

ASHP Guidelines on the Safe Use of Automated Compounding Devices for the Preparation of Parenteral Nutrition Admixtures

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Purpose

Automated compounding devices (ACDs) are frequently used by pharmacists for the extemporaneous preparation of parenteral nutrition (PN) admixtures. This continuing shift from manual compounding procedures comes as a result of significant advances in automated technology, as well as in response to changing

healthcare demands to provide admixture compounding in a safer, more efficient, and more accurate manner. As of 2019, approximately 29% of hospitals in the United States use ACDs. Larger teaching facilities are more likely to implement ACDs, with approximately 58% of hospitals with 400 beds or greater having an ACD in their workflow.¹ Compounders are also used for other types of intravenous (IV) admixtures and in other settings, including home care and long-term care facilities; therefore, the overall magnitude of their use is substantial. As with other automated systems or devices, the benefits can be realized only when the technology is used appropriately. Significant patient harm may occur when safety and quality assurance measures are overlooked or circumvented.²

The purpose of these guidelines is to outline key issues that should be considered to safely and cost-effectively incorporate this technology into the pharmacy operations of healthcare organizations. The guidelines focus on PN admixtures, but the recommendations may also be applicable to the use of compounders for other types of IV admixtures. The term “healthcare organization” is used throughout the guidelines as a general descriptor and is intended to be inclusive of any practice setting or type of facility in which compounders are used. These guidelines should be used in conjunction with the ASHP Guidelines on Compounding Sterile Preparations³; the American Society for Parenteral and Enteral Nutrition (ASPEN) Standards of Practice for Nutrition Support Pharmacists⁴; the ASPEN, Academy of Nutrition and Dietetics, and ASHP consensus statement on optimizing the electronic health record (EHR) in the parenteral nutrition

workflow⁵; and device manufacturers’ instruction manuals and training materials. The recommendations in these guidelines represent a consensus of professional judgment, expert opinion, and documented evidence. They are written to establish reasonable goals and to be progressive and challenging yet attainable as best practices in applicable settings. They do not represent minimum levels of practice, and pharmacy professionals are encouraged to exercise their professional judgment in assessing their organization’s needs for ACDs and in adapting these guidelines to meet those needs.

Background

The act of extemporaneously compounding any parenteral formulation is complex and not without inherent risks; therefore, compounding tasks are best performed by personnel most qualified to do so. An incompatible, unstable, or contaminated IV infusion may induce significant patient morbidity and even mortality.² Pharmacists are specifically educated and legally responsible for performing these tasks safely. Pharmacists are also responsible for training other personnel to perform relatively simple tasks with the least risk possible.

The extemporaneous preparation of multi-additive products, such as PN admixture compounding, should be performed under the direct supervision of a pharmacist and in the appropriate environment according to United States Pharmacopeia (USP) standards and regulatory guidelines.⁶ The historical method of compounding these multicomponent admixtures has been to manually use gravity-driven transfers for large-volume additives, such as amino acids, dextrose, lipids, and sterile water. Small-volume additives, such as electrolytes, trace minerals,

multivitamins, and drugs, have often been added manually and separately with a syringe. Thus, this compounding method is limited by the visual inspection of volumes transferred between stock containers, as well as by the precision of the calibrations marked on the stock containers or transfer devices.

The manual method of PN admixture compounding is labor-intensive and requires multiple manipulations of infusion containers, sets, syringes, needles, and other equipment, which can lead to extrinsic contamination of the final admixture with sterile and/or nonsterile contaminants. A sterile contaminant can be particulate matter from elastomeric vial enclosures (needle cores), and nonsterile contaminants can be bacteria and other infectious materials. Minimizing the number of extemporaneous manipulations of the parenteral infusion containers and supplies improves compounding efficiency and reduces the risk of extrinsic contamination and associated sequelae.⁷

Technology utilization as an alternative approach to PN admixture compounding has led to potentially improved compounding accuracy with the use of fluid pump technology and software that controls the compounder pump. Fluid can be delivered from the source container to the final container using either a volumetric or a gravimetric fluid pumping system. Volumetric systems transfer a specified volume of fluid from a source container to a final container via a rotary peristaltic pump. The tubing is stretched around a rotor and, as the rotor turns, the solution is pulled from the source container and pushed toward the final container. Measurements are based on the theory that each rotor movement advances a constant amount of fluid through the system. The total volume delivered is calculated by the volume pulled into the tubing by each rotor movement multiplied by the number of movements. These systems usually incorporate a final check of the *actual* total bag weight by comparing it with a calculated *expected* weight.

In gravimetric systems, measurement of fluid volume delivered from the source container to the final

container is performed by weighing the fluid transferred and dividing the weight by the solution's known specific gravity, thereby converting weight to volume. Two types of gravimetric pumps are available, additive and subtractive; additive pumps are the most common. With an additive pump, a single load cell is positioned to measure each fluid as it is delivered to the final container. With a subtractive pump, load cells are positioned beneath the source containers to measure each fluid as it is being pumped from its source container. Weight is determined by subtracting the post-transfer weight from the pre-transfer weight of the container for each source solution. When all transfers are completed, the system compares the *actual* total bag weight with a calculated *expected* weight.

Compared with manual methods, the software application available with ACDs leads to improved compounding accuracy, enforcement of proper compounding sequence, and a reduction in opportunities for human touch contamination. However, preparing PN admixtures with an ACD is not an error-free process. Previous literature has reported higher error rates with manual compounding than with ACDs.^{8,9} Organizations may improve the safety of using PN compounding systems by requiring that all doses being compounded pass through an order entry/clinical decision support system and by ensuring that those systems' clinical decision support features are properly enabled and configured.¹⁰

Justification for the use of ACDs

When is it appropriate to use compounders, and how will decisions affect others within and outside the pharmacy department? It is incumbent upon the pharmacist to ensure that the department is fully knowledgeable about the operation of the compounder and that a minimum acceptable standard of pharmacy practice is met. First, internal decisions need to be made to justify the expenses associated with this technology. Second, policies and

procedures should be in place to assess workflow, establish training programs, and standardize compounder use in the specific pharmacy practice setting. Third, changing current compounder contracts may result in more cost than the savings that might appear in the new contracts. Specifically, the initial incorporation of an automated compounder into daily pharmacy practice is a labor-intensive effort, and such transitions can be disruptive and can even increase the risk of errors, particularly during staff orientation to new devices. Such changes must be carefully reviewed and, if they are determined to be worthwhile, a well-coordinated transition plan should be devised in advance. Whether transition costs (including the potential for unused sets and supplies) can be deferred to the new contract is another factor for consideration.

The principal emphasis associated with using ACDs in healthcare organizations should be improving patient care and enhancing mixed PN prepared in the pharmacy while maintaining efficiency and cost-effectiveness. "Cost-effectiveness" is a relative term with respect to personnel, as the labor saved is often redirected to other aspects of pharmacist care that could also improve patient safety. Time that was previously spent on operations associated with PN admixture compounding can now be aimed at other issues, such as optimization of drug and nutritional therapies, reorganization of product utilization, quality assurance programs, and augmentation of other core pharmacy services.

Specific points related to cost justification of ACDs may include the following:

1. Enhanced efficiency and worker safety during the PN compounding process and patient safety with parenteral use.
2. Reduction in labor associated with manually compounded PN admixtures. Assessment of the overall labor and material costs associated with the current manual compounding methods should include hidden costs,

such as pharmacists' time to perform calculations, quality assurance checks, and compounder set-up, as well as staff training (initial and ongoing).

3. Reduction in waste through more efficient use of base solutions and additives. Inventory can often be reduced by consolidating source solutions to a few high-concentration, large-volume additives.

In some cases, in which the cost of implementing automated compounding technology in one facility is prohibitive, healthcare organizations have opted to explore regional compounding centers or outsourcing to contractors.

Performance requirements and responsibilities

Use of automated devices for compounding PN admixtures should be clearly defined by the healthcare organization and the manufacturer. This definition should include the ongoing responsibilities of the pharmacy department and those of the manufacturer during and after implementation of the compounder in the pharmacy practice setting.

Three areas need to be clearly defined before choosing an automated compounding system: (1) the system's performance requirements, (2) the manufacturer's responsibilities, and (3) the pharmacy department's responsibilities. Performance requirements of the automated compounding system should ensure the following at a minimum:

1. The compounder exceeds the level of accuracy achieved with manual compounding. The ACD should be accurate to within 5% of the amount programmed, with verification of the amount pumped versus the programmed amount for each ingredient.
2. The ACD has inherent safeguards (e.g., barcode technology), including the ability to detect inadvertent source-solution mix-ups; the ability to detect situations that could result in inaccurate deliveries, such as occluded

transfer-set tubing and empty source containers; and the ability to keep incompatible source solutions separate.

3. The automated compounding software alerts the user when formulation issues arise.
4. The automated compounding software meets ASPEN standards for PN label formats.¹⁰
5. The automated compounding software assists the pharmacist in producing physicochemically compatible PN formulations.
6. The automated compounding software provides useful clinical information.
7. The automated compounding software interfaces with the existing EHR wherever possible to allow orders transfer from the EHR to the compounder after pharmacist verification to help in optimizing patient care and avoiding therapeutic duplications.

The contractual agreement with the manufacturer should provide continuous support of the compounder and software, including information and software updates, problem solving, and emergency coverage. The Food and Drug Administration (FDA) considers all ACDs class II devices,¹¹ and as such they must comply with federal regulations. The manufacturer's responsibilities are as follows:

1. The manufacturer should ensure compliance with all FDA requirements for medical devices.
2. The manufacturer should provide support for the compounder and its software throughout the life of the contract.
3. The manufacturer should routinely provide the latest version of the compounder software in a timely manner.
4. The manufacturer should ensure adequate availability of compounding supplies.
5. The manufacturer should provide detailed information and instructions on the appropriate use of the compounder and its software. References should be provided when appropriate.
6. The manufacturer should comply with FDA requirements for reporting adverse events.

Within the pharmacy department, specific policies and procedures should be developed to address responsibilities for compounder operations and maintenance, staff training, and monitoring compounder performance at all times. Before selecting and implementing an automated compounder, the pharmacy department should do the following:

1. Define and agree on automated compounding system needs and performance requirements.
2. Develop an implementation team with a lead person.
3. Develop a set of policies and procedures.
4. Develop a well-defined plan for backup and downtime procedures.

Control of the ACDs in daily operations

The pharmacy department is responsible for the use, maintenance, and performance of the ACD, including decisions about who has access to the compounder and its operations. Specific consideration should be given to the following:

1. Only designated pharmacy department personnel should have access to the compounder and its software. The level of access should correspond to the level of authority and expertise of the personnel.
2. Before being granted access to a compounder, pharmacy personnel should pass established competency standard testing.
3. Access to and use of the compounder by pharmacy support personnel (e.g., pharmacy technicians, students, other designated support staff) should be directly supervised by an authorized pharmacist.
4. The additive configuration or sequence of the compounder for compounding PN admixtures should not be altered from the established format without the authorization of a designated pharmacist.
5. Unless allowed per approved facility specific policy, the compounder

should not be used for any purpose other than PN admixture compounding without authorization from a designated pharmacist. If the compounder is used for other extemporaneous drug preparation, this should be done separately from the schedule for PN admixtures. The use of the compounder in this manner will likely require the use of new compounding sets and admixture configurations.

6. Operation of the compounder should follow manufacturer recommendation (e.g., tubing changes).
7. With the current prevalence of medication shortages, pharmacist review and verification should be required for any changes to individual product ingredients (needed to reflect availability, shortages, and conservation, among other variables) and to prevent ordering of unavailable products.
8. Only the core equipment needed should be in the hood when compounding, and unnecessary items should not be kept or stored in the hood (e.g., extra labels and needles).
9. If the ACD will be used for multiple patient populations (e.g., adults and pediatrics), an authorized pharmacist should ensure the formula templates are clearly marked to avoid compounding errors, such as using incorrect ingredient concentrations.

Safety and efficacy features

The complexity of ACD functions makes it imperative that the pharmacy department develop a specific plan for ensuring safe and efficacious use at all times. The safety and efficacy features should outline the core principles necessary for carrying out the complex tasks of PN compounding. The plan should identify the minimum standards that are routinely assessed through an established monitoring and surveillance program. ACDs on the market differ in hardware design, mechanisms of fluid transfer, and software applications. Consequently, sterility and quality assurance testing procedures and measures are also different, including routine assessments of accuracy in the delivery

of correct amounts of nutrients. Consideration should be given to the following in accordance with the device manufacturer's specific instructions:

1. Establishing minimum competency standards for all personnel who have access to and operate the compounder. Competency standards should ensure that the compounder user has sufficient expertise to identify errors that may inadvertently bypass quality assurance systems. For all personnel operating the compounder, the competency standards should be reviewed and validated on a routine basis to ensure compliance with federal and local regulation along with sterile compounding standards (e.g., USP general chapter 797¹²).
2. Establishing specific procedures for the operation of the compounder that standardize its use, irrespective of the individual operator. Changes in compounder operations should occur only when authorized and should be communicated to all staff involved in compounding.
3. Including sterility and quality assurance measures that meet USP general chapter 797 sterile compounding standards to avoid extrinsic contamination and ensure accurate delivery of PN additives.¹²
4. Ensuring that compounder tubing changes occur at appropriate specified time intervals in accordance with the manufacturer's recommendations.
5. Devising methods for assessing and calibrating the accuracy of the compounder in delivering precise levels of substrates and additives in accordance with the manufacturer's recommendations.
6. Developing a plan on how to utilize reports included within the automated compounding in documenting daily activities.
7. Developing a contingency plan and a readily available backup system or method for providing uninterrupted PN therapy to patients in the event of compounder failure.
8. Ensuring that adequate amounts of solutions and supplies for automated compounding are on hand.

Quality assurance monitoring and documentation

ACDs are intended to provide a higher margin of accuracy and to streamline the labor-intensive tasks associated with the manual extemporaneous preparation of large-volume, multi-additive PN admixtures and other admixtures. The compounders are not designed to replace oversight functions, which require the expertise of a pharmacist.

The pharmacy department may work with other departments to assess the compounder's performance if such expertise is not available within the pharmacy department. For example, portions of PN admixtures may be sent to the healthcare organization's laboratory to determine dextrose content. However, laboratory methods are usually designed for biological rather than pharmaceutical systems and should be validated to meet USP requirements for the components being tested. If outside departments participate in the quality assurance program, their methods should be appropriately validated in accordance with USP specifications and the results documented within the pharmacy department records on the compounder's performance.

The pharmacy department should develop a monitoring and surveillance plan with output reports that encompasses the principles outlined under the section on safety and efficacy features. The plan should detail specific policies and procedures that will ensure the continuing operation of the ACD at optimum performance levels at all times. The data generated by the monitoring procedures should be reported to the pharmacy director and other appropriate oversight personnel and kept as a permanent record of the compounder's operations. These reports should be regularly reviewed in the assessment of trends and other long-term measures of performance. Specific consideration should be given to the following:

1. Establishing performance standards and continuous quality assurance measures for assessing the

compounder's performance and product quality during setup and in process (during compounding) and end-process testing.

- Establishing quality assurance testing of user-defined software variables validating that the correct responses to user commands occur.
- Validating all quality assurance testing before implementation.
- Establishing a minimum performance standard for each quality assurance test (e.g., deviations in the accuracy of delivering a single additive cannot exceed a predetermined percentage error without immediate corrective actions).
- Documenting all quality assurance data daily. A comprehensive review of the data and documentation of performance trends should be performed at scheduled intervals as necessitated by aseptic conditions. The compounder should have scheduled, routine cleaning and maintenance according to the manufacturer's recommendations to ensure proper operation.
- The availability of readily accessible reports from the compounding device is a feature that should be considered when selecting a device.

Storage, inventory, and medication shortages

The pharmacy department is responsible for housing the ACD, related disposable supplies, and admixture ingredients. Other departments, such as materials management or supply chain, may order and store additional supplies for the compounder yet defer to the pharmacy for the selection of the components necessary for proper compounder operation. Specific consideration should be given to the following:

- Maintaining an adequate inventory of supplies necessary for compounder operation and patient needs.
- Procuring large-volume PN components (amino acids, dextrose, and lipids) that have adequate physicochemical data that ensure the stability, compatibility, and safety of the final formulations commensurate

with the data for single-source products.³ Any proposed substitute products should be assessed for compatibility and approved by designated pharmacy personnel qualified to do so and possibly by the pharmacy and therapeutics committee if clinical issues are identified.

- If a healthcare organization's contract requires a change in the brand of parenteral products, designated pharmacy personnel should verify that the new products are compatible. If a new product is approved, designated pharmacy personnel should verify that the new product is compatible, add it to the compounder formulary, and revise the admixture requirements and instructions relevant to the compounder's operations. In addition, EHR updates need to happen in the same time to make the transition seamless

Hospitals and medical facilities across the nation are dealing with shortages of medications and supplies daily. The reasons behind drug shortages are varied and complex. According to the FDA, the leading causes of drug shortages are manufacturing problems, delays in manufacturing or shipping, and lack of availability of the active pharmaceutical ingredient.¹³ Specific consideration concerning drug shortages should be given to the following:

- Changes made in the EHR in response to a drug shortage should be associated with matching changes to the PN components within the ACDs. This is imperative to avoid patient harm in the midst of an urgent response to a critical medication shortage.
- Having multiple concentrations of a specific medication loaded in an automated dispensing cabinet carries a risk of infusing the wrong concentration; proper use of barcode technology and other safeguards built within the ACDs minimize that risk.

Education and training

PN is a complex therapeutic modality reflected in complex prescriptions with dozens of ingredients, each

with clinical rationales, dosing implications, and interaction potential. As such, the pharmacist reviewing the PN order should demonstrate competency to optimize the delivery of safe and effective therapy. In addition, the pharmacist and/or the pharmacy technician preparing or directly supervising the preparation of the PN should demonstrate competency to prepare an appropriate and safe admixture for each patient. Institutions should implement policies and procedures addressing determination of competent PN order review and preparation. Competence should be assessed initially and on an annual basis at a minimum. Any identified medication errors related to PN order review or preparation will necessitate more frequent competency assessment in addition to a systematic review of the PN use process.¹⁴ Specific consideration should be given to ensuring the following:

- Pharmacy administration determines the individuals who will be responsible for education and training in the use of the compounders.
- All education and training are documented in a permanent record maintained in the pharmacy department and in personnel files.
- All pharmacy personnel using or supervising compounder operations are tested at regular intervals to ensure that individuals meet the department's minimum competency standards.
- Retraining, competency assessment, and appropriate documentation accompany upgrades and new versions of the compounder to ensure the continued proficiency of personnel, safety of compounder operations, and adequacy of oversight.

Device variability

ACDs are marketed by several manufacturers. Even though there are similarities among compounders, there may be significant differences in the design, accuracy, operation, maintenance, software, and manufacturing support, among other things. The safe operation and supervision of any given

compounder depend on adherence to the manufacturer's specific instructions and continuous quality assurance monitoring of compounder performance. The safe and efficient operation of an automated compounding system depends on defined responsibilities for the pharmacy and manufacturer, as well as on strict adherence to policies, procedures, and quality assurance programs.

Conclusion

ACDs are frequently used for extemporaneous preparation of PN admixtures to provide admixture compounding in a safer, more efficient, and more accurate manner. As with other automated systems or devices, benefits can be realized only when the technology is used appropriately, and significant patient harm may occur when safety and quality assurance measures are overlooked or circumvented. These guidelines outline key issues that should be considered to safely and cost-effectively incorporate this technology into the pharmacy operations of healthcare organizations. Pharmacy professionals are encouraged to exercise their professional judgment in assessing their organization's needs for ACDs and in adapting these guidelines to meet those needs.

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Disclosures

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Additional information

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