Safe IV Compounding Procedures: The Release of ISMP Guidelines

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Objectives

• List system-based causes of medication errors associated with preparation of compounded sterile preparations (CSPs) in the acute care setting

• Identify storage, workflow, labeling, quality control, and documentation best practices that should be standardized and incorporated into the manual preparation of all CSPs

• Discuss current technologies and describe how each can be used to reduce the risk of error in the preparation of CSPs

• Learn how to participate in further development and finalizing of these draft best practice guidelines
Disclosure

Matthew Fricker declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.
Background: IV Compounding Sterility Issues: Pre-USP <797>

- 1975: “Nationwide epidemic of septicemia caused by contaminated intravenous products”

- 1984: 11 patients received cardioplegia solutions contaminated with *Enterobacter cloacae* – 5 deaths

- 1990-2005: 12 incidents of contaminated products in over 19,000 patients and 15 deaths.
  *ISMP Medication Safety Alert – Oct 8, 2012*

- FDA: 200 adverse events reported involving 71 compounded products since 1990.
  *The Guardian – Oct 10, 2012*
USP Chapter <797>

• 2004: Release of USP Chapter <797> Sterile Preparations.
• FDA left enforcement to the states
• 2012: only 18 states require compliance

www.clinicaliq.com/797-state-survey

– In survey of US hospitals, 65% say they comply with USP <797> clean room requirements


– 17% of hospitals comply with all requirements

    Pharmacy Purchasing & Products 2012 (Oct); 8(10):S4-24
IV Compounding Sterility Issues Since USP Chapter <797>

• Serious infections still occur
  – 2011-2012: 4 serious incidents of contaminated pharmacy-prepared sterile products resulting in harm to over 244 patients
    
  – October 23, 2012: Over 19,000 doses of contaminated pharmacy-prepared sterile products were dispensed by a compounding pharmacy sickening 720 people with meningitis & killing 51
    
IV Compounding Errors

• 2009: 30% of surveyed hospitals had a patient event involving a compounding error in the prior 5 years
  *Pharmacy Purchasing & Products*. 2009; 6(4):4-20

• Five hospital study found a mean daily error rate of 9% (highest for complex solutions like TPN – 22-37%)

• 2005-2011: Serious cases of sterile compounding errors involving 15 patients, 8 of which died, reported due to:
  – wrong concentration/strength of the product dispensed
  – wrong product or diluent used in compounding
  – product mislabeling by the pharmacy
  *ISMP Medication Safety Alerts*
Multiple fatal events related to IV admixture issues

- **Nevada** - Death from 1000-fold zinc overdose (mcg and mg zinc sulfate confused)
- **Illinois** - Child died after sodium chloride concentrate used in error during compounding
- **California, Tennessee, Florida** - Multiple patients blinded due to contamination of Avastin during compounding for wet macular degeneration patients
Multiple fatal events related to IV admixture issues

- **Alabama** - Nine deaths when PN solutions contaminated during compounding
- **Pennsylvania** - Three neonates die after heparin syringes inadvertently prepared in potassium chloride injection concentrate instead of dextrose 5% injection
- **Ohio** - Child died after compounding error led to administration of chemotherapy in 23.4% sodium chloride injection instead of 0.9%
Gaps in pharmacy IV compounding

- Absence of specific practice guidelines related to product preparation checks
- Variability in practices across the country
- Ambiguity in ability to validate compounding

Observations and analysis presented based on data from the ISMP Medication Error Reporting Program (MERP) and onsite risk assessments across the US
Gaps in pharmacy IV compounding

- Need for expanded technology solutions
- Lack of awareness of associated risks by pharmacists as well as senior leadership/RM
- Pharmacy and technician education/hands on training in the compounding of sterile preparations

Observations and analysis presented based on data from the ISMP Medication Error Reporting Program (MERP) and onsite risk assessments across the US
Risk points for the preparation of IV compounds

- Prescribing/Communication
- Technology/Automation
- Product production
- Product checking
- Environment
Risk related to prescribing/communication

• Open formulary
• No restrictions on prescribing
  – The use of non-standard concentrations
  – “Custom formulations”
Risk related to prescribing/communication

• No or incomplete preprinted templates or order sets
• Alignment of ingredients on order forms does not follow sequence of the order entry into a database
• Products ordered in g, mg, mcg, mEq, ratio, percent, mL, units, etc.
Risk related to technology/automation

• Using manual processes when automation is available
• Lack of/outdated clinical decision support in order verification, drug selection, and production
Risk related to production

• Not using commercially-available products when available
• No preparation ticket or directions (worksheet) for compounding; preparation from memory
Risk related to production

• No restrictions on time of day for ordering/production
• Using only the label to prepare IV compounded solutions
• Lack of standardization of preparation procedures between technicians and pharmacists
Risk related to production

- More than one patient-one product in the hood or isolator
- Flawed labeling procedures
- Low volume (rarely prepared) solutions made in house
- Lack of clinical expertise for specialty products
Risk related to IV checking

• Variable checks
  – Are dilutions checked if required for preparing the compounded sterile preparation (CSP)
  – When product is prepared--but before it is added to the solution
  – After compounding using a syringe pull back or other proxy methods
Risk related to the environment

- Insufficient space
  - Inadequate/improper storage
  - Hood space/number of hoods for amount of production
  - Sharing space in hood or isolator
  - Inadequate space for checking process
ISMP Sterile Preparation Compounding Safety Summit

- October 24th and 25th, 2011 near Philadelphia
- Pharmacists, pharmacy technicians, industry, nurses, consumers, medication safety, ASHP, ASPEN, FDA
- Developing core processes for the safe preparation and checking of compounded sterile preparations in the in-patient pharmacy setting

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Approach to the Summit

• Focus on sterile compounding within the hospital in-patient pharmacy

• Divide preparations into
  – Simple
  – Complex
  – Pediatric and neonatal
  – Chemotherapy
Goals of the Summit

• Identification of quality control practices that should be standardized and incorporated into the manual process for the preparation of CSPs.
• Discuss technologies that assist in the preparation of CSPs
• Identify the minimum safeguards that must be in place.
Consensus statements developed for core processes

- Policies and Procedures
- Order entry and verification
- Drug storage
- Assembling products and supplies for preparation
- Compounding
- Drug conservation
- Preparation of source/bulk containers

- Technology/Automation used for compounding CSPs
  - IV Workflow Software
  - Automated IV Compounders
- Quality control/final verification of manually prepared product
- Product labeling
- End product testing
- Record keeping
- Staff management
Definitions

• **Level 1** - used to indicate a best practice that is strongly encouraged but which may not be applicable to all institutions or in all circumstances.

• **Level 2** - used to indicate a minimum standard of practice set forth in this document.

• **Level 3** - used to indicate a requirement established by law, regulation, accrediting bodies, or other binding authorities.
Policies and Procedures for Compounding CSPs

- Organizational practices comply with USP <797> standards. (Level 2)
- Organizations have well-defined policies and procedures that guide the compounding of sterile preparations. (Level 3)
Policies and Procedures for Compounding CSPs

• Organizations identify standardized work flow processes that include quality control, process change control and documentation practices. (Level 3)

• Organizations develop detailed policies for BATCH production of CSPs. (Level 2)
Order Entry and Verification

- Orders transcribed into the pharmacy system are verified by a second QUALIFIED individual, even if the order was entered by a pharmacist, for specific types of CSPs and/or selected individual products as identified by the organization (e.g., chemotherapy, PN, other selected high-alert medications). (Level 2)
Order Entry and Verification

- For parenteral nutrition (PN), the sequence of ingredients on pre-printed order sets or order entry screens is consistent with that of the automated IV compounding screens, the patient-specific label and the medication administration record. *(Level 1)*
Drug Storage

• Minimize drug inventory to avoid intermingling of products.
• Provide sufficient space for drug storage to segregate each drug concentration.
• Concentrated electrolytes are isolated from other inventory. (Level 2)
• Labeling of bins or bin dividers include generic drug name, and concentration. (Level 1)
Drug Storage

• CSPs that have been compounded, and are waiting to be checked are placed in a clearly identified and designated storage location until the checking process has been completed. (Level 2)

• Environmental recommendations, as provided in the USP <1066>, for lighting, noise, workspace and distractions are followed. (Level 1)
Assembling Products and Supplies for Preparation

- Drugs, diluents, base solutions and other supplies are gathered and placed in a separate container, (e.g., a basket or bin) for each preparation or each batch to be prepared.

(Level 1)
Compounding

- When available, commercially-prepared, premixed IV products are used over manually compounded sterile products. (Level 1)
- Additives are not manually incorporated into a commercially-prepared, pre-mixed solution (Level 1)
- Standard base solutions (e.g., dextrose 5%) are used when available to prevent the error prone process of preparing unique/unusual base solutions (e.g., dextrose 3.5%). (Level 2)
Compounding

• Outsourcing the production of CSPs is considered as an alternative to in-house compounding when:
  – the volume of certain CSPs is very low
  – the volume for certain CSPs is high and staff resources are limited or unavailable to prepare this quantity
  – the organization does not possess the technological resources
  – commercially-prepared, premixed product is not available

(Level 1)
Compounding

- A preparation label, master formulation record, or worksheet is available for compounding complex, chemotherapy, and pediatric/neonatal CSPs. (Level 1)
Compounding

• Only one staff member is permitted to work in the direct compounding area when compounding chemotherapy and complex CSPs. (Level 2)

• Two staff members are permitted to work in the compounding area simultaneously provided that the hood is 6 feet in length and there is a physical divide. (Level 2)
Compounding

• Only one CSP is prepared at a time. An exception is:
  – One practitioner can prepare multiple CSPs safely in the hood at one time only if preparing the same doses of the same drug with the same route of administration for one or multiple patients. It is not safe to prepare multiple CSPs at the same time in the hood for different doses or routes of administration, or multiple products for the same patient.

(Level 1)
Compounding

• In facilities that care for adult, pediatric and neonatal patients, the computerized label runs for pediatric and neonatal CSPs are generated or printed separately from adult CSPs. (Level 2)

• In facilities that care for adult, pediatric and neonatal patients, the preparation of CSPs for each population is separated by time or location. (Level 2)
Compounding

• Pharmacies create standard processes to address the volume of base solution when compounding CSPs. Such standard work practices address:
  – if and when there is a need to remove base solution in amounts equivalent to drug additive(s).
  – if and when there is a need to eliminate the manufacturer overfill from the base solution and the method used to accomplish removal (Level 2)
Drug Conservation

• Partially used multidose vials, bulk containers or single dose containers ARE NOT be left in the hood or direct compounding area for future use. *(Level 1)*
  – However, single dose containers of drugs in short supply that are covered by an organization-specific, drug conservation policy may be left in the hood for use up to 6 hours after initial needle puncture in accordance with USP 797 guidelines. *(Level 2)*
Preparation of Source/Bulk Containers

• A detailed standard process is in place for preparing and checking pharmacy-compounded SOURCE/BULK CONTAINERS used to prepare multiple doses or batches.

(Level 2)

– A pharmacist conducts an INDEPENDENT DOUBLE CHECK of all diluents and drugs before the preparation of all source/bulk containers.

(Level 2)
Technology/Automation
General comments

• Organizations develop a strategic plan for implementation of automation and technology for the sterile products service.  
  (Level 1)

• Technology and automation such as bar code verification or IV robotics is utilized as much as possible for preparing and verifying CSPs.  
  (Level 1)
IV Workflow Software

• Intravenous workflow software is used to augment manual processes whenever possible.

(Level 1)
Automated IV Compounding Devices

- The use of a checklist/sign-off sheet is required when making modifications to the database.
- Organizations implement specific soft limits and hard (catastrophic) limits for ingredients that are consistent with the needs of their patient population.

(Level 2)
Automated IV Compounding Devices

• Only pharmacists are allowed to override alerts. (Level 2)

• A double check process for the initial daily setup is performed, with two staff members using a printed check list. Verbal affirmation takes place to validate placement. (Level 2)
Automated IV Compounding Devices

• If multiple containers of a single additive are used during the preparation of a single CSP, all empty containers are presented to the pharmacist as part of the final check process prior to dispensing the final CSP. (Level 2)

• Customized order entry templates created by organizations have a documented standard review process. (Level 1)
Automated IV Compounding Devices

• When an automated IV compounding device is used, it delivers all ingredients. Manual compounding is only used:
  – if the volume of an ingredient to be mixed is less than the compounding device can accurately deliver.
  – if there is an interaction between an ingredient and a component of the compounding device.
  – if there is a chemical interaction between ingredients that cannot be mitigated by sequencing the addition of ingredients.

(Level 1)
Quality Control/Final Verification of Manually Prepared Product

• All personnel are able to “stop the line” and question any concerns about any order or any sterile preparation to be compounded.

(Level 2)
Quality Control/Final Verification of Manually Prepared Product

- Identify those CSPs that require visual confirmation of the amount of each ingredient \(\textbf{prior to}\) addition to the final container. At a minimum this list SHOULD include:
  - chemotherapy
  - PN admixtures
  - pediatric and neonatal preparations
  - pharmacy prepared source/bulk containers
  - preparations requiring the use of multi-dose vials of high-alert medications
  - CSPs administered via high-risk routes of administration (Level 2)
Quality Control/Final Verification of Manually Prepared Product

- Proxy methods of verification such as the SYRINGE PULL-BACK method of verification are never be used in the preparation of chemotherapeutic, complex, pediatric / neonatal or high-alert CSPs and shall not be used without the presence of the actual, original source containers (medication and diluent).

(Level 2)
Quality Control/Final Verification of Manually Prepared Product

• The use of proactive risk assessments, such as failure modes and effects analysis (FMEA) are recommended prior to the implementation of process changes. (Level 1)

• Internal as well as external information about medication errors, from sources such as ISMP, are reviewed and used to modify practices and procedures as needed. (Level 1)
Product Labeling

• Labels generated by an automated IV compounding device match the format and units of measure of the prescriber’s order.
  (Level 1)

• For chemotherapy and other CSPs identified by the organization, the final volume to be infused is present on the label.
  (Level 2)
Staff Management

• Pharmacy technicians involved in preparation of CSPs are Certified Pharmacy Technicians. (Level 1)

• All staff members involved in preparing CSPs or supervising the preparation of CSPs SHALL participate in a comprehensive orientation and training program. (Level 2)
Staff Management

- Pharmacists and pharmacy technicians who prepare CSPs have annual competency evaluation for all aspects of sterile compounding.

(Level 1)
Staff Management

• A national certification program for sterile-compounding specialists should be developed. (Level 1)

• The American Association of Colleges of Pharmacy should instruct their Academic Affairs Committee to add hands-on experience with sterile compounding into pharmacy training. (Level 1)
Additional Topics

- Record Keeping
- Manufacturer overfill in IV solution containers
- End product testing technology (verification of accurate compounding)
Questions