Parenteral Nutrition Fundamentals: Navigating the Complexities

Phil Ayers, BS, PharmD, BCNSP, FASPEN. FASHP, FMSHP
Mississippi Baptist Medical Center
Clinical Associate Professor
University of Mississippi School of Pharmacy

1

Disclosures:

- American Regent-Advisory Board
- BBraun-Advisory Board
- Fresenius Kabi-Consultant, Speaker

BAPTIST Get Better.

2

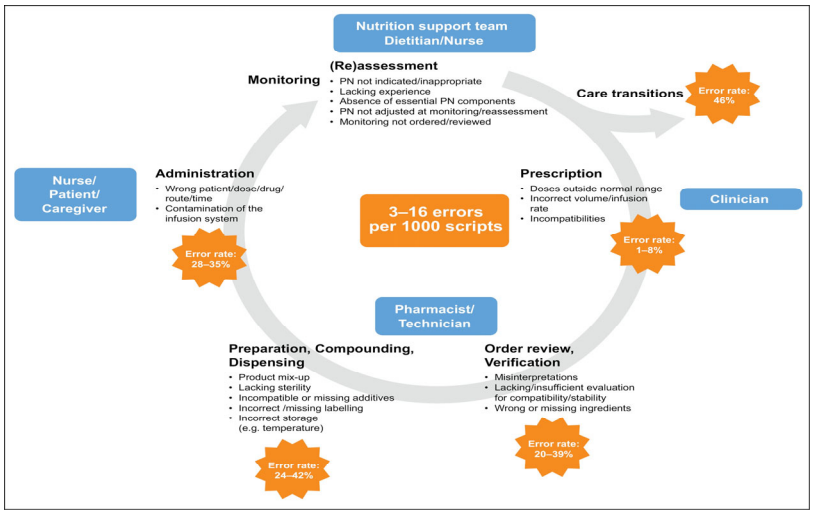
Objectives:

- Review practical considerations regarding parenteral nutrition compatibility and stability
- Discuss the recent Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey
- Describe recent updates to USP Chapter <797> and parenteral nutrition safety concerns

BAPTIST Get Better.

3

The PN Use Process: Potential Sources and Reported Incidence of Errors



Ayers P et al. *Am J Health-Syst Pharm*. 2024;81(suppl 3):S75-S88.

4

DOI: 10.1002/ncp.11189

REVIEW

Parenteral nutrition compatibility and stability: Practical considerations

Joseph I. Boullata PharmD, RPh[1] | Genene Salman PharmD[2] | Jay M. Mirtallo MS[3] | Todd W. Canada PharmD[4] | Jessica Monczka RD, LD[5] | Kathleen M. Gura PharmD[6] | Paul Kiritsy MS, PharmD, RPh[7]

Nutr Clin Pract. 2024;1-14. doi:10.1002/ncp.11189.

5

Definitions:

Compatibility

The uneventful physical and chemical coexistence of two or more components over time after being combined.

Incompatibility

An interaction between two or more substances (active ingredients, excipients, and/or materials) over time in a specific environment.

- Physical (e.g., complexation or leaching)
- Chemical (i.e., involve reactants of intermolecular and interionic forces)
- Manifest as a change in color, pH, osmolality or viscosity, formation of gas, or yielding of a precipitate (whether readily visible or not)
- Clinical consequences may include a limited therapeutic effect of one or more active ingredients or increased risk for toxicity including that from the infusion of precipitates

Nutr Clin Pract. 2024;1-14. doi:10.1002/ncp.11189.

6

Stability

The maintenance of the chemical integrity of each active ingredient or the physical integrity of the dosage form/system over time in a given environment.

Instability

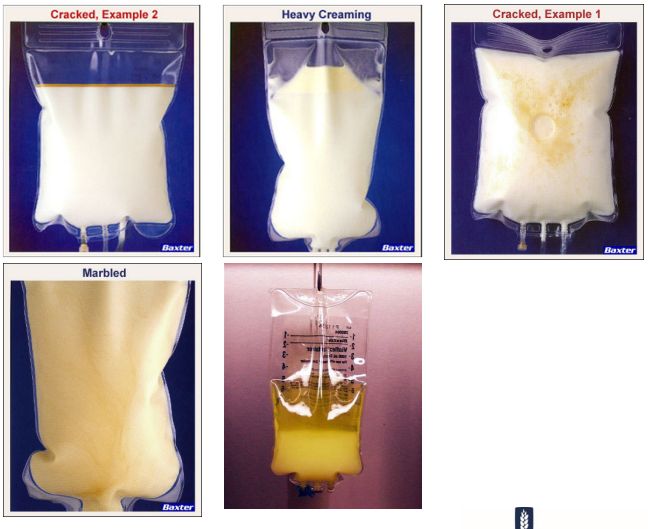
The irreversible decomposition of active ingredients or the dosage form/system as a result of pH, temperature, light, oxygen, solvents, and/or reactants.

- Physical (e.g., crystallization, adsorption, or broken emulsion)
- Chemical (e.g., hydrolysis or oxidation)
- Instability may manifest as increased particulate matter, a visible haze, visible oil, or other color change but, in most cases, may only be identified using appropriate stability-indicating methodology
- The ultimate result is that instability can take away from biological activity of the degraded component or generate risk from toxic byproducts or particulate matter, including large lipid droplets

Nutr Clin Pract.2024;1-14.doi:10.1002/ncp.11189.

BAPTIST Get Better.

7



aspen LEADING THE SCIENCE AND PRACTICE OF CLINICAL NUTRITION
American Society for Parenteral and Enteral Nutrition

8

Mixing sequence

The order in which component products are dispensed into the final PN admixture container. The order is deliberately chosen, whether using an automated compounding device or a manual preparation method.

Beyond use date

The date and time by which the PN infusion must be started at the latest, based on compatibility, stability, and sterility parameters.

Nutr Clin Pract. 2024;1-14. doi:10.1002/ncp.11189.

9

TABLE 1 Examples of concentration limits.

To avoid TNA instability	
Example 1[25]	
PN component product	Concentration
Amino acids injection (Aminosyn II 15%)	4%–7%
Dextrose (dextrose 70%)	10%–20%
ILE (Liposyn III[a] 20%)	2%–5%
Divalent cations (sum of calcium and magnesium)[b]	4–20 mEq/L
Monovalent cations (sum of sodium and potassium)[c]	0–150 mEq/L
Phosphate (as sodium and potassium)	15 mmol/L

Nutr Clin Pract. 2024;1-14.

10

Example 2[26]

PN component product	Concentration
Amino acids injection (Clinisol 15%)	8.8%–9.5%
Dextrose (dextrose 70%)	13.5%–15.7%
ILE (SMOFlipid 20%)	0.6%–0.7%[d]
Calcium (as gluconate)	0–10 mEq/L
Magnesium (as sulfate)	0–16 mEq/L
Sodium (as chloride and phosphate)	0–151 mEq/L
Potassium (as acetate)	0–150 mEq/L
Phosphate (as sodium)	0–15 mmol/L

To avoid calcium phosphate insolubility[27]

Nutr Clin Pract. 2024;1-14.

BAPTIST Get Better.

11

TABLE 4 Example of an acceptable mixing sequence.[40]

Order of mixing	PN component product	Notes
1	Amino acids	-
2	Dextrose	-
3	Sterile water for injection	-
4	Phosphate salt(s)	-
5	Other electrolytes (sodium, potassium, or magnesium)	Separate potassium acetate from magnesium sulfate
6	Trace elements	-
7	Vitamins	Except for PN at home, when added last by patient/caregiver just before infusion
8	Calcium gluconate	The preferred source of calcium when using inorganic phosphate salts
9	lipid injectable emulsion (if appropriate)	-

Abbreviation: PN, parenteral nutrition.

Nutr Clin Pract. 2024;1-14.

BAPTIST Get Better.

12

TABLE 5 Key take home points.

Topic	Points
Compatibility and stability, along with sterility	Determine both PN admixture safety and beyond use date
Organizations designing prescription templates/order sets for total nutrient admixture	Should consult the manufacturer's stability data for the specific combination of amino acids and lipid injectable emulsion products used by the organization
During product shortages/outages	PN component substitutions require compatibility and stability evaluation and, once confirmed, requires an associated revision to PN order templates/ order sets
Calcium phosphate solubility or compatibility	Do not rely solely on a solubility curve or a "green light" for calcium phosphate compatibility without knowing both the test conditions and acceptance criteria used to determine the data
PN incompatibility and instability	Is a preventable cause of patient morbidity and mortality

Abbreviation: PN, parenteral nutrition.

Nutr Clin Pract. 2024;1-14.

BAPTIST Get Better.

13

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- 280 Respondents (December 2024-January 2025)
  - Pharmacists 79%
  - Nurses 10%
  - Pharmacy technicians 4%
  - Dietitians 4%
  - Prescribers 2%
  - Others 1%

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

14

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Hospital Size
  - 26% 100-299 beds
  - 25% 300-499 beds
  - 22% 500 beds or more
  - 10% 26-99
  - 5% 25 beds or less
  - 12% NA

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

15

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Setting (87% United States)
  - 38% Community Hospitals
  - 28% Teaching Hospitals
  - 8% Critical Access Hospitals
  - 6% Home Infusion
  - 4% Pediatric Hospitals
  - 3% Cancer Care Hospitals
  - 2% Long Term Care Facilities
  - 1% Women and Children Hospitals
  - 10% Other

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

16

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Multi-Chamber Bag Parenteral Nutrition (MCB-PN)
  - 53% use MCB-PN
  - 26% use for all PN patients
  - 34% use in less than 25% of their patients
  - 34% said their organization had increased use in the last 3 years due to shortages

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

17

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Multi-Chamber Bag Parenteral Nutrition (MCB-PN)
  - 91% stored/dispensed from Pharmacy
  - 8% Combination Pharmacy/ADC
  - 2% Locked cabinet for nurses

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

18

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- MCB-PN Activation
  - 50% Most often in Pharmacy in sterile environment but not always (24%)
  - 11% Combination Nursing and Pharmacy
  - 11% Always by Nursing
  - 4% Patient/Nurse in the home

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

19

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- MCB-PN Additives
  - 83% Multivitamins
  - 77% Trace Elements
  - 52% Electrolytes
  - 30% Other medication (insulin, heparin, H2 antagonists)
  - 15% Lipid Injectable Emulsion
  - 13% Dextrose
  - 15% Amino Acids
  - 12% No Additives

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

20

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- MCB-PN Errors
  - 29% experienced or are aware of a close-call or error reached the patient
  - More than 40 errors described
  - Infused beyond 24 hours

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

21

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- MCB-PN Competency Assessment
  - 68% indicated that their organization does not provide initial and/or annual competency assessment for
    - Prescribing
    - Dispensing
    - Activating
    - Administering

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

22

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Custom PN
  - 78% indicated that their organization provides custom PN
    - 59% compound on-site
    - 35% Outsourced
    - 6% Combination
  - 49% work in organizations that have an interface between EHR and ACD
  - 48% were aware of an organization process for the pharmacy or provider to work with home infusion company to convert MCB-PN to custom PN

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

23

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Errors with Custom PN
  - 40% have experienced or are aware of a close call or a medication error
  - More than 80 errors described

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

24

Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey

- Custom PN Competency Assessment
  - 53% indicated that their organization does not provide an initial and/or annual competency
    - Prescribing
    - Dispensing
    - Compounding
    - Administration
- Standardized Cutoff times
  - 80% have standardized cutoff times for PN ordering and compounding
  - Adherence
    - Usually 58%
    - Always 30%
    - Sometimes 9%
    - Rarely 3%

ISMP March 13, 2025 Volume 30 Issue 5

BAPTIST Get Better.

25

ISMP Safe Practice Recommendations

- Conduct a Failure Mode and Effects Analysis (FMEA)
  - Labeling and Packaging
  - How PN is ordered in EHR
  - Displayed on MAR
  - MCB activation

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

26

ISMP Safe Practice Recommendations

- Implement Standard Times
  - Cutoff times
  - Transmit during day shift for outsourcing
  - Pharmacy should be aware of all PN patients

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

27

ISMP Safe Practice Recommendations

- Prevent Transcription Errors
  - Automated compounding devices (ACD) interfacing with EHR
  - If no interface, independent double check

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

28

ISMP Safe Practice Recommendations

- Evaluate System Functionality
  - EHR functionality
    - Drug-drug interaction
    - Duplicate therapy
    - Cyclic PN
    - Central versus peripheral

BAPTIST Get Better.

29

ISMP Safe Practice Recommendations

- Conduct Effective Verification Processes in Pharmacy
  - Pharmacist verification of PN order
  - Quality control checks and verification of replacement solutions
  - Intravenous workflow management with barcode scanning

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

30

ISMP Safe Practice Recommendations

- Gather Stability Data
  - Contact manufacturers and document stability data
  - Information should be readily available
  - ASPEN: 30 hours room temperature and 9 days refrigerated unless there is specific extended stability data for the components
  - Hang time should not exceed 24 hours
  - Separate lipid injectable emulsion (ILE) emulsion 12 hours

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

31

ISMP Safe Practice Recommendations

- Store MCB-PN Safely
- Require Pharmacy Activation and Compounding

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

32

ISMP Safe Practice Recommendations

- Apply Auxiliary Labels
- Employ Barcoding Technology

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

33

ISMP Safe Practice Recommendations

- Administer PN using a 1.2 micron filter
- Reconcile Medication Including Home PN
- Document and Communicate

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

34

ISMP Safe Practice Recommendations

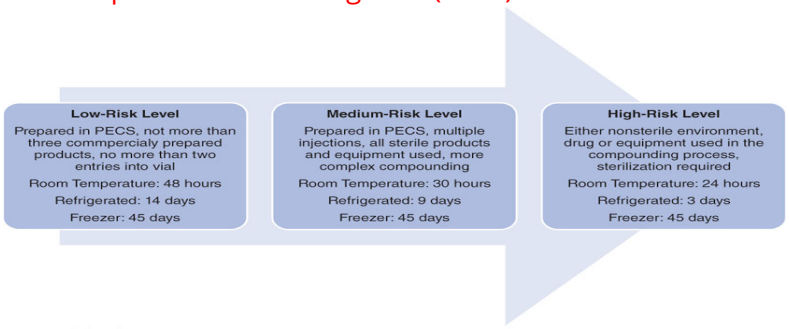
- Educate Practitioners
- Report Errors and Share Lessons Learned

ISMP March 27, 2025 Volume 30 Issue 6

BAPTIST Get Better.

35

USP Chapter 797 Risk Categories (2008)



source: S. Scott Sutton:
McGraw-Hill's NAPLEX® Review Guide, Third Edition
Copyright © McGraw-Hill Education. All rights reserved.

PECs = Primary engineering controls (PECs)

Citation: Chapter 76 Sterile Compounding Regulations and Best Practices for Sterile Compounding per USP 797, Sutton S. *McGraw-Hill's NAPLEX® Review Guide, 3e;* 2019. Available at: https://accesspharmacy.mhmedical.com/content.aspx?sectionid=201036417&bookid=2512&Resultclick=2 Accessed: December 27, 2023

36

USP Chapter 797 (2008) Parenteral Nutrition

Examples of Medium-Risk Compounding

- Compounding of total parenteral nutrition fluids using manual or automated devices during which there are multiple injections, detachments, and attachments of nutrient source products to the device or machine to deliver all nutritional components to a final sterile container

USP General Chapter 797

37

ASPEN Parenteral Nutrition Guidelines

Clinical Guidelines

A.S.P.E.N. Clinical Guidelines: Parenteral Nutrition Ordering, Order Review, Compounding, Labeling, and Dispensing

Joseph I. Boullata, PharmD, RPh, BCNSP, FASPEN[1]; Karen Gilbert, RN, MSN, CNSC, CRNP[2]; Gordon Sacks, PharmD, BCNSP, FCCP[3]; Reginald J. Labossiere, MD[4]; Cathy Crill, PharmD, BCNSP[5]; Praveen Goday, MD, MBBS, CNSC[6]; Vanessa J. Kumpf, PharmD, BCNSP[7]; Todd W. Mattox, PharmD, BCNSP[8]; Steve Plogsted, PharmD, BCNSP, CNSC[9]; Beverly Holcombe, PharmD, BCNSP, FASHP[10]; and the American Society for Parenteral and Enteral Nutrition

aspen

Journal of Parenteral and Enteral Nutrition
Volume 38 Number 3
March 2014 334–377

DOI: 10.1177/0148607114521833
jpen.sagepub.com
hosted at
online.sagepub.com

SAGE

6. What macronutrient dosing limits are expected to provide for the most stable 3-in-1 admixtures? We recommend that TNAs maintain final concentrations of amino acid ≥4%, monohydrated dextrose ≥10%, and injectable lipid emulsion ≥2% to be more likely to remain stable for up to 30 h at room temperature (25°C) or for 9 d refrigerated (5°C) followed by 24 h at room temperature. Strong

Boullata JI et al. *JPEN J Parenter Enteral Nutr.* 2014;38(3):334-377.

38

Revised USP Chapter 797

Table 13. BUD Limits for Category 2 CSPs[a]

Preparation Characteristics		Storage Conditions		
Compounding Method	**Sterility Testing Performed and Passed**	**Controlled Room Temperature (20°–25°)**	**Refrigerator (2°–8°)**	**Freezer (−25° to −10°)**
Aseptically processed CSPs	No	Prepared from one or more nonsterile starting component(s): 1 day	Prepared from one or more nonsterile starting component(s): 4 days	Prepared from one or more nonsterile starting component(s): 45 days
		Prepared from only sterile starting components: 4 days	Prepared from only sterile starting components: 10 days	Prepared from only sterile starting components: 45 days
	Yes	30 days	45 days	60 days
Terminally sterilized CSPs	No	14 days	28 days	45 days
	Yes	45 days	60 days	90 days

[a] A shorter BUD must be assigned when the physical and chemical stability of the CSP is less than the BUD limit stated in the table.

https://www.usp.org/compounding/general-chapter-797

39

Revised USP Chapter 797

Table 13. BUD Limits for Category 2 CSPs[a]

Preparation Characteristics		Storage Conditions		
Compounding Method	**Sterility Testing Performed and Passed**	**Controlled Room Temperature (20°–25°)**	**Refrigerator (2°–8°)**	**Freezer (−25° to −10°)**
Aseptically processed CSPs	No	Prepared from one or more nonsterile starting component(s): 1 day	Prepared from one or more nonsterile starting component(s): 4 days	Prepared from one or more nonsterile starting component(s): 45 days
		Prepared from only sterile starting components: 4 days	Prepared from only sterile starting components: 10 days	Prepared from only sterile starting components: 45 days
	Yes	30 days	45 days	60 days
Terminally sterilized CSPs	No	14 days	28 days	45 days
	Yes	45 days	60 days	90 days

[a] A shorter BUD must be assigned when the physical and chemical stability of the CSP is less than the BUD limit stated in the table.

https://www.usp.org/compounding/general-chapter-797

40

Key Takeaways:

- Importance of parenteral nutrition compatibility and stability
- Reviewed the Institute for Safe Medication Practices (ISMP) Parenteral Nutrition Survey
- Understand recent updates to USP Chapter <797> in relation to parenteral nutrition safety

BAPTIST Get Better.

41

Self Assessment Question 1

- Studies have shown the PN transition of care error percentage to be?
  1. 12%
  2. 13%
  3. 46%
  4. 60%

BAPTIST Get Better.

42

Self Assessment Question 1

- Studies have shown the PN transition of care error percentage to be?
  1. 12%
  2. 13%
  3. 46%
  4. 60%

BAPTIST Get Better.

43

Self Assessment Question 2

- A recent ISMP Survey indicated what percentage of organizations utilize MCB-PN
  1. 23%
  2. 33%
  3. 53%
  4. 63%

BAPTIST Get Better.

44

Self Assessment Question 2

- A recent ISMP Survey indicated what percentage of organizations utilize MCB-PN
  1. 23%
  2. 33%
  3. 53%
  4. 63%

BAPTIST Get Better.

45

Self Assessment Question 3

- According to the revised USP Chapter <797>, PN is stable for 4 days at room temperature.
  1. True
  2. False

BAPTIST Get Better.

46

Self Assessment Question 3

- According to the revised USP Chapter <797>, PN is stable for 4 days at room temperature.
  1. True
  2. False

BAPTIST Get Better.

47

References

Ayers P, Berger MM, Beriana D, et al. Expert consensus statements and summary of proceedings from the International Safety and Quality of Parenteral Nutrition Summit. *Am J Health-Syst Pharm* 2024;81(suppl 3):S75-S88.

Mirtallo JM, et al. Parenteral nutrition compatibility and stability: practical considerations. Nutr Clin Pract. 2024;1-14. doi:10.1002/ncp.11189.

Acute Care ISMP Medication Safety Alert. March 13, 2025. Volume 30 Issue 5.

Acute Care ISMP Medication Safety Alert. March 27, 2025. Volume 30 Issue 6.

USP General Chapter 797. Assessed July 3 , 2025.

Boullata, J.I., Gilbert, K., Sacks, G., Labossiere, R.J., Crill, C., Goday, P., Kumpf, V.J., Mattox, T.W., Plogsted, S., Holcombe, B. and (2014), A.S.P.E.N. Clinical Guidelines. Journal of Parenteral and Enteral Nutrition, 38: 334-377. https://doi.org/10.1177/0148607114521833

BAPTIST Get Better.

48

Questions?

BAPTIST Get Better.

49