Standardization of intravenous medication beyond use dating at a large health-system

by

Margaret J. Kronz

PharmD, Lake Erie College of Osteopathic Medicine, 2019

Submitted to the Graduate Faculty of the

Graduate School of Public Health in partial fulfillment

of the requirements for the degree of

Master of Public Health

University of Pittsburgh

2021

UNIVERSITY OF PITTSBURGH

GRADUATE SCHOOL OF PUBLIC HEALTH

This essay was submitted

by

Margaret J. Kronz

It was defended on

April 30, 2021

and approved by

David Finegold, MD, MPH, Director, Multidisciplinary Master of Public Health

Tina Batra Hershey, JD, MPH, Assistant Professor, Health Policy and Management

Arpit Mehta, PharmD, MPH, MHA, Director of Pharmacy, Allegheny General Hospital

Thesis Advisor: David Finegold MD, MPH, Director, Multidisciplinary Master of Public Health

Standardization of intravenous medication beyond use dating at a large health-system

Margaret J. Kronz, PharmD, MPH

University of Pittsburgh, 2021

Abstract

Within a large, nine-hospital health-system, there are a number of hospitals that have historically reviewed the current literature individually to establish hospital-specific non-hazardous compounded sterile product (CSP) beyond-use date (BUD) lists. Creating and standardizing the list on a system level is a potential model that could reduce work at the individual site level, increase network patient safety, and facilitate the implementation of network technology. Researchers reviewed the most up-to-date literature and current non-hazardous CSP BUD lists at each site for inconsistencies to highlight the value and increased safety associated with standardizing this resource across the network.

Table of Contents

List of Tables

List of Figures

Preface

This paper was largely made possible by the opportunities and experiences I gained through the Health-System Pharmacy Administration and Leadership (HSPAL) residency at Allegheny General Hospital and the Allegheny Health Network leadership team. The mentorship and support the program provides has allowed for learning and achievement in a year of many disruptors. For this and much more, I am incredibly grateful.

1.0 Background

Compounding medications is a key component to the practice of pharmacy. In the last one hundred years, commercial manufacturing of medications at a large scale became less common. Medications that are commercially available for purchase may not be compounded to protect the manufacturer's patent on the product[1]. There is still a need for medications to be compounded especially in situations where the available formulation is unsuitable for the patient as well as for many compounded sterile products (CSPs) that would have short expiration dates if they were to be manufactured.

As the role of hospital pharmacists was defined throughout the twentieth century, inpatient facilities began to rely more heavily on pharmacies to mix CSPs[2,3]. CSPs were historically mixed by the nursing team at the patient's bedside, but this is recognized as a potential danger to patient safety[1,3]. CSPs are regulated by the Food, Drug, and Cosmetic Act (FDCA) which requires all medications to meet United States Pharmacopeia (USP) standards[1]. USP standards had existed as quality guides since 1820, but until this point, they were simply a best practice rather than a legal requirement[1]. As patient-specific compounding became more infrequent and quality standards for manufacturing became more stringent, the USP organization began to draft standards directed at compounding quality[1,2,3]. These were organized into three chapters: non-sterile (USP <795>), sterile (USP <797>), and hazardous (USP <800>). The scope of this project focuses specifically on products regulated under USP <797>. Hazardous products were excluded from the project and are a source for future quality improvement in the health system.

USP <797> discusses the two components of how long a CSP can be used for: stability and sterility[7]. Stability is defined as "the extent to which a product retains, within specified limits and

throughout its period of storage and use, the same properties and characteristics that it possessed at the time of [compounding].” Stability is dependent on the medication and its chemical properties, medication concentration, the diluent, the container that the medication is stored in, exposure to light, and the storage temperature.

Sterility is defined as “freedom from the presence of viable microorganisms.” Sterility is dependent on the storage temperature and level of risk associated with the compounding procedure. Risk is defined in USP <797> as either high, medium, or low. USP <797> specifically calls out sterility. Personnel and compliance with USP regulations can also affect the sterility of a product. Stability is often determined by the manufacturer or published stability studies. It is important to match and consider the other factors that could affect stability, such as concentration, diluent and container, when reviewing stability studies. A product’s beyond-use date (BUD) can be assigned by reviewing the stability from the available data and sterility dictated by USP <797> and choosing the time that is the most conservative.

Table 1 USP <797> Beyond Use Dating

Risk Level	Controlled Room Temperature (20 – 25°C)	Refrigerator (2 – 8°C)	Freezer (-25 – -10°C)
Low Risk	48 hours	14 days	45 days
Medium Risk	30 hours	9 days	45 days
High Risk	24 hours	3 days	45 days

The variables and potential downfalls when compounding sterile products are numerous. With an increasing number of mergers and acquisitions creating large health-systems, standardizing different populations and practices is a challenge. There are a number of reasons why creating standard network beyond-use-dating resource for compounded sterile products is advantageous. Without standardization, sites likely have their own resource that are updated and validated at variable frequencies. One standard document owned at a health-network level is likely to save time across the network and prevent duplicative work. This standard document may lead to an increased level of patient safety by reducing errors due to lack of sterility or unstable medications administered to patients. Additionally, standardizing CSP practices such as BUD can facilitate the implementation of intravenous (IV) workflow technology. IV workflow technology has been shown to significantly decrease the number of medication errors as well as wasted and missing doses[4,5]. This decreases cost associated with wasted doses and increases patient safety. In 2018, a survey of United States hospitals showed that only 16.4% of hospitals use sterile compounding technology and practices of how sterile products are tracked and maintained varied widely in the survey. This statistic showcases another barrier created when a merger or acquisition is conducted considering that new sites are likely to have different CSP practices[6]. While it is known that other hospitals and health-systems have a similar resource, it is not well documented how many health-systems have beyond use dating documents or use standard beyond use dating in their IV workflow solutions. The publication of the project aims to promote public health information sharing and encourage the use of standardized documents such as this one in the healthcare community.

This paper details a quality improvement project conducted at a nine-hospital health-system in the north-eastern United States in an attempt to standardize the CSP BUDs across the network. The health-system has undergone several mergers and acquisitions throughout the last two decades. Historically, each hospital has managed their CSP beyond-use dating at the site-level. The manager at each site is then responsible for implementing any changes and educating staff. Currently, only one of the nine hospitals, the flagship hospital, utilizes IV workflow technology for compounding. Seven of the hospitals use a tracking system built into the electronic health record (EHR).

The objective of this project is to standardize the beyond-use-dating of non-hazardous CSPs throughout a nine-hospital health-system in preparation for the implementation of IV workflow technology. Several secondary objectives were also explored during this project. The researchers sought to capture the number of discrepancies between the CSP BUD lists and the current literature, develop a standardized process to maintain accuracy of the list over time, and implement the list into IV workflow technology. It is hypothesized that creating and standardizing the list on a health-system level is a potential model that could reduce work on the level of the individual site and facilitate the implementation of IV workflow technology in the near future.

2.0 Methods

The assembled research team consists of one site-lead from each of the nine hospitals. Each site-lead provided their CSP BUD resource(s) to the primary researcher. The CSP BUD list from the flagship hospital would be used as the template and information from other hospitals was added or amended using the existing structure. The primary researcher reviewed the medications listed to ensure that they are in-line with the current literature with clear source citations (Figure 1).

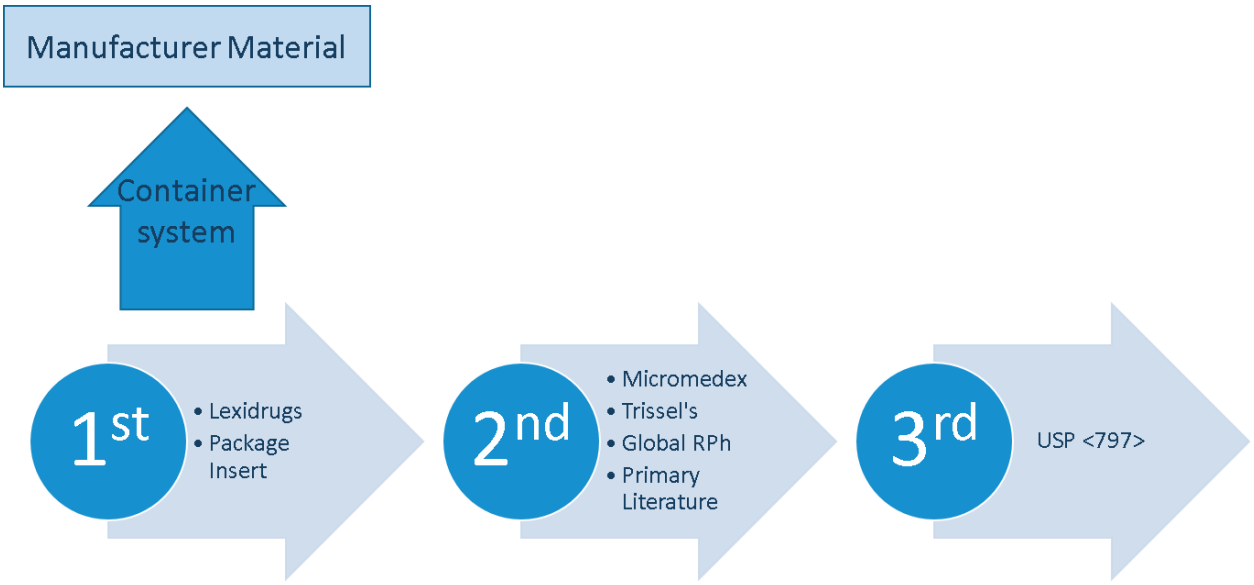

Figure 1 Research Methodology

Stability data is analyzed first by looking at the information provided in the product's package insert and Lexicomp. If stability could be obtained and validated using both sources, the researchers did not proceed with a more detailed investigation of stability and proceeded to the third step in Figure 1. If the sources do not match or one or both of those resources is incomplete, other tertiary resources are explored until two sources confirmed the medication's stability. If this

cannot be achieved through review of available tertiary resources, a database search is run with to consider primary literature exploring stability information. The key words used in this data base search is the name of the medication, “IV,” and “stability.” Once the stability is established, sterility is determined using USP <797> guidance. Many medications at these hospitals are made in batches, so the researchers assumed that all compounding is at the medium risk level. If sterility is shorter than stability, the sterility would dictate the BUD. If stability is shorter than sterility, the stability would dictate the BUD.

Discrepancies are tracked to show the value of standardization. Then, the researcher compares the resources with one another, adds missing medications, and compiles an up-to-date list of medications, their concentrations, and their sterility and stability. This tool returns to the site-leads for review, suggestions, and updates until a final product is approved. The site-leads are responsible for rolling out the product at their site. The primary researcher is responsible for an update at the decided upon frequency and would work with the site-leads to create a process of updating the resource at the decided upon interval and as needed in the future. The team did not perform any advanced statistical analysis.

Several adjustments to the original methods were made during the project. First, the team removed all stability on the chart for premixes removed from foil packing and stability secondary to medication container systems such as Mini-bag Plus or Vial-mate. This information was initially included because these items are processed in the pharmacy workflow in a similar way to CSP, but these items are not CSPs and have generic beyond-use-dating. Next, primary literature is used several times when multiple tertiary sources confirmed shorter stability. All primary literature that supersedes multiple tertiary databases is peer reviewed literature, and studied the CSP under the same conditions that the health-system uses (same diluent, concentration, container, temperature

etc.). Extended-stability studies became more useful and advantageous than initially anticipated by the team, and several sites had this literature readily available, and it is utilized to justify extending the CSP's BUD. These changes to the methodology are detailed as key lessons learned throughout the discussion.

3.0 Results

Six of the nine hospitals in the health-system had an available BUD and concentration resource prior to the beginning of the project. Three of the hospitals report no resource prior to this project and confirmed that stability and sterility information is researched each time a medication is compounded. 352 unique CSPs were reviewed. 10% of the CSPs reviewed (35 medications) showed updated stability information since the last review. One hospital's resource had been updated within the last calendar year, more recently than other hospitals' resources, and of the 50 CSPs on the hospital's list, 2 of those medications required updates to their stability.

In November 2020, the health-system established version one of the standard network resource. The site-leads noted many differences from their previous CSP BUD resources, and work on a second version of the document began shortly after implementation.

Table 2 Version One to Version Two Key Changes

Medication	Version One	Version Two
Dexmedetomidine	24 hours refrigerated	9 days refrigerated
FEIBA	Not included	Included
Medication container system stability	Included	Not included
Morphine	30 hours room temperature	Option for 9 days refrigerated as well
Octreotide	24 hours refrigerated	30 hours room temperature
Protect from light (PFL) medications	Listed in the comment section	Listed in a separate column; also added columns to denote high alert medications and medications that require a filter

Revisions include CSPs compounded infrequently or compounded outside of the EHR that were not included on the list or extended-stability data. The group begans revisions to create a second version of the network resource in December 2020 and the second version was finalized in April 2021. This revision included the addition of three columns: protect from light, high alert, and filter to alert the user of additional stickers or post-preparation instructions; this is counted as one change although it affected many of the medications. The version also removed all stability secondary to medication container systems such as such as Mini-bag Plus or Vial-mate; this is counted as one change although it affected many of the medications. 41 total changes were made to the document between version one and version two; some important examples are highlighted in Table 2. This final list was provided to the new network IV workflow technology system for a planned implementation of this list electronically in October 2021.

4.0 Discussion

This project led to many benefits such as information sharing among sites, ease of technology implementation, and it is believed, but not proven, that the project also created increased patient safety and cost savings in the network. The project succeeded largely because the team was nimble enough to respond to challenges and embrace lessons learned.

Sites within the network had site-leads compiling their lists with a variety of experience with USP regulation and CSPs. The comprehensiveness of each site's list varied greatly, and some of the initially collected resources referenced a combination of extended stability and manufacturer stability data as well as just sterility data. The group took longer than anticipated to agree on the structure of the document. Each hospital provides a different perspective, and the expectations of what the final product would like varied. This could have been anticipated considering that there are many variables that must be considered when assigning a BUD and could be broken down further to consider the components that factor into choosing appropriate sterility and stability information. There were moments where the project experienced scope creep in an attempt to accommodate all site needs in one comprehensive document. This quickly became unrealistic and less user-friendly for the primary user of the document, technicians compounding in the buffer room. This had was mitigated by a phone call with all group members to discuss perspectives and expectations until a consensus was reached. The team kept some of the information utilizing the "hide" feature in Microsoft Excel to maintain information in the electronic copy maintaining a user-friendly resource that accommodates the variety of practices and populations around the network.

In addition to the many lessons learned coordinating the project, several adjustments were made to the original strategy to improve the final product as briefly discussed above. The medication container system beyond-use dating and premix stability out of the foil packaging is now excluded after discussion. The researchers agreed that these products are not CSPs and the end-user friendliness would be greatly increased with the removal of these items. The intention behind relying on tertiary data sources as the preferred source of data is ease of standardization as well as updating and validating the information. The addition of primary literature to displace tertiary literature seems logical, but it presented more variables and required a deeper understanding of the principles behind medication stability. Extended-stability studies became more useful and advantageous than initially anticipated by the team, and several sites had this literature readily available and used it to justify extending the CSP's BUD. These extended-stability studies also lead to more medication that were able to be assigned longer beyond-use dates. Several medications were also indicated low risk compounds rather than medium risk if they are always compounded for a specific patient one dose at a time and the stability data would allow for a longer BUD if the medication were compounded under low risk conditions. These two nuances allowed several medications to be assigned longer BUDs than the health-system historically assigned.

This project likely results in overall departmental efficiency and soft-dollar cost savings that, while challenging to quantify, are crucial to consider. One cost-saving mechanism across the network is through the reduction of the burden on the site-level leads when compiling the beyond-use-dating list. Pharmacy management salaries are large expenses for inpatient pharmacies considering that the average hospital operates with tight financial margins; leveraging their time in the most efficient and cost-effective is preferred. This project removes the burden of updating

and validating this list annually and remove the step of concentration and BUD standardization when implementing the network IV workflow technology. The sites also worked together in the draft process to obtain the best stability data each location had access to, which increased the BUD on many medications. When a medication is compounded but not given to the patient, there is opportunity for the dose to be reused if an identical compound is needed for another patient within the BUD. This naturally becomes more likely when the BUD is longer. When this concept is extrapolated across all nine hospitals within the health-system, there is likely to be cost-savings associated with decreased waste. The cost of medication waste is not and was not being captured prior to the project and is unfortunately unavailable for formal analysis.

Standardization of IV medication BUDs promotes larger public health goals. This project leads to a higher level of standardization and creates safer environments for patients. When patients enter a health care facility, they expect to have knowledgeable clinicians taking care of them and receive a high level of care. Deviations from this expectation are, at the very least, frustrating for patients and may cause patient harm. Generally, standardization in the health care leads to fewer deviations in data-driven, best-practices. Patient harm due to health care issues is an epidemic of great scale. Medical mistakes are the third leading cause of death in the United States[8]. Rates of errors in IV compounds is estimated to be nearly 9%[8]. Standard concentrations and beyond-use dating has been adopted and studies at organizations across the country as an error reducing strategy[9]. The prevalence of administration of unstable or contaminated medications is largely unstudied and extremely challenging to capture. Errors caused by beyond use date errors or inaccuracies are likely to be underreported and generally challenging to capture considering that patients who are taking IV medications in the hospital setting typically present with a complicated, multifactorial, clinical pictures which muddies the waters of underlying causes. Even if this were

examined more closely, it is unlikely to lead to significant differences in errors due to low reporting and the challenge associated with realizing this error caused patient harm. Though it is challenging to capture, prevention of patient harm due to medication instability or lack of sterility may result from this project. This error prevention is an important public health outcome of this project but is not likely to be quantifiable at a single health-system level.

While obtaining data on error prevention rate is unlikely to be quantifiable, cost savings to the health-system and health care cost savings generally may result from this project. Using the best stability information available and recognized by hospitals in the health-system allows more time to use or reuse an IV product after compounding. This leads to less waste and reduces health care spend overall. Some of the hospitals in the health-system compound infrequently and did not historically have this information readily available to them. Historically, each medication that was compounded was either researched or assigned a conservative BUD. The time spent researching the beyond use dating reduces departmental efficiency and creates a cost burden on the department. Additionally, this practice takes time, emphasis, and focus away from the checking the validity of the compounded product. Adding this additional mentally taxing step could lead to missed errors and patient harm. Through information sharing and extended beyond use dating, it is likely that health care spend decreases; this would be a potential area for future studies to more closely consider as this would assist in quantifying the public health impact.

Overall, the team found many of the anticipated benefits sat the conclusion of the project, but there are also many lessons learned. In the current health care climate, a focus on projects that benefit public health and create a high quality of care is crucial to modernizing health care practices. Publishing projects such as this one and sharing this information with other health care providers is key to promoting standardization and data-driven health care. The standardization of

this intravenous beyond-use dating list at hospitals across a health-system was a key quality improvement project that led to cost-savings, increased data-driven medication safety and overall, better patient care.

5.0 Appendix A: IV BUD Version 2

Drug	Strength/Volume	Diluent	BUD	Store	PFL	Filter	High Alert	Additional Comments
Acetazolamide sodium	Diluted in 50 mL	NS	12 hrs	RT				
			3 days	REF				
Acetylcysteine	6,000 mg/200 mL	D5W	24 hrs	RT				
	12,000 mg/400 mL							
	30,000 mg/1000mL							
Acyclovir	Dilute in 100 mL to 250 mL - see comments	D5W	24 hrs	DNRF				< 700mg diluted in 100ml >/= 700mg diluted in 250ml
Alfa1-Proteinase Inhibitor (Prolastin)	Follow manufacturer reconstitution instructions	Iso-osmotic Diluent	3 hrs	RT		X		Administer within 3 hours Filter during administration with a 5 to 15 micron filter
Alteplase	10 mg/50 mL	NS	8 hrs	DNRF				
	6 mg/120 mL							
	12 mg/240 mL							
Amikacin		NS/D5W	24 hrs	RT				</= 500mg diluted in 100ml

	Dilute in 100 mL to 250 mL - see comments		14 days*	REF				> 500mg diluted in 250ml *Assuming low risk compounding
Amiocaproic Acid	1-5 g/100 mL	NS	48 hrs*	RT			X	*Assuming low risk compounding
	25 g/250 mL	D5W						
Aminophylline	50 mg/10 mL	Bacterio static water	14 days*	REF	X			Syringes for stress lab Supplied as vials containing 25 mg/mL. Withdraw 2 mL (25 mg/mL) into a 20 mL syringe, further dilute with 8 mL bacteriostatic water for injection. Protect from light *Assuming low risk compounding
	50 mg/50 mL	D5W	24 hrs	RT				
Amiodarone	450 mg/250 mL	D5W	24 hrs	REF		X		Use a DEHP free bag If using a glass bag; 24 hours at room temperature
Amphotericin B Conventional (Fungizone IV)	10 mg/100 mL	D5W	24 hrs	RT	X	X		Reconstitute with SWFIPeripheral line = 0.1mg/mLCentral line = 0.25mg/mLADULT</=25mg diluted in 250ml26-50mg
			48 hrs	REF				
	50 mg/10 mL		24 hrs	RT				
			48 hrs	REF				

	Dilute in 250 to 1,000 mL - see comments		24 hrs	RT				diluted in 500ml> 50mg diluted in 1000ml
			48 hrs	REF				
Amphotericin B Lipid Complex (Abelcet)	Dilute in 250 or 500 mL - see comments	D5W	6 hrs	RT	X			Filter when adding to IV bag Do not use in-line filter Do not mix with saline containing solutions Begin administration within 6 hours of compounding < 400mg diluted in 250ml >/= 400mg diluted in 500ml
			48 hrs	REF				
Amphotericin B Liposomal (AmBisome)	40 mg/40 mL 200 mg/250 mL	D5W	24 hrs	REF		X		Filter when adding to IV bag Do not mix with saline-containing solutions
Ampicillin	1 gm/50 mL 2 gm/100 mL	NS	48 hrs	REF				Admixure Protect from freezing

	3000 mg/100 mL		24 hrs					
Ampicillin/ Sulbactam	1.5 gm/50 mL	NS	8 hrs	RT				Admixture
			48 hrs	REF				
	3 gm/100 mL		8 hrs	RT				
			48 hrs	REF				
Antithymocyte globulin rabbit (Thymoglobulin)	-	NS	24 hrs	RT		X	X	25mg vial should be diluted in 50mL Send with primed IV line with 0.22 micron inline-filter
Argatroban	50 mg/50 mL	NS	96 hrs	REF	X		X	Admixure Protect from light
Ascorbic Acid	1,500 mg/50 mL	NS or D5W	96 hrs	REF	X			Protect from light
Azithromycin	500 mg/250 mL	D5W	7 days	REF				Admixure
Aztreonam	20 mg/50 mL	NS	24 hrs	RT				Admixure
	12 mg/5 mL		48 hrs	RT				
	1 gm/50 mL		48 hrs	RT				
			7 days	REF				
	2 gms/100 mL		48 hrs	RT				
			7 days	REF				
Basiliximab	20 mg/50 mL	NS	4 hrs	RT				Immediate use is recommended per PI
			24 hrs	REF				

Bivalirudin	50mg/500 mL 250 mg/50 mL	D5W	24 hrs	RT			X	
Belatacept	Dilute in 50-250 mL	NS/D5W	24 hrs	REF		X		Infusion must be completed within 24 hrs of reconstitution with a maximum of 4 hours of the 24 hours at room temperature Send 0.2 to 1.2 micron low protein-binding filter
Bumetanide	10 mg/40 mL Dilute dose in 50 mL	- NS	24 hrs	DNRF	X			Protect from light Undiluted and admixed in empty e-vac bag UNLESS dose is greater than 4g (dilute with NS to achieve a total volume of 50 mL)
Bupivacaine	375mg/300mL	NS	48 hrs* 9 days	RT REF				For Epidural Not for IV Use *Assuming low risk compounding For Anesthesia only
Caffeine citrate	60 mg / 3 mL	D5W	24 hrs	RT			X	Stock vials should be discarded from the IV room every 8 hours.
Calcitonin	Injection	n/a	30 hrs 9 days	RT REF				Draw up weight based dose using the 200 units/1 mL product undiluted in a syringe Protect from freezing

Calcium Chloride	Dilute in 100 mL	NS or D5W	24 hrs	DNRF				
Calcium Gluconate	Dilute in 100 mL	NS or D5W	24 hrs	RT				
Cangrelor	50 mg/250 mL	NS	24 hrs	RT				Avoid vigorous mixing
Capsofungin	Dilute dose in 250 mL	NS	24 hrs	RT				Admixture
			48 hrs	REF				
Cefazolin	Injection		24 hrs	RT				
			10 days	REF				
	2 gm/50 mL	D5W	48 hrs*	RT				Admixure *Assuming low risk compounding
			14 days*	REF				
	3 gm/100 mL		48 hrs*	RT				
			14 days*	REF				
	6 gm/250 mL		48 hrs*	RT				
			14 days*	REF				
Cefepime	1 gm/100 mL	NS	24 hrs	RT				Admixure
			7 days	REF				

	2 gm/100 mL		24 hrs	RT				
			7 days	REF				
Cefotaxime	Dilute dose in 50 mL	NS or D5W	24 hrs	RT				
			5 days	REF				
Cefotetan	1 gm/50 mL 2 gm/50 mL	D5W	96 hrs	REF	X			Protect from light
Cefoxitin	Dilute dose in 50 mL	NS or D5W	6 hrs	RT				
			7 days	REF				
Ceftaroline	Dilute in 100 mL	NS	24 hrs	REF				Can be stored at room temperature for 6 hours if needed
Ceftazidime	Dilute dose in 50 mL	NS	3 days	REF				Admixture
Ceftazidime/ avibactam (Avycaz)	2.5 gms/100 mL	NS or D5W	12 hrs	RT				Admixture
			24 hrs	REF				
Ceftolozane/ Tazobactam (Zerbaxa)	1.5 gm/50 mL	NS	24 hrs	RT				
			7 days	REF				
Ceftriaxone	1 gm/50 mL	NS	48 hrs	RT				

	2 gms/50 mL*							Doses greater than 2 g should be diluted in 100 mL
Cefuroxime	Dilute dose in 50 mL	NS or D5W	24 hrs 7 days	RT REF	X			Protect from light
Chlorpromazine	25 mg/50 mL	NS	24 hrs	RT	X			Protect from light
Ciprofloxacin	200 mg/100 mL	D5W	30 hrs	RT	X			Protect from light
	400 mg/200 mL	D5W	24 hrs	REF				
Cisatracurium	100 mg/100 mL	NS	24 hrs	REF			X	
Clindamycin	600 mg/50 mL	D5W	30 hrs 9 days	RT REF				
	900 mg/50 mL		30 hrs 9 days	RT REF				
Colistimethate	150 mg/100 mL	NS	24 hrs	RT				
Conivaptan	20 mg/100 mL	D5W	24 hrs	RT				
Dalbavancin	Dilute dose in 100 - 250 mL - see comments	D5W	48 hrs*	RT				</=500mg diluted in 100ml >500mg diluted in 250ml *Assuming low risk compounding
Dalfopristin/ quinupristin (Synercid)	Dilute dose in 250 mL	D5W	5 hrs 30 hrs	RT REF				

Dantrolene (Revonto)	Dilute to maintain concentration	SWFI	6 hrs	RT	X			Protect from light
Daptomycin (Cubicin®)	Dilute dose in 50 mL	NS	12 hrs	RT				Refer to manufacturer specific beyond use dating - some products are stable for longer than this conservative estimate
			48 hrs	REF				
Deferoxamine	500-1,000 mg/250mL	SWFI	24 hrs	DNRF				Manufacturer recommends use within 3 hours of reconstitution
Desmopressin	Dilute dose in 50 mL	NS	24 hrs	RT				
Dexamethasone	Dilute dose in 50 mL - see comments	NS or D5W	24 hrs	RT	X			Protect from light Doses </=10mg may be given undiluted Doses >10mg diluted in 50mL
Dexmedetomidine	20 mcg/5 mL	NS	9 days	REF			X	
	40 mcg/10 mL							
	0.2 mg/50 mL		48 hrs	RT				
	0.4 mg/100 mL							
Digoxin Immune fab	Dilute in 50 mL	NS	4 hrs	REF		X		Send with 0.22 micron filter Do not shake vials
Diltiazem	100 mg/100 mL	D5W	24 hrs	RT				
	125 mg/125 mL							
Diphenydramine	50 mg / 1 mL	-	30 hrs	RT	X			Protect from light *Assuming low risk compounding
	Dilute dose in 50 mL	NS	14 days*	REF				

Dobutamine	500 mg/250 mL	D5W	24 hrs 48 hrs	RT REF			X	
Dopamine	400 mg/250 mL	D5W	36 hrs	RT	X		X	Protect from light
Dornase alfa	5 mg/30 mL	NS	24 hrs	REF	X			Protect from light Do not expose to room temperature for > 60 hours total (including administration)
Doxycyline hyclate	Dilute dose in 250 mL	NS/D5 W	30 days 72 hrs	RT REF	X			Protect from light
Eculizumab	900 mg / 180 mL 1200 / 240 mL	NS	24 hrs	RT			X	
Epinephrine	5 mg/250 mL	NS or D5W	9 days	REF	X		X	Protect from light
	10 mg/250 mL		9 days					Protect from light High concentration sticker
Ertapenem	Dilute dose in 50 mL	NS	4 hrs 24 hrs	RT REF				Admixure
Erythromycin lactobionate	Dilute dose in 100-250 mL - see comments	NS	24 hrs	REF				Reconstitute vial with SWFI </= 250mg diluted in 100ml> 250mg diuted in 250ml
Ethacrynic Acid	Dilute dose to achieve	NS	24 hrs	RT				

	concentration of 1 mg/1 mL							
Famotidine	10 mg/ 10 mL	NS	48 hrs	REF				
	20 mg / 50 mL							
Feiba	n/a	SWFI	3 hr	RT	X			Protect from light
Fenoldopam	10mg/250ml	NS or D5W	4 hrs	RT				
			24 hrs	REF				
Fentanyl	See Epic Standard Concentrations	NS	30 hrs	RT	X		X	Protect from light Admixture
Ferric carboxymaltose	Undiluted	-	30 hrs	RT				Concentration must always be greater than or equal to 2 mg/mL
	Dilute dose in 250 mL	NS						
Fluconazole	100 mg/50 mL	NS	24 hrs	RT				Expiration date applies when Premix bag is split into multiple doses
	600 mg/300 mL		24 hrs					
	800 mg/400 mL							
Folic Acid	1 mg/0.2 mL	-	24 hrs	RT	X			Protect from light Undiluted
	1 mg/50 mL	NS						
Fomepizole	1,600 mg/100 mL	D5W	24 hrs	RT				
	2,400 mg/100 mL							

Fosaprepitant	150 mg/150 mL 150 mg/250 mL	NS	24 hrs	RT				
Foscarnet	Dilute dose to achieve concentration of 12 mg/mL	NS	24 hrs	RT				
Fosphenytoin	Dilute dose in 50-100 mL - see comments	NS/D5W	48 hrs* 14 days*	RT REF				</=200mg may be given undiluted >200mg to 749mg diluted in 50ml >/= 750mg diluted in 100ml *Assuming low risk compounding
Furosemide	Dilute dose in 50 mL - see comments 300 mg/100 mL	NS	24 hrs	RT	X			</= 160mg may be undiluted>160mg diluted in 50ml Protect from light High concentration sticker
Gentamicin	Dilute dose in 50 - 250 mL - see comments	NS	48 hrs*	RT				Admixure Expiration date is the same at RT and REF </=100mg diluted in 50ml > 100mg to 250mg diluted in 100ml > 250mg diluted in 250ml *Assuming low risk compounding
Glucagon	10 mg/100 mL	D5W	24 hrs	RT	X			Protect from light For immediate use 1 mg = 1 unit

Heparin	500 units/500 mL	NS	24 hrs	RT			X	Admixure
	25,000 units/500 mL	D5W		RT				
	25,000 units/250 mL			REF				
Hydrocortisone	100 mg/100 mL	NS	48 hrs*	RT	X			Protect from light *Assuming low risk compounding
Hydromorphone	Dilute dose in 50 to 250 mL	NS	30 hrs	RT	X		X	Protect from light
			9 days	REF				
Hydroxocobalamin	5 g/200 mL	NS	6 hrs	DNRF				Do not shake
Ibutilide	Dilute dose in 50 mL	NS or D5W	24 hrs	RT				Note that the medication is more stable at RT
			48 hrs	REF				
Imipenem/ Cilastatin	500 mg/100 mL*	NS	4 hrs	RT				*Doses greater than 500 mg should be diluted in 250 mL
			24 hrs	REF				
Immune Globulin (GammaGard)	-	D5W	24 hrs	RT				Send with tubing Do not shake
Infliximab	Dilute in 250 mL	NS	5 hrs**	RT		X		**Start infusion within 3 hours of preparation Send with 1.2 micron (or smaller) filter
Insulin, regular	100 units/100 mL	NS	14 days*	REF			X	Expiration date for insulin used for IV infusion *Assuming low risk compounding

Insulin U-500	500 units/100 mL	NS	24 hrs 14 days*	RT REF			X	Undiluted in a syringe - High concentration sticker **Date when vial is opened and expiring** *Assuming low risk compounding
Iron Dextran	25 mg/0.5 mL 100 mg/2 mL Dilute dose in 500 mL	NS	24 hrs	RT				
Iron Sucrose	Dilute dose in 250 mL	NS	7 days	REF				</=200mg given undiluted >200mg diluted in 250ml
Isoproterenol	0.2mg/100mL 1mg/250mL 1 mg/500mL	NS or D5W	24 hrs	REF	X			Protect from light
Kcentra	n/a	SWFI	8 hrs	RT	X			Protect from light
Ketamine	500 mg/500 mL 1,000 mg/500 mL	NS	24 hrs	RT	X		X	Protect from light Protect from light High concentration sticker
Labetalol	500 mg/100 mL	Undiluted	24 hrs	RT	X		X	Protect from light Expiration date is the same at RT and REF
Lacosamide	Dilute dose in 100 mL	NS	24 hrs	DNRF				
Leucovorin	25 mg/50 mL 50 mg/50 mL	Bacteriostatic water	30 hrs	RT	X			Protect from lightSolutions reconstituted with SWFI must be used immediately

	200 mg/50 mL							
Levetiracetam	Dilute dose in 100 mL	NS	24 hrs	DNRF				Refer to manufacturer specific beyond use dating - stability is formulation depedent
Levocarnitine	Dilute dose in 250 mL	NS	24 hrs	RT				
Levofloxacin	250 mg/50 mL	D5W	24 hrs	RT	X			Protect from light
Levothyroxine	-	NS	7 days	REF	X			Protect from light Syringes
	200mcg/500ml	NS	18 hrs	RT				Protect from light For organ harvest
Lidocaine	2 gms/250 mL	D5W	30 hrs	RT				
Lorazepam	40 mg/250 mL	D5W	24 hrs	DNRF	X	X		Protect from light Use a DEHP-free bag Send with 0.22 micron filter
	160 mg/40 mL							High concentration sticker
Magnesium Sulfate	Dilute dose in 50 - 1,000 mLs*	NS	30 hrs	DNRF			X	Admixture 1-4 grams diluted in 50-1,000 mLs depending on order
Meropenem	500 mg/50 mL	NS	15 hrs	REF				Admixure
	1 gm/100 mL							
	2 gms/100 mL							
Mesna	1 gm/10 mL	NS or D5W	24 hrs	RT				Dose dependent on indication

Methocarbamol	Dilute dose in 250 mL	NS	30 hrs	DNRF				
Methyldopate	Dilute dose in 100 - 250 mL - see comments	D5W	24 hrs	RT				</= 125mg diluted in 100ml >125 mg diluted in 250ml
Methylene Blue (Provay Blue)	Dilute dose in 100 mL	D5W	1 hr*	RT	X			Protect from light Keep in the original packaging *Immediate use
Methylprednisolone	250 mg/100 mL 500 mg/100 mL 750 mg/250 mL	NS	30 hrs	RT	X			Protect from light
Metoclopramide	10 mg/2 mL Dilute dose in 50 mL	NS	48 hrs*	DNRF	X			Protect from light </= 10mg may be given undiluted >10mg diluted in 50ml *Assuming low risk compounding
Metoprolol tartrate	5 mg/50 mL	D5W	36 hrs*	DNRF				*Assuming low risk compounding
Metronidazole	250 mg/50 mL 500 mg/100 mL	NS	48 hrs* 48 hrs*	RT				*Assuming low risk compounding
Micafungin	Dilute dose in 100 mL	NS or D5W	24 hrs	RT	X			Protect from light Admixture
Midazolam	50 mg/50 mL	D5W	30 hrs 9 days	RT REF			X	
Milrinone	20 mg/100 mL		30 hrs*	RT			X	Admixture *Assuming low risk compounding

Minocycline	100 mg/250 mL	NS or D5W	4 hrs 24 hrs	RT REF				Admixture
Morphine	Dilute dose in 100 mL	NS or D5W	30 hrs 9 days	RT REF	X		X	Protect from light
Multivitamin Infusion	Dilute in 500 or 1000 mL	NS or D5W	24 hrs	RT	X			Protect from light
Nafcillin	Dilute in 500 mL	D5W	7 days	REF				Admixture
Naloxone	2 mg/500 mL	NS	24 hrs	RT	X		X	Protect from light
Nicardipine	50 mg/100 mL	NS	24 hrs	RT	X		X	Protect from light High concentration sticker
	25 mg/250 mL							Protect from light
Nitroglycerin	100 mg/250 mL	D5W	48 hrs 7 days	RT REF	X		X	Protect from light
Nitroprusside	50 mg/250 mL	D5W	24 hrs	RT	X		X	Protect from light Expiration date is the same at ART and REF
Norepinephrine	4 mg/250 mL	D5W	9 days	REF	X		X	Admixure Protect from light
	16 mg/250 mL	D5W	24 hrs					
	4 mg/250 mL	NS	7 days					
	16 mg/250 mL	NS	24 hrs					
Octreotide	250 mcg/50 mL 500 mcg/100mL	NS	30 hrs	RT	X		X	Protect from light

Ondansetron	Dilute dose in 50 mL	NS or D5W	48 hrs*	RT	X			Protect from light 8 mg or fewer may be given undiluted *Assuming low risk compounding
Oxacillin	Dilute dose in 50 mL	NS	6 hrs	RT				Admixture
Oxytocin	30units/500mL	NS	30 hrs	RT	X		X	Protect from light
			7 days	REF				
Palifermin	5 mg/mL	NS	1 hr*	RT	X			Protect from light
Pamidronate	60 mg/250 mL	NS	24 hrs	RT				
	90 mg/250 mL							
	30 mg/500 mL							
	60 mg/500 mL							
	90 mg/500 mL							
Pantoprazole	80 mg/250 mL	NS	24 hrs	RT				
			9 days	REF				
Penicillin G Potassium	4 million units/50 mL	D5W	7 days	REF				Admixure
	10 million units/250 mL							
	12 million units/250 mL							
Pentamidine	Dilute dose in 50 mL	D5W	24 hrs	DNRF	X			Protect from light
Pentobarbital	500 mg/ 100 mL	NS	24 hrs	RT			X	

Peramivir	Dilute dose in 100 mL	NS or D5W	24 hrs	RT				
Phenobarbital	Dilute dose in 100 mL	NS	24 hrs	DNRF	X			Protect from light
Phenylephrine	Dilute in 250 mL	NS or D5W	4 hrs 9 days	RT REF			X	High concentration sticker if needed
Phenytoin	Dilute dose in 100 mL	NS	4 hrs	DNRF	X	X		Protect from light Send with 0.22 filter </=200mg may be given undiluted > 200mg diluted in 100ml
Phytonadione	Dilute dose in 50 mL	NS	24 hrs	RT	X			Protect from light
Piperacillin/ Tazobactam	2.25 gm/50 mL 3.375 gm/100 mL 4.5 gm/100 mL	NS	24 hrs	RT				
	Dilute dose in 500 mL	NS or D5W	12 hrs	RT				
Polymyxin B	Dilute dose in 100 mL	D5W	72 hrs	REF	X			Protect from light
Posaconazole	300 mg/250 mL	NS or D5W	24 hrs	REF				
Potassium chloride	Dilute dose in 50-100 mL*	NS or D5W	24 hrs	RT			X	Admixture Always use premix if availible Do not exceed a concentration of 0.4 mEq/mL
Potassium phosphate	Dilute dose in 250 mL	NS	48 hrs*	RT			X	

Procainamide	2 gm/500 mL Dilute dose in 50 mL	NS	24 hrs	RT				
Promethazine	Dilute dose in 50 mL	NS	24 hrs	RT	X			Protect from light
Prothrombin Complex Concentrate	500 units/20 mL 1000 units/40 mL	SWFI	4 hrs	RT	X			Protect from light Actual potency varies vial to vial
Rasburicase	1.5 mg/50 mL 3 mg/50 mL	NS	24 hrs	REF	X			Protect from light
Ravulizumab	Dilute dose in 50 mL	NS	6 hrs 24 hrs	RT REF	X	X		Protect from light Send with 0.2 or 0.22 micron filter
Remdesivir	Dilute dose in 250 mL	NS	24 hrs 48 hrs	RT REF				
Remifentanyl	1 mg/20mL 2 mg/40 mL	NS or D5W	24 hrs	RT				
Rifampin	Dilute in 100 mL	NS	30 hrs	RT	X			Protect from light
Rocuronium	100 mg/100 mL	NS	24 hrs	RT				
Ropivacaine	2.5 mg/250 mL	NS	24 hrs	RT			X	
Sargramostim	250 mcg/mL	SWFI	6 hrs	RT				
Sodium Bicarbonate	50 - 150 mEq/1,000 mL	D5W, D5W 1/2NS, 1/2	24 hrs	REF				

		NS, D10W						
Sodium Ferric Gluconate Complex	125 mg/250 mL	NS	24 hrs	RT				
Sodium Phosphate	Dilute dose in 250 mL	NS	24 hrs	RT				
Sodium thiosulfate	25 g/200 mL	NS or D5W	48 hrs*	RT				*Assuming low risk compounding
Streptomycin	Dilute dose in 100 mL	D5W	24 hrs	RT	X			Protect from light Some manufacturers show longer stability - check with manufacturer specific product
Talc (Sterile Talc)	Dilute dose in 100 mL	NS	12 hrs	RT	X			Protect from light
Tenecteplase	n/a	SWFI	8 hrs	REF				
Thiamine	Dilute dose in 100 mL	NS	24 hrs	RT				
Tigecycline	50 mg/100 mL	NS	24 hrs	RT				Admixture
			48 hrs	REF				
Tobramycin	Dilute dose in 100 mL	NS	48 hrs*	RT				*Assuming low risk compounding
		D5W	24 hrs	RT				
Tocilizumab	Diliute dose in 100 mL	NS	24 hrs	RT	X	X		Protect from light Send with 0.22 micron filter

Tranexamic Acid	1000 mg/100 mL	NS	48 hrs*	RT				*Assuming low risk compounding
Treprostinil	n/a	**Flolan Diluent**	48 hrs*	RT				**Check for opened vials in the IV room** Flolan diluent found in central pharmacy *Assuming low risk compounding
Trimethoprim/Sulfamethoxazole	80 mg/125 mL	D5W	6 hrs	RT				For 6 hr stabilty, every 80 mg of trimethoprim requires 125 mL of D5W For 4 hr stability, every 80 mg of trimetheprim requires 100 mL of D5W
	160 mg/250 mL							
	200 mg/250 mL		4 hrs					
	320 mg/400 mL							
	400 mg/500 mL							
	480 mg/600 mL							
Valproate	Dilute dose in 100 mL	D5W	24 hrs	DNRF				
Vancomycin	500 mg/ 100 mL	NS/D5W	9 days	REF				Concentration to be ≤5 mg/mL
	750 mg/250 mL							
	1 gm/250 mL							
	1250 mg/250 mL							
	1500 mg/300 mL							
	1750 mg/500 mL							
Vasopressin	20 units/50 mL	NS/D5W	24 hrs	REF			X	

	20 units/100 mL							
Vecuronium	50 mg/50 mL	NS/D5 W	24 hrs	REF			X	
Vedolizumab	300 mg/250 mL	NS	12 hrs	RT				
			24 hrs	REF				
Verapamil	40 mg/250 mL	NS	24 hrs	RT	X			Protect from light
Voriconazole	Dilute dose in 100 - 250 mL - see comments	NS	24 hrs	REF				<500mg diluted in 100ml >/= 500mg diluted in 250ml
Zidovudine	400 mg/100 mL	D5W	8 hrs	RT				
			24 hrs	REF				
Zoledronic acid	4 mg/100 mL	NS	24 hrs	REF				
	5 mg/100 mL							

6.0 Bibliography

1. *From guesswork to standards: The history of medicine quality | USP*. (2020). United States Pharmacopeia.

2. Brown TR. *Handbook of Institutional Pharmacy Practice.* Bethesda, MD: American Society of Hospital Pharmacists; 2006.

3. Urick BY, Meggs EV. Towards a Greater Professional Standing: Evolution of Pharmacy Practice and Education, 1920–2020. *Pharmacy*. 2019;7(3):98. doi:10.3390/pharmacy 7030098

4. Deng, Y., Lin, A. C., Hingl, J., Huang, G., Altaye, M., Maynard, H., Mayhaus, D., & Penm, J. (2016). Risk factors for i.v. compounding errors when using an automated workflow management system. *American Journal of Health-System Pharmacy*, *73*(12), 887–893. https://doi.org/10.2146/ajhp150278

5. Lin, A. C., Deng, Y., Thaibah, H., Hingl, J., Penm, J., Ivey, M. F., & Thomas, M. (2018). The impact of using an intravenous workflow management system (IVWMS) on cost and patient safety. *International Journal of Medical Informatics*, *115*, 73–79. https://doi.org/10.1016/j.ijmedinf.2018.04.004

6. Pedersen, C. A., Schneider, P. J., Ganio, M. C., & Scheckelhoff, D. J. (2019). ASHP national survey of pharmacy practice in hospital settings: Monitoring and patient education—2018. *American Journal of Health-System Pharmacy*, *76*(14), 1038–1058. https://doi.org/10.1093/ajhp/zxz099

7. *United States Pharmacopeia and National Formulary* (USP 797-NF 36). United States Pharmacopeial Convention; 2016.

8. Deng Y, Lin AC, Hingl J, et al. Risk factors for i.v. compounding errors when using an automated workflow management system. Am J Health Syst Pharm. 2016;73(12):887-893.

9. Leigh Briscoe-Dwyer, Dan Degnan et al. Standardize 4 Safety: Guiding principles, decision matrix, and other considerations. American Society of Health-System Pharmacists. 2016