STANDARDIZE 4 SAFETY INITIATIVE

Standardize 4 Safety is the first national, interprofessional effort to standardize medication concentrations to reduce errors, especially during transitions of care.

These national standards will cover:

- Concentrations and dosing units for intravenous continuous medications for adult patients.
- Concentrations for compounded oral liquid medications.
- Concentrations and dosing units for intravenous continuous medications for pediatric patients.
- Doses for oral liquid medications.
- Concentrations for intravenous intermittent medications.
- Concentrations for PCA and epidural medications.

The Standardize 4 Safety initiative began in 2008 when a multi-stakeholder IV summit was held to address preventing patient harm and death from intravenous (IV) medication errors. Among the recommendations made by the participants was to establish national standards for IV medications in hospitals including standardized concentrations and dosing. In addition, it was recommended that the national standards be created in collaboration with the Food and Drug Administration (FDA), the pharmaceutical industry, and other stakeholders. Since the summit, establishing standardized concentrations has garnered strong support from ASHP members, the Joint Commission, the Institute for Safe Medication Practices (ISMP), and others. 1 2 3 4

In 2015 the FDA, through its Safe Use Initiative, awarded ASHP a grant to develop and implement national standardized concentrations for IV and oral liquid medications. The aims of the grant were to: (1) identify a nationwide expert interprofessional panel consisting of physicians, nurses, and pharmacists; (2) create standards for adult continuous IV infusions, compounded oral liquid medications, pediatric continuous IV infusions, doses for liquid medications, intravenous intermittent infusions, and PCA and epidural medications; (3) disseminate the standards and assess their adoption.

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WHY STANDARDIZE

To Err is Human was published in 1999 and highlighted the harm to patients from healthcare error. In that report, medication errors were stated to be responsible for one of 131 outpatient and one of 854 inpatient deaths.⁵ Healthcare continues to struggle to eliminate harm to patients. A systematic review and meta-analysis in 2019 estimated one in 20 patients are exposed to preventable medical harm with the highest incidence of events due to medications. Compounded medications,⁶ especially those given intravenously, are known to be high risk for error due to added complexity and multiple steps required for determining dosing when ordering, concentrations for preparation and rates of infusion for administering.⁷ ⁸ Using standardization as a quality improvement tool decreases variation, improves safety, and is the foundation for using clinical pathways and evidence-based guidelines. Standardization allows providers to manage excessive and unintended variation as they customize care for patients.⁹

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HOW THE NATIONAL MEDICATION CONCENTRATION STANDARDS WERE DEVELOPED

A comprehensive environmental scan was conducted to identify the appropriate medications to be addressed in the respective standard concentrations. A multi-disciplinary expert panel was convened for each standard concentration category. Members were selected based on their expertise in the subject matter and identified with assistance from organizations such as The American Society of Anesthesiologists, Society of Critical Care Medicine, and American Association of Critical-Care Nurses. Each expert panel was charged to establish standard principles to guide their decisions in creating the respective standard concentration recommendations. Once a draft of standards was established, it was released for public comment and review by ASHP staff and ISMP. The expert panel subsequently met to address all comments and generate the National Medication Concentration Standards.

PRINCIPLES FOR EXPERT PANEL DELIBERATIONS

- **Patient clinical needs**
- **FDA-approved commercial products**
- **Limit to one concentration when possible**
- **Use more concentrated when possible**
- **Operational considerations (costs and waste)**
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DISCLAIMERS

- Suggested concentrations may differ from the package insert (PI) information for a drug. This is due to clinical needs that may have transpired postmarket. When this is the case, studies are available to support the use of a concentration different than what the parent company originally pursued through the new drug application (NDA) process.

- Please use the utmost caution when using a concentration different than the PI, especially if rate information is used from the PI.

- 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. We strongly encourage that drug libraries and electronic health records (EHRs), including the electronic medication administration record, make distinct differences for weight-based vs. non-weight-based dosing so nurses can easily distinguish what pump programming is needed.

- These concentrations are guidelines only and are not mandatory. It is our hope 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.

- The information contained in this table is subject to the professional judgment and interpretation of the practitioner. ASHP has made reasonable efforts to ensure the accuracy and appropriateness of the information presented. However, any reader of this information is advised that ASHP is not responsible for the continued currency of the information, for any errors or omissions, and/or for any consequences arising from the use of the information in the self-assessment tool. Any user of the table is cautioned that ASHP makes no representation, guarantee, or warranty, express or implied, as to the accuracy and appropriateness of the information contained in it, and will bear no responsibility or liability for the results or consequences of its use.

CONSIDERATIONS IN USING THE ADULT CONTINUOUS INFUSION STANDARDS

The 80/20 rule was applied by the expert panel to determine recommended standard concentrations. The concentrations listed reflect those applicable to most patient care circumstances. The panel recognizes situations occur where the most appropriate concentration for a patient may not be the recommended standard.

Whenever possible one standard infusion concentration is the recommendation. When more than one standard concentration was recommended it was to accommodate patient care needs for fluid restrictions, differences required for peripheral versus central lines, to simplify calculations and accommodate limitations of pump infusion rates.

Medications with more than one recommended concentration are listed from lowest to highest concentration, with the numbering corresponding to the respective stability reference(s).
<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration Standards</th>
<th>Dosing units</th>
<th>Commercially available</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alteplase</strong></td>
<td>1 mg/mL</td>
<td>mg/hour</td>
<td>Yes, comes in a kit with diluent</td>
<td>1. Product Information: Activase(R) intravenous injection, alteplase intravenous injection. Genentech, Inc.(per Manufacturer), South San Francisco, CA, 2015</td>
</tr>
<tr>
<td><strong>Amiodarone</strong></td>
<td>1. 1.8 mg/mL</td>
<td>mg/min</td>
<td>Yes</td>
<td>1. Product Information: amiodarone HCl intravenous injection, Teva Canada Limited (per Health Canada), Toronto, ON, Canada, 2016. - 2. Product Information: amiodarone HCl intravenous injection, Teva Canada Limited (per Health Canada), Toronto, ON, Canada, 2016.</td>
</tr>
<tr>
<td></td>
<td>2. 3.6 mg/mL</td>
<td></td>
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</tr>
<tr>
<td><strong>Bumetanide</strong></td>
<td>0.25 mg/mL</td>
<td>mg/hour</td>
<td>Administer undiluted</td>
<td>1. Hospira. Bumetanide Injection, USP. Lake Forest, IL. 2021 March.</td>
</tr>
<tr>
<td><strong>Cisatracurium</strong></td>
<td>2 mg/mL</td>
<td>mcg/kg/min*</td>
<td>Administer undiluted</td>
<td>1. Abbv. Nimbex® (cisatracurium besylate) injection prescribing information. North Chicago, IL; 2016 Dec.</td>
</tr>
<tr>
<td><strong>Dexmedetomidine</strong></td>
<td>4 mcg/mL</td>
<td>mcg/kg/hour</td>
<td>Yes</td>
<td>1. Hospira. Precedex® (dexmedetomidine) injection prescribing information. Lake Forest, IL; 2016 Apr.</td>
</tr>
<tr>
<td><strong>Diltiazem</strong></td>
<td>1 mg/mL</td>
<td>mg/hour</td>
<td>No</td>
<td>1. Diltiazem HCL 0.5% intravenous injection, Akor, Inc. (per DailyMed) Lake Forest, IL. 2012.</td>
</tr>
<tr>
<td><strong>Dobutamine</strong></td>
<td>4000 mcg/mL</td>
<td>mcg/kg/min</td>
<td>Yes</td>
<td>1. Hospira. Dobutamine in 5% dextrose injection prescribing information. Lake Forest, IL; 2006 June.</td>
</tr>
<tr>
<td><strong>Dopamine</strong></td>
<td>1. 1600 mcg/mL</td>
<td>mcg/kg/min</td>
<td>Yes</td>
<td>1. Hospira. Dopamine hydrochloride and 5% dextrose injection prescribing information. Lake Forest, IL; 2014 May. 2. Hospira. Dopamine hydrochloride and 5% dextrose injection prescribing information. Lake Forest, IL; 2014 May.</td>
</tr>
<tr>
<td>Drug</td>
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<tr>
<td></td>
<td>2. 40 mcg/mL</td>
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<tr>
<td></td>
<td>2. 20 mg/mL</td>
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<tr>
<td></td>
<td>2. 50 mcg/mL</td>
<td></td>
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</tbody>
</table>
| Furosemide     | 1. 2 mg/mL              | mg/hour            | Yes                    | 1. Donnelly RF. Chemical stability of furosemide in minibags and polypropylene syringes. Int J Pharmaceut Compound. 2002:6:468-70  
<p>|                | 2. 10 mg/mL             |                    |                        |                                                                           |
| Heparin⁶       | 100 units/mL            | units/hour or units/kg/hour | Yes                     | 1. B.Braun Medical Inc. Heparin Sodium in Dextrose Injection prescribing information. Bethlehem, PA. 2018. April |</p>
<table>
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<tr>
<td>INSULIN (regular)</td>
<td>1 unit/mL</td>
<td>units/hour, DKA protocols may require units/kg/hour</td>
<td>Yes</td>
<td>1. Product Information: HUMULIN(R) R subcutaneous injection, intravenous injection, insulin human subcutaneous injection, intravenous injection. Lilly USA LLC (per FDA), Indianapolis, IN, 2018. Micromedex</td>
</tr>
<tr>
<td>ISOProprenaline</td>
<td>4 mcg/mL</td>
<td>mcg/min or mcg/kg/min</td>
<td>No</td>
<td>1. ISUPREL (R) IV injection, isoproterenol hcl IV injection. Hospira, Inc, Lake Forest, IL, 2004.</td>
</tr>
<tr>
<td>Labetalol</td>
<td>1. 1 mg/mL</td>
<td>mg/min</td>
<td>Yes</td>
<td>1. Labetalol Hydrochloride in Sodium Chloride and Labetalol Hydrochloride in Dextrose Injection. Hikma Pharmaceuticals USA Inc. Eatontown, NJ. 2020</td>
</tr>
<tr>
<td></td>
<td>2. 5 mg/mL</td>
<td></td>
<td></td>
<td>2. Product Information: labetalol HCl intravenous injection, labetalol HCl intravenous injection. Hospira, Inc. (per DailyMed), Lake Forest, IL, 2015.</td>
</tr>
</tbody>
</table>
## ADULT CONTINUOUS INFUSION STANDARDS

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</thead>
</table>
| Milrinone    | 200 mcg/mL              | mcg/kg/min   | Yes                    | 1a. Wilson TD, Forde MD, Crain AVR, Dombrowski LJ, Joyce MA. Stability of milrinone in 0.45% sodium chloride, 0.9% sodium chloride, or 5% dextrose injections. *Am J Hosp Pharm*. 1986;43(9):2218-2220.  
   1b. Wong F, Gill MA. Stability of milrinone lactate 200 mcg/mL in 5% dextrose injection and 0.9% sodium chloride injection. *Int J Pharm Compound*. 1998; 2(2):168b |
| Naloxone     | 1. 16 mcg/mL            | mg/hr*       | No                     | 1a. Product Information: Naloxone Hydrochloride Injection, solution. Hospira Inc. Lake Forest, IL. 9/2019. 4 mcg/ml  
<table>
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<tr>
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</thead>
</table>
| Nicardipine  | 1. 0.1 mg/ml             | mg/hour      | Yes - 0.1 mg/mL        | 1. Product Information: CARDENE(R) IV solution for IV infusion, nicardipine HCL solution for IV infusion. EKR Therapeutics, Inc, Bedminster, NJ, 2014.  
|              | 2. 0.5 mg/ml             |              |                        |                                                                                                                                                                                                             |
| Nitroglycerin| 200 mcg/mL               | mcg/min      | Yes                    | 1. Product Information: Nitroglycerin Injection. Abbott Laboratories, North Chicago, IL, October 2014                                                                                                           |
| Nitroprusside| 1. 200 mcg/mL            | mcg/kg/min   | No                     | 1. Product Information: NIPRIDE RTU intravenous injection, sodium nitroprusside intravenous injection. Exela Pharma Sciences, LLC (per FDA), Lenoir, NC, 2017.  
|              | 2. 500 mcg/mL            |              |                        |                                                                                                                                                                                                             |
| Norepinephrine4 | 1. 16 mcg/mL           | mcg/kg/min   | Yes - 16 mcg/mL and 32 mcg/mL | 1. Allwood MC. The stability of four catecholamines in 5% Glucose Infusion. J Clin Pharm Ther. 1991; 16:337-40.  
3a. Gilliot S, et.al. Long-term stability of ready-to-use norepinephrine solution at 0.2 and 0.5 mg/ml. Eur J of Hosp Pharm. 2020; 27:e93-98.  
|              | 2. 32 mcg/mL             |              |                        |                                                                                                                                                                                                             |
|              | 3. 128 mcg/mL            |              |                        |                                                                                                                                                                                                             |
| Phenylephrine| 1. 80 mcg/mL             | mcg/kg/min   | No                     | 1a. West-Ward Pharmaceuticals. Phenylephrine hydrochloride injection prescribing information. Eatontown, NJ; 2012 Dec  
1b. Éclat Pharmaceuticals. Vazculep* (phenylephrine hydrochloride) injection prescribing information. Chesterfield, MO; 2014  
<p>|              | 2. 400 mcg/mL            |              |                        |                                                                                                                                                                                                             |</p>
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<tr>
<td>Propofol</td>
<td>10 mg/mL</td>
<td>mcg/kg/min</td>
<td>Yes</td>
<td>1. Fresenius Kabi USA, LLC. Diprivan® (propofol) injectable emulsion prescribing information. Lake Zurich, IL; 2017 Nov.</td>
</tr>
<tr>
<td>Rocuronium¹</td>
<td>10 mg/mL</td>
<td>mcg/kg/min</td>
<td>Administer undiluted</td>
<td>1. Hospira. Rocuronium bromide injection prescribing information. Lake Forest, IL; 2014 Feb.</td>
</tr>
</tbody>
</table>
| Vasopressin⁶ | 1. 0.2 unit/mL          | units/min or units/kg/min | No                      | 1. Par Pharmaceutical. Vasostrict® (vasopressin injection, USP) For Intravenous Infusion. 2021. Chestnut Ridge, NY. 
| Vecuronium¹  | 1 mg/mL                 | mcg/kg/min*  | No                     | 1. Product Information: Vecuronium bromide Intravenous Injection Lyophilized powder for solution. Fresenius Kabi USA, LLC (per DailyMed) Lake Zurich, IL. 2016 |

*BOLD - dosing units differ from concentration units*

ISMP’s List of Error-Prone Abbreviations, Symbols, and Dose Designations
Use mcg for Microgram

*Updated: October 2023*

**NOTES**
1 Paralytics are recommended to be administered as straight drug. This provides consistency between operating room and the ICU, and eliminates potential compounding errors.

2 This is a concentration that differs from the package insert, therefore infusion related calculations will differ from the PI

3 Consider limiting to one bag size for each recommended concentration (250 vs 500 ml). This may reduce errors and also reduce inventory needs.

4 The group intentionally made epinephrine and norepinephrine concentrations different to avoid confusion between the two agents.

5 These concentrations are for continuous infusions not delivered by a PCA device.

6 We recommend trying to standardize dosing units but understand some protocols may use “flat” dosing while others may require weight based dosing.