By James Ruble, PharmD, JD

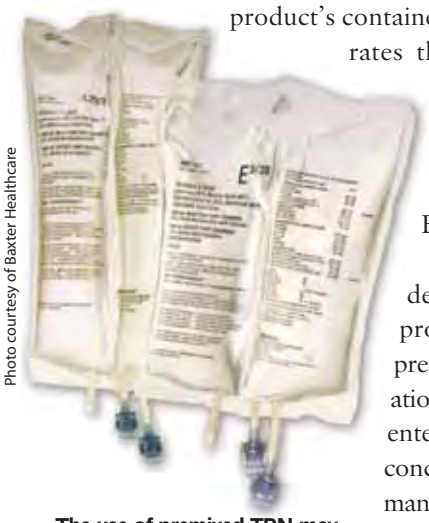
Impact Safety, Efficiency, and the Bottom Line With **Premixed IV Products**

Photo courtesy of B. Braun Medical, Inc.

To ensure the proper activation of products utilizing isolation technologies, provide nurse training and use secondary labels to remind nurses to activate the product.

The availability of premixed IV products and their role in the health care environment have grown exponentially with the release of the widely known Institute of Medicine (IOM) report, as well as the USP and Joint Commission's increased expectations regarding sterile product compounding and medication management. Litigation may also make the utilization of premixed IV products an attractive option. However, decisions to use premixed products should not be made without due diligence.

The terms premixed, ready-to-use (RTU), and point-of-care (POC) are often used synonymously; however, they may describe slightly different products. Premixed products generally involve an absolutely RTU container of medication. The product may be frozen to extend beyond-use dating. A POC product's container may use an isolation technology that separates the drug and diluent until administration. Examples include ADD-Vantage, Mini-Bag Plus, Duplex, and Vial-Mate. There are several reputable manufacturers of premixed, RTU, and POC products, including B. Braun, Baxter, and Hospira.



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The use of premixed TPN may allow your facility to initiate therapies at various times throughout the day, regardless of pharmacy's compounding workload.

A variety of factors may be involved in the decision to use premixed, RTU, and POC IV products. Accordingly, this article will examine premixed IV products in regard to safety, considerations specific to concentrated electrolytes and parenteral nutrition, dosage standardization, labeling concerns, bar coding options, changes to inventory management and dispensing workflow, staff education, and finally, decision analysis.

Safety Concerns

Decisions to purchase and stock premixed products often rally around the flag of safety. Extemporaneous compounding of IV admixtures has been shown to lead to error in 9% of doses compounded, and 2% of extemporaneously compounded IV products may involve clinically significant errors. In contrast, ready-to-use pharmaceutical products are suggested to have an error rate of less than 1%.[1]

On the other hand, premixed products also present some safety concerns. Many of the safety concerns with these products are not related to their pharmaceutical production, but rather their packaging and labeling, which can lead to product selection errors during dispensing. For instance, several years ago, confusion resulted between a manufacturer's premixed esmolol and dopamine infusion products, both of which were contained within a foil overwrap that listed the drug name on one side only; when the bags rested with the identity side facing down, the products could be mistaken for one another. As a partial solution to this problem, the manufacturer issued special labels to be affixed to both sides of the esmolol over-wraps upon dispensing from the pharmacy. In addition, there were recommendations to avoid storing these products on the care units.

Another safety concern was identified with glass bottles of dextrose 5% in water (D5W) and premixed nitroglycerin bottles, both of which featured similar label colors and lettering. In this circumstance, there were isolated cases of nurses hanging a bottle of D5W that was assumed to be premixed nitroglycerin. This problem was addressed primarily through staff education.

Look-alike premixed bags can easily be confused for one another, and ultimately, the wrong medication can be dispensed. Ciprofloxacin (5 mg/mL) and fluconazole (2 mg/mL) premixed products are available in approximately 200 mL volumes and have similar over-wrap packaging. While both are anti-infective agents, their misapplication could have profound consequences in a critically ill patient. To avoid these errors, physically separate these products in drug storage areas.

Another premixed product prone to dispensing errors is heparin. Some of these products have red lettering on their labels and can be confused with premixed potassium chloride, which also features red lettering. Premixed heparin products have also been confused with hetastarch products. In spite of these observations, there remains general agreement that premixed products and POC technologies do result in fewer errors.[2]

Potassium Chloride/Magnesium Sulfate and TPN

Electrolyte homeostasis in clinical care often involves potassium and magnesium supplementation. These agents can be simultaneously viewed as critical agents in patient care and error-prone IV products. Vials of concentrated potassium chloride and magnesium sulfate are frequently used to prepare electrolyte replacement solutions. Compounding errors can result in a replacement therapy of a higher dose or concentration than intended. The Joint Commission (TJC) now prohibits floor stock storage of any concentrated potassium chloride product in patient care units. The Institute for Safe Medication Practices (ISMP) has further recommended that only premixed

solutions or commercially outsourced admixed solutions be made available in these areas.[3]

There has been much debate over the benefits of premixed versus customized parenteral nutrition formulations.

- Arguments against premixed TPN include:
  - May limit the ability to fine tune electrolyte homeostasis
  - May limit the ability to optimize caloric needs of patient
  - May make prescribers feel a loss of control in patient care
  - Difficulty in gaining prescriber acceptance may increase inventory, should both premixed and customized TPN be offered by pharmacy

- Arguments in favor of premixed TPN include:
  - May reduce compounding workload and simplify USP <797> compliance
  - May allow for greater variability in start/hang times, regardless of pharmacy's compounding workflow (In many institutions, hang times are standardized to evening/late evening hours. If premixed TPN is being utilized, TPN could start at nearly any time of the day.)
  - May lead to decreased product contamination (Pharmacy-prepared products are subject to variability in the staffing/environment of the compounding area.)

Dosage Standardization

There are often legitimate clinical reasons for relatively small changes to the dosages and concentrations of IV medications or for orders for atypical dosages. Nevertheless, those who routinely work in IV admixture services frequently observe these highly customized products being returned unused to pharmacy within 24 to 48 hours. Premixed and RTU products can both reduce waste and serve to establish reasonable limitations for dosage standardization.

Pharmacy, in conjunction with the P&T committee, may decide to implement a standardized dosage program utilizing premixed IV products. The hospital may still compound non-standard doses, but the availability of predetermined premixed products may channel providers into more cost-effective orders.

Labeling Concerns

Many health care enterprises encounter errors associated with the mislabeling of IV medications. While premixed and RTU products are not immune from these types of errors, many now undergo substantial scrutiny of their packaging prior to market release. Specialists in human factors engineering may be involved to identify packaging or processes that would contribute to such errors.

Thought should be given to the placement of patient-specific labels on premixed IV products that require over-wrap packaging to maintain optimal storage conditions. Removal of the over-wrap may subject the product to dosage concentration changes resulting from the evaporation of water or exposure to light. Whenever possible, the pharmacy should defer to manufacturer recommendations on over-wrap packaging. In some circumstances, over-wraps may be partially opened and rescaled so that a patient-specific label can be placed on the immediate container.

Bar Coding Options

The use of bar coded medication administration (BCMA) technology is growing exponentially in hospitals and is contributing to favorable cost-benefit analyses and substantially reducing errors.[4] FDA regulations now require that pharmaceutical products contain a machine readable bar code, which, at a minimum, contains the NDC number. Many manufacturers have moved beyond this minimum requirement to include the lot number and beyond-use date in the product's bar code.

The FDA requires that bar codes be present on a drug product's overwrap, as well as on its immediate container, unless the immediate container's bar code is readily visible and machine-readable through the overwrap (such as an overwrap with a transparent section over the label bar code). To prevent medication errors, a bar coded overwrap is important, even if the overwrap will be removed prior to administration, because hospital personnel may need to scan the bar code at several points in the dispensing process and prior to administration. Some institutions use software to generate bar coded, patient-specific medication labels for premixed products.

Changes to Inventory Management and Dispensing Workflow

Automated dispensing cabinets (ADCs) are a natural fit with the dispensing of oral and topical medications. However, the placement of extemporaneously compounded IV medications into ADCs is complicated by storage requirements and shortened beyond-use dating. Some ADCs have refrigerated compartments, but even so, some compounded medications may allow for storage of only a few days, making their availability in ADCs less than optimal. In contrast, premixed and POC products are ideally suited for incorporation into ADCs.[5]

Premixed products often have extended beyond-use dating and, therefore, may be kept in ADCs for longer times, providing a shelf-life that will likely result in clinical utilization and reduce medication wastage. Pharmacy can monitor unit-based ADCs to optimize inventory par levels and ensure product availability.

Automated inventory management systems track product utilization and can help pharmacy contain costs associated with excess inventory levels. Data is most often captured when nurses remove a product from an ADC prior to patient administration and either scan the product's bar code or record it as removed using the ADC's on-board computer. Furthermore, by stocking premixed and POC medications in ADCs, hospitals stand to improve their medication delivery and administration times.

Even for hospitals not using ADCs to dispense medications on the nursing units, premixed IV products can present several inventory management benefits. For instance, pharmacies may witness a decrease in the ancillary products required for the production of IV medications, and medication wastage may decrease due to the extended beyond-use dating offered by premixed products, in comparison to sterile preparations compounded in the pharmacy. Moreover, some institutions may heavily depend on batch production of common dosages, such as cefazolin 1 g, nafcillin 2 g, and vancomycin 1 g. Substitution of premixed products for some of these products may result in reduced cleanroom-related costs. The reduction in overhead may result from a smaller portion of space dedicated to compounding, reduction of staff hours needed for compounding, and reductions in ancillary costs for compounding equipment and supplies.

Nursing Education

Nurses remain primarily responsible for the administration of medication products; however, physicians and other prescribers also need to be considered in the education process. Premixed and RTU products typically require no significant difference in education compared to their extemporaneous counterparts. However, POC products that utilize isolation technologies require additional training, as they are prone to improper activation. For example, ADD-Vantage systems require digital manipulation of a latex stopper to allow the mixture of the diluent and drug. Unfortunately, it remains possible for nursing personnel

to administer the diluent without fully activating the drug. Likewise, Mini-Bag Plus and Vial-Mate systems require bending a connecting cannula to allow mixing of drug and diluent. If the mixture is not accomplished first, the patient typically receives a small saline dextrose or isotonic fluid bolus, without any medication. Problems with improper activation can be minimized or entirely overcome through nursing education and the use of secondary labels, placed nearby the patient-specific label, that remind nurses to activate the product prior to hanging it.

Decision Analysis

To date there are no large-scale literature analyses of the economic impact of premixed, RTU, and POC products. A small pharmacoeconomic analysis on the cost-savings from RTU products was conducted in Belgium. This study was limited to the use of dobutamine (extemporaneous compounded versus premixed) in cardiac surgery patients. Overall, the investigators found a 60% cost-reduction from using premixed dobutamine versus conventional admixture.[6]

In addition, Kenneth Witte and his colleagues developed a decision analysis model for frozen premixed IV products, primarily frozen cefazolin. They developed a nine-point, weighted decision process.[7] The decision analysis demonstrated their institution could save approximately $5,000 by utilizing frozen, premixed cefazolin products. Accounting for inflation, this would amount to approximately a $10,000 savings today.

Carl Geberbauer described general guidelines to consider when purchasing premixed products.[8] A favorable cost-management outcome can be achieved by utilizing premixed, small-volume parenteral products. With the use of small-volume parenteral products, Geberbauer observed better inventory control (fewer items to purchase); a reduction in waste, equipment costs, and the need for specialized compounding staffing; and improved quality assurance for parenteral products.

Summary

Many health care enterprises are making decisions to utilize premixed, RTU, and POC IV products instead of performing in-house compounding, in order to improve safety, ease USP and TJC compliance burdens, improve medication delivery times, and reduce medication wastage. Furthermore, by reducing your compounding workload, the use of premixed IV products can promote quality assurance for your institution's IV products, reduce the costs associated with compounding supplies and IV product components, and allow your pharmacists to dedicate their time to other worthwhile tasks, both within and outside the walls of the pharmacy department. ■

With more than 20 years' experience in health care, James Ruble, PharmD, JD, is manager of infusion services for the pharmacy department at the University of Utah. In addition, he provides pharmacy law and ethics instruction for the University of Southern Nevada and is on the auxiliary faculty at the University of Utah.

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Vendor	Reader Service Number
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Hospira, Inc.	138
PharMEDium Services, LLC	141