Efficiencies gained by using manufactured premixes

Part 1 of a multi-article series that explores how premixed IV products can positively impact your pharmacy operations

Introduction

The goal of this article series is to explore important variables that should be considered when making decisions around IV dosage forms.

Typically, when an IV medication is added to formulary through the Pharmacy and Therapeutics (P&T) committee, the pharmaceutical is added to formulary while the decision to utilize a specific dosage form commonly lies in the hands of operational leaders. To determine the impact that IV dosage forms have on operational efficiency, we must first understand the dosage form options that may be available (Table 1), including Ready-to-Administer products (RTAs), Ready-to-Use products (RTUs) and Compounded Sterile Products (CSPs). Due to the number of IV dosage forms that may be available for a given medication, selecting one or multiple dose forms for your pharmacy operation may seem like a daunting task. We will take a systematic approach to assist with IV dosage form evaluation by first looking at its impact on operational efficiency.

Labor Impact

The specific IV dosage form chosen has the potential to impact pharmacy department labor. Typically, a pharmacy technician performs the compounding, assembly and/or labeling of IV products while a pharmacist monitors and checks the final product before it is released for patient use. A complex process with numerous steps in the IV dose preparation will require more pharmacy department time and labor.

The additional labor component for IV dosage forms that also must be evaluated is the impact to the end-user, which is most commonly a nurse but may also be an anesthesia provider (e.g., CRNA, MD) or another healthcare professional. Undoubtedly, end-users prefer the IV dose to be ready to administer to the patient without any additional manipulation. As such, end-users prefer RTA's over any options that require additional steps, such as assembly and/or activation, prior to administration.

Table 2 compares the IV dosage forms based on the amount of labor needed, according to the number of steps and/or manipulations that may be required.

Below is a summary of the labor impact in Table 2:

1. **RTAs have the least amount of labor involved:**
   - No manipulations required
   - Premix directly from the pharmaceutical company
   - Overwrap may need to be removed prior to administration

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Table 1.

Dose Type	Meaning	Description
RTA	ready-to-administer	Premixed from manufacturer and can be administered without any further manipulation
RTU	ready-to-use	Premixed product requires activation prior to use or Premixed product requires thawing or some type of storage manipulation prior to use or Product requires both assembly and activation prior to use
CSP	compounded sterile product	Sterile product that is prepared using component ingredients by a qualified individual or device in a sterile environment Preparation options include: – Robotic preparation – Human preparation with assistive technology – Human preparation with no assistive technology

Labor Impact (cont.)

2. RTUs requiring activation (e.g., multi-chamber bags such as commercially prepared parenteral nutrition solutions) have an increased labor impact compared to RTAs:

- Final dosage form must be activated either by pharmacy personnel prior to dispensing or by end-users prior to administration
- Requires one or more seals to be broken
- Must be mixed thoroughly prior to administration

3. Premixes requiring storage manipulation (e.g., commercially prepared frozen premixes) require significant preparation by the pharmacy team:

- Requires modification of storage conditions and continuously rotating stock
- Operation must be highly-reliable
- Must have the ability to dynamically modify practices based on utilization trends

4. RTUs that need to be assembled and activated have significant labor requirements: (Figure 1).

- Must aseptically assemble products together
- Must perform a critical activation step prior to administration
- Can be assembled in the pharmacy department and then activated by end-users, or assembly and activation may both be delegated to end-users such as a nurse

Due to increasingly high demands for pharmacy compounding efforts (e.g., COVID-19 response), pharmacy leaders are prioritizing compounding efforts for those situations with limited IV dosage form options, such as preparing unit-dose syringes for COVID-19 vaccine and preparing monoclonal antibodies used to combat COVID-19. Pharmacy labor is being reserved for these high priority efforts that have limited IV dose options; thereby allowing pharmacy leaders to switch from compounding to the use of RTA or RTU products wherever feasible.

5. CSPs produced through a robotic operation still require considerable human effort and can vary depending on the robotic technology being utilized:

- Must load the robotic device
- Must remove completed CSPs from the robotic device
- Must check the final CSP and in some cases relabel the final CSP

6. CSPs produced via a human process, with or without assistive technology, is without a doubt the most complex and laborious process (Figure 1).

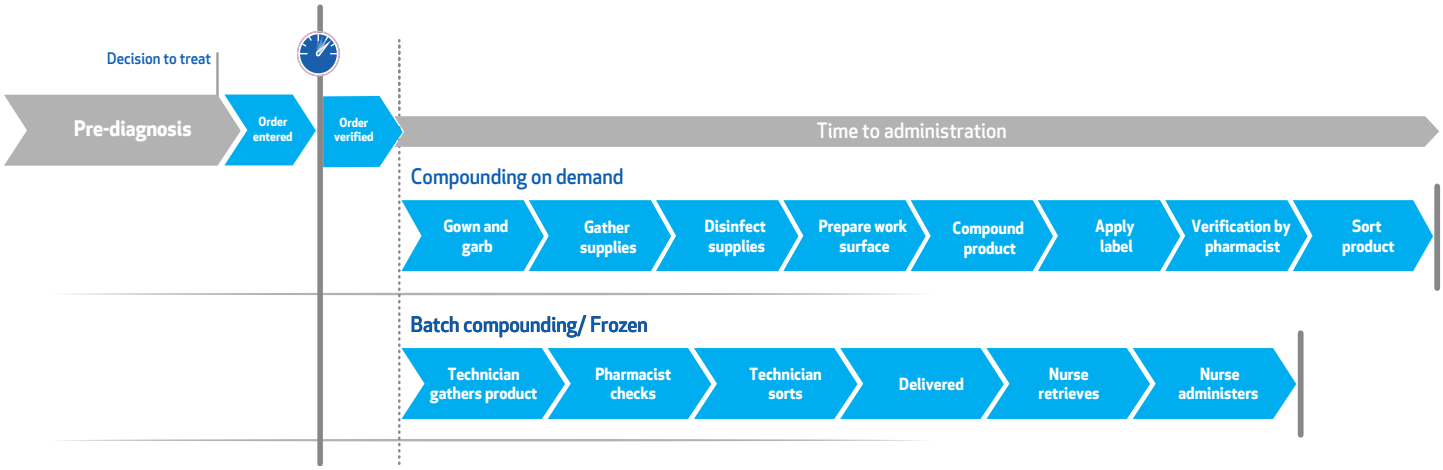
- Must gather supplies and perform a myriad of steps
- Requires labeling and final verification from a pharmacist
- Process is lengthy and requires involvement from both pharmacy technicians and pharmacists

Table 2. Labor impact based on IV dose type

Labor intensity	IV Dosage Form
Least labor ↓ Most labor	RTA
	RTU requiring activation
	RTU requiring storage manipulation
	RTU requiring assembly and activation
	CSP: robotic process
	CSP: human process with or without assistive technology

RTA: ready-to administer
RTU: ready-to-use
CSP: compounded sterile product

Figure 1. Typical steps involved in compounding sterile products in a hospital pharmacy department

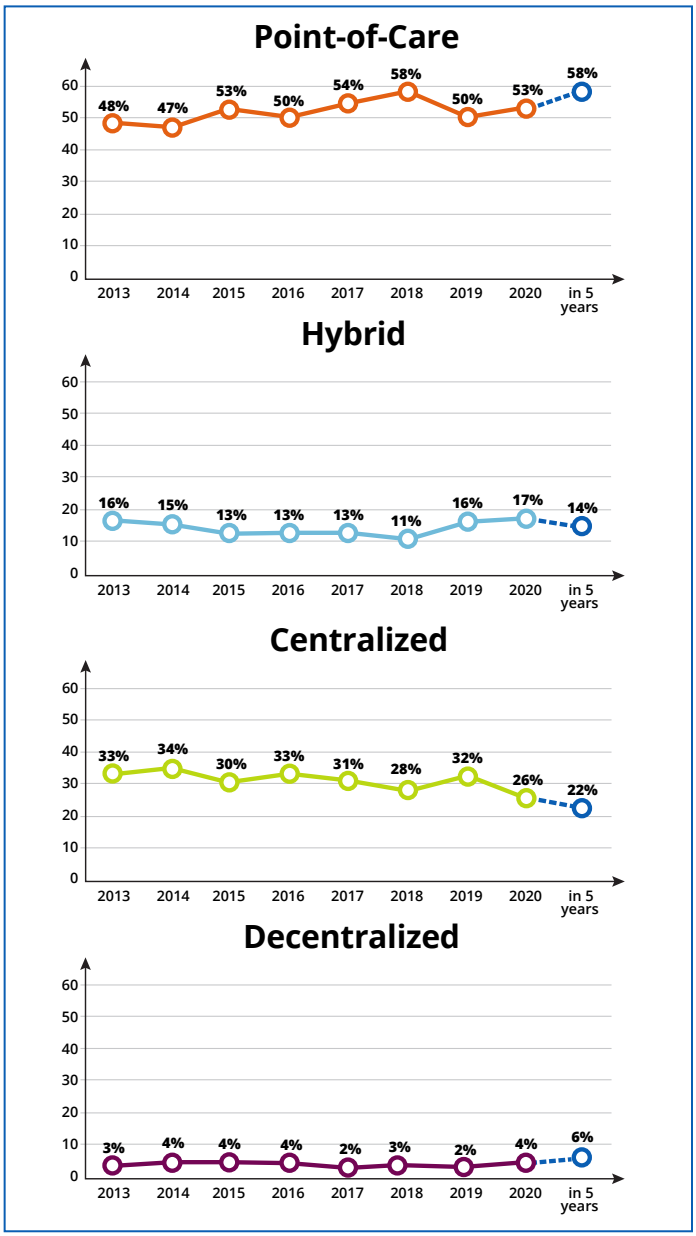


Medication Distribution Model

The popularity of the point-of-care (POC) medication distribution model, where the majority of medications are placed in automated dispensing cabinets (ADCs), continues to dominate the hospital market[1]. Figure 2 outlines the prevalence between medication distribution models based on the author's hospital experience. Key drivers for the popularity of the POC distribution model include: decreased time from provider order entry to administration as well as decreased efforts for end-users to assemble/activate medications.

In reviewing IV dosage form options, RTA and RTU dosage forms are the most likely candidates for placement in ADCs due to storage considerations (usually room temperature). These dose forms also have a manufacturer's expiration date or have a relatively longer beyond-use date (BUD); therefore, RTA and RTU options are highly supportive of the POC medication distribution model and can also support other distribution models as well. While CSPs can be stored in ADCs, their BUD restrictions and limited storage options (usually refrigerated) serve as barriers for widespread adoption in ADCs.

Figure 2.



Definitions

Centralized: The majority or more of inpatient beds receive medications from the central pharmacy, and/or robot/carousel is the main dispensing platform to unit dose carts

Decentralized, supported by satellite pharmacy: The majority or more of inpatient beds receive medications from satellite pharmacies and/or ADCs restocked from satellite pharmacies

Point-of-care The majority or more of inpatient beds receive medications from ADCs on the patient unit, which are restocked from central pharmacy

Hybrid: a combination of the above dispensing methods

Waste

Minimizing waste of essential medications is an important part of operating efficiency that must not be overlooked. Waste not only impacts efficiency, but also intersects with safety and financial factors as well. Since waste can come in many forms, we are referring to waste that's due to an IV product not being utilized by either its manufacturer's expiration date, or by its BUD after assembly or compounding. Most pharmacy operations do not prospectively monitor and evaluate IV product waste, which may represent a significant impact to the overall IV medication budget[2-4].

The general hypothesis is that a longer expiration date or BUD will translate to decreased product waste, due to more time available for its potential use in the clinical setting. This hypothesis generally holds true, however, it is important to note that using an IV dosage form with a shorter shelf life (i.e., short BUD) does not automatically translate to increased waste. When dealing with a shorter shelf life, it is paramount that the operation monitors key inventory variables, such as production quantity, on-hand inventory (including Max and Par values) and inventory turnover rates to minimize waste associated with assembled or compounded IV products. Given operational complexities, priorities and demands associated with a hospital pharmacy operation, it is difficult to fully mitigate waste associated with IV dose types with a short BUD, thereby making IV dosage types with a manufacturer's applied expiration date generally preferred. It is a common strategy to transition CSP dose types with a short BUD to an RTA product to minimize waste[5].

Another scenario that may cause waste is related to the storage of a product under the wrong conditions. This situation usually occurs when a refrigerated medication is sent from the pharmacy to the patient care unit. The medication may not be stored in the refrigerator upon arrival or it may be removed from the refrigerator for an extended period of time. In either case, the time elapsed at room temperature is usually unknown, thereby requiring the product to be discarded.

For both RTA and RTU premixed requiring activation will be evaluated based on the manufacturer's applied expiration date, which is typically 12 to 60 months from the time the product was manufactured.

For all other IV dosage forms listed in Table 1, the BUD will be used to determine how long the dose type is viable. Typical BUDs range from hours up to several weeks depending on the preparation and storage conditions.

Inventory Control and Storage Considerations

Managing product inventory and storage are also variables to consider when selecting an IV dosage form. Additional inventory products or locations needed for a given IV dosage form will add complexities to the inventory control process, thereby requiring additional resources and effort to manage inventory properly. The following list provides commentary on inventory control concepts and storage considerations for the various IV dosage forms:

RTA's and premix requiring activation:

- Stored centrally
  - Higher overall availability due to point of care storage
  - Simplified inventory process when stored centrally
- Room temperature

RTU requiring manipulation;

- Stored centrally in 2 locations
  - Frozen
  - Refrigerated
- Added complexity
  - Inventory control
  - Temperature control
- Added cost - physical infrastructure

Centralized Inventory Management is required for:

- Each component of RTU products that require assembly and activation
- Multiple products including medication vials and proprietary containers
- Ancillary supplies needed for preparation e.g. needles, syringes, alcohol swabs, etc...
- Some component ingredients will require refrigeration; however, the majority of component ingredients can be stored at room temperature. In addition to managing component ingredients, management of completed CSPs may be indicated in some instances, given the specifics of the operation. The storage of the final CSP may occur under various conditions, which will usually have an impact on its BUD.

Management of a multitude of products with various BUDs can be extremely difficult to manage. It is important to utilize a First-In, First-Out (FIFO) method which assumes the product with the earliest BUD is dispensed first. This is difficult to achieve in a controlled setting, like a centralized pharmacy department, and futile to manage when inventory is placed in ADCs.

To fully evaluate the impact of an IV dosage form on your operation's inventory management, it is important to understand how many inventory locations will be needed and the storage conditions required for each of these locations.

Dosage form consistency

When evaluating IV dosage forms available for a given pharmaceutical, it is important to consider if all doses can be provided in the same dosage form. Having a standardized dosage form will have a positive, wide-sweeping impact on your operation, including improved inventory control, simplified electronic health record build as well as streamlined educational efforts.

As an example, let's consider that you are evaluating the latest drug approval, a hypothetical drug called NewDrug. In this example, NewDrug is commonly administered as an intermittent IV infusion to adults in 0.5, 1 and 2 gram doses. When looking at available IV dosage forms for NewDrug, it is preferred that all three doses are available in the same dose form. If different dosage forms are chosen for the three doses, this has potential to negatively impact your operation by not having a standardized practice.

Conclusion

As technologies and options for IV dosage forms continue to increase, pharmacy leaders must take into account multiple variables when making a decision for their operation. In terms of operational efficiency, RTA products offer superiority when compared to other dose types. RTA's confer the following advantages:

–minimizing the impact to pharmacy and nursing labor

–versatility with any medication distribution model including the popular POC model, which prioritizes placement in ADCs

–high potential for waste minimization due to longer expiration dates

–improved management through a lower number of physical inventory locations and storage usually at room temperature

Lastly, it is important to standardize your IV dosage form selection for a given pharmaceutical to streamline your operation and minimize operational inconsistencies.

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