

## Standardize 4 Safety: Concentrating on Concentrations

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<https://www.ashp.org/Pharmacy-Practice/Standardize-4-Safety-Initiative>

### Conflict of Interest

- Funding for Standardize 4 Safety is a three year contract with the FDA under the Safe Use Initiation Section 8.5
- The PI has no other conflicts of interest

### Partners



### Learning Objectives

- Define the Standardize 4 Safety initiative and the phases of the project.
- Describe why standardization for IV and oral liquid medications is an error reduction strategy.
- Review considerations that were made for proposed concentrations.
- Identify what steps you can take to ensure compliance with the initiative at your institution.

### Back to the beginning

- Henry Ford first developed standard work for car production lines in early 1900's
  - First time standardization used to ensure quality work
- LEAN concepts carried into the 1950's with the Toyota way
- LEAN enters into healthcare in late 1990's
- Smart infusion devices enter into the market place late 1990's but robust adoption started 2000, however some hospitals still do not use this technology
- High reliability

### ASHP IV Summit 2008

- The effort to standardize IV concentrations started in 2008 when a multi-stakeholder IV summit was held in Maryland to address preventing patient harm and death from IV medication errors. Three main barriers were identified at the summit
  - Lack of standardization and good process design for IV medications
  - Lack of shared accountability for safety among members of different healthcare disciplines
  - High-volume, high-demand environments in which safety may be sacrificed for other priorities

Proceedings of a summit on preventing patient harm and death from i.v. medication errors. July 14-15, 2008, Rockville, Maryland. Am J Health-Syst Pharm. 2008; 65:2367-79

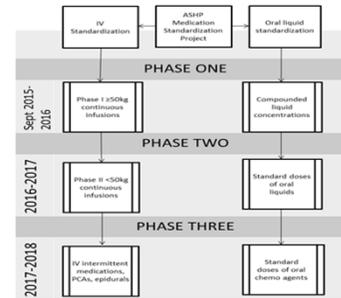
### Statement of the Problem

- Currently, no national consensus for standard concentrations of IV medications (continuous, intermittent, etc)
- Patients are transferred between patient care areas
  - Within each hospital
  - Within same city
  - Within same state
  - Out of state
- Each time a patient needs an IV medication, there is potential for error if a concentration different from the previous patient care area is used
- Often vulnerable patient populations involved
  - Critically ill
  - Pediatric, neonate
  - Geriatric

### Standardize 4 Safety



- Standardize 4 Safety* is the first national, interprofessional effort to standardize medication concentrations in order to reduce errors and improve transitions of care
- Standardize 4 Safety* is creating, testing, publicizing, and supporting the adoption of these national standardized medication concentrations
- Key partners include AAMI, PPAG, and ISMP



### Status of S4S

- Half-way through

Done	In process (done 2017)	Not started (2018)
Phase One, V 1.01 adult continuous	Phase Two, V 1.02 adult continuous	Intermittent IV meds
Phase One, V 1.01 Cmpd oral liquids	Phase Two, V 1.02 cmpd oral liquids	PCA's, epidurals
	Phase One, pediatric continuous	
	Phase One, standard doses oral liquids	

### Exclusions for IV Project

- Infusions related to extracorporeal modalities (Extracorporeal Membrane Oxygenation, Continuous Renal Replacement Therapies, etc.)
- Concentrations for non-treatment indications (i.e., heparin for line patency, etc.)
- Compounded infusions final volumes
- Diluents — selection of dextrose, saline, or a combination
- Library nomenclature and profile naming
- Chemotherapy drugs

### Goals for S4S

- *Goal 1. Form a nationwide expert faculty panel*
- *Goal 2. Create the standards*
- *Goal 3. Disseminate the standards and assess their adoption*

### Methods: Formation of Expert Panels

- **IV Panel**
  - 7 pharmacists
  - 3 nurses
  - 3 MD's
  - 1 consultant
  - 2 informaticists (ASHP)
- **Oral Panel**
  - 7 pharmacists
  - 3 nurses
  - 3 MD's
  - 1 Parent
  - 2 informaticists (ASHP)

### Methods: Data Analysis

- Data was collected from a variety of diverse sources:
  - Standardized lists from state and regional efforts in Maine, Indiana, North Carolina, and San Diego
  - Information gathered from the 2008 IV Summit
  - Information previously gathered by the University of Utah Drug Information Service
  - Expert panel members' lists from their respective organizations
  - De-identified information from 503b companies
  - Other offerings from large health systems nationwide
- A draft list was released for public comment, and then revisions were conducted based on feedback collected.

### Methods: Meetings

- The expert panel convened in March 2016 to review the list and narrow the scope for version 1.01 to 32 drugs
- Expert panel members continue to have one to two calls per month to continue work

### Methods: Guiding Principles for IV

<p><b>Safety first – use commercial when possible</b></p>	<p><b>Try to limit to one concentration when possible</b></p>
<p><b>Patient needs/clinical</b></p>	
<p><b>Consider concentration relative to fluid status Use more concentrated whenever possible</b></p>	<p><b>Operational dispensing aspects and steps including waste</b></p>

### Methods: Quality Assurance

- The finalized list has been reviewed by expert panel members, internal ASHP staff, and ISMP for accuracy of drug name, concentrations, and dosing units
  - ASHP used the FDA and ISMP recommendations for tallman lettering.
- ASHP validated with the FDA that it is permissible to recommend a concentration other than that stated in the PI, given the inclusion of a disclaimer statement and the existence of evidence-based published literature for the concentration recommended

### Disclaimers

- This project is supported by a contract with the FDA, Safe Use Initiative, FDA-BAA-15-00121, Section 8.5
- This document is a working draft. Additional sections and lists will be added as the project moves forward
- Suggested concentrations may differ from the package insert (PI) information for a drug. This is due to clinical needs that may have transpired post-market. When this is the case, studies are available to support the use of a concentration different than what the parent company

### Disclaimers

- Dosing units were derived from
  - PI information
  - Commonly used drug-reference guides and clinical practice guidelines
  - Of special note, the expert panel is recommending that weight-based dosing be used for vasopressors (i.e., per kg, per minute), which may differ from institution- specific guidelines.
- These concentrations are *guidelines only and are not mandatory*.
- It is the vision of the project that organizations will voluntarily adopt these concentrations and join a national movement to use standardization across the care continuum as an error-prevention strategy for patient safety

### Results for IV Version 1.01

### ≥50kg Continuous Infusions Version 1.01 drug list

Alteplase	Isoproterenol
Amiodarone	Labetalol
Argatroban	Lidocaine
Bumetanide	Lorazepam
Cisatracurium	Morphine
Dexmedetomidine	Midazolam
Diltiazem	Mirinone
Dobutamine	Nicardipine
Dopamine	Nitroglycerin
Epinephrine	Nitroprusside
Esmolol	Norepinephrine
Fentanyl	Phenylephrine
Furosemide	Propofol
Heparin	Rocuronium
Hydromorphone	Vasopressin
Insulin	Vecuronium

<https://www.ashp.org/-/media/assets/pharmacy-practice/045/00c3/045-iv-adult-continuous-infusion-guiding-principles-ashp-04-08-17.pdf?rev=27487778C2096C705F3946765CE68198&C=1710D6C>

### Compounded Oral Liquids

### Problem Statement

- Currently, no national standard concentrations
- Hospital pharmacies and community pharmacies use different recipes
  - Why?
    - Availability of recipes
    - Availability of ingredients
    - Ease of preparation
    - Reimbursement
- Medication errors occur through improper med rec
  - Caregivers usually know doses in mL's, not mg
  - Concentrations are not readily known unless verify with bottle or speak to pharmacy (difficult to do during non-business hours)

### Problem Statement con't

- Nearly 75% of the drugs available in the US for adults have not been labeled for use in infants and children <12 years
- Off label drug use results in:
  - Using drugs that have not been adequately tested
  - Using dosage forms that are not suitable for administration to infants and children
  - Using a portion of solid dosage form
  - Increased demand for extemporaneous liquid formulations

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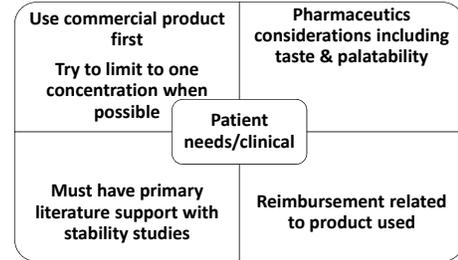
### Oral compounded liquid medication arm

- Standardized list for oral compounded liquid medications
  - For all patients needing a liquid dosage form
  - Will use the Michigan effort as a starting point
    - [www.mipedscompounds.org](http://www.mipedscompounds.org)
- Accurate measurement and measurement literacy
  - Smart phone App to show consumer a visual display of an oral syringe and appropriate measurement for patient specific dose
- What products could be commercially produced and how to keep cost down?
- Standardize liquid doses (example: Amoxicillin 256.5mg to 250mg)
- What other dosage forms could be developed (more solutabs, etc)?

### Challenges in using oral compounded medication formulations

- Lack of stability and sterility studies
- Short shelf-life
- Lack of pharmacokinetic/dynamic studies
- Efficacy and safety
- Palatability and compliance
- Variations in compounding practice

### Oral compounded liquid medications Decision matrix tool



### Methods: Guiding Principles

- Version 1.01 is finalized, 29 drugs
- These are recommended/highly suggested concentrations at this time
  - For a recipe to be considered, there must be a peer-reviewed published article
    - Abstracts are considered on a case-by-case basis
  - Stability needs to be longer than seven days to accommodate reasonable patient refill schedule

### Guiding principles (Continued)

- Ease of compounding: simple ingredients that are readily available, doesn't require pH testing or addition of multiple complex ingredients
- Ease of measurement: for example, if the concentration is 1 mg/mL then dose = mL
- Concentration can be used for the majority of doses and won't result in doses less than 0.1mL
- Can be used for ketogenic diets (preference for sugar free compounding ingredients when possible)
- Preference for dye-free compounding ingredients when possible
- Preference for commonly used and accepted concentrations
- Existing USP monograph
- Avoid potential for tenfold dosing errors
- Cultural considerations related to ingredients

### Methods for Oral Compounded Liquids

- Creation of expert panel
  - Differs from IV that does involve parent member
- Create the standards (remember the easy, peasy)
  - EXTENSIVE work for recipe review
- Formulations (recipes) will be made available once the rights are formalized by the FDA

### Version 1.01 drug list compounded oral liquids

Amiodarone 5 mg/mL or 20 mg/mL	Metronidazole 50 mg/mL
Atenolol 2 mg/mL	Metoprolol 10 mg/mL
Baclofen 5 mg/mL	Morphine (NAS) 0.4 mg/mL
Bethanacol 5 mg/mL	Nifedipine 4 mg/mL
Captopril 1 mg/mL	Pyrazinamide 100 mg/mL
Clonidine 20 mcg/mL	Rifampin 25 mg/mL
Chloroquine 10 mg/mL	Sodium chloride 4 mEq/mL
Flecainide 20 mg/mL	Spirolactone 5 mg/mL <sup>2</sup>
Flucytosine 50 mg/mL	Tacrolimus 1 mg/mL
Hydralazine 4 mg/mL <sup>1</sup>	Thioguanine 20 mg/mL
Hydrochlorothiazide 5 mg/mL	Topiramate 20 mg/mL <sup>4</sup>
Hydrocortisone 2 mg/mL <sup>2</sup>	Ursodiol 60 mg/mL
Hydroxyurea 100 mg/mL	Valacyclovir 50 mg/mL
Labelalol 40 mg/mL	Zonisamide 10 mg/mL
Lansoprazole 3 mg/mL	

### Methods: Open Comment Periods

- Done via ASHP Connect community
- Postings will be internally moderated
  - Please use professional language
  - If you or the organization you represent feel strongly opposed to a particular concentration please respond with a suggested alternative concentration, literature support, and patient clinical indication
    - The reason “we have always done it this way” is not evidence based

### Challenges and questions along the way

### IV Challenges

- Differences between the OR and other areas
  - Paralytics
  - Chose to use straight drug vs. a pharmacy compounding infusions
- Stability data
  - Some have used just because “we’ve always done it this way”
- Drug shortages
- Other concentrations are needed
  - Dexmedetomidine, Esmolol, Nicardipine, Hydromorphone
  - Role of pharmaceutical industry
- Package size mismatches
  - Example esmolol
  - Amiodarone

### Compounded oral liquid challenges

- DATA!
  - Formulations (i.e. recipes)
  - Some internal
  - Literature review was intense and took much longer than anticipated
  - Some information in abstract only
  - Rights to information: Example is topiramate (owned by USP)
  - Competing with large compounding groups
- Ingredient availability
  - Common ingredients vs. extensive formulations
  - Powders vs. solid dosage forms
    - Reimbursement
    - Larger compounding facilities want/use powders (ex. Nifedipine)
- Kits
  - Not FDA approved
  - Not in First Data Bank
  - Lansoprazole, Magic Mouthwash, Baclofen 5 mg/mL, Metronidazole 50 mg/mL
  - We want to use these when possible
- Drug shortages
  - Keep information for compounding
  - Example is chlorthiazide (on and off market)

## What You Can Do

- START TALKING!!!!
- Be a champion, cheerleader, sponsor
- Don't just get buy-in, take ownership
- Remember to take an inter-professional approach
- Start talking to the informatics team now
- Everyone can make a difference
- Resources: IPI, Bainbridge Health, ASHP, eBroselow, new potential tools in the pipeline

## The Role of PhRMA

- Once standard concentrations can be agreed upon the manufacturers could potentially make
  - Lisinopril, spironolactone
- We do recognize the pricing can be prohibitive
- We want to help guide appropriate concentrations, palatability, dye-free, sugar-free

## Collaborations

- Regenstrief center
- Bainbridge Health
- eBroselow
- Shonna Yin
- Dan Budnitz
- Joe Massimo (Patient Safety Movement)
- NIH: Anne Zajicek and Majid Tanas
- Nat Sims and Mass General
- Vizient
- Canadian and European groups now interested
- Vendors: CareFusion, Baxter, Smiths-Medical
- PhRMA – Baxter, Fresenius-Kabi, J&J

## What does the future hold?

## Questions?



<http://www.ashp.org/menu/PracticePolicy/Standardize-4-Safety.aspx>  
<http://www.ashp.org/menu/AboutUs/ForPress/PressReleases/PressReleases.aspx?id=948>

## Audience participation

1. Standardization can be used as an error prevention strategy
  - a. True
  - b. False
2. The most important reason to adopt national standards is:
  - a. It's a Joint Commission standard
  - b. You won't get reimbursed if you don't
  - c. The right thing to do for patient safety
  - d. Makes the pharmacy more efficient

## Audience participation

3. Ways to get involved with S4S include:
  - a. Start talking about the project
  - b. Be a champion at your institution
  - c. Your hospital or health-system becomes an early adopter of the standards
  - d. Talk to your patients that receive compounded oral liquids and explain the new standards and why they are important
  - e. All of the above