CHANGES IN PHARMA REGULATIONS
HOW IT AFFECTS THE OR NURSE

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DISCLOSURE

I, John Karwoski, RPH, MBA have business relationships with the companies MOBIUS THERAPEUTICS, LLC, Cubex, and PharMEDium.

There is no conflict of interest between these relationships and the presentation I will deliver today.

OBJECTIVES

1. At the conclusion of this webinar, operating room nursing staff will be able to confidently comply with USP <797>
2. Recognize non-compliance of injectable medications used in the operating room
3. Identify pertinent components of Track & Trace (DSCSA) as it concerns common used OR medications

USP <797>

THE UNITED STATES PHARMACOPEIA CONVENTION(USP)

USP sets standards for the quality of drug products The USP is a large book of standards and monographs broken into chapters (eg., chapter 797). The chapter describing how sterile products are to be handled. It can be enforced by the state boards of pharmacy and the Food and Drug Administration.

USP <797>

Chapter 797 will affect anyone or any facility that handles injectables and other products that require sterility.

USP <797> REVISIONS

USP <797>

"*USP* General Chapter <797> provides standards for compounding sterile preparations to promote patient safety and prevent harm. These standards help ensure patients receive quality preparations that are free from contaminants and are consistent in intended identity, strength and potency. This General Chapter describes a number of requirements, including responsibilities of compounding personnel, training, environmental monitoring, storage and testing of finished preparations."

DEFINITIONS

Compounding is defined as the combination of three or more commercially manufactured packages of sterile-nonhazardous products from the manufacturer's original containers

Compounded biologics include nasal inhalations, baths and soaks for live organs and tissues, injections, irrigations, ophthalmic drops and ointments, and tissue implants

CSP is an abbreviation used for Compounded Sterile Preparations

BUD is an abbreviation for Beyond Use Date is NOT to be confused with an expiration date. A BUD is the date and time after which a CSP shall not be stored or transferred

OBJECTIVE OF USP <797>

The objective of USP <797> is to prevent harm as result of:

- Microbial contamination (nonsterility)
- Excessive bacterial endotoxins
- Variability in the intended strength of correct ingredients
- Unintended chemical and physical contaminants
- Ingredients of inappropriate quality

COMPOUNDED STERILE PREPARATIONS (CSPs)

- Compounded biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals
  - Aqueous bronchial and nasal inhalations, baths and soaks for live organs and tissues
  - Injections INCLUDING colloidal dispersions, emulsions, solutions, and suspensions, irrigations for wounds and body cavities, ophthalmic drops and ointments, and tissue implants
- Manufactured sterile products
  - The FDA states that, "Compounding does NOT include mixing, reconstituting, or similar acts that are performed in accordance with the directions contained in approved labeling provided by the product's manufacturer…"

PERSONNEL ABLE TO COMPOUND

All sterile compounding is likely to be performed under the supervision of a licensed pharmacist.

All individuals who prepare CSPs are responsible for upholding the standards set in USP <797>

- Pharmacists
- Nurses
- Pharmacy technicians
- Physicians

CATEGORIZING COMPOUNDING

- USP <797> revisions have categorized compounding into 4 levels:
  - Low-risk
  - Medium-risk
  - High-risk
  - Immediate Use
- CSPs are classified according to the potential for microbial, chemical, and physical contamination

LOW-RISK COMPOUNDING

- ISO Class 5 Environment (air quality control)
- Transfer, measuring, or mixing of not more than 3 packages of sterile products
- Manipulations are limited to opening ampules, penetrating vials, and transferring liquids for storage and dispensing
- Meets requirements for storage conditions and periods
- Example: "single volume transfers of sterile dosage forms from ampules, bottles, bags, and vials using sterile syringes with sterile needles, other administration devices, and other sterile containers".

IMMEDIATE-USE CSPs

- Exempt from Low-Risk CSP compounding criteria ONLY if:
  - Simple transfer of NO more than 3 products from original containers
  - Compounding procedure does not take more than 1 hour
  - Aseptic technique is followed
  - Administration of CSP is no later than 1 hour after preparation of CSP
  - Labeling requirements are met

THE ONE-HOUR RULE

"Opened or needle-punctured single-dose containers, such as bags, bottles, syringes, and vials of sterile products and CSPs shall be used within 1 hour if opened in worse than ISO class 5, and any remaining contents must be discarded"

MULTIPLE-DOSE VIALS

- Multiple-dose containers, i.e. vials, are formulated for multiple entries
- This is possible because the vial contains antimicrobial preservatives
- BUD after initial entrance of a multiple-dose vial is 28 days unless specified otherwise by the manufacturer
- NOTE: All injectable medications(single use vials and multiple dose vials)must be used for one patient when accessed in the OR.

ADDITIONAL NURSE TRAINING REQUIREMENTS

- Not yet clear if nursing staff will require additional training
- FDA registered 503B outsourcing facilities must provide training materials for caregivers and patients
- Education and competencies are required for individuals compounding anything more than immediate-use CSPs

USP <797> REGULATORY EFFECTS

- The Drug Quality and Security Act (DQSA)
  - Signed into law November, 2013
  - Includes Sections 503A and 503B defining traditional compounding and outsourcing facilities
  - Removed uncertainty of governing oversite for compounders by granting the FDA regulatory control
- Centers for Medicare and Medicaid Services (CMS)
  - USP <797> has influenced CMS infection control regulation
  - One-hour rule, labeling practices, multiple- and single-dose containers
- Accrediting bodies such as AAAHC and TJC

THE DRUG SUPPLY CHAIN SECURITY ACT (DSCSA)

COMMONLY KNOWN AS "TRACK & TRACE"

TRACK & TRACE BACKGROUND

- **The Drug Supply Chain Security Act (DSCSA)**, otherwise known as Track & Trace, was signed into law in November, 2013
- Went into effect on January 1, 2015 for manufacturers, re-packagers, and wholesalers, and July 1, 2015 for dispensers
- The objective of Track & Trace is to identify and remove potentially harmful pharmaceuticals from the market… primarily, counterfeit drugs
- Many of you may think that counterfeit drugs aren't a problem for your facility, but are you willing to risk your patients' safety?

THE EPOGEN TRAIL TO TIMOTHY FAGAN

- 16 year old Timothy Fagan received liver transplant
- Prescribed Epogen for anemia
  - SDV, 40,000 U/mL dose, was $470
  - Tim experienced severe reactions such as severe cramping, convulsions, and seizing, none of which were known side effects
  - Drug did not have desired effect
- The Epogen Tim was taking had been counterfeit
- The drug had a weaker strength AND was potentially supplemented with unknown substances

THE BASICS

- All ***trade partners*** are required to pass along certain information about prescription drugs, upon the transfer or purchase of the drug, to the subsequent owner:
  - Documents
    - Transaction Statement
    - Transaction History
    - Transaction Information
  - All three documents may be located on a single page

TRACK & TRACE APPLICATION

- To comply with Track & Trace regulation:
  - Implement internal policy to comply
  - Include a protocol about receiving and storing transaction documents, IF you plan on retaining these records
  - The policy may state that your suppliers will maintain the required documentation for the requisite 6 years
- Ask your suppliers to provide a notice, in writing, that they comply with the DSCSA

THE FUTURE OF TRACK & TRACE

Present Day-2022: The FDA will prepare pilot projects with stakeholders to enhance security of the drug supply chain

2021: Development of regulations establishing drug distribution security measures for electronic tracing of drugs

2022: FDA to establish guidance for secure tracing and data exchange at the package level

Ultimately, the FDA seeks to establish regulation requiring NDC or barcodes on all drugs passed through the supply chain to ensure integrity

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