Baxter ExactaMix Automated Compounding Device (ACD)
Valve Set Supply Disruption Considerations
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On April 19, 2022, Baxter announced a supply disruption of the ExactaMix valve sets (ExactaMix 1200 Valve Set H938792 and ExactaMix 2400 Valve Set H938724) due to raw material constraints that are impacting production volumes. As a result, healthcare providers and institutions are driven to consider conservation measures when compounding using the ExactaMix Automated Compounder.

However, the nature of this supply disruption is of grave concern, limiting the ability to safely prepare parenteral nutrition and other intravenous sterile products compounded using the ExactaMix device. Typical strategies for conservation may not easily translate to this supply disruption. As such, to assist, the information found within this document provides considerations for potential approaches and subsequent considerations for healthcare providers and organizations.

This document was collaboratively prepared and approved by:

- the American Society for Parenteral and Enteral Nutrition (ASPEN),
- the American Society for Health System Pharmacists (ASHP),
- the Institute for Safe Medication Practices (ISMP), and
- the National Home Infusion Association (NHIA)

The above listed organizations collaborated in the preparation of these guidance considerations and respectively represent the interests of physicians, nurses, dietitians, pharmacists, other allied health professionals, and researchers. Collectively, they envision an environment in which every patient receives safe, efficacious, and high-quality care. They have developed these considerations to assist their members in responding to the supply disruption of Baxter ExactaMix valve sets in order to avoid interruptions in therapy and minimize potential errors.

Important Notes:

- These recommendations do not constitute medical or professional advice and should not be taken as such. To the extent the information published herein may be used to assist in the care of patients, this is the result of the sole professional judgment of the attending health professional whose judgment is the primary component of quality medical care. The information presented herein is not a substitute for the exercise of such judgment by the health professional and healthcare institution.

- No single strategy will work for all organizations, and all are less than ideal for providing safe and optimal patient care. Institutions must carefully consider options and weigh the risks and benefits prior to implementation.

- The use of the valve sets outside of the Operator Manual by extending the use of the valve sets for longer than 24 hours or to deliver more than 150 liters of fluid, whichever comes first, has not been validated and is not recommended by Baxter.

- Baxter is not aware of any other valve set that is compatible with, works with, or has been validated with the ExactaMix Automated Compounding Device.

During the shortage period, consider the following:

1. Purchase only as much supply as needed. In the interest of patient safety and fair allocation to all patients nationally, please do not stockpile.
2. Continue to observe and maintain compliance with product labeling (e.g., package insert), USP General Chapter <797> Pharmaceutical Compounding-Sterile Preparations and associated USP chapters, and State Boards of Pharmacy and federal rules and regulations.
3. Report severe drug product shortage information to ASHP Drug Shortages website and the FDA Drug Shortage Program (DSP). Report device shortages to FDA Center for Devices and Radiological Health.
4. Report medication errors or near misses related to shortages to the ISMP National Medication Errors Reporting Program (ISMP MERP).

Below, two tables are included outlining considerations for the following:

- Table 1. Considerations for Automated Compounding Devices
- Table 2. Additional Parenteral Nutrition (PN) Specific Considerations for Automated Compounding Devices

Note: For PN specific considerations, the intent is for the considerations in Table 2 to be used in conjunction with those presented in Table 1.

Table 1. Considerations for Automated Compounding Devices (ACD)

Potential Approach to Consider	Select Factors to Consider
Use commercially available products and alternatives, where able and clinically appropriate. - Account for all products prepared using the ACD, including continuous renal replacement therapy (CRRT), cardioplegia solutions, parenteral nutrition, and other admixtures and sterile products.	- Prescribing and electronic health record (EHR) considerations - Workflow and labeling considerations - Administration considerations - Clinical appropriateness
Reduce the number of ACDs in use. For example, if your institution employs more than one ACD, consider consolidating all compounding to a single ACD.	- Accuracy of measurement when the 150 liter volume maximum has been exceeded - Feasibility of using single ACD for different patient populations (e.g., adults, pediatrics/neonates)
Use alternative compounding devices, if appropriate and available.	
Consolidate ACD compounding to a single, central location (e.g., the organization's centralized sterile compounding pharmacy).	- Accuracy of measurement when the 150 liter volume maximum has been exceeded
Outreach to other healthcare facilities in your region or organization to consolidate sterile compounding via ACD to one facility.	- Prescribing and workflow considerations - Accuracy of measurement when the 150 liter volume maximum has been exceeded (e.g., consider combined compounding volume from consolidating institutions) - Compliance with USP General Chapter <797> Pharmaceutical Compounding-Sterile Preparations and associated chapters, State Boards of Pharmacy and federal rules and regulations - Additional logistic, financial, legal, and privacy considerations
Outsource to a sterile compounding facility.	- Prescribing and workflow considerations
If necessary, after other measures have been considered, perform manual compounding and preparation of admixtures instead of ACD preparation	- Use ACD software/intravenous (IV) workflow technology for calculations and production labeling - Ensure adequate safety checks are in place, including barcode ingredient verification, in-process ingredient checking, and/or the use of IV workflow technology[1]

Table 2. Parenteral Nutrition (PN) Specific Considerations for Automated Compounding Devices (ACD)
Note: In addition to the considerations presented in Table 1, Table 2 presents additional considerations for parenteral nutrition, specifically. The intent is for these considerations to be used in conjunction with those presented in Table 1.

Potential Approach to Consider	Select Factors to Consider
Assess and routinely reassess each patient for PN indication and appropriateness; provide nutrition via the oral or enteral route when possible.	
Prioritize ACD for compounding of neonatal and pediatric PN admixtures and lipid injectable emulsions (ILEs) when possible.	
Use commercially available multi-chamber PN products, where available and clinically appropriate.	- Prescribing and electronic health record (EHR) considerations - Workflow and labeling considerations (e.g., CPOE changes, changes to established standard PN administration times, etc.) - Activation and compounding (e.g., adding multivitamins, trace elements) considerations - Administration considerations - Assuring PN formulation contains all necessary components, is stable and compatible - Clinical appropriateness of commercially available multi-chamber bag PN products (Note: may require co-administration of other parenteral fluids; may not be appropriate for neonatal and pediatric patients)
Reduce the number of days the ACD is in use, for example: - Stagger timing of PN compounding using the ACD to optimize the 24-hour limit on the valve sets. For example, begin preparing bags at noon on day 1 and finish preparing bags before noon on day 2. - Eliminate weekend PN compounding using the ACD by delaying new PN initiation until Monday and compounding weekend PN supply on Fridays. - Batch PN compounding using the ACD by preparing more than one PN bag per patient at a time. (Note: These strategies may only be effective for conservation if the use of ACD can be avoided entirely on certain days of the week. If the ACD must be used on any given day, the use of the ACD and valve set should be optimized.)	- Prescribing and EHR considerations - Workflow and labeling considerations - Administration considerations - Storage considerations - Compliance with USP General Chapter <797> Pharmaceutical Compounding-Sterile Preparations and associated chapters, State Boards of Pharmacy, and federal rules and regulations for anticipatory compounding - Beyond use dating limitations per USP <797> ***Important Note****: Avoid extending the beyond-use date (BUD) for individual PN admixtures as a strategy to reduce compounding days. Adhere to the limits expressed in USP Chapter <797> when assigning BUDs for PN.*
For hospitalized patients receiving home PN, if the patient is clinically stable, PN has been stored appropriately, and appropriate verification procedures are in place, allow for home PN to be used while the patient is admitted to the hospital.	- Prescribing and EHR considerations - Pharmacy review and verification processes - Workflow and labeling considerations - Administration considerations - Nursing considerations - Storage considerations - Patient clinical status and appropriateness to receive home PN admixture - Consultation with home infusion pharmacy

On days when the 150 liter volume maximum has not been met, pre-prepare PN bags with commonly prescribed concentrations of amino acids, dextrose, ILE, and electrolytes that may be used for clinically stable adult and older pediatric patients.	- Clinical appropriateness - Compliance with USP General Chapter <797> Pharmaceutical Compounding-Sterile Preparations and associated chapters, State Boards of Pharmacy, and federal rules and regulations for anticipatory compounding - Beyond use dating limitations per USP <797> ***Important Note**: Avoid extending the beyond-use date (BUD) for individual PN admixtures as a strategy to reduce compounding days. Adhere to the limits expressed in USP Chapter <797> when assigning BUDs for PN.*
If the institution has evaluated other measures, reviewed and assessed available literature and data, and deems it necessary to extend the use of the valve set beyond the description in the Operator Manual and published recommendation from the manufacturer[2], the following additional measures should be considered: - In an inpatient setting, discussion of the risks and benefits with the pharmacy and therapeutics committee or another hospital interprofessional stakeholder group(s), including epidemiology and risk management. - In the home infusion setting, discussion of the risks and benefits with the organization, leadership, and key stakeholder group(s) including epidemiology and risk management. - Initiate or increase microbiological testing of samples of PN admixtures and ILE prepared on days valve set use is extended. - Development of procedures for ensuring sterility of the valve set is maintained. - Increasing vigilance and visual inspection for the presence of precipitates or particulate matter.	- Sterility/infectious risk - Durability of valve set - Accuracy of measurement when the 150 liter volume maximum has been exceeded - Integrity of plastic and components of valve set - Ensure PN admixtures are filtered per ASPEN recommendations[3] - Re-sterilization of valve sets, by any means, has not been qualified and re-use is not supported
If necessary after other measures have been considered, perform manual compounding and preparation of admixtures instead of ACD preparation	- Use ACD software/ intravenous (IV) workflow technology for calculations and production labeling - Ensure adequate safety checks are in place, including barcode ingredient verification, in-process ingredient checking, and/or the use of IV workflow technology[1] - Ensure appropriate order of addition of PN components and additives to maximize solubility, compatibility, stability and avoid precipitation

Table References

1. Institute for Safe Medication Practices (ISMP). *ISMP Targeted Medication Safety Best Practices for Hospitals*; 2022. https://www.ismp.org/guidelines/best-practices-hospitals.
2. Baxter "Dear HealthCare Professional" letter dated April 19, 2022.
3. Worthington P, Gura KM, Kraft MD, Nishikawa R, Guenter P, Sacks GS; ASPEN PN Safety Committee. Update on the Use of Filters for Parenteral Nutrition: An ASPEN Position Paper. Nutr Clin Pract. 2021 Feb;36(1):29-39.

Select Resources for Clinicians:

Topic	Select Resources
Valve Set Supply Status	- ASHP Drug Shortage Bulletin: ExactaMix Valve Set
Parenteral Nutrition Solution Center (ASPEN)	- https://www.nutritioncare.org/PNResources/
PN Indication	- When Is Parenteral Nutrition Appropriate? JPEN J Parenter Enteral Nutr. 2017 Mar;41(3):324-377.
PN Dosing and Safe Practices	- Appropriate Dosing for Parenteral Nutrition: ASPEN Recommendations. - American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. JPEN J Parenter Enteral Nutr. 2014 Mar-Apr;38(3):334-77. - American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. parenteral nutrition safety consensus recommendations. JPEN J Parenter Enteral Nutr. 2014 Mar-Apr;38(3):296-333.
PN Compatibility and Stability	- Parenteral nutrition compatibility and stability: A comprehensive review. JPEN J Parenter Enteral Nutr. 2022 Feb;46(2):273-299.
Lipid Injectable Emulsions	- ASPEN Lipid Injectable Emulsion Safety Recommendations, Part 1: Background and Adult Considerations. Nutr Clin Pract. 2020 Oct;35(5):769-782. - ASPEN lipid injectable emulsion safety recommendations part 2: Neonate and pediatric considerations. Nutr Clin Pract. 2021 Dec;36(6):1106-1125.
PN Filters	- Update on the Use of Filters for Parenteral Nutrition: An ASPEN Position Paper. Nutr Clin Pract. 2021 Feb;36(1):29-39.
Multi-chamber PN Bags	**Multi-Chamber Bag Parenteral Nutrition (MCB-PN) Series**: Addresses the appropriate use of multi-chamber bag parenteral nutrition. (Sponsored by Fresenius Kabi) *2018* • Part 1: Introduction, Indications, and Decision Tool • Part 2: Prescribing and Order Review • Part 3: Preparing, Labeling, and Dispensing • Part 4: Administration and Monitoring

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