concerning ordering of drugs and biologicals by practitioners.
- Verify that there are policies and procedures approved by the medical staff covering who is authorized to administer medications, and that the policies are followed.
 - Verify nursing staff authorized to administer drugs and biological are practicing within their State-permitted scope of practice.
 - Are personnel other than nursing personnel administering drugs or biologicals? If yes, determine if those personnel are administering drugs or biologicals in accordance with Federal and State laws and regulations, including scope of practice laws, hospital policy, and medical staff by-laws, rules and regulations. Use the above procedures to determine compliance.
- Verify that there are policies and procedures approved by medical staff addressing the timing of medication administration.

- Verify that the hospital has, consistent with its policies, identified medications: which are:
 - not eligible for scheduled dosing times;
 - Eligible for scheduled dosing times and are time-critical; and
 - Eligible for scheduled dosing times and are not time-critical.
- Verify the hospital has established total windows of time that do not exceed the following:
 - 1 hour for time-critical scheduled medications
 - 2 hours for medications prescribed more frequently than daily, but no more frequently than every 4 hours; and
 - 4 hours for medications prescribed for daily or longer administration intervals.
- Verify that the hospital's policy describes requirements for the administration of identified time-critical medications. Is it clear whether time-critical medications or medication types are identified as such for the entire hospital or are unit-, patient diagnosis-, or clinical situation- specific?
- Review a sample of medical records to determine whether medication administration conformed to an authorized practitioner's order, i.e., that there is an order from an authorized practitioner, or an applicable standing order, and that the correct medication was administered to the right patient at the right dose via the correct route, and that timing of administration complied with the hospital's policies and procedures. Check that the practitioner's order was still in force at the time the drug was administered.
- Observe the preparation of drugs and their administration to patients [medication pass] in order to verify that procedures are being followed
 - Is the patient's identity confirmed prior to medication administration?
 - Are procedures to assure the correct medication, dose, and route followed?
 - *If immediate-use CSPs are prepared outside of the pharmacy, are practices consistent with USP <797>?*
 - Are drugs administered in accordance with the hospital's established policies and procedures for *safe and* timely medication administration?
 - Does the nurse remain with the patient until oral medication is taken?
- Are patients assessed by nursing and/or other staff, per hospital policy, for their risk to their prescribed medications?

- Are patients who are at higher risk and/or receiving high-alert medications monitored for adverse effects?
- Are staff knowledgeable about intervention protocols when patients experience adverse medication-related events?
- Interview personnel who administer medication to verify their understanding of the policies regarding timeliness of medication administration.
 - Are they able to identify time-critical and non-time-critical scheduled medications? Medications not eligible for scheduled dosing times?
 - Are they able to describe requirements for the timing of administration of time critical and non-time critical medications in accordance with the hospital's policies?

A-0489
(Rev.)

§482.25 Condition of Participation: Pharmaceutical Services.

The hospital must have pharmaceutical services that meet the needs of the patients. The institution must have a pharmacy directed by a registered pharmacist or a drug storage area under competent supervision. The medical staff is responsible for developing policies and procedures that minimize drug errors. This function may be delegated to the hospital's organized pharmaceutical service.

Interpretive Guidelines §482.25

A hospital must provide pharmaceutical services that meet the needs of its patients. The services must include either a pharmacy that is directed by a pharmacist, or, when appropriate, a drug storage area that is competently supervised. The hospital's medical staff is responsible for developing pharmaceutical policies and procedures that minimize the potential for medication errors, but may delegate this function to the pharmaceutical service.

The manner or degree of noncompliance with the requirements of this Condition and its component standards must be evaluated to determine whether there is substantial noncompliance with the Condition, warranting a Condition-level citation.

A-0490
(Rev.)

Standard-level Tag for

§482.25 Condition of Participation: Pharmaceutical Services.

The hospital must have pharmaceutical services that meet the needs of the patients....

Interpretive Guidelines §482.25

What is included in pharmaceutical services?

Pharmaceutical services encompass the functions of procuring, storing, compounding, re-packaging, and dispensing all medications, biologicals, chemicals and medication-related devices within the hospital. They also include providing medication-related information to care professionals within the hospital, as well as direct provision of medication-related care.

Meeting patient needs

Hospitals must provide pharmaceutical services that meet the needs of their patients. The scope and complexity of pharmaceutical services available in the hospital must be consistent with the volume and types of patients the hospital serves. Except in unusual circumstances, the pharmaceutical service is expected to make available in a timely manner the volume and types of medications typically needed. These would be those medications typically prescribed by the hospital's practitioners for hospital patients receiving inpatient services, surgical services, diagnostic services involving medications as a component of testing, and outpatient drug therapies administered while the patient is in the hospital.

Not every hospital is expected to offer the same level of pharmaceutical services. For example:

- *It would not be uncommon for a psychiatric hospital to maintain a relatively limited pharmaceutical service, due to minimal need for compounding, and/or dispensing multiple types and forms of medications and biologicals.*
- *On the other hand, a short-term acute care hospital with a busy oncology outpatient service and other complex medical and surgical departments would be expected to provide a wider range of pharmaceutical services that are ready to be furnished when needed.*

Survey Procedures §482.25

- *Ask the hospital for evidence of the scope and complexity of its pharmaceutical services.*
- *Ask how the hospital has determined that the services meet the needs of its patients.*

- *Ask unit nursing staff if prescribed medications are routinely available and timely. If there are reports of frequent delays or other problems, probe further with the director of pharmaceutical services.*

A-0491

(Rev.)

[\$482.25 Condition of Participation: Pharmaceutical Services

.....The medical staff is responsible for developing policies and procedures that minimize drug errors. This function may be delegated to the hospital's organized pharmaceutical service.]

§482.25(a) Standard: Pharmacy Management and Administration

The pharmacy or drug storage area must be administered in accordance with accepted professional principles.

Interpretive Guidelines §482.25(a)

Pharmaceutical services must be administered in accordance with accepted professional principles. Accepted professional principles includes compliance with applicable Federal and State laws, regulations, and guidelines governing pharmaceutical services, as well as, standards or recommendations promoted by nationally recognized professional organizations, *such as those found in the U.S. Pharmacopeia/National Formulary (USP/NF).*

The hospital's pharmacy service must ensure safe and appropriate procurement, storage, preparation, dispensing, use, tracking and control, and disposal of medications and medication-related devices throughout the hospital, for both inpatient and outpatient services.

Hospitals may choose how to set up the pharmaceutical services utilizing various methods including, but not limited to:

- *a unit dose system (i.e.; single unit package, dispensed in most ready to administer form possible),*
- *individual prescription (i.e.; instruction for a single patient, written by a medical practitioner for a medication or treatment),*
- *floor stock system (i.e.; storage of pharmaceutical and over-the-counter drugs on the patient care unit), or*
- *a combination of these systems, as long as they are properly stored.*

However, hospitals with only a drug storage area must only use drugs that are pre-packaged and need no further preparation beyond that required at the point of care.

The *hospital must* develop, implement and periodically review and revise *as needed* policies and procedures governing provision of pharmaceutical services. *The regulation makes the hospital's medical staff responsible for the policies and procedures, but also permits the medical staff to delegate this function to the hospital's pharmaceutical services. The policies and procedures must reflect accepted professional pharmacy principles, and the pharmacy director must be able to identify the source(s) used when developing and adopting the policies and procedures. There must also be a process to train staff on the applicable policies and procedures and to monitor their adherence.*

Policies and Procedures for Minimizing Drug Errors

Medication errors are a substantial source of morbidity and mortality risk in the hospitalized setting. Therefore, hospitals must take steps to prevent, identify, and minimize these errors. These steps must be based on accepted professional principles. This includes not only ensuring that the pharmacy processes conform to of accepted standards of pharmacy practice but also proactively identifying and reviewing Adverse Drug Events (ADE) that occur. Pharmacies also need to be aware of external alerts to real or potential pharmacy-related problems in hospitals.

The *pharmaceutical services* policies and procedures *must be designed* to minimize drug errors and are expected to address:

- *High-alert medications - are considered inherently high risk for adverse drug events. High alert drugs may include controlled medications, medications not on the approved FDA list, medications with a narrow therapeutic range, psychotherapeutic medications, look-alike/sound-alike medications and those new to the market or new to the hospital. Although mistakes may or may not be more common with these drugs, the consequences of errors are often harmful, sometimes fatal, to patients. Examples of ways to minimize high alert medication errors include, but are not limited to, the following: dosing limits, administration guidelines, packaging, labeling and storage.*
- *Investigational medications - hospitals that conduct research involving investigational medications must have a policy and procedure in place to ensure that investigational medications are safely controlled and administered. Procedures for the use of investigational medications include, but are not limited to, the following: A written process for reviewing, approving, supervising and monitoring investigational medications specifying that when pharmacy services are provided, the pharmacy controls the storage, dispensing, labeling, and distribution of the investigational medication.*
- *Adherence to professional standards of practice for all compounding, packaging dispensing and drug disposal activities;*
- *Standardizing medication-related devices and equipment where feasible. For example, limit the types of general-purpose infusion pumps to one or two;*
- *Availability of up-to-date medication information and pharmacy expertise on-call when pharmacy does not operate 24 hours a day;*

- *Standardization of prescribing and communication practices to include:*
 - *Avoidance of dangerous abbreviations;*
 - *All elements of the order – dose, strength, units (metric), route, frequency, and rate;*
 - *Alert systems for look-like and sound-alike drug names;*
 - *Use of facility approved pre-printed order sheets whenever possible.*
- *Prohibition of orders to “resume previous orders;”*
- *Availability of patient-specific information to all individuals involved in provision of pharmaceutical services. The patient information must be sufficient to properly order, prepare, dispense, administer and monitor medications as appropriate;*
- *Identification of when weight-based dosing for pediatric populations is required; and*
- *A voluntary, non-punitive, reporting system to monitor and report adverse drug events (including medication errors and adverse drug reactions);*
- *Monitoring drug alerts and/or recalls. The hospital should have a means to incorporate external alerts and/or recommendations from national associations and governmental agencies for review and facility policy and procedure revision consideration. National associations could include Institute for Safe Medications Practice and National Coordinating Council for Medication Error Reporting and Prevention. Governmental agencies may include: Food and Drug Administration, Med Watch Program; and*
- *The hospital’s pharmacy services must be integrated into its hospital-wide QAPI program and therefore, it is important to flag new types of mistakes and continually improve and refine policies and procedures as a result of analyses of errors and adverse events.*

Survey Procedures §482.25(a)

- *Is the hospital’s organized pharmaceutical services responsible for the procurement, distribution and control of all medication products used in the hospital (including medication-related devices) for inpatient and outpatient care?*
- *If the hospital has a drug storage area instead of a pharmacy, does it use only drugs that are pre-packaged and need no further preparation beyond that required at the point of care?*
- *Is there evidence that the hospital’s medical staff has either adopted pharmaceutical services policies and procedures, or has delegated this task to the pharmaceutical services?*

- *Can the pharmacy director provide evidence that the policies and procedures are consistent with accepted professional principles?*
- *Can the pharmacy director provide evidence that policies and procedures address key areas to prevent medication errors?*
- *Is there evidence of training staff on applicable pharmaceutical policies and procedures?*
- *Is there a process in place to monitor adherence to policies and procedures?*

A-0492

(Rev.)

[\$482.25 Condition of Participation: Pharmaceutical Services

The hospital.... must have a pharmacy directed by a registered pharmacist or a drug storage area under competent supervision....

§482.25(a)(1) - A full-time, part-time, or consulting pharmacist must be responsible for developing, supervising, and coordinating all the activities of the pharmacy services.

Interpretive Guidelines §482.25 and §482.25(a)(1)

Pharmaceutical services offered throughout the hospital must be under the direction of a pharmacist, who may be full-time, part-time, or consulting. This is required even in the case of a hospital that has a drug storage area instead of a pharmacy. The director must have documented training or expertise in hospital pharmacy practice and management. The hospital must have written criteria for the qualifications of the pharmacy director in accordance with the scope of services provided.

The extent of pharmaceutical services provided by the hospital determines whether a part-time director of the services is sufficient. Depending on the volume and complexity of the hospital's services, oversight may not require full-time on-site management at the hospital's pharmacy, but may be accomplished through regularly scheduled visits, and/or use of telecommunications in accordance with federal and state law and accepted professional principles. If the hospital does not have a full-time pharmacist, it must be able to provide evidence of how a part-time or consulting pharmacist is able to perform all functions relating to developing, supervising and coordinating all pharmacy services activities.

In general, hospital pharmacies are staffed with registered pharmacists and pharmacy technicians who perform various functions, including, but not limited to, compounding, labeling, and dispensing of various drugs and biologicals.

There may be instances of small hospitals that do not have a pharmacy but utilize a drug storage area for dispensing pre-packaged drugs only. If the hospital has a drug storage area in lieu of a

pharmacy, the day-to-day operations of pharmaceutical services must be under the supervision of an individual who, if not a pharmacist, nevertheless has documented competency to oversee compliance with all the pharmaceutical services regulatory requirements (e.g., security, access to locked areas, etc.). The hospital must establish in writing the qualifications of the drug storage area supervisor.

Likewise, if a hospital has remote locations or satellites that rely on the pharmacy of the main campus and maintain only drug storage area(s) on-site, there must be competent day-to-day supervision of those storage area(s), under the overall direction of the pharmacist who manages the hospital's pharmaceutical services.

The job description or the written agreement for the responsibilities of the pharmacist director should be clearly defined and include development, supervision and coordination of all the activities of pharmacy services, including active leadership of those committees responsible for establishing medication-related policies and procedures.

Survey Procedures §482.25 and §482.25(a)(1)

- *Does the hospital have a pharmacist who has been appointed to direct the pharmaceutical services?*
 - *Are there written criteria for the qualifications of the pharmacist director?*
 - *Is there evidence in the pharmacist's file that he/she satisfies the criteria?*
- *If the hospital has a drug storage area in lieu of a pharmacy, is there evidence the storage area is under competent supervision?*
- *Review the pharmaceutical services Director's file to verify that he or she meets the qualifications established by the medical staff and has been granted privileges as a pharmacist.*
- *If the Director is a part-time employee or consultant, ask him/her how much time/week is spent on developing, supervising and coordinating pharmaceutical services.*
- Review the implementation of the pharmacy *director's* responsibilities by:
 - Reviewing minutes of meetings (if any) with facility staff regarding pharmaceutical services;
 - Reviewing the job description or the written agreement to see that the responsibilities of the pharmacist are clearly defined and include development supervision and coordination of all the activities of pharmacy services;

Determining whether the pharmacy *director/manager* routinely evaluates the performance and competency of pharmacy personnel?

- *Ask the pharmacy director to describe how policies and procedures related to pharmaceutical services are developed, approved, and implemented. What is his/her role in this process?*
- *Is there any evidence of problems within the pharmaceutical services that suggest lack of supervision?*

A-0500
(Rev.)

§482.25(b) Standard: Delivery of Services

In order to provide patient safety, drugs and biologicals must be controlled and distributed in accordance with applicable standards of practice, consistent with Federal and State law.

Interpretive Guidelines §482.25(b)

Drugs and biologicals must be controlled and distributed in accordance with applicable Federal and State laws and regulations, and in accordance with applicable standards of practice. Applicable standards of practice include compliance with all Federal and State laws, regulations, and guidelines. The procedures established to prevent unauthorized usage and distribution must provide for an accounting of the receipt and disposition of drugs subject to the Comprehensive Drug Abuse Prevention and Control Act of 1970.

Other sources of additional guidelines could include, but are not limited to: American Society of Health-System Pharmacists, American College of Clinical Pharmacy, American Pharmacists Association, United States Pharmacopeia, etc.

Note re: US Pharmacopeia/National Formulary (USP/NF)

According to the Federal Food, Drug and Cosmetic Act (FCDA), the official compendia of the United States for excipients, drug substances, and drug products is the USP/NF. It is published every year in November by the United States Pharmacopeial Convention (<http://www.usp.org/>) and includes two supplements published in February and June.

The USP is a not-for-profit, non-governmental organization that since 1820 has established quality standards for, among other things, drug substances, drug products and compounded preparations. Congress established a role for USP standards in the adulteration provision of the 1906 Food and Drug Act. That role was expanded in the modern Food, Drug and Cosmetic Act (FDCA) beginning in 1938, with a role for USP compendial standards for naming and identity; strength, quality, and purity; and packaging and labeling, in both the adulteration and misbranding provisions of FDCA. (See, for example, §501(b) of the FDCA regarding compendial standards for strength, quality and purity, §502(g) for compendial standards for packaging and labeling). Under the FDCA, a drug with a name recognized in the USP/NF must comply with compendial identity standards, or be deemed adulterated, or misbranded, or both. To avoid being deemed adulterated, such drugs must also comply with compendial standards for strength, quality, and purity, unless labeled to show all respects in which the drug differs.

The hospital must have a process in place for medication orders to be received in the pharmacy and dispensed in a safe and timely manner. Safe dispensing of medications must be in accordance with accepted standards of practice and includes, but is not limited to, the following:

- *Implementing systems such as dose limits, pre-printed orders, special labeling, or double checks to minimize adverse drug events, especially for high alert medications;*
- *Reviewing all medication orders (except in emergency situations) for appropriateness by a pharmacist before the first dose is dispensed. A process is established for resolving questions with the prescribing practitioner and the discussion and outcome are documented in the patient's medical record or pharmacy copy of the prescriber's order;*

This review should include:

- *Therapeutic appropriateness of a patient's medication regimen;*
 - *Therapeutic duplication in the patient's medication regimen;*
 - *Appropriateness of the drug, dose, frequency, and route of administration;*
 - *Real or potential medication-medication, medication-food, medication-laboratory test and medication-disease interactions;*
 - *Real or potential allergies or sensitivities; and*
 - *Other contraindications.*
- Medications dispensed by the hospital are retrieved when recalled or discontinued by the manufacturer or the Food and Drug Administration (FDA) for safety reasons;
 - *Policies and procedures that address the use of medications brought into the hospital by patients or their families when self-administration of medications is permitted by hospital policy; and*
 - *Having a system in place to reconcile medications that are not administered (e.g., left in the patient's medication drawer) when the pharmacy inventories patient medications or restocks patient medications.* For example, did the patient refuse the medication, was there a clinical or treatment reason the medication was not used, or was the medication not used due to an error?

Monitoring the Effects of Medications

The pharmaceutical service may be responsible for monitoring the effects of medication(s) specified per hospital policy to assure medication therapy is appropriate and minimizes the occurrence of adverse events. Typically this occurs with anticoagulant therapy and antibiotics

prescribed for the pharmacy to establish or adjust the dosage (i.e.; “pharmacy to dose” order). In such cases, the pharmacy’s monitoring process includes:

- *Clinical and laboratory data to evaluate the efficacy of medication therapy to anticipate or evaluate toxicity and adverse effects;*
- *Physical signs and clinical symptoms relevant to the patient’s medication therapy;*
- *Assessing the patient’s own perceptions about side effects, and, when appropriate, perceived efficacy.*

(See also the Nursing CoP discussion regarding monitoring of patients at §482.23(c)(4)).

Survey Procedures §482.25(b)

- *Are medication orders routinely reviewed by the pharmacy before the first dose? What evidence can the hospital present that such reviews take place?*
- *Are questions regarding **medication** orders resolved with the prescriber and a written notation of these discussions documented in the patient’s medical record or pharmacy copy of the prescriber’s order?*
- *Does the hospital pharmacy have a system for monitoring the effects of medication therapies for cases specified per hospital policy?*
- *Does the hospital retrieve and remove medications available or patient use when the hospital has been informed of a drug recall?*

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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:

- *manufacturers,*
- *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 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/pharmacycompounding/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 USP <795> and <797> requirements, 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 practice equivalent to or more stringent than those described in the compounding-related chapters in the United States Pharmacopeia and the National Formulary (USP) published by the U.S. Pharmacopeial Convention, which are recognized as authoritative guidance regarding minimum standards of safe practice applicable to both sterile and non-sterile compounding.

The definition of compounding as that term is used in the USP is found in USP Chapter <795> (USP <795>):

“The preparation, mixing, assembling, altering, packaging and labeling of a drug, drug-delivery device, or device 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:

- Preparation of drug dosage forms for both human and animal patients*
- Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns*
- Reconstitution or manipulation of commercial products that may require the addition of one or more ingredients*
- Preparation of drugs or devices for the purposes of, or as incident to, research (clinical or academic), teaching or chemical analysis*
- Preparation of drugs and devices for prescriber’s office use where permitted by federal and state law.”*

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.

USP <797> outlines minimum standards of practice to be followed by all health care personnel in any setting when preparing, storing and transporting “compounded sterile preparations” (CSPs). Its stated objective is “to describe conditions and practices to prevent harm, including death, to patients that could result from...microbial contamination...excessive bacterial endotoxins...variability of intended strength of correct ingredients...unintended chemical and physical contaminants...and ingredients of inappropriate quality....” Contaminated CSPs are especially hazardous if administered into body cavities, the central nervous system, vascular system, eyes, joints, and/or used as baths for live organs and tissues. “All compounded dosage forms that must be sterile when they are administered to patients” are considered by USP <797> to be CSPs, including but not limited to:

- *“Aqueous bronchial and nasal inhalations;*
- *Baths and soaks for live organs and tissues;*
- *Injections [and infusions];*
- *Irrigations for wounds and body cavities;*
- *Ophthalmic drops and ointments;*
- *Tissue implants.”*

USP <797> specifies differing standards for the physical layout and structure of the locations in which compounding takes place as well as processes, precautions and quality assurance practices to be implemented during the preparation, transport and storage of CSPs. The standards differ in part based on the level of risk of microbial contamination of the CSP, and the risk level has implications for whether a CSP must be terminally sterilized before being dispensed and for how long a CSP may be stored before use. The risk categories and accompanying standards are based on specific criteria, including but not limited to, factors such as:

- *The structural design, environmental controls, air quality levels (based on International Organization for Standardization (ISO) standards for particulate matter in air) and air flow patterns in and surrounding the environment to which the contents of the CSP as well as the surfaces of devices and containers for the preparation, transfer, sterilization and packaging of CSPs are exposed.*
- *The sterility of the original ingredients and/or device(s) used in compounding, the number of containers that need to be entered, how many times they need to be entered, the nature and complexity of the manipulations and length of time required to prepare the CSP.*
- *Whether compounding personnel are appropriately garbed and gloved.*
- *Whether multiple doses of sterile products are pooled to produce a CSP that will be administered on more than one occasion or to more than one patient.*

The goal of the USP <797> standards is to prevent and/or minimize the risk of microbial contamination of CSPs, whether by direct contact, exposure to particles in air generated by personnel or objects, or other mechanisms. A major concern is preventing contamination of “critical sites,” which include “any component or fluid pathway surfaces (e.g., vial septa, injection ports, beakers) or openings (e.g., opened ampules, needle hubs) exposed or at risk of direct contact with air...moisture...or touch contamination.”

USP <797> describes two basic structural designs for the physical layout and environmental controls intended to minimize airborne contamination of critical sites during preparation of CSPs. The risk level of the CSPs a facility can produce depends, in part, on which USP <797> environmental quality and control/facility design standards the hospital (or its vendor) is able to meet (low-risk level, medium-risk level and high-risk level are discussed here; see §482.23(c) for a discussion of “immediate-use” CSPs):

- *Some facilities may only prepare low-risk level nonhazardous and radiopharmaceutical CSPs pursuant to a physician order for a specific patient, and administration must commence within the lesser of 12 hours of preparation or as recommended in the manufacturer’s package insert. Such a facility would have a designated, demarcated room or space that is the “segregated compounding area (SCA),” which contains a device that provides unidirectional airflow of International Standards Organization (ISO) Class 5 air quality (quality class ranges from class 0, the most stringent, to class 9, the most relaxed). The SCA may not be in an area with unsealed openings/potential openings to high traffic locations, the outdoors and other proscribed environmental conditions, and the SCA area may not contain any materials or be the site of any activities unrelated to preparing low-risk CSPs.*
- *If a facility is preparing high- or medium-level risk CSPs or low-risk CSPs with a beyond-use date of greater than 12 hours, it must meet additional environmental design and monitoring/testing standards in the buffer and ante-areas.*
- *USP<797> contains separate standards for the safe compounding of hazardous medications (defined as “...if studies in animals or humans indicate that exposures to them have a potential for causing cancer, development or reproductive toxicity, or harm to organs...”), radiopharmaceuticals and allergen extracts.*

In addition, USP <797> includes standards for various processes, precautions and quality assurance practices required and recommended for the safe preparation of all risk levels of CSPs. These address issues such as:

- *The responsibilities of compounding personnel and their supervisors to implement and maintain proper procedures and quality assurance checks.*
- *Issues specific to “immediate use” CSPs; single- and multiple-dose containers; CSPs containing hazardous drugs; radiopharmaceuticals; allergen extracts; and automated compounding devices used for parenteral nutrition compounding.*
- *Methods for sterilization, depyrogenation and for verifying compounding accuracy and sterility.*
- *Specifications for environmental quality and control, including but not limited to:*
- *Specifications and related personnel training, including competency assessment and evaluation of skill in aseptically preparing CSPs using visual observation as well as bacterial sampling of glove fingertips and “media-fill testing” at specified intervals.*

- *Evaluation and monitoring/testing of the environment in which compounding takes place and, if applicable, the adjacent “ante-” and “buffer” areas, including facility layout, design, environmental controls, restricted access, air quality standards and testing, surface characteristics, furnishings, cleaning and disinfection procedures, and standards for personnel health, attire/cosmetics, cleansing/garbing/gloving, aseptic work practices, etc.*
- *Suggested standard operating procedures to protect the quality of the environment in which CSPs are prepared.*
- *Quality control related to ingredients, devices and equipment used in relation to CSPs.*
- *Quality checks to be performed before CSPs are dispensed or administered.*
- *Issues related to beyond-use dating and packaging, storage and transportation conditions for CSPs.*
- *Protecting dispensed and distributed CSPs.*
- *Patient education issues.*
- *Monitoring for and reporting adverse patient events related to CSPs.*
- *Requirements for a formal quality assurance program to be maintained by providers of CSPs.*

For Information – Not Required/Not to be Cited

USP <797> Appendices I and III-V contain summaries and assessment tools that hospitals may find helpful. However, there is no requirement to use specific forms or materials as long as the hospital and/or its external sources of CSPs are implementing plans, procedures, testing and documentation consistent with applicable standards for safe compounding. These USP <797> materials are referenced here only as examples:

- *“Appendix I: Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required...and Recommended in USP Chapter <797>”*
- *“Appendix III: “Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel”*
- *“Appendix IV: “Sample Form for Assessing Aseptic Technique and Related Practices of Compounding Personnel”*
- *“Appendix V: “Sample Form for Assessing Cleaning and Disinfection Procedures”*

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). It should be noted that, for multi-dose medication vials with antimicrobial preservatives which have been opened or entered (e.g., needle-punctured), the USP standard is that the BUD is 28 days, unless otherwise specified by the manufacturer. 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 be accessed by authorized personnel.*
- *Policies and procedures must address who can access medications during after-hours.*

For Information Only – Not Required/Not to be Cited

When utilizing automated dispensing cabinets (ADCs), the Institute for Safe Medication Practices recommendations include the following:

(See: <http://www.ismp.org/Newsletters/acutecare/articles/20090212.asp> and http://www.ismp.org/Tools/guidelines/ADC_Guidelines_Final.pdf)

Security processes are established to ensure adequate control of medications outside of the pharmacy and to reduce the potential for medication diversion from ADCs.

- *Utilize biometric user identification or, at a minimum, change user passwords quarterly.*
- *Link the ADC to the pharmacy computer to allow for patient “profiling,” so that a pharmacist can review each medication order and screen it for safety before the drug is dispensed or accessed by the nurse or other healthcare professional.*
- *Limiting the availability of overrides to the ADC system.*
- *Limiting access to drugs based on the patients profile so to decrease medication selection errors.*
- *Store each medication and strength in an individual lidded ADC compartment that opens only when the specific medication is selected.*

- *Document the destruction of medication waste at the time of removal of the medication whenever possible. Record this waste via the ADC, and match the administered dose with ordered dose. Have a process to routinely review/reconcile the documented medication waste.*
- *Return all medications to a common secure one-way return bin that is maintained by pharmacy, not to an individual pocket or bin within the ADC.*

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 equivalent to or more stringent than the standards described in USP <795> and <797>?*
 - *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 equivalent to or more stringent than the standards described in USP <795> and <797>?*
 - *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? For example, does the contract include provisions ensuring that the hospital has access to quality assurance data verifying that the vendor is adhering to current USP <795> and <797> requirements, and can the hospital document that it obtains and reviews such data?*
- *Can the pharmacy director explain the risk level(s) of the CSPs being produced in-house and/or obtained from external sources? Can he or she demonstrate that the assigned risk levels are consistent with USP <797> or equivalent/more stringent standards?*

- *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 USP <797> or equivalent/more stringent 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?*

A-0502
(Rev.)

§482.25(b)(2)(i) - All drugs and biologicals must be kept in a secure area, and locked when appropriate.

Interpretive Guidelines §482.25(b)(2)(i)

A secure area means that drugs and biologicals are stored in a manner to prevent unmonitored access by unauthorized individuals. Drugs and biologicals must not be stored in areas that are readily accessible to unauthorized persons. For example, if medications are kept in a private office, or other area where patients and visitors are not allowed without the supervision or presence of a health care professional (for example, ambulatory infusion), they are considered secure. Areas restricted to authorized personnel only would generally be considered “secure areas.” If there is evidence of tampering or diversion, or if medication security otherwise becomes a problem, the hospital is expected to evaluate its current medication control policies and procedures, and implement the necessary systems and processes to ensure that the problem is corrected, and that patient health and safety are maintained. (71 FR 68689)

All controlled substances must be locked. Hospitals are permitted flexibility in the storage of non-controlled drugs and biologicals when delivering care to patients, and in the safeguarding of drugs and biologicals to prevent tampering or diversion. An area in which staff are actively providing care to patients or preparing to receive patients, i.e., setting up for procedures before the arrival of a patient, would generally be considered a secure area. When a patient care area is not staffed, **both** controlled and non-controlled substances are expected to be locked.

Generally labor and delivery suites and critical care units are staffed and actively providing patient care around the clock, and, therefore, considered secure. However, hospital policies and procedures are expected to ensure that these areas are secure, with entry and exit limited to appropriate staff, patients and visitors.

The operating room suite is considered secure when the suite is staffed and staff are actively providing patient care. When the suite is not in use (e.g., weekends, holidays and after hours), it would not be considered secure. A hospital may choose to lock the entire suite, lock non-mobile carts containing drugs and biologicals, place mobile carts in a locked room, or otherwise lock drugs and biologicals in a secure area. If an individual operating room is not in use, the hospital is expected to lock non-mobile carts, and ensure mobile carts are in a locked room. (71 FR 68689)

This regulation gives hospitals the flexibility to integrate patient self-administration of non-controlled drugs and biologicals into their practices as appropriate. When a hospital allows a patient to self-administer selected drugs and biologicals, the hospital authorizes the patient to have access to these medications. This regulation is consistent with the current practice of giving patients access at the bedside to urgently needed medications, such as nitroglycerine tablets and inhalers. It supports the current practice of placing selected nonprescription medications at the bedside for the patient’s use, such as lotions and creams, and rewetting eye

drops. Hospitals are expected to address patient self-administration of non-controlled drugs and biologicals in their policies and procedures (*see self-administration discussion at §§482.23(c)(6)(i) and 482.23(c)(6)(ii)*). This regulation supports hospital development, in collaboration with the medical staff and the nursing and pharmacy departments, of formal patient medication self-administration programs for select populations of patients, including hospital policies and procedures necessary to ensure patient safety and security of medications. The policies and procedures are expected to include measures to ensure the security of bedside drugs and biologicals. They are also expected to address both the competence of the patient to self-administer drugs and biologicals as well as patient education regarding self-administration of drugs and biologicals. (71 FR 68689)

Due to their mobility, mobile nursing medication carts, anesthesia carts, epidural carts and other medication carts containing drugs or biologicals (hereafter, all referred to as “carts”) must be locked in a secure area when not in use. Hospital policies and procedures are expected to address the security and monitoring of carts, locked or unlocked, containing drugs and biologicals in all patient care areas to ensure their safe storage and to ensure patient safety. (71 FR 68689)

Medication automated distribution units with security features, such as logon and password or biometric identification, are considered to be locked, since they can only be accessed by authorized personnel who are permitted access to the medications. Such units must be stored in a secure area.

Survey Procedures §482.25(b)(2)(i)

- Review hospital policies and procedures governing the security of drugs and biologicals to determine whether they provide for securing and locking as appropriate.
- Review hospital policies and procedures governing patient self-administration of drugs and biologicals.
- Observe whether medications in various areas of the hospital are stored in a secure area, and locked when appropriate. *Are medication storage areas periodically inspected by pharmacy staff to make sure medications are properly stored?*
- Determine that security features in automated medication distribution units are implemented and actively maintained, e.g., that access authorizations are regularly updated to reflect changes in personnel, assignments, etc.
- Interview staff to determine whether policies and procedures to restrict access to authorized personnel are implemented and effective.
- *If patient self-administration of drugs and biologicals is permitted, interview* patients and staff to determine whether policies and procedures are implemented and effective.

A-0505
(Rev.)

§482.25(b)(3) - Outdated, mislabeled, or otherwise unusable drugs and biologicals must not be available for patient use.

Interpretive Guidelines §482.25(b)(3)

The hospital must have a pharmacy labeling, inspection, and inventory management system that ensures that outdated, mislabeled, or otherwise unusable drugs and biologicals are not available for patient use. *This would include drugs that are the subject of a manufacturer's recall.*

A drug or biological is outdated after its expiration date, which is set by the manufacturer based on stability testing under specified conditions as part of the FDA approval process. It should be noted that a drug or biological may become unusable prior to its expiration date if it has been subjected to conditions that are inconsistent with the manufacturer's approved labeling.

A drug or biological is also outdated after its "beyond-use date" (BUD), which may be reached before the expiration date, but never later. The BUD takes into account the specific conditions and potential for deterioration and microbial growth that may occur during or after the original container is opened, while preparing the medication for dispensing and administration, and/or during the compounding process if it is a compounded medication.

The BUD is to be based on information provided by the manufacturer, whenever such information is available. The hospital must maintain and implement policies and procedures that provide clear and consistent direction to pharmacy staff regarding how to determine a BUD when complete BUD information is not available from the manufacturer. The policies and procedures must be based on accepted professional principles which are equivalent to, or more stringent than, those described in the United States Pharmacopeia-National Formulary (USP).⁴

According to Chapters <795> and <797> of the USP, the BUD must be safe for patients, and determined conservatively. The section in USP <797> entitled "Determining Beyond-Use Dates," which addresses sterile compounding, notes that "the truly valid evidence for predicting beyond-use dating can be obtained only through product-specific experimental studies." It provides an example of testing considered more appropriate for certain types of compounded sterile preparations (CSPs) such as "CSPs with a narrow therapeutic index, where close monitoring or dose titration is required to ensure therapeutic effectiveness and to avoid toxicity...." It also provides examples of important issues that a pharmacist must be able to critically interpret and evaluate when consulting literature sources in the process of determining a BUD; and distinguishes between reviewing literature specific to a particular drug, composition, concentration of ingredients, fill volume, container, storage conditions and duration of use, etc., versus merely reviewing available publications or tables. The former is the

⁴ All references to "USP" herein are from: United States Pharmacopeial Convention. *USP on Compounding: A Guide for the Compounding Practitioner. Current with USP 37-NF32 through First Supplement.* Rockville, MD: United States Pharmacopeial Convention, 2014.

preferred approach, while the latter results in a “theoretical BUD,” which has an inherent likelihood of inaccuracy or 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 BUD. It should be noted that, for multi-dose medication vials with antimicrobial preservatives which have been opened or entered (e.g., needle-punctured), the USP standard is that the BUD is 28 days, unless otherwise specified by the manufacturer. 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.

Survey Procedures §482.25(b)(3)

- Spot-check the labels of individual drug containers to verify that they conform to *Federal and State laws*, and/or contain the following minimal information:
 - Each patient’s individual drug container bears his/her full name, and strength and quantity of the drug dispensed. Appropriate accessory and cautionary statements are included as well as the expiration date *and/or, if applicable, a BUD*.
 - Each floor stock container bears the name and strength of the drug, lot and control number of equivalent, expiration date.
- If the unit dose system is utilized, verify that each single unit dose package bears name and strength of the drug, lot and control number equivalent, expiration date *and/or, if applicable, a BUD*.
- Inspect patient-specific and floor stock medications to identify expired, mislabeled or unusable medications.
- *Review the pharmacy policies and procedures for determining BUDs (for medications compounded in-house as well as from external sources).*
 - *Can the hospital demonstrate that the policies and procedures are consistent with or more stringent than the applicable USP standards?*
 - *Can it demonstrate that the pharmacy personnel assigned to determining BUDs when a manufacturer’s instructions are not available have the expertise and technical support needed to properly conduct the assessments needed to make such determinations in a manner consistent with standards and hospital policies?*

- *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?*

A-0507

(Rev.)

§482.25(b)(5) - Drugs and biologicals not specifically prescribed as to time or number of doses must automatically be stopped after a reasonable time that is predetermined by the medical staff.

Interpretive Guidelines §482.25(b)(5)

In accordance with accepted standards of practice, the medical staff, in coordination and consultation with the pharmacy service, determines and establishes the reasonable time to automatically stop orders for drugs and biologicals not specifically prescribed as to time or number of doses. The hospital must implement, monitor, and enforce this automatic stop system.

It is important to note that hospitals with an electronic health record (EHR) system may have time and dose parameters automatically built into computerized provider order entry (CPOE) screens. These may be part of the hospital's plan for addressing automatic stop orders.

Survey Procedures §482.25(b)(5)

- Review policies and procedures to determine that there is a protocol established by the medical staff to discontinue and review patients' medical records to determine compliance with stop-order policy.
- *Ask unit staff what happens in the case of drugs with no stop date or prescribed number of doses. Are they aware of the automatic stop policy? Can they describe how it is enforced?*

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§482.25(b)(8) - Information relating to drug interactions and information of drug therapy, side effects, toxicology, dosage, indications for use, and routes of administration must be available to the professional staff.

Interpretive Guidelines §482.25(b)(8)

The pharmacy must be a resource for medication-related information to the hospital's health-care practitioners and other health care personnel to optimize therapeutic outcomes and

minimize adverse drug events. Information must be available concerning drug interactions and information of drug therapy, side effects, toxicology, dosage, indications for use, and routes of administration. The pharmacy may also assist other health care professionals with the following medication-related functions:

- *Collection and organization of patient-specific information (height, weight, allergies);*
- *Identification of the presence of medication-therapy problems, both potential and actual, such as drug-drug interactions, excessive doses;*
- *Identification and specification of pharmaco-therapeutic goals;*
- *Implementation of a monitoring plan in collaboration with the patient, if applicable, and other health-care professionals;*
- *Monitoring the effects of the pharmacotherapeutic regimen – could include adjusting doses based on lab values (i.e.: Coumadin dosing); or*
- *Redesigning the regimen and monitoring plan as indicated.*

For example, practitioners may write an order for “pharmacy to dose” an antibiotic. The pharmacist would then take patient-specific information, review the patient’s current medication therapies for any problems, and then calculate the dose required to meet therapeutic goals.

Increasingly, as hospitals move to computerized physician-order entry (CPOE) of medication orders, much of this consultation function (e.g.; dosage, path of administration, drug-drug interactions and other contraindications, etc.) is built in to the electronic health record (EHR) system. However, the pharmacy service remains responsible for the provision of accurate, up-to-date information to meet the needs of the hospital’s practitioners, nursing staff and patients.

The *hospital must also have immediately available sufficient up-to-date reference material* on drug therapy, *whether in electronic or hard copy format*. A pharmacist also should be readily available by telephone or other means to *respond to questions from* practitioners and nursing personnel.

Survey Procedures §482.25(b)(8)

- *Is drug information readily available to nurses and practitioners, whether in hard copy or electronic format?*
- *If drug information is built in to the hospital’s EHR system, ask the pharmacy director how the hospital ensures that the information is accurate and up-to-date.*
- *Ask practitioners whether needed reference information is available to them when*

prescribing drugs.

- *Ask nursing staff whether needed reference information is available to them when administering drugs or biologicals and when monitoring patients for effects of medication therapies.*