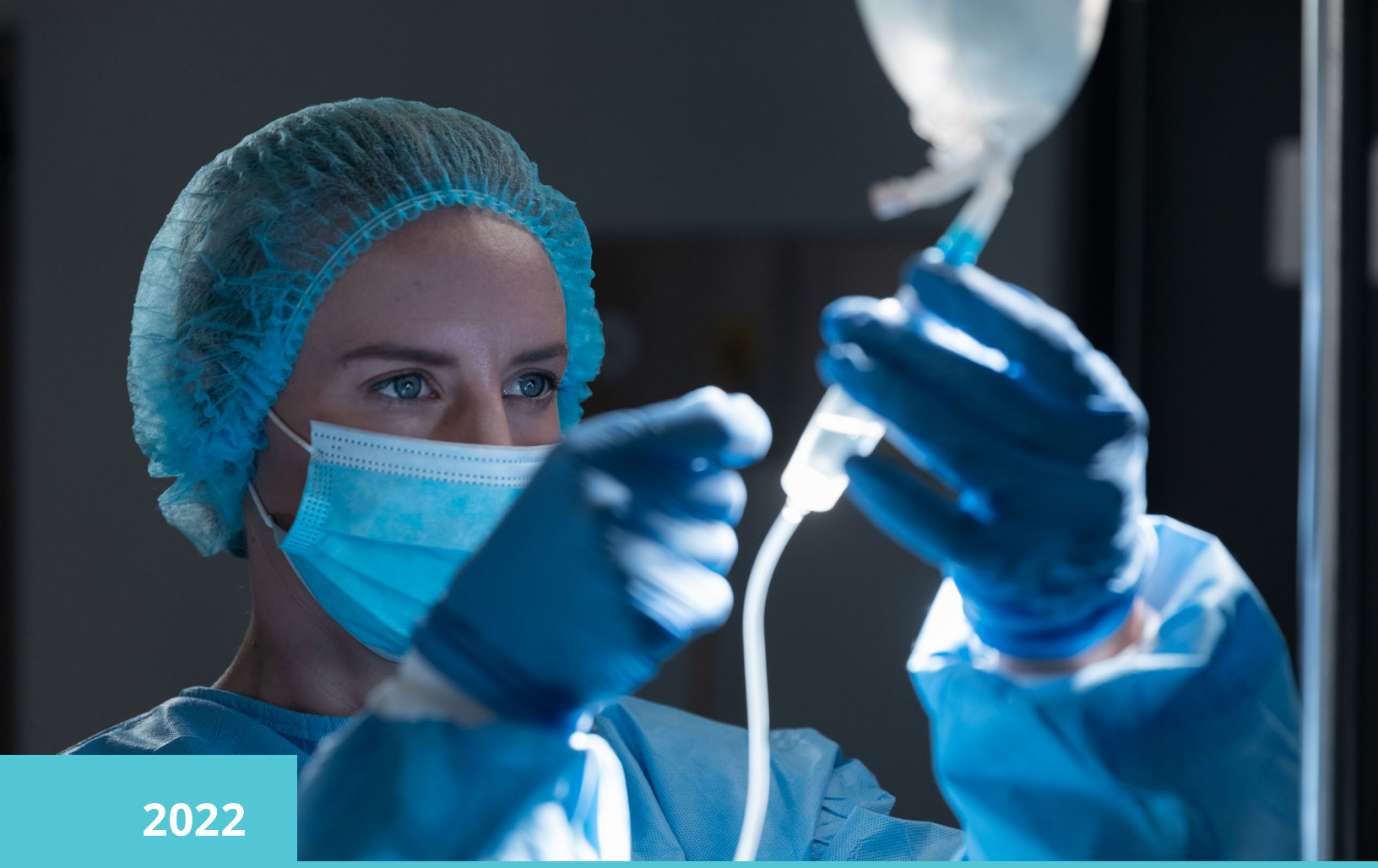

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ISMP Guidelines for Sterile Compounding and the Safe Use of Sterile Compounding Technology

ISMP
Institute for Safe Medication Practices
An ECRI Affiliate

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Introduction and Background

In 2011, in response to several serious and fatal compounding errors reported to the ***Institute for Safe Medication Practices National Medication Errors Reporting Program*** *(ISMP MERP)*, the first national ISMP Sterile Product Compounding Safety Summit was held to address best practices for preparing and verifying sterile preparations.

The inaugural summit resulted in the far-reaching, and frequently referenced, ***ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations*** (released 2013, revised 2016).

In the 10 years since that summit, the sterile compounding technology market has widened with more products available and more organizations adopting use of technology solutions in the sterile compounding process.[1,2] Despite these advancements, an ISMP survey on pharmacy compounding practices revealed that opportunities remain to improve the safety of sterile compounding practices as well as increase and enhance the safe use of technology in the process.[3]

To this end, ISMP convened an invitational, virtual sterile compounding safety summit to address safe practices related to the use of sterile compounding workflow management systems, automated compounding devices, and robotic compounding automation.

Summit Goals

The summit's objectives were four-fold: review current state of the use of technology and automation in compounding sterile preparations, examine sterile compounding-related events and published studies on the use of various forms of technology in the compounding process, identify best practices for the safe use of technology and automation in sterile compounding processes, and recommend best practices associated with sterile compounding when technology cannot be used.

Our goal was to produce best practice guidelines to support safe use of technology and automation in sterile compounding. We recognize that use of compounding technologies is a growing area of pharmacy practice, and we expect that as use of technology expands, and technology and automation evolve, so too will these recommendations.

We also recognize these guidelines may not address every concern or provide an answer or perfect solution for every issue; however, we believe that our efforts have produced a best practice guidance that will improve safe medication practices in this important area of practice.

We plan to revisit these guidelines in two-to-three years, after assessing and observing how organizations have used and implemented technology and automation in sterile compounding practices, and the degree to which this technology and automation have evolved.

Stakeholder Collaboration

A multi-stakeholder group was assembled, consisting of an expert advisory panel, informed users, compounding technology vendors, professional healthcare organizations, and experts in medication safety and regulations. Guideline development followed a three-phase approach plan (Figure 1, page 5). The pre-summit phase included gathering and analyzing event data from the ISMP MERP, performing a literature search and review, surveying summit participants' agreement level with existing ISMP guideline statements, and reviewing published surveys on implementation rates for specific compounding technologies. In the second phase, the multi-stakeholder group attended a summit held virtually over three days. Event data and evidence from a literature review were presented to the group. Summit attendees addressed three topics: essential technology attributes, safe pharmacy processes, and best practices for mitigating harm due to system safety gaps, related to the three technologies. Following the summit, guideline statements were developed based on the consensus of summit attendees. The draft guideline statements were shared with the multi-stakeholder group for review and commentary and subsequently opened for public comment. The final guidelines reflect feedback received.

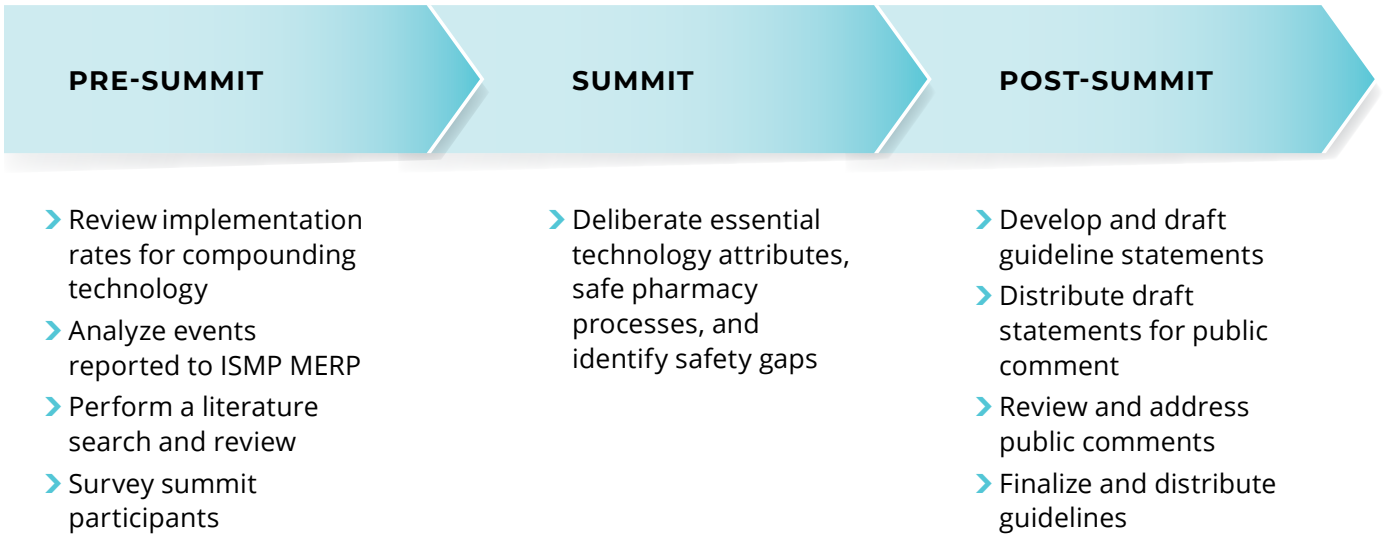
Literature Search

A broad literature search was conducted in five bibliographic databases: Medline, Embase, the Cumulative Index of Nursing and Allied Health Literature (CINAHL), Scopus, and PubMed. The major search terms and concepts included sterile compounding, sterile preparations, IV compounding, workflow, software, robotics, technology, and automation. In addition, technology brand names were used to identify additional studies. Searches were limited to articles published in English but were not limited by publication year. Literature was evaluated based on relevance to the summit's target of safe practices related to the use of sterile compounding workflow management systems, automated compounding devices, and robotic compounding automation. We excluded from review abstracts that focused on contamination, sterility, compounding without use of technology, non-sterile compounding, prescribing, pharmacist order/prescription verification, comparing manual systems to technology, or cost comparisons. We screened 111 abstracts and identified 46 initially relevant texts for full-text review. The reviewed articles addressed technology performance, accuracy, precision, productivity, production time, ability to detect and prevent errors, and users' perceptions related to safety when technology was used. None of the articles focused on safety gaps that could lead to an error despite use of the technology. As such, the goal to identify best practices for use of technology and automation in sterile compounding by balancing technology attributes with pharmacy processes was validated as a means to achieve safe use.

How to Use These Guidelines

These guidelines should be used in concert with other relevant sources, including guidelines and recommendations from USP, the American Society of Health-System Pharmacists (ASHP) and the American Society for Parenteral and Enteral Nutrition (ASPEN) and after careful review of applicable regulatory standards.

Figure 1: Process for Developing Guideline Statements



1. Paytes A, Hansen KN, Boiallis CJ. The state of sterile compounding technology. *Pharmacy Purchasing & Products.* March 2022;19(3):s2-4.
2. Pedersen CA, Schneider PJ, Ganio MC, Scheckelhoff DJ. ASHP National survey of pharmacy practice in hospital settings: Dispensing and administration- 2020. *Am J Health-Syst Pharm.* 2021;78:1074–93.
3. Institute for Safe Medication Practices. Survey Provides Insights into Pharmacy Sterile Compounding Systems and Practices. *ISMP Medication Safety Alert!* 2020;25(21):1-5.

Technologies

AUTOMATED COMPOUNDING DEVICES

Essential Technology Attributes for Automated Compounding Devices

- Automated compounding devices are interfaced with the electronic health record to eliminate transcription errors.

  Interfacing automated compounding devices with electronic health records is a key safety strategy, and every effort should be made to implement this wherever possible. Interfacing the electronic health record with the automated compounding device eliminates the error-prone process step of transcribing multi-ingredient compounded sterile preparation orders and prescriptions into the automated compounding software system.

  - If an interface between the electronic health record and the automated compounding device is not available, a process is in place for transcribed orders/prescriptions to be verified by a second individual using an independent double check and the technology prompts for the second check.
- Clinical decision support with soft warnings and hard stops are available and warn practitioners when approaching or exceeding dose limits (e.g., single dose, daily dose, infusion rate).
- Clinical decision support is customized to specific patient populations (e.g., adult, pediatric, neonatal).
- Clinical decision support warns practitioners when solution contents are incompatible or unstable.
- Clinical decision support warns practitioners when solution osmolarity approaches maximum limits for peripheral administration.
- Parenteral formulations are ordered in concentrations and dosing units that match those available in the automated compounding device.
- Patient and/or condition-based standard ordering templates are available when ordering parenteral nutrition and dosing units match those available in the automated compounding device.
- Machine-readable coding (e.g., barcode scanning, radio frequency identification [RFID]) is used to verify additives on the automated compounding device.
- Automated compounding devices track beyond-use dates of additives.
- Automated compounding devices record lot numbers and expiration dates of additives, and this information is easily retrievable (i.e., in the event of a product recall).
- At the completion of the compounding process there is a gravimetric check of the preparation to ensure the correct volume of additives have been included.
- Auxiliary product information (e.g., storage conditions, filter use during administration) should be incorporated in the automated compounding device dispensing label.
- A process is in place for calibrating the automated compounding device.
  - Standard operating procedures define how often and who performs the calibration process.
  - Only those trained in the calibration process complete this function.
  - Calibration is verified by an independent double check.
  - Gravimetric analysis may be used during the calibration process, when appropriate.

- Close call compounding events (e.g., wrong drug scans) intercepted by the technology are captured in a report to facilitate compounding error analysis and process improvement.
  - Data in vendor-supplied reports are in a useful format and do not require significant manipulation by the end user.
- When a system update is available, automated compounding device vendors ensure all customers receive and install the update in a reasonable timeframe.

Safe Pharmacy Processes for Automated Compounding Devices

- Automated compounding devices are used for all compounded parenteral nutrition infusions.
- A workflow process is in place to identify new products and enter them into the automated compounding device database before they are available for use.
- When a new drug (or a new manufacturer of a drug that is already in the system) is entered into the automated compounding device database, an assessment of information needed to ensure safe use of the drug is completed (e.g., soft warnings, hard stops).
  - Drug-specific information in the automated compounding device database is reviewed and updated as necessary and annually to ensure the content is up to date.
- The number of staff who have access to change the automated compounding device database is limited.
- Staff who are granted access to change the automated compounding device database are trained, and their competency to perform database functions is assessed.
- A second practitioner performs an independent double check anytime a change is made to the automated compounding device database, and the double check is documented in the system.
  - When applicable, have staff test changes made to the database (e.g., verifying that a newly entered barcode scans correctly).
- All practitioners approved to access and change the automated compounding device database have their own unique login and password.
- Staff are adequately trained, and their competency for operating automated compounding devices is assessed before use.
- At the completion of the compounding process, the final preparation is visually inspected according to USP standards and applicable regulations and guidelines.
- Standard operating procedures define when and how to clear or change automated compounding device tubing in between the preparation of different compounds.
- Backup, emergency power is available to avoid an abrupt shutdown in the case of an unexpected power outage while the automated compounding device is running.
- Defined downtime procedures exist and include backup equipment needs, and an annual tabletop simulation is conducted to identify gaps and revise procedures as necessary.
  - Downtime procedures address standard workflow for both hardware and software failures.
  - Downtime procedures dictate under which circumstances a switch to manual processes is necessary.
  - Downtime procedures define documentation and labeling processes.
  - Tabletop simulations include assessment of users' competency with manual standard operating procedures.

- Vendor-suggested preventive maintenance is followed to avoid unexpected hardware and/or software downtime.

Safety Gaps and Associated Best Practices for Automated Compounding Devices

Safety Gap	Associated Best Practice
Connecting tubing to source products	• A dedicated primary engineering control is available for each automated compounding device. ▬ If a dedicated primary engineering control is not available, when the automated compounding device is in use, no other sterile compounding activities take place in that primary engineering control. • Policies and procedures define the steps required to set up the automated compounding device before use and when tubing and source products need to be changed. • Machine-readable code (e.g., barcode, RFID) verification and line tracing are used when setting up source products on the automated compounding device. • A second individual documents and verifies automated compounding device setup steps, including machine-readable coding (e.g., barcode, RFID) verification for the connection of products to tubing and line tracing.
Use of compounded stock solutions (e.g., diluted trace element solutions)	• IV workflow management systems are used to prepare compounded solutions for use on the automated compounding device.
Manually adding products (e.g., separately using a syringe) to a compounded sterile product prepared using an automated compounding device	• Use of the automated compounding device is maximized to limit the number of products that must be added manually. • If a product must be added manually to a sterile product prepared using an automated compounding device, an intravenous (IV) workflow management system is used during the manual compounding step. ▬ If an IV workflow management system is not available, a second individual performs an independent verification of manual additions to ensure that the proper medications (and diluents, if applicable) are added, including confirmation of the proper volume of each medication (and diluent, if applicable) before its addition to the final container. • Machine-readable coding (e.g., barcode, RFID) is used to verify manually prepared additives. • Policies define the order for adding manually prepared solutions to compounded sterile preparations to minimize the risk of precipitation.

Alert Overrides	• Organizations should define how overrides of system warnings or alerts are to be managed considering the overall goal is to limit overrides, building in a second verification before a warning is overridden, and being sensitive to operations that may unnecessarily lead to care delays. • Limit warnings to those with the most value. • Regularly review alert overrides to determine appropriateness and to facilitate process improvement.

IV WORKFLOW MANAGEMENT SYSTEMS

Essential Technology Attributes for IV Workflow Management Systems

- IV workflow management systems are interfaced with the electronic health record to eliminate order transcription from one system into another.
  - If a compounded sterile preparation has been discontinued before initiation of the compounding process, the system interface allows for the removal of these products from the queue.
- IV workflow management systems allow users to create a master formulation record for non-patient-specific batch, stock solution, and patient-specific compounded sterile preparations.
- When master formulation records are created, the IV workflow management system prompts for an independent double check, which is documented in the system.
- Master formulation record changes are timestamped, saved, and identify the user who made the modification.
- IV workflow management systems provide an electronic log of changes made to the database by users.
- IV workflow management systems allow users to customize the incoming order queue to prioritize work.
- Machine-readable coding (e.g., barcode, RFID) is used to verify source products, including diluents, during the compounding process.
- IV workflow management systems automatically perform calculations or conversions.
- IV workflow management systems guide users through essential steps in the compounding process including which steps require video or still images or gravimetric analysis.
- Image-capture pictures are clear such that syringe graduation marks, drug and/or diluent names, lot numbers, and expiration dates are easily visible.
- IV workflow management systems that use gravimetric analysis prevent users from creating master formulation records for preparations that are outside the system's tolerance limits, and if staff attempt to weigh a volume outside the integrated scale's tolerance limit the IV workflow management system alerts the user.
- IV workflow management systems document all steps and components of the compounding process (e.g., products used, the practitioner who performed the compounding, the primary engineering control, machine-readable code scans, date and time of preparation, alerts or warnings presented during the process, the practitioner who verified the preparation), and the information is available to users in a log and/or report.

- IV workflow management systems allow for remote verification using video or image capture, and, when used, gravimetric analysis.
- IV workflow management systems track beyond-use dating of opened or reconstituted products to warn practitioners and prevent use of an expired product.
- IV workflow management systems allow for customization of labels (e.g., tall man lettering, color print, reverse print, electronic health record compatible barcode).
- IV workflow management systems limit the printing of the dispensing label until the compounding process is complete.
- Workload (e.g., incoming load) is documented by the technology and captured in a report to inform and facilitate operational improvement.
- Close-call compounding events (e.g., wrong drug scans) intercepted by the technology are captured in a report to facilitate compounding error analysis and process improvement.
  - Data in vendor reports are provided in a useful format and do not require significant manipulation by the end user.
- When a system update is available, IV workflow management system vendors ensure all customers receive and install the update in a reasonable timeframe.

Safe Pharmacy Processes for IV Workflow Management Systems

- Use of an IV workflow management system is the minimum safety standard for preparing compounded sterile preparations.
- A workflow process is in place to identify new products and enter them into the IV workflow management system database before they are available for use.
- When a new drug (or a new manufacturer of a drug that is already in the system) is entered into the IV workflow management system database, an assessment of information needed to ensure safe use of the drug is completed.
  - Drug-specific information in the IV workflow management system database is reviewed and updated as necessary and annually to ensure the content is up to date.
- The number of staff who have access to change the IV workflow management system database is limited.
- Staff who are granted access to change the IV workflow management system database are trained, and their competency to perform database functions is assessed.
- A second practitioner performs an independent double check anytime a change is made to the IV workflow management system database, and the check is documented in the system.
- When applicable, test changes made to the database (e.g., verifying that a newly entered barcode scans correctly).
- All practitioners approved to access and change the IV workflow management system database have their own unique login and password.
  - Staff are adequately trained and their competency for operating the IV workflow management system is assessed before use.

- Master formulation records are customized and include specific directions for each process step (e.g., volume of fluid to withdraw, volume of fluid to add, concentrations, formulations, special filters, tubing, diluents, supplies, storage instructions, protection from light guidance), and this information is presented to the user before initiation of the compounding process.
- Compounding staff prepare and label one patient-specific product at a time and avoid printing multiple patient-specific labels at once.
- The final label applied to the compounded sterile preparation is a dispensing label intended for the healthcare practitioner (or patient) who will be administering the medication.
- IV workflow management system hardware is set up in a manner that facilitates compounding without increasing the potential for frequent sterility breaches.
- Movement out of the primary engineering control when using IV workflow management systems is minimized decreasing the number of times gloves must be disinfected.
- At the completion of the compounding process, the final preparation is visually inspected according to USP standards and applicable regulations and guidelines.
  - IV workflow management systems support documentation of this visual inspection.
- Routinely observe the compounding process to identify risks and ensure that IV workflow management systems are being used as designed and described in standard operating procedures.
- Anytime a change to the workflow process is planned, the change is evaluated using simulation to identify gaps and revise procedures as necessary.
- Backup, emergency power is available to avoid an abrupt shutdown in case of an unexpected power outage while the IV workflow management system is running.
- Defined downtime procedures exist and include backup equipment needs, and an annual tabletop simulation is conducted to identify gaps and revise procedures as necessary.
  - Downtime procedures address standard workflow for both hardware and software failures.
  - Downtime procedures dictate under which circumstances a switch to manual processes is necessary.
  - Downtime procedures define documentation and labeling processes.
  - Tabletop simulations include assessment of users' competency with manual standard operating procedures.
- Vendor-suggested preventive maintenance is followed to avoid unexpected hardware and software downtime.

Safety Gaps and Associated Best Practices for IV Workflow Management Systems

Safety Gaps	Associated Best Practices
Compounds that need multiple vials or infusion bags for preparation	• Every vial or bag needed for compounding should have a machine-readable code (e.g., barcode, RFID) that is scanned during the compounding workflow process.
Tolerance limits when using gravimetric analysis	• Users should follow guidance from product vendors when gravimetric analysis is used to determine the minimum volume that can be accurately measured by the integrated scale. • Product vendors should communicate the minimum volume that can be accurately measured by the integrated scale to users and build this information into the IV workflow management system's master formulation records. • Users should follow product vendors recommendations for initial system settings and IV workflow management system setup. • Drug manufacturers should publish and/or share densities of their drug products. • Product vendors should supply densities if available and assist users in setting up tolerance limits. • Users should partner with product vendors to support compounding process challenges (e.g., accuracy when measuring products in syringes, small dose accuracy, accounting for drug left in the hub of needles, quality of the integrated scale).
Alert overrides	• Organizations should define how overrides of system warnings or alerts are to be managed considering the overall goal is to limit overrides, building in a second verification before a warning is overridden, and being sensitive to operations that may unnecessarily lead to care delays. • Limit warnings to those with the most value. • Regularly review alert overrides to determine appropriateness and to facilitate process improvement.
Label swapping	• Prepare one product at a time allowing dispensing labels to remain in the queue until the time of compounding to ensure the correct label is affixed to the product at the proper time. • If separate production and dispensing labels are used, application of the dispensing label should be verified by machine-readable coding (e.g., barcode, RFID). • Develop standard operating procedures to prevent unnecessary reprinting of production and/or dispensing labels.
Incomplete auxiliary product information	• Auxiliary product information (e.g., storage conditions) should be incorporated in the IV workflow management system dispensing label.

IV ROBOTS

Essential Technology Attributes for IV Robots

- IV robots are interfaced with the electronic health record to eliminate order transcription from one system into another.
  - IV robots are interfaced with IV workflow management systems if the IV workflow management system is used to compound solutions for use in the IV robot.
  - If a compounded sterile preparation has been discontinued before initiation of the compounding process, the system interface allows for the removal of these products from the queue.
- IV robots allow users to create a master formulation record for non-patient-specific batch, stock solution, and patient-specific compounded sterile preparations.
  - Master formulation records include additional steps required for IV robot set up and programming (e.g., needle angle, agitation time for reconstitution).
  - When master formulation records are created, the IV robot prompts for an independent double check and the check is documented in the system.
  - IV robot master formulation records are easily accessible, organized, and easy to maintain.
  - Master formulation record changes are timestamped, saved, and identify the user who made the modification.
- Machine-readable coding (e.g., barcode scanning, RFID) and/or image capture for non-barcoded items, is used to verify products, including diluents, during the compounding process.
  - If a machine-readable code (e.g., barcode, RFID) is manually added to a product so that it can be used in the IV robot, a second individual verifies the code using an independent double check.
  - At the completion of the compounding process, there is a gravimetric check of the preparation to ensure the correct volume of additives have been included.
  - The IV robot applies a dispensing label to the completed compounded sterile preparation.
  - IV robots allow for customization of labels (e.g., tall man lettering, color print, reverse printing, electronic health record-compatible barcode).
  - IV robots prompt users when maintenance is needed.
  - IV robot vendors supply a comprehensive user service agreement that specifically addresses, at a minimum, expectations related to service, hardware and software maintenance and update, training, and retraining of staff.
  - When a system update is available, IV robot vendors ensure all customers receive and install the update in a reasonable timeframe.

Safe Pharmacy Processes for IV Robots

- IV robots are considered when preparing products with high volume of use and/or products that require large batch preparations.
- Standard operating procedures are defined for IV robot operations.
- Staff are adequately trained and their competency for operating IV robots is assessed before use.
- Annual vendor-supported training is offered to all IV robot staff operators.
- Staff are assessed annually for their competence with IV robot operations.
- Standard operating procedures define the process required to program the IV robot.
- Staff who are granted access to program or change the IV robot database are trained, and their competency to perform database functions is assessed.
- All practitioners approved to access and change the IV robot database have their own unique login and password.
- The number of staff who have access to program or modify the IV robot database is limited.
  - Modifications to the IV robot database are documented along with the reason the change was made.
- When modifications are made to the IV robot database staff follow a defined change control process including an assessment of information required to ensure safe use of the new product (e.g., specific gravity, agitation time for reconstitution).
  - Drug-specific information in the IV robot database is reviewed and updated (as necessary) annually to ensure the content is up to date.
- A second practitioner performs an independent double check anytime a change is made to the IV robot and the check is documented in the system.
- When using the IV robot for large batches, staff attempt to secure a large volume of products from the same manufacturer production lot.
- Staff ensure that routine calibration and certification of IV robot equipment components are performed according to vendor requirements.
  - Each calibration and certification are documented.
- Maintenance, media fills, monthly surface sampling, and cleaning follow vendor recommendations, USP standards and applicable regulations and guidelines.
- At the completion of the compounding process, the final preparation is visually inspected in compliance with USP standards and applicable regulations and guidelines.
- Backup, emergency power is available to avoid an abrupt shutdown in case of an unexpected power outage while the IV robot is running.
- Defined downtime procedures exist and include different levels of operational failures including hardware and software issues.
- An annual tabletop downtime simulation is conducted to identify gaps and revise procedures as necessary.
- Downtime procedures address varying levels of hardware and software failures.
- Downtime procedures dictate under which circumstances a switch to manual processes is necessary.

- Downtime procedures define documentation and labeling processes.
- Tabletop simulations include assessment of users' competency with manual standard operating procedures.
- Vendor-suggested preventive maintenance is followed to avoid unexpected hardware and/or software downtime.

Safety Gaps and Associated Best Practices for IV Robots

Safety Gap	Associated Best Practices
Machine-readable codes that are not readable	• When possible, users should avoid the use of products with difficult-to-read machine-readable codes (e.g., barcodes, RFID). • When possible, users should use IV workflow management systems to provide a product with reliable machine-readable codes (e.g., barcode, RFID).
Label swapping when the dispensing label is applied to the compounded sterile preparation manually	• Label one product at a time immediately after generation of the dispensing label to ensure the correct label is affixed to the product. • Application of the dispensing label is verified by machine-readable coding (e.g., barcode, RFID).
Incomplete auxiliary product information	Auxiliary product information (e.g., storage conditions) should be incorporated in the IV robot dispensing label.

GENERAL BEST PRACTICES FOR COMPOUNDING TECHNOLOGY

- Before implementing compounding technology, include appropriate stakeholders in a failure mode and effects analysis (FMEA) performed for the proposed new system to identify possible failure points, their causes, and their effects. The identified failure modes are addressed by introducing safeguards to avoid unintended consequences and to improve reliability.
- Organizations employing the use of compounding technology develop an overarching technology infrastructure.
  - The infrastructure ensures that new products introduced to the institution have been appropriately added to all affected technology systems.
  - Before new product use, the infrastructure supports a verification process to confirm that each technology system has been properly updated with complete information.
- Human factors engineering principles (e.g., consistency, standardization, user-centered perspective), focusing on the interaction between staff and the technology (i.e., human-technology interface), are used when designing new workflow processes to reduce the risk for human error and enhance safety.
- Use of compounding technologies is optimized by conducting preventive maintenance procedures to ensure minimal downtime and achieve the maximum medication safety benefit.
- Competency of staff using compounding technology is assessed during initial training and at least annually thereafter.
- Close call compounding events captured in technology reports are reviewed regularly (at a minimum quarterly) to facilitate error analysis and process improvement.

GENERAL BEST PRACTICES FOR STERILE COMPOUNDING

- Sterile compounding outside the pharmacy should be minimized.
- To the extent possible, commercially manufactured parenteral products are used over manually compounded sterile preparations.
- Organizational practices employed for compounding sterile preparations follow USP standards and applicable regulations and guidelines.
- Standard operating procedures for compounding are defined and include quality control, change control, and documentation.
- Standard operating procedures for labeling preparations are defined, sufficiently detailed, and used to prevent process variation among staff.
- Standard operating procedures for verification of compounded sterile preparations are defined, sufficiently detailed, and used to prevent process variation among staff.
- Staff who prepare and/or verify compounded sterile preparations are trained, and their competency to perform sterile compounding procedures is assessed at least annually.
  - Competency assessments for specific aspects of sterile compounding could include performing calculations, preparing dilutions, compounding base solutions, preparing medications for specific administration routes (e.g., intrathecal administration), demonstrating proper use of devices (e.g., filter needles/straws), and operating technology used in the compounding process.
  - Competency assessments follow USP standards and applicable regulations and guidelines.
- Organizations include additional training and competency assessment for preparing chemotherapy, hazardous drugs, parenteral nutrition, neonatal and pediatric preparations, and high-risk compounding.
- All orders (or prescriptions) that are transcribed, including entry into a pharmacy information system, a chemotherapy dosing system, or an automated compounding device, are verified by a pharmacist.
- Master formulation records are verified by a second individual using an independent double check before use.
- A process is in place (e.g., the use of bins) to allow for the separation of products and supplies used during the compounding process for each preparation or batch preparation.
- Compounding dose volume information is available on a production label, master formulation record, or other approved document to avoid the need for manual calculations.
- Production labels, if used, are not the final dispensing label.

The information contained on a production label can be confusing to the practitioner or patient who will be administering the product.

- If multiple vials, bottles, bags, or syringes of a specific product are used during the preparation process, all vials, bottle, bags, and syringes, whether partially full or empty, are presented to the pharmacist as part of the final verification process.
- Clearly defined and segregated areas exist for products (and corresponding materials) awaiting verification by a pharmacist.
- In organizations that care for adult, pediatric, and neonatal patients, strategies are implemented to differentiate compounding productions (e.g., separate the timing for preparation of pediatric and neonatal patients from adult patients, prepare in different locations, adjust/customize labeling).

- Batch preparations are logged, and documentation includes the theoretical versus actual yield and all waste.
  - Discrepancies that vary from expected yield are documented and further investigated.
- Organizations consider outsourcing sterile compounding services as a strategic option to inhouse compounding based on an in-depth assessment that considers organizational, operational, staffing, financial, quality, and regulatory issues.
- Organizations maintain a drug conservation policy to address and maintain the integrity and sterility of drugs in short supply during their handling and dispensing.
- Machine-readable coding (e.g., barcode, RFID) verification is used during replenishment and removal of medication stock used for sterile compounding.
- Pharmacists who practice primarily in sterile compounding should obtain advanced training (e.g., a certificate program).
- Pharmacists in charge of sterile compounding may consider Board of Pharmacy Specialties (BPS) Board Certification in Compounded Sterile Preparations (BCSCP).
- Technicians expected to perform sterile compounding may consider Pharmacy Technician Certification Board (PTCB) Compounded Sterile Preparation Technician (CSPT) certification.
- Errors and close calls that occur during the preparation of compounded sterile preparations are documented through the organization's reporting system for analysis.
- Errors and close calls should be reported to the ISMP MERP or ***ISMP National Vaccine Errors Reporting Program (ISMP VERP)*** for learning purposes and dissemination of prevention measures.

The following recommendations should be considered to safely prepare compounded sterile preparations when no technology is available or when no pharmacy or pharmacist is available (e.g., ambulatory settings):

- Maximize the use of manufacturer-prepared products.
- Purchase products in patient-specific doses that are ready to administer.
- If a commercially manufactured product is not available, investigate the use of a commercially prepared product (e.g., from a compounding pharmacy or outsourcing facility). See reference section for *ASHP Guidelines on Outsourcing Sterile Compounding Services.*
- When sterile compounding is performed in a pharmacy, multiple compounded sterile preparations of the same drug, dose, and administration route for one or multiple patients can be compounded at the same time.
- When sterile compounding is performed in a pharmacy (without use of compounding technology) the pharmacist independently verifies that the proper medications and diluents are added, including confirming the proper volume of each medication and/or diluent before their addition to the final container.
- If compounding (e.g., dilution, reconstitution) must occur outside a pharmacy environment, aseptic techniques, processes and procedures, and USP standards for beyond-use dating, as well as other applicable regulations and guidelines are followed.
- If compounding must occur outside a pharmacy environment, standard operating procedures for compounding and labeling preparations are defined.

- If compounding must occur outside a pharmacy environment, have a second practitioner independently verify the proper medications (and diluents, where applicable) are added, including confirming each ingredient's proper volume before their addition to the final container.
  - Investigate the ability to have a pharmacist perform the verification remotely using video or still images.
- If compounding must occur outside a pharmacy environment, staff who prepare and/or verify compounded sterile preparations are trained, and their competency to perform sterile compounding and associated procedures is assessed annually.
- Errors and close calls that occur during the preparation of compounded sterile preparations are documented through the organization's reporting system for analysis.

Moving Forward

Summit participants discussed ways that sterile compounding technology vendors and developers could help practitioners close the safety gaps presented during the summit. The following list represents recommendations for future consideration.

- Establish bi-directional interfaces for compounding technologies (e.g., automated compounding devices, IV workflow management systems, IV robots).
- Provide additional wireless hardware to facilitate compounding without increasing the potential for frequent sterility breeches when using IV workflow management systems.
- Deliver a human-readable master formulation record from IV workflow management software systems and IV robots that is suitable for use during system downtime.
- Investigate the ability to have common language between technologies so that practitioners do not need to reenter data into each system.
- Define standards for implementing sterile compounding technology, including physical operations and procedural requirements to facilitate adoption and successful application of the technology.
- Define the role of flow metrics in sterile compounding.

Definitions

Automated compounding device: A device used to accurately combine multiple drugs and sterile component solutions into a single final container. These devices are commonly used for parenteral nutrition preparation, but may be used for cardioplegia, continuous renal replacement therapy, or other complex preparations.

Batch: A specific quantity of compounded sterile preparations prepared as described in the master formulation record in a single, discrete process, and expected to have uniform character and quality within specified limits.

Close call: An event, situation, or error that took place but was captured before reaching the patient.

Compounding staff: Pharmacists and/or pharmacy technicians who perform compounding duties.

Dispensing label: The final label that is attached to the compounded sterile preparation with information intended for the healthcare practitioner (or patient) who will be administering the medication.

Gravimetric analysis: A method that uses an electronic balance and the density of a solution as a quality assurance check to confirm the accuracy of volumes.

Independent double check: A procedure in which two individuals independently check each targeted component of the work process that requires verification.

IV Robot: Automated pharmacy IV robotic systems intended to prepare compounded sterile preparations.

IV workflow management systems: Pharmacy IV workflow systems intended to facilitate safe preparation of compounded sterile preparations by standardizing workflow and providing a means to verify and document the compounding steps.

Label swapping: When the wrong label is applied to a compounded sterile preparation, often caused by not following a one-by-one process flow (one-piece flow).

Master formulation record: A detailed record of procedures that describes how a compounded sterile preparation is to be prepared.

Production label (may be referred to as preparation label): A document that is designed for use by compounding staff and includes preparation-specific information such as what may be found in a master formulation record.

Primary engineering control: A device or zone that provides an International Organization for Standardization (ISO) Class 5 air quality environment for sterile compounding.

Quality control: The sampling, testing, and documenting of results that, taken together, ensure that specification have been met before releasing the compounded sterile preparation.

Related Guidelines and References

American Society of Health-System Pharmacists (ASHP) *Guidelines on the Safe Use of Automated Compounding Devices for Preparation of Parenteral Nutrition Admixtures*

ASHP *Guidelines on Compounding Sterile Preparations*

ASHP *Guidelines on the Selection, Implementation, and Utilization of Workflow and Robotic Technologies for Preparing Intravenous Compounded Sterile Preparations,* in press

ASHP *Guidelines on Outsourcing Sterile Compounding Services*

Proceedings from the Cleveland Clinic International IV Robotics Summit *American Journal of Health-System Pharmacy,* Volume 78, Issue 9, 1 May 2021, Pages 800–805

American Society for Parenteral and Enteral Nutrition (ASPEN) *Clinical Guidelines Parenteral Nutrition Ordering, Order Review, Compounding, Labeling, and Dispensing*

ASPEN *Parenteral Nutrition Safety Consensus Recommendations*

ASPEN *Safety Checklists*

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The Institute for Safe Medication Practices (ISMP) is the nation's first 501c (3) nonprofit organization devoted entirely to medication error prevention. During its more than 25-year history, ISMP has made a difference in the lives of millions of patients and the healthcare professionals who care for them. ISMP is known and respected for its medication safety information and has served as a vital force for progress by securing numerous necessary changes in clinical practice, public policy, and drug labeling and packaging. ISMP operates the only national voluntary practitioner medication error reporting program, publishes newsletters with real-time error information trusted by the global healthcare community, and offers a wide range of educational programs, tools, and guidelines. In 2020, ISMP affiliated with ECRI to create one of the largest healthcare quality and safety entities in the world. ISMP receives no advertising revenue and relies on charitable donations, educational grants, newsletter subscriptions, and volunteer efforts. For more on ISMP's lifesaving work, visit www.ismp.org.

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