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Special article

[Translated article] Spanish consensus on the preparation of parenteral nutrient mixtures – General aspects☆

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ABSTRACT

Parenteral nutrition is a complex therapeutic intervention, particularly in pediatric and critically ill patients, requiring strict standards of safety, stability, and compatibility during its preparation. To update and harmonize clinical practice, the Pharmacy Working Group of the Spanish Society of Clinical Nutrition and Metabolism and the Spanish Society of Hospital Pharmacy have developed a new multidisciplinary consensus. This document addresses key practical questions and provides recommendations grounded in scientific evidence and clinical experience.

The consensus focuses on six key areas related to parenteral nutrition preparation: lipid emulsion stability and lipid peroxidation; calcium-phosphate precipitation risk; stability of amino acids, vitamins, and trace elements; quality control and labeling; automated compounding systems and multi-chamber bags; and drug-parenteral nutritioncompatibility. It outlines strategies to minimize physicochemical instability, including guidelines on analytical techniques, the recommended sequence of component addition, and preventive measures to avoid destabilization phenomena.

This document serves as a practical guide for healthcare professionals involved in the compounding and administration of parenteral nutrition across various clinical settings. Recommendations were developed using a structured consensus methodology (adapted Delphi technique) and were unanimously endorsed by all participating experts. The result is a reference tool that supports safety, quality, and efficiency in parenteral nutrition preparation throughout Spain.
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Consenso español sobre preparación de mezclas de nutrientes parenterales: aspectos generales

Palabras clave:
Nutrición parenteral
Estabilidad
Compatibilidad
Seguridad

R E S U M E N

La nutrición parenteral constituye una terapia compleja, especialmente en pacientes pediátricos y críticos, cuya preparación exige estándares rigurosos de seguridad, estabilidad y compatibilidad. Con el objetivo de actualizar y estandarizar la práctica, el Grupo de Trabajo de Farmacia de la Sociedad Española de Nutrición Clínica y Metabolismo y la Sociedad Española de Farmacia Hospitalaria han desarrollado un nuevo consenso multidisciplinar. Este documento responde a preguntas clave y aporta recomendaciones prácticas basadas en evidencia científica y experiencia clínica.

El consenso aborda 6 áreas fundamentales dentro de la preparación de la nutrición parenteral: estabilidad de la emulsión lipídica y procesos de peroxidación; riesgo de precipitación calcio-fosfato; estabilidad de aminoácidos, vitaminas y oligoelementos; orden de adición, control de calidad y etiquetado; automatización y uso de bolsas multicámara; y compatibilidad entre nutrición parenteral y fármacos.

Se presentan estrategias para minimizar riesgos de inestabilidad física y química, así como directrices sobre técnicas analíticas, orden de adición de componentes y medidas preventivas frente a procesos de inestabilización. El documento representa una guía práctica, útil para profesionales que elaboran o administran nutrición parenteral en diversos entornos asistenciales. Las recomendaciones se han desarrollado mediante metodología de consenso (técnica Delphi adaptada), y se ha alcanzado la unanimidad entre los expertos participantes. Este trabajo constituye una herramienta de referencia que promueve la seguridad, la calidad y la eficiencia en la preparación de nutrición parenteral en España.

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Introduction

Parenteral nutrition (PN) is an important therapeutic intervention for paediatric and adult patients who cannot be fed via the enteral route. PN mixtures are complex, comprising more than 50 components that interact with one another.[1,2] The complexity of PN mixtures makes an up-to-date practical guide necessary for healthcare professionals. This consensus document on PN compounding summarises the recommendations of the Pharmacy Working Group of the Spanish Society of Clinical Nutrition and Metabolism (SENPE) and the Clinical Nutrition Group of the Spanish Society of Hospital Pharmacy (SEFH), with both groups represented by the hospital pharmacists who are signatories to this document. This article addresses key issues to guide PN compounding and provides recommendations that have been agreed upon by consensus. These recommendations are based on clinical and scientific evidence, as well as the practical experience of the signatories.

One of the main aims of this document was to report the consensus recommendations on common practical and clinical issues related to PN compounding across all settings, organised under the following topics:

1. Lipid emulsion stability and peroxidation processes.
2. Calcium-phosphate precipitation.
3. Stability of amino acids, vitamins, and trace elements.
4. Order of addition, quality control, and labelling of PN.
5. Automated compounding systems and multi-chamber bags.
6. Compatibility of PN with medications.

In addition to updating the 2008 consensus document, the other main aim was to provide practical guidance and consensus-based recommendations on all aspects of PN compounding across various populations and practical settings.[3] The format and design of this document were developed to foster interactive discussion and facilitate consensus-building. The resulting consensus statements represent the collective opinion of all signatories, grounded in and supported by scientific evidence and practical and clinical experience. This article summarises the key points of the consensus document statements.

Methods

A steering committee was set up comprising hospital pharmacists with PN experience. They were selected on the basis of their involvement in the SENPE and SEFH working groups. Participants in the consensus process were formally invited via the SENPE and SEFH professional networks. Participation was voluntary. The purpose of the initiative was to update the 2008 consensus document on PN compounding.[3]

The consensus statements were prepared using an adapted version of the Delphi technique.[4] Although a formal systematic review was not conducted, each topic was developed by a published expert in the field based on a critical review of the relevant literature and clinical experience. Each topic addresses the current state of knowledge and the most relevant recommendations as formulated by the expert participants. The initial draft for each topic was discussed by all members in a round-table format to identify priority issues and draft the corresponding consensus statements.

Each draft was submitted to a consensus vote to finalise the recommendations. The topics were discussed in structured group sessions, although standardised questionnaires or formal numerical rounds were not used. The consensus statements were refined over several rounds of discussion, with annotated versions returned for review and approval. After each round of discussion, the resulting document was finalised with the full agreement of all participants. This consensus was not recorded in any public protocol registry. The consensus-building process took place between January 2022 and February 2025, during regular virtual meetings of the participants.

Results

All signatories to this document, representing the SENPE Pharmacy Working Group and the SEFH Clinical Nutrition Working Group, agreed with all the consensus statements presented below. This section summarises the key points of each of the topics addressed.

Lipid emulsion stability and peroxidation processes

Lipid emulsions consist of lipid droplets stabilised with phospholipids derived from egg lecithin. Their stability is compromised by multiple factors that promote aggregation, coalescence, and cracking, which can pose a clinical risk, particularly in neonates.[5,6] The destabilisation of the lipid emulsion begins with flocculation, followed by creaming and coalescence. The formation of droplets larger than 5 μm can obstruct the pulmonary microvasculature. Among other factors, stability is influenced by pH (optimal 6–9), amino acid composition, glucose concentration, electrolytes, type and quantity of lipids, order of addition, and temperature and storage conditions.[5–7] Amino acids stabilise the emulsion through their buffering capacity and interaction with divalent ions, whereas electrolytes such as iron, calcium, and magnesium tend to destabilise it.[8]

To detect instability, visual inspection should be supplemented with optical microscopy or other techniques such as dynamic light scattering. Key parameters include pH, osmolarity, the critical aggregation number, and the percentage of droplets larger than 5 μm. An increase in this percentage indicates a risk of phase separation.[9,10]

Peroxide formation is another problem observed in PN mixtures.[11] Peroxides form through the action of oxygen combined with exposure to light or high temperatures. Lipids are the components most susceptible to peroxidation, but this phenomenon can also occur in lipid-free formulations containing amino acids and vitamins, with trace elements exacerbating the effect.[11,12] These radicals are harmful as they cause tissue damage and systemic inflammation, particularly in low-birth-weight preterm infants, whose immature enzymatic systems and environmental conditions increase their susceptibility.

Overall, the main factors affecting lipid emulsion stability are as follows[7,13,14]:

- Solution pH: a decrease in pH reduces emulsion stability by lowering the negative charge of the phospholipids.
- Amino acid concentration: amino acids stabilise ternary PN mixtures by counteracting the flocculating effects of electrolytes and glucose.
- Glucose concentration: direct addition of glucose to the lipid emulsion can destabilise it.
- Electrolyte concentration: as the positive electrolytic charge increases, emulsion stability decreases, because cations neutralise the negative charge on the surface of the lipid droplets.
- Lipid concentration: very low lipid concentrations can also destabilise the emulsion.
- Type of lipids: the stability of the lipid emulsion largely depends on the type and proportion of fatty acids it contains. Emulsions containing long-chain triglycerides appear less stable than those with medium-chain triglycerides in varying proportions, structured lipids, or those based on olive or fish oil.
- Order of addition: the amino acids and glucose should be mixed first, with the lipids added last, to minimise the destabilising effect of the acidity of the glucose solution.
- Temperature and time: extreme temperatures and prolonged storage/administration times can reduce stability.

The main recommendations for maintaining lipid emulsion stability are as follows[7,12,14–16]:

- Do not mix glucose and lipids directly without amino acids, to prevent emulsion destabilisation.
- To facilitate visual inspection, first mix amino acids and glucose, followed by the remaining components, with fat-soluble vitamins and the lipid emulsion added last.
- Never add electrolytes directly to the lipid emulsion.
- The lipid source should be the most stable emulsion containing medium-chain triglycerides in varying proportions, such as those based on olive or fish oil, avoiding emulsions composed entirely of long-chain triglyceride emulsions whenever possible.
- Do not prepare ternary PN mixtures with low glucose concentrations.
- Do not use ternary PN mixtures when there is a risk of destabilisation. Parenteral nutrition mixtures are complex, and their stability is determined by multiple chemical and physical interactions, making their study challenging. Therefore, very high or very low concentrations of macronutrients or micronutrients are generally not recommended.
- Monitor environmental conditions during the compounding, storage and administration of PN mixtures to minimise peroxidation.
- Use multi-layer bags, protect them from light, and store the mixtures in a refrigerator.
- Minimise oxygen ingress into the bag at all times, particularly during compounding and administration.
- Use opaque administration systems to protect against light exposure, particularly for paediatric patients.

Maximum safe electrolyte concentrations exist for organic and inorganic calcium and phosphorus salts, and these limits vary with the amino acid concentration.[7] During compounding, lipids should not be mixed with acidic solutions or divalent cations; standardised protocols and appropriate additive methods should be followed.[7,15,17] Knowledge of these recommendations and their implementation improves the stability and safety of PN mixtures in clinical practice.

Calcium-phosphate precipitation in parenteral nutrition

Calcium-phosphate precipitation is one of the most important complications in the formulation of PN mixtures, particularly in newborns. It may cause fatal complications (e.g., pulmonary embolism) if particles larger than 5–6 μm are administered.[18,19]

One of the most important factors is the choice of chemical forms of calcium and phosphorus. Organic salts, such as calcium gluconate and sodium glycerophosphate, have a lower tendency to precipitate, even at high concentrations.[19–21] In contrast, inorganic salts, such as monobasic or dibasic phosphate or calcium chloride, must be used with caution. The main species involved in precipitation are monobasic and dibasic calcium phosphate, the latter being significantly less soluble. At pH values below 6.4, monobasic phosphate predominates, as it is the more soluble form, whereas higher pH values favour the formation of dibasic phosphate and, consequently, precipitation. The most decisive factors in precipitate formation are the concentration and type of calcium and phosphorus, pH of the mixture, temperature (particularly critical in neonatal units), order of addition, infusion rate, and storage time.[7,18,20]

The order of addition is a key factor for compatibility. Phosphate should be added first, followed by magnesium, and finally calcium, each dissolved in the largest possible volume. This sequence reduces the likelihood of immediate interactions between phosphate and calcium. Polyelectrolyte solutions typically contain inorganic magnesium and calcium. If used, the polyelectrolyte solution may be incorporated first, allowing calcium to be added at the start and phosphorus at the end.[6,12] In general, it is advisable to use organic sources of phosphorus and calcium, as they offer greater stability. Calcium and phosphate must never be added together to the same initial mixture. Addition must always be carried out in amino-acid-rich mixtures, as the amino acids act as complexing agents, reducing the availability of calcium and phosphate. During patient administration, safety strategies include the use of 0.2-μm filters for binary mixtures or 1.2-μm filters for ternary mixtures, employing separate syringes for each additive, and staggering the addition of calcium and phosphorus.[1,3,7,21] Furthermore, the mixture must be gently shaken after each addition.

Finally, maximum limits are established based on amino acid concentration: in binary mixtures (2-in-1) containing ≥2.5% amino acids, up to 56 mEq/L of calcium and 48 mmol/L of phosphorus may be tolerated when using organic salts.[3,7,18] A critical approach should be adopted when extrapolating these limits to ternary mixtures, under the supervision of a pharmacist, taking into account additional factors introduced by the lipid emulsion, such as its stability and its phosphate content. The use of nomograms and tables based on recent studies is essential for safe PN formulation. However, the validation of these concentrations must be supported by experimental data and methods, such as microscopy, turbidimetry, or particle counting.[22]

Stability of amino acids, vitamins, and trace elements

Amino acids, vitamins, and trace elements are particularly sensitive to light, oxygen, temperature, and pH conditions; in addition, incompatibilities among these components can compromise their integrity and clinical safety.[7,23]

Amino acids can degrade under light exposure or through reactions with glucose. Until used, they should be stored in their original packaging and protected from light.[7,23] Amino acids such as tryptophan, methionine, and cysteine are particularly photosensitive, and riboflavin accentuates their oxidation. However, vitamin C acts as a protective agent.[7,23,24] Maillard reaction products form when amino acids and glucose interact. This reaction, exacerbated by heat and alkaline pH, can generate pigments, cause the loss of essential amino acids such as lysine, and produce potentially toxic compounds. To minimise these risks, use multi-layer EVA bags, control storage temperature, and avoid exposure to light and oxygen during processing.[25]

Vitamins are the most unstable components of PN mixtures; exposure to light, oxygen, temperature, and certain metal ions necessitates strict measures. It is crucial to protect from light, store under refrigeration, and use multilayer bags.[7,26–28] Water-soluble vitamins such as B_1 and C, and fat-soluble vitamins, such as A and E, are susceptible to oxidation and photolysis.[29] Vitamin C can oxidise readily, generating oxalic acid, which can precipitate as calcium oxalate. Because vitamins have a low pH that can destabilise mixtures, they should not be added to glucose solutions above 40% concentration. Trace elements and vitamins should be added separately. To minimise vitamin degradation, avoid high temperatures and minimise contact with oxygen.[25,27] Using light-protective overbags and opaque infusion systems is essential to prevent losses during storage and administration.

The stability of trace elements depends on pH, the concentration of electrolytes such as phosphorus, and the amino acid profile.[30–32] Precipitates of metal phosphates such as iron, zinc, copper, and manganese may form, particularly at low pH or in the presence of amino acids with sulphhydryl groups, such as cysteine. Avoid adding trace elements directly to lipid emulsions, as their cationic charge can destabilise the emulsion. Instead, add them to amino acid solutions, which provide a buffering effect. Avoid high concentrations of vitamin C in the presence of selenium or calcium, as insoluble calcium oxalate may form.[7]

Finally, attention must be paid to contaminating trace elements, such as aluminium, chromium, or cadmium, which can originate from raw materials and packaging, as well as from differences in PN bags, whether multi-chamber or ready-to-use.[32,33] Contaminating trace elements can accumulate in paediatric patients or those with renal dysfunction and cause toxicity. Avoid glass containers and monitor intake, particularly in neonates.

Order of addition, quality control, and labelling of parenteral nutrition

The order of component addition when compounding PN mixtures is crucial for maintaining physicochemical stability, preventing precipitates, and minimising nutrient interactions. Accumulated experience, consensus recommendations, and current literature allow the establishment of an optimal addition order, which must be adapted to the formula's characteristics and the centre's technical resources. The following order of mixing and addition to an empty PN bag is recommended for manual or automated preparation:

1. Phosphate (preferably organic).
2. Amino acids.
3. Glucose.
4. Monovalent cations (Na^+, K^+).
5. Magnesium.
6. Calcium (always separate from phosphate).
7. Vitamins and trace elements separately, without mixing them together.
8. Lipids (at the end, to facilitate visual inspection).

Use a separate syringe and line for each incompatible additive, flushing between steps with a diluent or a compatible solution, generally water for injection. Key steps to ensure mixture homogeneity include gentle shaking after each addition and inverting the bag twice after adding lipids. This sequence can be adapted depending on the type of PN mixture in automated systems or the need to prepare small volumes, particularly for paediatric patients.

Correct labelling and quality control of PN mixtures are essential to ensure patient safety, facilitate traceability, and minimise errors during administration. The label must provide clear, structured information consistent with the prescription, including patient identification (at least 2 non-redundant identifiers), a detailed description of macronutrients, micronutrients, additives, and calories, as well as the route of administration, infusion rate, compounding date, and specific warnings such as "DO NOT ADD MEDICATIONS" and "HIGH-RISK MEDICINE".[1,3,34,35] In particular, the route of administration must be visually highlighted using colour or typographic cues. Reconstituted multi-chamber formulations, once modified by the pharmacy department, must meet the same labelling criteria.

We highlight the importance of including these recommendations through specific warnings on the label and using light-protective systems for both the bag and infusion equipment, particularly for paediatric patients, to minimise oxidative stress.[11–13] Using multilayer bags further helps to maintain stability during refrigerated storage.[15,36]

Quality control of PN mixtures must form part of a comprehensive quality assurance system under the direct responsibility of pharmacists, as recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN) and the American Society of Hospital Pharmacists (ASHP).[15,36] Quality control involves verifying that all operations are performed according to predefined and documented procedures. This approach allows errors to be identified and corrective measures taken, while also preventing the administration of PN mixtures that do not meet the required standards.[34–36] During compounding, implement independent double-checks at 3 key stages: selecting vials and bottles, loading syringes with additives, and performing a final review of the prepared mixture against the compounding sheet.[35]

Once compounding is complete, perform a rigorous visual inspection of the mixture to rule out the presence of particles, colour changes, emulsion breakdown, or compromised closure integrity, as well as verify the components used and the suitability of the devices.[1,35,37,38] Gravimetric analysis, based on comparing the actual and theoretical weights calculated from the density and volume of the components, must have an error margin of less than 5%, as recommended by the European Medicines Agency and the United States Pharmacopoeia (USP).[38–40] Furthermore, physicochemical analyses (pH, osmolarity, glucose, electrolytes) and microbiological testing may be performed on selected samples.[37,38]

Finally, in line with USP 797, systematic sterility testing is not mandatory if the IV solution is prepared under validated aseptic conditions: ISO Class 5 cleanroom, rooms certified every 6 months, written

procedures, initial and annual staff training, environmental and microbiological monitoring, verification of materials, systematic disinfection, and adherence to storage times.[34,41]

Automated compounding systems and multichamber bags

Modern PN compounding faces the challenge of ensuring safety, efficacy, and efficiency. This challenge is addressed by 2 technological solutions: automated compounding systems (ACSs) and multichamber bags (MCBs). Both solutions have advantages and limitations relevant to different clinical and organisational contexts, thereby providing alternatives in clinical practice.

Automated compounding systems use software-controlled pumps to deliver nutrients, enabling precise dosing, enhanced traceability, and fewer manual errors. There are two main types of ACS: peristaltic pumps and volumetric syringe-based systems. However, ACSs require rigorous staff training, constant validation, and stringent quality control. Furthermore, the investment in infrastructure is substantial, as it requires adequate facilities, including large laminar flow cabinets, and materials compatible with disinfectants. It is essential to document every step of the process, perform daily quality controls, and ensure interoperability with medical prescription systems.[1,15]

The system should incorporate scanning technologies and alarms to detect potential errors, such as incompatible PN mixtures, blockages, and empty sources. Implementation must include continuous staff training, thorough process documentation, and daily verification of system operation. Safety is enhanced by pre-calibration, barcode technology, and incompatibility alarms. However, systematic errors may occur if the configuration is incorrect. Although the cost of acquisition and implementation can be high, it is offset by a reduction in errors and the number of staff involved.[17,42]

By contrast, MCBs are widely used in Europe and provide an efficient and safe alternative. They contain the 3 macronutrients in separate chambers, allowing mixing before administration. Vitamins, trace elements, and electrolytes can then be added safely, but strictly within a controlled environment. This approach reduces costs, compounding times, and errors, which is particularly important in hospitals without compounding facilities or for home PN.[43] However, owing to their fixed composition and the absence of trace elements and vitamins, their use is limited in patients with specific requirements, such as paediatric patients, those with renal failure or obesity, and in patients requiring long-term PN.

Key advantages include shorter compounding times, a low risk of contamination and fewer errors.[43,44] When handling, always adhere to aseptic practices and avoid adding components outside the pharmacy's controlled environment. During compounding, the manufacturer's information on stability and compatibility can provide useful guidance. Despite these limitations, previous studies suggest that more than 80% of hospitalised patients could benefit from their use. Given the potential release of plastic particles from multi-chamber bags, 1.2-μm filters should always be used during administration, even when no additives are included.

The use of ACSs and MCBs must comply with national guidelines, follow the most current international recommendations, such as those from ASPEN, ASHP, or USP 797, and adhere to standardised protocols.[17,34,45] The decision to use ACSs or MCBs should be based on clinical, logistical and economic factors. Whereas ACSs provide flexibility and precision in high-complexity hospitals with a large patient load and advanced technical resources, multi-chamber PN bags are distinguished by their simplicity, safety, and low cost, offering a standardised and effective solution for most hospital and home-based patients.[46] The appropriate integration of both systems can optimise safety, efficiency, and quality of care. A strategic approach involves using ACSs for individualised cases while employing multi-chamber PN bags for the majority of stable patients. This approach provides safer, more cost-effective PN provision tailored to the specific needs of each centre.

Compatibility of parenteral nutrition and medications

To minimise risks, specific recommendations must be followed to manage compatibility between PN and medications. Firstly, assess the patient's clinical condition and overall treatment, prioritising avoidance of concurrent administration whenever possible.[47] Consider alternatives such as switching to oral administration, peripheral infusion, cyclic PN infusion, or the use of a multilumen catheter before proceeding.

If concurrent administration is unavoidable, carefully assess the medication's stability with PN, thoroughly review the literature and specialised databases, and ensure that specific conditions, such as concentration, type of lipid, infusion time, and patient population (paediatric or adult), are considered. Verify the quality of the original studies, since variations in compounding conditions and PN components can affect compatibility. Conduct risk assessment using structured tools that classify medications as low- or high-risk for incompatibility, based on environmental variables and the characteristics of supporting studies.[48]

The stability assessments in these studies should include analytical methods such as turbidimetry, light absorption, or estimation of lipid droplet size, as recommended by the USP, since these methods indicate coalescence, which may pose a risk to neonates and paediatric patients.[10]

Regarding paediatric IV therapies, compatibility findings from adults should not be extrapolated because of differences in composition and infusion rate; thus, greater caution is required.[7] Incompatibilities, particularly in children, can have fatal consequences such as embolisms; consequently, concurrent administration should be avoided unless strictly necessary, and safe alternatives should always be considered for each clinical situation.

When addressing a compatibility query, the following steps are recommended: assess clinical need, consider alternative routes, evaluate the drug profile, and thoroughly document the decision.[7,47,48] Concurrent administration should be authorised only in justified cases, and only after a critical review of the literature, avoiding exclusive reliance on compatibility tables without verifying their methodological quality and clinical context.[1,7] In summary, the decision to administer medications with PN must be carefully tailored to each patient, always prioritising safer alternatives. Ensure access to up-to-date databases referencing well-designed studies and promote collaboration among hospital pharmacy, medical, and nursing teams.

Conclusions

This consensus document offers a reference tool for standardising PN compounding in the clinical setting. Using a practical question-based approach, clear and up-to-date recommendations have been agreed upon to address the real needs of healthcare professionals involved in the formulation, validation, and administration of PN. Notable methodological limitations include the lack of a formal analysis of response rates or the statistical representativeness of the panel, which are inherent to the design of an informal consensus. However, this document provides consistent criteria aligned with scientific evidence, promoting the implementation of good practices across diverse healthcare settings, from high-complexity hospitals to home parenteral nutrition units. The aim was to reduce variability in processes, improve patient safety, and optimise the efficiency of pharmaceutical and clinical practice. Furthermore, the document provides a solid foundation for future updates and research lines, highlighting the role of hospital pharmacists in ensuring the safety and quality of intravenous nutritional therapy.

Contribution to the scientific literature

This consensus article provides a comprehensive, up-to-date review of parenteral nutrition compounding procedures, combining scientific evidence and clinical experience. The consensus methodology employed ensures the practical applicability of the recommendations in

real-world hospital and home settings. Furthermore, it is an update of the 2008 Spanish consensus and incorporates aspects such as automation and error prevention. This document can help reduce variability between centres, improve patient safety, and serve as an educational reference. In addition, it represents a step forward in standardising hospital pharmacy practice in clinical nutrition.

Artificial intelligence

The authors declare that they have not used artificial intelligence (AI) or any tool utilising AI in the preparation of this article.

Conflicts of interest

None declared.

CRediT authorship contribution statement

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References

1. Ayers P, Adams S, Boullata J, et al. A.S.P.E.N. Parenteral nutrition safety consensus recommendations. *JPEN J Parenter Enteral Nutr*. 2014;38(3):296–333. doi:10.1177/0148607113511992.
2. Berlana D. Parenteral nutrition overview. *Nutrients*. 2022;14(21):4480. doi:10.3390/nu14214480.
3. Calvo Hernández MV, Sirvent Ochando M, coords. Estandarización del soporte nutricional especializado Grupo de Trabajo de Nutrición. *Farm Hosp*. 2009;33(suppl 1):3–107.
4. Hsu CC, Sandford BA. The Delphi technique: making sense of consensus. *Pract Assess Res Eval*. 2007;12(10):1–8.
5. Driscoll DF. Globule-size distribution in injectable 20% lipid emulsions: compliance with USP requirements. *Am J Health Syst Pharm*. 2007;64(19):2032–2036. doi:10.2146/ajhp070097.
6. Driscoll DF. Pharmaceutical and clinical aspects of lipid injectable emulsions. *JPEN J Parenter Enteral Nutr*. 2017;41(1):125–134. doi:10.1177/0148607116673187.
7. Boullata JI, Mirtallo JM, Sacks GS, et al. Parenteral nutrition compatibility and stability: a comprehensive review. *JPEN J Parenter Enteral Nutr*. 2022;46(2):273–299. doi:10.1002/jpen.2306.
8. Otero-Millán L, Lago Rivero N, Blanco Rodicio A, García Beloso N, Legido Soto JL, Piñeiro-Corrales G. Stability of lipid emulsion in total parenteral nutrition: an overview of literature. *Clin Nutr ESPEN*. 2021;45:19–25. doi:10.1016/j.clnesp.2021.06.027.
9. Hanifah S, Maulidani Y, Nugroho BH, Sari CP. All-in-one versus lipid-free parenteral nutrition for premature infants: visual, ph, and particle size analyses. *Nutr Hosp*. 2019;36(6):1237–1240. doi:10.20960/nh.02758.
10. Klang MG. PFAT5 and the evolution of lipid admixture stability. *JPEN J Parenter Enteral Nutr*. 2015;39(suppl 1):67S–71S. doi:10.1177/0148607115595976.
11. Boullata JI, Berlana D, Pietka M, Klek S, Martindale R. Use of intravenous lipid emulsions with parenteral nutrition: practical handling aspects. *JPEN J Parenter Enteral Nutr*. 2020;44(S1):S74–S81. doi:10.1002/jpen.1737.
12. Karthigesu K, Bertolo RF, Brown RJ. Parenteral nutrition and oxidant load in neonates. *Nutrients*. 2021;13(8):2631. doi:10.3390/nu13082631.
13. Driscoll DF, Thoma A, Franke R, Klutsch K, Nehne J, Bistrian BR. Lipid globule size in total nutrient admixtures prepared in three-chamber plastic bags. *Am J Health Syst Pharm*. 2009;66(7):649–656. doi:10.2146/ajhp080164.
14. Gomis Muñoz P. Preparación de las nutriciones parenterales pediátricas. *Nutr Hosp*. 2017;34(suppl 3):44–49. doi:10.20960/nh.1380.
15. Boullata JI, Holcombe B, Sacks G, et al. Standardized competencies for parenteral nutrition order review and parenteral nutrition preparation, including compounding. *Nutr Clin Pract*. 2016;31(4):548–555. doi:10.1177/0884533616653833.
16. Lobo BW, da Veiga VF, Cabral LM, Michel RC, Volpato NM, de Sousa VP. Influence of the relative composition of trace elements and vitamins in physicochemical stability of total parenteral nutrition formulations for neonatal use. *Nutr J*. 2012;11:26. doi:10.1186/1475-2891-11-26.
17. Iredell B, Mourad H, Nickman NA, et al. ASHP guidelines on the safe use of automated compounding devices for the preparation of parenteral nutrition admixtures. *Am J Health Syst Pharm*. 2022;79(10):730–735. doi:10.1093/ajhp/zxac004.
18. MacKay M, Anderson C. Physical compatibility of sodium glycerophosphate and calcium gluconate in pediatric parenteral nutrition solutions. *JPEN J Parenter Enteral Nutr*. 2015;39(6):725–728. doi:10.1177/0148607114528982.
19. Ribeiro DDO, Lobo BW, Volpato NM, Da Veiga VF, Cabral LM, De Sousa VP. Influence of the calcium concentration in the presence of organic phosphorus on the physicochemical compatibility and stability of all-in-one admixtures for neonatal use. *Nutr J*. 2009;8:51. doi:10.1186/1475-2891-8-51.
20. Newton DW, Driscoll DF. Calcium and phosphate compatibility: revisited again. *Am J Health Syst Pharm*. 2008;65(1):73–80. doi:10.2146/ajhp070138.
21. Barnett MI, Pertkiewicz M, Cosslett AG, Mühlebach S. Basics in clinical nutrition: parenteral nutrition admixtures, how to prepare parenteral nutrition (PN) admixtures. *e-SPEN*. 2009;4(3):e114–e116. doi:10.1016/j.eclnm.2009.01.011.
22. Gonyon T, Carter PW, Phillips G, et al. Probability-based compatibility curves for calcium and phosphates in parenteral nutrition formulations. *JPEN J Parenter Enteral Nutr*. 2014;38(6):717–727. doi:10.1177/0148607113495415.
23. Unger N, Holzgrabe U. Stability and assessment of amino acids in parenteral nutrition solutions. *J Pharm Biomed Anal*. 2018;147:125–139. doi:10.1016/j.jpba.2017.07.064.
24. Kearney MCJ, Allwood MC, Martin H, Neal T, Hardy G. The influence of amino acid source on the stability of ascorbic acid in TPN mixtures. *Nutrition*. 1998;14(2):173–178. doi:10.1016/S0899-9007(97)00430-9.
25. Balet A, Cardona D, Jane S, et al. Effects of multilayered bags vs ethylvinyl-acetate bags on oxidation of parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2004;28(2):85–91. doi:10.1177/014860710402800285.
26. Ribeiro DO, Pinto DC, Lima LMTR, Volpato NM, Cabral LM, De Sousa VP. Chemical stability study of vitamins thiamine, riboflavin, pyridoxine and ascorbic acid in parenteral nutrition for neonatal use. *Nutr J*. 2011;10:47. doi:10.1186/1475-2891-10-47.
27. Allwood MC, Martin HJ. The photodegradation of vitamins A and E in parenteral nutrition mixtures during infusion. *Clin Nutr*. 2000;19(5):339–342. doi:10.1054/clnu.2000.0109.
28. Dupertuis YM, Morch A, Fathi M, et al. Physical characteristics of total parenteral nutrition bags significantly affect the stability of vitamins C and B1: a controlled prospective study. *JPEN J Parenter Enteral Nutr*. 2002;26(5):310–316. doi:10.1177/0148607102026005310.
29. Allwood MC, Martin H, Greenwood M, Maunder M. Precipitation of trace elements in parenteral nutrition mixtures. *Clin Nutr*. 1998;17(5):223–226. doi:10.1016/s0261-5614(98)80063-0.

30. Thibault M. Possible incompatibility between amino acids and copper in solutions for pediatric parenteral nutrition. *Can J Hosp Pharm*. 2014;67(2):160–164. doi:10.4212/cjhp.v67i2.1345.
31. Gomis Muñoz P, Arrieta M, Rosas C, Spiers S, Shinn M, Orbaneja MÁ. Influence of the type of amino acids in the formation of precipitates of copper and sulfur in parenteral nutrition. *Nutr Hosp*. 2019;36(4):764–768. doi:10.20960/nh.02661.
32. Olson LM, Wieruszewski PM, Jannetto PJ, Abbott JC, McMahon MM, Nystrom EM. Quantitative assessment of trace-element contamination in parenteral nutrition components. *JPEN J Parenter Enteral Nutr*. 2019;43(8):970–976. doi:10.1002/jpen.1668.
33. Berlana D, López-Hellín J, Pau-Parra A, Ferrer-Costa R. Comparing aluminum concentrations in adult and pediatric parenteral nutrition solutions: multichamber-bag versus compounded parenteral nutrition. *Nutrients*. 2024;16(7):1024. doi:10.3390/nu16071024.
34. Okeke CC, Newton DW, Kastango ES, Allen LV. Basics of compounding: United States pharmacopeia general chapter 797 pharmaceutical compounding - sterile preparations, part 10: first revision: the main changes, events, and rationale. *Int J Pharm Compd*. 2008;12(6):530–536.
35. Instituto para el Uso Seguro de los Medicamentos. Recomendaciones para la prevención de errores de medicación. Instituto para el Uso Seguro de los Medicamentos. Boletin no 27. Actualizada: 18 de enero de 2025. [accessed 7 Oct 2025]. Available from: https://www.ismp-espana.org/ficheros/Boletín%2027%20Junio%202,008.pdf.
36. Mirtallo J, Canada T, Johnson D, et al. Safe practices for parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2004;28(6):S39–S70. doi:10.1177/0148607104028006S39.
37. Corriol O, Crauste-Manciet S, Arnaud P, et al. Recommendations for the preparation of parenteral nutrition mixtures. *Nutr Clin Metab*. 2005;19(1):30–55. doi:10.1016/j.nupar.2005.01.003.
38. Ortuño AM, Jiménez RR, Navarro CO, Flores MF, Sáez MS. Quality control of parenteral nutrition compounding: gravimetric and component verification control. *Nutr Hosp*. 2020;37(4):667–671. doi:10.20960/nh.03037.
39. Gómez-Costas D, Romero-Jiménez RM, Lobato-Matilla ME, et al. Detection and reduction of errors in parenteral nutrition compounding through gravimetric and product control. *Farm Hosp*. 2024;48(3):116–121. doi:10.1016/j.farma.2023.11.007.
40. European Medicines Agency. Guideline on manufacture of the finished dosage form. European Medicines Agency. 2017. Actualizada: 17 de marzo de 2025. [accessed 7 Oct 2025]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-manufacture-finished-dosage-form-revision-1_en.pdf.
41. Romero Jiménez RM, Sagrario Pernía López M, Fresneda NS, Sáez MS. Validación de la técnica aséptica de elaboración de nutrición parenteral en un servicio de farmacia según el capítulo 797 de la USP. *Nutr Hosp*. 2013;28(5):1494–1497. doi:10.3305/nh.2013.28.5.6689.
42. Perrier Q, Piquemal M, Leenhardt J, et al. A quality by design approach for the qualification of automating compounding device for parenteral nutrition. *Eur J Pharm Sci*. 2022;179:106275. doi:10.1016/j.ejps.2022.106275.
43. Alfonso JE, Berlana D, Ukleja A, Boullata J. Clinical, ergonomic, and economic outcomes with multichamber bags compared with (hospital) pharmacy compounded bags and multibottle systems: a systematic literature review. *JPEN J Parenter Enteral Nutr*. 2017;41(7):1162–1177. doi:10.1177/0148607116657541.
44. Berlana D, Almendral MA, Abad MR, et al. Cost, time, and error assessment during preparation of parenteral nutrition: multichamber bags versus hospital-compounded bags. *JPEN J Parenter Enteral Nutr*. 2019;43(4):557–565. doi:10.1002/jpen.1436.
45. Boullata JI, Gilbert K, Sacks G, et al. A.S.P.E.N. Clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. *JPEN J Parenter Enteral Nutr*. 2014;38(3):334–377. doi:10.1177/0148607114521833.
46. Wischmeyer PE, Klek S, Berger MM, et al. Parenteral nutrition in clinical practice: international challenges and strategies. *Am J Health Syst Pharm*. 2024;81(suppl 3):S89–S101. doi:10.1093/ajhp/zxae079.
47. Farhan M, Bennett J, Cram A, McCallion N, O'Brien F. Risk assessment tool for compatibility of concurrent administration of intravenous medications with parenteral nutrition admixture. *Eur J Pharm Biopharm*. 2025;207:114614. doi:10.1016/j.ejpb.2024.114614.
48. Négrier L, Martin Mena A, Lebuffe G, Odou P, Genay S, Décaudin B. Strategies to prevent drug incompatibility during simultaneous multidrug infusion in intensive care units: a literature review. *Eur J Clin Pharmacol*. 2021;77(9):1309–1321. doi:10.1007/s00228-021-03112-1.