

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

Original Publication: 2013

Revised: 2016



TABLE OF CONTENTS

Table of Contents	2
Background on STERILE PREPARATION COMPOUNDING Safety.....	3
Stakeholder Collaboration	4
Goals for the Summit	4
Disclosure	5
About ISMP	6
Policies and Procedures for Compounding Sterile Preparations	6
Order Entry and Verification	7
Drug Inventory Storage	7
Assembling Products and Supplies for Preparation	8
Compounding	8
Drug Conservation	11
Compounding Performed Outside the Pharmacy IV Admixture Service	11
Preparation of Source/Bulk Containers	11
Technology/Automation Used for Compounding CSPs	12
Automated Compounding (Pumping) Systems	14
Quality Control/Final Verification	15
Product Labeling	15
Staff Management	16
Glossary and Abbreviations	16
References	18
APPENDIX A: Summit Participant List	20

Note: Words within the text of the document presented in all capital letters have a definition in the glossary section at the end of the document.

BACKGROUND ON STERILE PREPARATION COMPOUNDING SAFETY

General information

Errors during pharmacy preparation of parenteral products and admixtures have frequently been reported to the ISMP National Medication Errors Reporting Program (ISMP MERP) and have also been a topic of discussion in the *ISMP Medication Safety Alert!*¹⁻⁸ In addition, a five-hospital observational study on the accuracy of preparing small- and large-volume injectables, chemotherapy solutions, and parenteral nutrition (PN) showed a mean error rate of 9%, meaning almost 1 in 10 products was prepared incorrectly prior to dispensing.⁹ Error rates for complex solutions such as PN were especially high—37% for manual preparation and 22% for preparations that were partly automated. A 2009 State of Pharmacy Compounding Survey showed that 30% of hospitals have experienced a patient event involving a compounding error in the past 5 years.¹⁰

Clearly national efforts are needed to identify and eliminate or reduce errors and their causative factors. The Institute for Safe Medication Practices (ISMP) held a national invitational Sterile Preparation Compounding Safety Summit on October 25-26, 2011 at the ACE Conference Center in Lafayette Hill, PA. Errors identified through the ISMP MERP and other reporting programs (e.g., US Food and Drug Administration MedWatch, MEDMARX), were reviewed. A literature review was also conducted to identify additional published admixture-related errors. Reports highlighted fatal medication errors associated with intravenous (IV) compounding in pharmacies, often involving infants or children.

During the 2011 summit, participants were asked a variety of questions regarding best practices when applied to preparation of 1) simple compounded sterile preparations (CSPs) (those with one or two ingredients, such as patient controlled analgesia infusions, single electrolyte infusions, bolus doses, or maintenance IV infusions with no more than two ingredients), 2) complex CSPs (those with greater than two ingredients, such as PN, cardioplegia solutions, or dialysis solutions), 3) pediatric and neonatal preparations, and 4) chemotherapy. The summit effort resulted in the 2013 publication of ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations.

However, since then, ISMP has continued to learn of sentinel events involving IV admixture preparation and dispensing errors. One event that took place was particularly instructive about the need for additional actions to help prevent errors. A woman arrived for treatment in the emergency department (ED) following brain surgery performed at a different out-of-state hospital. She was supposed to receive IV fosphenytoin for seizure control. Instead, the pharmacy accidentally added rocuronium to the IV bag, which was labeled as fosphenytoin. Barcode scanning of the medication was not available in the pharmacy at the time of the event, and the preparation error was not identified manually before the medication was dispensed to the ED. The rocuronium was administered and caused respiratory paralysis. The patient experienced cardiopulmonary arrest, and suffered anoxic brain injury. She was taken off of life support 2 days later and died shortly thereafter. Because the bag was labeled as fosphenytoin, ED staff had no way of knowing the medication within the bag was rocuronium. Fosphenytoin is generally not considered a high-alert medication, so the drug may not have stepped-up procedures during prescribing, preparing, administering, the drug, or monitoring the patient, that might

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

have provided an opportunity to prevent or catch the error before reaching the patient.

As a result of the above case and many others like it that continue to this day, and in light of the fact that barcoding and other IV admixture associated technologies have become available at reasonable cost but are still not widely implemented, it became clear that the previously published guidance needed to be updated and revised where necessary.

STAKEHOLDER COLLABORATION

Over 60 invitees agreed to attend the original summit (see Appendix A). Those who participated came from a variety of backgrounds, including medication safety officers, experts in IV safety technology, pharmacy technicians, pharmacists, nurses, healthcare consumers, and representatives of the medical product vendor community. The meeting was cosponsored by the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) and the American Society of Health-System Pharmacists (ASHP) and attended by a representative from the US Food and Drug Administration (FDA) as well as a representative of the United States Pharmacopeia (USP) Committee that is overseeing future revisions of USP Chapter <797>.

Attendees were surveyed prior to the summit to gather information about their facilities, types of preparations compounded, standard practices, quality controls, automated processes, and software used related to CSPs. Participants were asked to review and comment on a compendium of ISMP recommended best practices that were sent to all attendees prior to the summit. Those practices with less than 90% agreement by attendees were included for discussion during the summit. Based on the pre-summit survey, one-third of responding participants represented hospitals with 100-299 beds and half were from hospitals with over 500 beds.

The summit comprehensively reviewed current methods used to prepare CSPs, identified manual and automated safeguards to provide assurance that the proper preparation is dispensed, addressed barriers that might inhibit safe practices, and sought to identify and standardize critical quality control practices needed for preparing and verifying the quality and safety of the final CSP. The summit resulted in a set of guidelines and safe practices, that were agreed upon by consensus to ensure the safe preparation of CSPs.

For this revision, ISMP formed an advisory panel composed of members of the Medication Safety Officers Society (MSOS). Participants in the revision process are acknowledged in Appendix A. There was also a period for public comment, during which we received multiple comments.

GOALS FOR THE SUMMIT

The goals for the summit included:

1. Review currently employed quality control measures used to ensure the correct preparation of

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

CSPs.

2. Identify quality control practices that should be standardized for incorporation into the manual process to ensure the correct preparation of CSPs.
3. Describe current and emerging technologies that assist the preparation and quality control of CSPs and how these technologies are utilized.
4. Identify the minimum safeguards that must be in place to prepare and dispense CSPs.
5. Recommend best practice guidelines to ensure the safe preparation of CSPs by pharmacies.

Please note: Revisions to the original document have occurred throughout the publication. A particular emphasis was made to address the use of IV admixture technologies.

Please also note: USP Chapter <797> provides a set of standards for assuring that compounded products are sterile at the time of dispensing. The ISMP summit was focused on another critical aspect of IV solution compounding: IV admixture error prevention. Summit attendees agreed to fully support the quality standards outlined in USP Chapter <797> and no discussion was specifically held to suggest any additions or revisions.

The remainder of this report will discuss agreed upon consensus statements for CSPs. Most of the consensus statements fit with a particular core process, but some span several core processes. Consensus statements are provided for the following core processes in the following order:

- Policies and Procedures for Compounding Sterile Preparations
- Order Entry and Verification
- Drug Inventory Storage
- Assembling Products and Supplies for Preparation
- Compounding
- Drug Conservation
- Compounding Performed Outside the Pharmacy IV Admixture Service
- Preparation of Source/Bulk Containers
- Technology/Automation Used for Compounding CSPs, including barcode scanning and gravimetrics
- Automated Compounding (Pumping) Systems
- Quality Control/Final Verification
- Product Labeling
- Staff Management

DISCLOSURE

All participants in the original summit and the revision were volunteers and received no compensation other than travel and meeting expense reimbursement. ISMP acknowledges the expertise of these volunteer practitioners and appreciates their assistance in developing these guidelines. The original summit and production of this guidance document was funded by the generous support of Ameridose, Baxa, Baxter, B. Braun, and Hospira. The revision of these guidelines took place without additional funding.

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

ABOUT ISMP

The Institute for Safe Medication Practices (ISMP) is an independent, nonprofit charitable organization that works closely with healthcare practitioners and institutions, regulatory agencies, consumers, and professional organizations to provide education about medication errors and their prevention. ISMP represents more than 35 years of experience in helping healthcare practitioners keep patients safe, and continues to lead efforts to improve the medication use process. ISMP is a federally certified patient safety organization (PSO). For more information about ISMP or its medication safety alert newsletters and other tools for healthcare professionals and consumers, visit www.ismp.org. For access to our consumer website, please visit www.consumermedsafety.org.

POLICIES AND PROCEDURES FOR COMPOUNDING STERILE PREPARATIONS

- Organizational practices employed for compounding sterile preparations are in compliance with USP standards related to sterile compounding.
- The organization implements well-defined policies and procedures to guide the compounding of sterile preparations.
- Standardized workflow processes that include quality control, PROCESS CHANGE CONTROL, and documentation are implemented by the organization, recognizing that workflow processes may vary depending on the type and quantity of CSPs prepared and the sophistication of technology employed in each organization or location.
- Detailed policies to guide BATCH compounding of CSPs have been implemented by the organization.
 - A Master Formulation Record is maintained for each BATCH of prepared CSPs and includes the following information:
 - Preparation name, strength, and dosage form
 - Physical description of the final preparation
 - Identities and amounts of all ingredients
 - Theoretical (expected) yield
 - Appropriate container–closure systems
 - Complete instructions for preparing the CSP, including equipment, supplies, and a

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

description of the compounding steps

- Beyond-use date (BUD) and storage requirements
 - Quality control procedures (e.g., pH, filter integrity, and visual inspection)
 - Sterilization method, if applicable (e.g., filter, steam, or dry heat)
 - Any other information needed to describe the operation and ensure its consistent repeatability (e.g., adjusting pH, tonicity and/or temperature)
 - A Master Formulation Record exists for all BATCH sizes (e.g., preparation of a quantity of 50 units versus a 250-unit BATCH) that are compounded
- Each BATCH preparation is logged and documentation includes the theoretical versus actual yield, and all waste. Discrepancies that vary from expected yield are documented and further investigated.
 - Whether entered into an electronic database or documented on paper, Master Formula Records are verified by a pharmacist using an INDEPENDENT DOUBLE CHECK (IDC).

ORDER ENTRY AND VERIFICATION

- All orders entered into a computerized prescriber order entry (CPOE) system are verified by a pharmacist.
- All orders that are transcribed, including entry into a pharmacy information system, an automated compounding device, a chemotherapy dosing system, etc., are verified by a pharmacist. Ideally, any order entry, even by a pharmacist, should be checked by a second individual. A pharmacy technician can serve in this role.
- The sequence of ingredients for PN displayed on any pre-printed order sets or order entry screens is consistent with that of entry screens for the automated CSP compounding system (when utilized), the patient-specific label, and the medication administration record.

DRUG INVENTORY STORAGE

- Drug inventory in the compounding area is minimized to avoid intermingling of products.
- Sufficient space for drug storage is provided to permit SEGREGATION of each drug and concentration.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

- Concentrated electrolytes are SEGREGATED (stored separately) from other inventory.
- Neuromuscular blockers are SEGREGATED from all other medications in the pharmacy by placing them in separate lidded containers in the refrigerator or other secure, isolated storage area. All storage bins of NMBs state: **“WARNING: PARALYZING AGENT-CAUSES RESPIRATORY ARREST.”**
- Storage bins or bin dividers are labeled with the generic drug name and concentration.
- Barcode verification is used during replenishment and removal from stock.
- FDA and/or ISMP tall man lettering is used to distinguish look-alike drug names on bin labels (and is incorporated into CPOE systems, pharmacy information systems, and product labels).
- CSPs that have been compounded and are waiting to be checked are placed in a clearly identified and SEGREGATED storage location until the checking process has been completed.
- Recommendations for safe working environments related to lighting, noise, workspace, and distractions, such as those in USP general chapter <1066>, are implemented.
- Medications are stored in accordance with USP <800> and the organization’s Assessment of Risk for Hazardous Drugs.

ASSEMBLING PRODUCTS AND SUPPLIES FOR PREPARATION

- When using SEMIAUTOMATED-MANUAL or manual systems, drugs, diluents, base solutions, and other supplies required to make CSPs are gathered and placed in a separate container (e.g., a basket or bin) for **each** preparation or **each** BATCH to be prepared. When possible, the person gathering products is different than the person preparing the CSPs.

COMPOUNDING

- To the maximum extent possible, COMMERCIALY-PREPARED, premixed parenteral products and unit dose syringes are used versus manually compounded sterile products.
- The organization utilizes standard intravenous drug concentrations as much as possible to avoid confusion. The number of unique concentrations is minimized.
- Additives are not incorporated into COMMERCIALY-PREPARED, pre-mixed preparations other than those designed for the addition of additives (e.g., multi-chambered bags for PN).
- COMMERCIALY-MANUFACTURED base solutions (e.g., dextrose 5%, 0.9% sodium chloride) are

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

used to prevent the error-prone process of preparing unique/unusual base solutions (e.g., dextrose 3.5%).

- Outsourcing the preparation of CSPs is **considered** as an alternative to in-house compounding when:
 - the frequency of use for certain CSPs is very low, thus making it difficult to maintain staff competency for preparing the product
 - the volume of use for certain CSPs is high, and staff resources are limited or unavailable and/or infrastructure is limited to prepare the quantity needed
 - the organization does not possess the technological or infrastructure resources to ensure the sterility of compounded products according to USP
 - a **COMMERCIALY-MANUFACTURED** product is not available, including product shortages
- When selecting an outsourcer for parenteral products (see www.ismp.org/sc?id=2802):
 - Only a 503B registered outsourcing facility may compound non-patient specific products.
 - A 503A compounding pharmacy may compound only patient specific products such as PN pursuant to individual prescriptions/orders. When a 503A compounding pharmacy is utilized, the hospital should ensure the outsourcing facility is in compliance with USP and the requirements of Section 503A of the Food Drug and Cosmetic Act.
 - The ASHP Foundation's document, "Outsourcing Sterile Products Preparation: Contractor Assessment Tool" (www.ashpfoundation.org/sterileproductstool), is used as one of the resources to analyze the capabilities and quality of external compounding providers prior to selecting a vendor.
- Standard Operating Procedures (SOPs) for compounding and checking all CSPs are utilized and are sufficiently detailed to prevent process variation in practice among staff.
- Standardized formulas (ingredients and the process to prepare) are implemented and used to guide the compounding of **COMPLEX** CSPs, (e.g., dialysis solutions, cardioplegia solutions).
 - SOPs and formulas are supported by current literature.
 - The organization has implemented a regular cycle for review of SOPs and formulas (e.g., every 2 to 3 years).
 - Pharmacy staff members compounding CSPs follow the sequence of steps and processes specified in the formulas and SOPs.
- A preparation label, worksheet, or Master Formulation Record is used to guide compounding of all

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

CSPs. This document expresses the drug name, base solution, patient-specific dose, preparation calculations, final volume of the preparation, and identifies the appropriate drug dosage form to be used (e.g., concentration and size of the container) and includes the name or initials of the person(s) who prepared and verified the preparation.

- Organizations provide sufficient space for staff working simultaneously in the DIRECT COMPOUNDING AREA to ensure sterility of CSPs is not compromised. Only one staff member is permitted to work in the DIRECT COMPOUNDING AREA when compounding chemotherapy and COMPLEX CSPs.
- Only one CSP is prepared by one staff member at a time. Except:
 - One staff member can prepare multiple CSPs safely if preparing the same dose 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 for different doses or routes of administration, or multiple different products for the same patient.
 - Two staff members are permitted to work independently in the compounding area simultaneously, if necessary, provided that the hood is 6 feet in length, a physical divide can be maintained between staff members, and the products being compounded are non-chemotherapy CSPs.
- Heparin and insulin vials are never in the hood at the same time unless on an automated CSP compounding system.
- In facilities that care for adult, pediatric, and neonatal patients, the computerized label batches printed for pediatric and neonatal CSPs are generated or printed separately from adult CSPs.
- If using a SEMIAUTOMATED-MANUAL workflow system, consider routing of pediatric and neonatal CSPs to a separate workflow system if available.
- In facilities that care for adult and pediatric and/or neonatal patients, the preparation of CSPs for each population is separated by time or location. Separation strategies can include the use of different color bins for assembling products to be prepared and/or different colored or differentiated labels.
- For each type of CSP prepared (e.g., chemotherapy, PN), the organization will ensure the availability of qualified staff resources and appropriate environmental control requirements.
 - Prescribers comply with predetermined ordering deadlines that are required by the organization to permit safe preparation of CSPs.
- Standard processes are implemented to address the volume of the base solution when compounding CSPs. Such standard work practices address:
 - If and when there is a need to remove base solution when compounding certain CSPs.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

- If and when there is a need to eliminate the manufacturer overfill from the base solution and the method used to accomplish removal (e.g., direct removal of overfill volume or pumping the amount of base solution from a commercial container into an empty bag).

DRUG CONSERVATION

- A drug conservation policy has been developed to address and maintain the integrity and sterility of drugs during their handling and dispensing, including the use of single dose vials for more than one dose, especially for those products in short supply due to market conditions, as these shortages can affect workflow.
- Organization-specific drug conservation policies include safe practices that address:
 - Maintaining the integrity and sterility of these medications.
 - Methods used to segregate the drug from the DIRECT COMPOUNDING AREA.
 - Regular observations by a pharmacist to monitor drug products are stored in compliance with this policy.

COMPOUNDING PERFORMED OUTSIDE OF THE PHARMACY ADMIXTURE SERVICE

- The director of pharmacy is responsible for oversight and ongoing monitoring of CSP preparation occurring in any department within the institution (e.g., pharmacy, nursing units, OR, physician offices, outpatient clinic, etc.). Basic guidelines should be provided that include staff training to assure use of proper aseptic technique, proper preparation of the compounding area prior to mixing, and labeling of all items prepared. Periodic competency assessments should be performed.
- The following are at-risk behaviors that must be avoided:
 - Preparing IV flush syringes from liter bags of IV solutions
 - Attaching administration sets to IV infusions hours in advance of infusion start time
 - Transferring an injectable medication from one syringe to another
 - Pooling contents from partially used vials
 - Using prefilled saline flush syringes to reconstitute parenteral drugs, then drawing the medication back up into the prefilled syringe
 - Diluting prefilled syringes containing IV push medication unnecessarily

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.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

- A pharmacist conducts an INDEPENDENT DOUBLE CHECK of all diluents and drugs before the preparation of all SOURCE/BULK CONTAINERS. If a pharmacist prepares the SOURCE/BULK CONTAINER and a second pharmacist is unavailable a technician may perform the INDEPENDENT DOUBLE CHECK.
- SOURCE/BULK containers prepared for use during compounding are labeled with the following information:
 - drug name
 - drug concentration
 - diluent
 - total volume
 - date and time of preparation
 - the identity of preparer and identity of person performing the IDC (these names must also be available permanently either electronically or via paper records)
 - beyond-use date (and time as applicable)
 - handwritten labels are avoided

TECHNOLOGY/AUTOMATION USED FOR COMPOUNDING CSPs

Important note: *Data submitted to the ISMP MERP has repeatedly shown that the manual inspection of IV admixture ingredients by pharmacy technicians and pharmacists is not a totally effective deterrent in preventing preparation and dispensing errors. ISMP believes that barcode scanning of base solutions and ingredients should now be considered the minimum requirement for pharmacy IV admixture services. Therefore, hospital leadership must support acquisition of IV admixture technologies that incorporate barcoding and other safety features. This should be done as soon as possible in organizations with pharmacy IV admixture programs that lack such technology.*

- Organizations have a strategic plan for implementation of automation and technology for sterile compounding.
- Technology solutions (e.g., systems that include barcode scanning verification of ingredients, gravimetric verification of drug and diluent volumes, and/or robotic image recognition) are utilized to augment manual processes for preparing and verifying CSPs.
 - At a minimum both barcoding and gravimetrics are used when preparing chemotherapy and ideally, for pediatric CSPs (several SEMIAUTOMATED-MANUAL systems and highly automated robotic systems utilize barcoding and gravimetrics). See FAQ below.

FAQ: *If we already have IV workflow software with barcoding and imaging in place to identify ingredients and base solutions used during IV admixture, is gravimetrics still necessary?*

While barcoding does help in documenting that the correct ingredients for admixture are available, and imaging allows visualization of the volumes used for admixing, neither can be used to confirm that the ingredients have actually been added to the correct patient's IV container in the correct amount.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

Gravimetrics provides a quality control step by confirming the expected weight of the ingredients and combined base solution and additives for the individual CSP. For hospitals and other IV admixture locations that regularly provide parenteral cancer chemotherapy, or ideally, where pediatric patients are treated, gravimetrics should be used when information about specific gravity of ordered medication is available.

*In any facility that has yet to install the above technologies, at a minimum, products with high-alert medications (e.g., chemotherapy, PN, electrolytes, neonatal/pediatric infusions) should employ an **INDEPENDENT DOUBLE-CHECK** of the vials, prepared syringes, and container labels (drug and diluent) prior to adding them to the final solution.*

- Overriding compounding technology-based alerts requires a pharmacist; a technician may override an alert only under the direct supervision of a pharmacist.
- A checklist/sign-off sheet process is used when adding new products, new concentrations, new generics, and changes in package size, or when making other modifications to the database (e.g., changes in privileges, changes in data requirements). Two staff members possessing training and experience with this technology, one of whom is a pharmacist, are required to sign off or validate changes. (Exception: entering a new lot number for a product that already exists in the database.)
- Privileges to make changes to compounding technology databases are restricted to staff members who are well-trained in both the theory and the mechanics of this process.
- Routine calibration and certification are performed and documented for equipment used during the compounding of CSPs, including balances used for weighing. These processes are noted in the SOPs.
- Preventive maintenance is performed, to assure proper operation of technology used in the compounding process, including updates to software, required cleaning of equipment, maintenance of hardware, archiving images, etc.
- All current service releases for software in use are installed, tested, and documented.
- Staff members are trained in the use of automated CSP compounding technology, and there is documentation of initial training, as well as ongoing competency assessment.
- When technology is in use to assist with sterile compounding, organizations have SOPs that ensure that the final check of the preparation has been completed prior to dispensing by a pharmacist possessing training and experience with the technology.

continued on next page >

AUTOMATED COMPOUNDING (PUMPING) SYSTEMS (E.G., FOR COMPOUNDING PARENTERAL NUTRITION)

- Organizations implement specific SOFT LIMITS and HARD (catastrophic) LIMITS that are consistent with the needs of their patient population.
- Weight-based warning limits for doses are developed by vendors. Ensure that these vendor-developed warning limits are appropriate for your institution. In addition, as appropriate, organizations utilize their own weight-based warning limits.
- Barcode verification is used to verify product identity during set up and replacement of ingredients.
- An INDEPENDENT DOUBLE-CHECK process for the initial daily set up and changes made (tubings, vials, etc.) during the work shift is performed with two staff members. A check list is used for the initial set up.
 - Verbal affirmation with two staff members takes place to validate placement of all additives and base solutions including name, concentration, and container size.
- Tubing set(s) should be labeled and traced from the source container to the port where it is attached during the initial daily set up and with each change in the source container.
- 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 checking process prior to dispensing the CSP.
- CUSTOMIZED ORDER ENTRY TEMPLATES are implemented by the organization, as appropriate. When implemented, a review process includes testing of clinical decision support that alerts the pharmacist to significant warnings.
- When an automated CSP compounder is used, it delivers all ingredients needed for the final CSP, except:
 - when the required volume of an ingredient is less than the compounder can accurately deliver,
 - when there is an interaction between an ingredient and a component of the compounder (e.g., insulin and tubing),
 - when there is a chemical interaction between ingredients that cannot be mitigated by sequencing the addition of ingredients,
 - when the automated compounder provides insufficient ports for the number of additives.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

- Operation of CSP automated compounders follows manufacturer recommendations (e.g., tubing changes).
- Preventative maintenance is completed in compliance with manufacturer guidelines.

QUALITY CONTROL/FINAL VERIFICATION

- All personnel have the authority to “stop the line” (i.e., call a halt to compounding activities) and question any concerns about any order or any sterile preparation to be compounded.
- For batched CSPs, a quality assurance plan shall include written standards for qualitative and quantitative integrity, potency, and labeled strength.
- Proxy methods of verification of ingredients, such as the SYRINGE PULL-BACK METHOD of verification are never used.
- Errors and near misses that occur during the compounding of CSPs and are identified by either the pharmacist or technician prior to dispensing are documented and reported through the organization’s reporting system for analysis.
- Serious incidents are reported to the ISMP MERP (ISMP forwards reports to FDA MedWatch) for learning purposes and dissemination of prevention measures.
- Proactive risk assessments, such as failure mode and effects analysis (FMEA) are used prior to the implementation of process changes.
- 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.

PRODUCT LABELING

- ISMP label guidelines are utilized when formatting computer generated labels for CSPs. These are available at: www.ismp.org/Tools/guidelines/labelFormats/default.asp.
- Labels are applied immediately after manual preparation of CSPs.
- Labels generated by an automated CSP compounding device match the format and units of measure of the prescriber’s order, and include the beyond-use date.
- If pharmacy compounding preparation labels are in use, they are never applied as the final product label.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

- For chemotherapy and selected other CSPs identified by the organization, the total volume (e.g., bag volume + manufacturer’s overfill + additive volume) is present on the label.
- Information on the final label matches the format and units of measure of the prescriber’s order and the medication administration record. The product label does not contain unnecessary information (e.g., vial size used to prepare the CSP).
- Labeling practices follow USP Chapters <7> and <17>, as well as all legal requirements.

STAFF MANAGEMENT

- Pharmacy technicians involved in the preparation of CSPs are Certified Pharmacy Technicians having passed the appropriate tests administered by the Pharmacy Technician Certification Board (PTCB).
- Pharmacists and pharmacy technicians who perform sterile compounding should participate in a certificate program in sterile compounding, when possible. In addition, when and if Board of Pharmaceutical Specialties approves certification in sterile compounding, the pharmacist in charge of sterile compounding should obtain such certification.
- All staff members involved in preparing CSPs or supervising the preparation of CSPs participate in a comprehensive orientation and training program as well as an ongoing competency assessment program.
- Pharmacists and pharmacy technicians who prepare CSPs have competency evaluations for aspects of sterile compounding which might include:
 - performing calculations and preparing dilutions
 - compounding base solutions (if necessary)
 - preparing medications for complex routes of administration (e.g., intrathecal)
 - demonstrating proper use of technology (if available)
 - completing competency assessments in compliance with USP, State Boards of Pharmacy, and other required oversight agencies

GLOSSARY AND ABBREVIATIONS

- **Batch**—Preparing a number of non-patient specific doses with the intention to use based upon anticipated patient needs.
- **Commercially-manufactured**—A product available from a commercial manufacturer.
- **Commercially-prepared**—A product available from either a commercial manufacturer or compounding facility.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

- **Complex CSPs**—Preparations with complexity in the compounding processes (e.g., number of manipulations).
- **Customized order entry templates**—Templates created in Automated CSP Compounders that are not part of the manufacturer's original library and are created by the individual institution.
- **Direct compounding area**—A critical area within the ISO Class 5 primary engineering control where critical sites are exposed to unidirectional HEPA-filtered air, also known as first air.
- **Hard limits**—Alerts that indicate something is outside a determined safe range. Hard limits will not allow the staff member to proceed with the selection.
- **Independent double check**—A procedure in which two individuals, preferably two practitioners, separately check each component of the work process. An example would be one person calculates a medication dose for a specific patient and a second individual independently performs the same calculation (not just verifying the calculation) and then matching their results.
- **Process change control**—A formal process used to ensure that changes to a product or system are introduced in a controlled and coordinated manner.
- **Segregated**—Stored apart from other drugs.
- **Semiautomated-manual systems**—Technology that employs a combination of manual (e.g., visual confirmation and handling of products by humans required) and automated (e.g., verification using barcode technology) processes.
- **Soft limits**—Alerts that are displayed but can be overridden by the staff member who may then proceed with the selection.
- **Source/bulk container**—A sterile container (bottle, vial, or bag) manufactured by a commercial vendor or prepared by pharmacy, which is then used as a source from which to withdraw multiple doses.
- **Syringe pull-back method**—A retrospective verification process whereby a syringe with its plunger is pulled back to indicate the amount of medication or diluent that was added to the infusion container. The syringe is placed next to the actual drug or diluent source container(s) from which the drug or diluent was withdrawn.

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

CITED REFERENCES

1. Pharmaceutical compounding-sterile preparations (general information chapter 797). In: The United States pharmacopeia, 27th rev., and The national formulary, 22nd ed. Rockville, MD: The United States Pharmacopeial Convention, 2004:2350-70.
2. <800> Hazardous Drugs – Handling in Healthcare Settings. United States Pharmacopoeia Web site. http://www.usp.org/sites/default/files/usp_pdf/EN/m7808.pdf. Accessed August 23, 2016.
3. Institute for Safe Medication Practices. Unfortunately, this time it wasn't the equipment. *ISMP Medication Safety Alert!* 2005;10(20):1-2.
4. Institute for Safe Medication Practices. Colchicine deaths. *ISMP Medication Safety Alert!* 2007;12(21):1,3.
5. Institute for Safe Medication Practices. Fatal 1,000-fold overdoses can occur, particularly to neonates, by transposing mcg and mg. *ISMP Medication Safety Alert!* 2007;12(18):1-4.
6. Institute for Safe Medication Practices. Post-production IV admixture checks less than ideal. *ISMP Medication Safety Alert!* 2010;15(13):3.
7. Institute for Safe Medication Practices. TPN-related deaths call for FDA guidance and pharmacy board oversight of USP Chapter <797>. *ISMP Medication Safety Alert!* 2011;16(7):1-3.
8. Institute for Safe Medication Practices. Another tragic parenteral nutrition compounding error. *ISMP Medication Safety Alert!* 2011;16(8):1-3.
9. Institute for Safe Medication Practices. Safe practices in pharmacy sterile compounding areas. *ISMP Medication Safety Alert!* 2011;16(11):1-4.
10. Institute for Safe Medication Practices. Failed check system for chemotherapy leads to pharmacist's no contest plea for involuntary manslaughter. *ISMP Medication Safety Alert!* 2009;14(8):1-2.

ADDITIONAL REFERENCES

1. Flynn EA, Pearson RE, Barker KN. Observational study of accuracy in compounding i.v. admixtures at five hospitals. *Am J HealthSyst Pharm.* 1997;54(8):904-12.
2. Pharmacy Purchasing & Products. State of pharmacy compounding 2009: Survey findings. *Pharm Purchasing Products.* 2009;6(4):4–20.
3. Cohen MR. Safe Practices for Compounding of Parenteral Nutrition. *JPEN J Parenter Enteral Nutr.* 2012;36(2 suppl):14S-19S.
4. O'Neal BC, Worden JC, Couldry RJ. Telepharmacy and bar-code technology in an IV chemotherapy admixture area. *Am J Health-Syst Pharm.* 2009;66(13):1211-7.
5. American Society of Health-System Pharmacists. Proceedings of a summit on preventing patient harm and death from IV medication errors. *Am J HealthSyst Pharm.* 2008;65(24):2367-79.
6. Sanborn MD, Moody ML, Harder KA, et al. Second Consensus Development Conference on the Safety of Intravenous Drug Delivery Systems—2008. *Am J HealthSyst Pharm.* 2009;66(2):185-92.
7. Rinehart JR, Chan D, Cunningham M, et al. ASHP guidelines on outsourcing sterile compounding services. *Am J HealthSyst Pharm.* 2010;67(9):757-65.
8. American Society of Health-System Pharmacists. ASHP Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products. *Am J HealthSyst Pharm.* 2000;57(12):1150-69.
9. Outsourcing Sterile Products Preparation: Contractor Assessment Tool. American Society of Health-System Pharmacists Research and Education Foundation Web site. www.ashpfoundation.org/sterileproductstool. Accessed August 23, 2016.
10. Speth SL, Fields DB, Schlemmer CB, Harrison C. Optimizing i.v. workflow. *Am J HealthSyst Pharm.* 2013;70(23):2076, 2078-80.

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

11. Moniz TT, Chu S, Tom C, et al. Sterile product compounding using an i.v. compounding workflow management system at a pediatric hospital. *Am J HealthSyst Pharm.* 2014;71(15):1311-7.
12. Reece KM, Lozano MA, Roux R, Spivey SM. Implementation and evaluation of a gravimetric i.v. workflow software system in an oncology ambulatory care pharmacy. *Am J HealthSyst Pharm.* 2016;73(3):165-73.
13. Deng Y, Lin AC, Hingl J, et al. Risk factors for i.v. compounding errors when using an automated workflow management system. *Am J HealthSyst Pharm.* 2016;73(12):887-93.
14. Institute for Safe Medication Practices. Failed check system for chemotherapy leads to pharmacist's no contest plea for involuntary manslaughter. *ISMP Medication Safety Alert!* 2009;14(8):1-2.
15. Neuenschwander M, Fahrni J. In the clean room. A review of technology-assisted sterile compounding systems in the United States. 2014. www.slideshare.net/JFahrni/in-the-clean-room-39946082. Accessed on August 30, 2016.

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

APPENDIX A

SUMMIT PARTICIPANT LIST

Nathan Ash, PharmD, CACP
St. Rita's Medical Center/Catholic Health Partners
Lima, OH

Mary Baker, PharmD, MBA
Hospira, Inc.

Bona Benjamin, BS Pharm
American Society of Health-System
Pharmacists

Joe Boullata, PharmD, RPh, BCNSP
University of Pennsylvania
Philadelphia, PA

Deborah Bruggman, PharmD
Kaiser Foundation Hospital
Los Angeles, CA

LTC Jorge Carrillo, PharmD, MS, BCPS
US Army Medical Command
Fort Sam Houston, TX

Stacy Carson, PharmD, BCPS, FISMP
ISMP
Horsham, PA

Wayne Chun,
Pharmacy Technician
Kaiser Permanente Medical Center
Walnut Creek, CA

William Churchill, MS, RPh
Brigham and Women's Hospital
Boston, MA

Michael Cohen, RPh, MS, ScD, FASHP
ISMP
Horsham, PA

Janice Dunsavage, RPh, MAS
PinnacleHealth System
Harrisburg, PA

Scarlett Eckert, PharmD
University of California
San Francisco Medical Center
San Francisco, CA

Frank Federico, RPh
Institute for Healthcare Improvement

Charles Ferris, RPh
Baxter Clinical Center of Excellence

Janice Figuracion, Pharmacy Technician
University of California
San Francisco Medical Center
San Francisco, CA

Ryan Forrey, PharmD, MS
James Cancer Hospital
and Solove Research Institute
Ohio State University Medical Center
Columbus, OH

Matthew Fricker, MS, RPh, FASHP
ISMP
Horsham, PA

Catina Greer, CPhT
St. Jude Children's Research Hospital
Memphis, TN

Peggi Guenter, PhD, RN
American Society for Parenteral and Enteral
Nutrition
Silver Spring, MD

Patricia Holbrook, BSP, MS
Baltimore VA Medical Center
Baltimore, MD

Michelle Holtorff, PharmD
Hinsdale Hospital/Adventist
Hinsdale, IL

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

Christopher Jerry
The Emily Jerry Foundation
Chagrin Falls, OH

Eric Kastango, MBA, RPh, FASHP
Clinical IQ
Florham Park, NJ

Patti Kienle, RPh, MPA, FASHP
Cardinal Health

Chris Kutza, PharmD
Advocate Lutheran General Hospital
Park Ridge, IL

Rebecca Lamis, PharmD, FISMP
Horsham, PA

Stuart Levine, PharmD
ISMP
Horsham, PA

Sue Liu, PharmD, FISMP
ISMP
Horsham, PA

Chris Lomax, PharmD
B. Braun Medical

Nicole Mollenkopf MacLaughlin, PharmD,
BCPS
Johns Hopkins Hospital
Baltimore, MD

Michelle Mandrack, RN, MSN
ISMP
Horsham, PA

Shane Marshall, PharmD
St. Jude Children's Research Hospital
Memphis, TN

Melissa McAuley, PharmD, FISMP
ISMP
Horsham, PA

Judy McMeekin, PharmD
U.S. Food and Drug Administration
Div. of Prescription Drugs

Christina Michalek, BSc Pharm, RPh, FASHP
ISMP
Horsham, PA

Cindy Mitman, PharmD
Lehigh Valley Health Network Cedar Crest
Allentown, PA

Susan Paparella, RN, MSN
ISMP
Horsham, PA

Sophia Pasedis, PharmD, RPh
Ameridose

Bruce Pleskow, BS Pharm
Baxter Clinical Center of Excellence

Amy Poppy, PharmD
The Children's Hospital
Aurora, CO

Dennis Schneider
Baxa

Dan Sheridan, MS, RPh
Marion General Hospital OhioHealth
Marion, OH

Lee Steindl, BS, RPh
Cleveland Clinic
Cleveland, OH

Nissa Stevens, CPhT
Johns Hopkins Hospital
Baltimore, MD

continued on next page >

ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations

Dennis Tribble, PharmD, FASHP
Baxa

Allen Vaida, PharmD, FASHP
ISMP
Horsham, PA

Chris Walsh, PharmD, RPh, FISMP
St. Joseph Medical Center
Catholic Health Initiatives
Reading, PA

Mary White, CPhT
Washington DC VA Medical Center
Washington, DC

Heather Zimmer, CPhT
Cleveland Clinic
Cleveland, OH

STERILE COMPOUNDING ADVISORY BOARD MEMBERS - 2016 Revision

LilyAnn Jeu, PharmD, BCPS
SUNY Downstate Medical Center
Brooklyn, NY

Dan Ross, PharmD
D Ross Consulting
Glendale, CA

Milan Moncilovich, PharmD, MJ, Bpharm
UHS of Delaware
Dover, DE

Salma Al-Khani, B.Sc, MHHA, CPHQ
King Faisal Specialist Hospital & Research
Center
Riyadh, Saudi Arabia

Rabih Dabliz, PharmD, FISMP
Cleveland Clinic Abu Dhabi
Abu Dhabi, United Arab Emirates

Misty Vo, PharmD, MSPharm
Banner Compounding Pharmacy
Chandler, AZ

Jennifer Burgess, PharmD
Sentara Albemarle Medical Center
Elizabeth City, NC

Jay Lewandowski, RPh
University of Utah Home Infusion Pharmacy
Salt Lake City, UT

Peter J. Post, PharmD, RPh
Mayo Clinic
Rochester, MN

Amy Marie Zehring, PharmD
Soin Medical Center