Use of Filters During the Administration of Parenteral Nutrition

Position Statement issued on behalf of British Pharmaceutical Nutrition Group

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Recommendations

1. All parenteral nutrition (PN) admixtures should be administered via a filter with a pore size of 1.2 µm (micron).
2. Aqueous (lipid-free) PN admixtures can be administered via 0.2 µm filter. This is considered good practice.
3. PN filters and administration sets should be changed with each new PN container, based on PN admixture shelf-life, local infection control policies, and as per filter manufacturer shelf life.
4. Use of filters integrated into giving sets, where available is preferable to separate filters, to reduce the number of connections, and thereby, infection risk.
5. Compatibility of IV administration sets and filters is dependent on the make of infusion pump and must be considered during the procurement process.
6. All manufacturer Summary of Product Characteristics (SPC) for PN bags/components need to be standardised and indicate minimum filtering requirements.
7. Infusion duration of PN and filter use outside of the product licence should be supported by a local risk assessment.

Introduction

PN is an aseptically produced mixture of medicinal products intended for intravenous use, and therefore known as an *admixture*. It is administered to patients with intestinal failure when nutritional requirements cannot be met using the gastro-intestinal tract. It is a complex medicinal product containing over 40 ingredients including amino acids, lipid emulsion, glucose, vitamins, trace elements, electrolytes and water. It is most commonly infused as a rate-controlled infusion by the central venous route. Concerns about physico-chemical stability, microbial contamination, catheter-related sepsis coupled with high monitoring demands categorise PN as a high-risk associated medicine.[1]

Patient safety incidents and harmful events related to PN contaminated by particulate matter or micro-organisms that enter during the compounding or administration processes, or precipitates that develop in the bag due to physico-chemical processes are not uncommon and need to be controlled. Identifying a root cause for each incident can be difficult and the use of filters during administration may help by removing particulate matter, and some micro-organisms. The success of this approach will depend on the pore size of the filters used and nature of the infusion. Filters are a special porous device used to prevent the passage of air or particulate matter. Available filters vary in pore size and presentation, and it is vital that the nature of the filtrate is considered with filter pore size (see Table 1).[2]

Table 1. Common filters in healthcare

Filtrate	Filter pore size
Clear fluids e.g. crystalloid	15 µm
Blood components	170-200 µm
Lipid infusions	1.2 µm

The aim of this position statement is to review the available evidence, international best practice guidance and to provide advice on best practice for UK healthcare professionals involved in the provision of PN. This guidance is applicable to PN administration in hospital and at home; for clarity, it will not differentiate between patient groups.

Current UK guidance

In 2001 a British Pharmaceutical Nutrition Group (BPNG) working group published a position statement on the use of filters during PN preparation and administration.[3] The Group reviewed particle sizes of potential contaminants at different stages of the PN manufacturing cycle and recommended 1.2 µm filters for the administration of lipid containing admixtures, and 0.2 µm endotoxin-retaining filters for non-lipid containing admixtures.

The National Institute for Health and Care Excellence (NICE) guidelines for PN for adults[4] and neonates[5] provide no guidance on the use of filters for PN administration. The Royal College of Nursing (RCN) in their *Standards for infusion therapy*, which are currently under review, state that for lipid infusions or total nutrient preparations that require filtration, a 1.2 µm filter should be used.[2] The UK Injectable Medicines Guide (Medusa) in their PN monographs advise the use of 1.2 µm filters, and in their paediatric guide, 1.2µm filters for lipid-containing bags and syringes and 0.2µm filters for aqueous (lipid-free) admixtures.[6,7] To our knowledge there is currently no other UK-based national guidance on filtering PN admixtures.

Different manufacturer SPCs for licensed multi-chamber bags and PN lipid and/or amino acid components vary in their statements around the use of filters for PN administration.[8] Some omit any reference to filters, others advise *if used* should

be ≥1.2 µm and permeable to lipids, or they recommend the use of a filter without reference to pore size. We found one product SPC that stated the use of a 1.2 µm filter recommended for administration.

Global recommendations

There is varying global guidance from organisations with regards to PN administration and the use of filters. These differences in the most recent guidance are outlined in Table 2. The US Food and Drug Administration (FDA) first issued a statement in 1994 recommending the use of a filter when infusing PN, suggesting 0.22 µm air-eliminating filters for non-lipid mixtures, and 1.2 µm air-eliminating filters for lipid PN.[9]

Despite recommendations there remains a wide variation in practice.[10] This may be related to the questionable strength of available evidence, lack of awareness of the risks related to particulate contamination, the role of filters in eliminating microbes, and problems such as low flow rates and occlusions during infusions. There may also be barriers related to cost pressures, strength of justification to senior managers, or procurement issues.

Table 2. Outline of differences between global guidelines for the use of filters during PN administration.

Group (Country, Year)	Patient group included			Filter recommendation
	Neonates	Paediatrics	Adults	
IRSPEN (Ireland, 2024)[11]	Yes	Yes	No	0.2 µm filter for aqueous PN and 1.2 µm for lipid PN. For 3-in-1 PN mixtures 1.2-1.5 µm filter
ASPEN (USA, 2021)[12]	Yes	Yes	Yes	1.2 µm filter for all PN admixtures
HAS (France, 2018)[13]	Yes	No	No	Use antibacterial (0.22 µm) and anti-particulate (1.2 µm) filters. Antibacterial filters cannot be used with lipids
ESPGHAN, ESPEN, ESPR, CSPEN (Europe & China, 2018)[14]	No	Yes	No	PN admixtures may be administered through a terminal filter: lipid emulsions (or all-in-one mixes) through 1.2-1.5 µm filter; aqueous admixtures through a 0.22 µm filter
BPNG (UK, 2001)[3]	Yes	Yes	Yes	1.2-µm filters should be used for lipid-containing admixtures including all-in-one admixtures (changed every 24 hours). 0.2-µm endotoxin-retaining filters should be used for non–lipid admixtures (changed every 96 hours).

Abbreviations: American Society for Parenteral and Enteral Nutrition (ASPEN); Irish Society for Clinical Nutrition & Metabolism (IRSPEN); Haute Autorité De Santé (HAS); European Society for Paediatric Gastroenterology Hepatology Nutrition (ESPGHAN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society for Paediatric Research (ESPR); Chinese Society for Parenteral and Enteral Nutrition (CSPEN); British Pharmaceutical Nutrition Group (BPNG)

Particulate contamination

When clinicians consider contamination in respect to PN, the default may be to first consider microbial contamination (viable). However physical particulate contamination (non-viable) may be introduced via a number of mechanisms; during the manufacture of source or final containers, during the compounding of preparations (e.g. glass or rubber), incompatibility caused by storage or transport processes, or at the point of administration. Particulate matter could be visible or subvisible and is categorised by the European Pharmacopoeia (EP) Chapter 2.9.19 and the United States Pharmacopoeia (USP) Chapter <788> as undissolved particles contained in infused solutions.[15,16] The Pharmacopoeias seek to define particle limits in infusion solutions, but consideration should be given to how the processes above could further increase the particulate levels within PN admixtures. Methods to reduce particulate load with the administration of PN are vital to ensure patient safety.[17] The number and size of particulates reported in PN admixtures has been reported in literature and results vary in sampling strategy, timing and with differing formulation. There is a potential for particle size of lipid containing admixtures to increase with time throughout the infusion duration.[18,19]

Compounding practices vary according to process design; from manual additions, gravity fill methods, semi and automated compounding devices. Compounders will seek to minimise the number of manipulations in order to minimise both microbial and particulate risk which in turn could lead to variations in practice, such as the use of terminal filters during the production processes.[3,20] The expectation is for robust quality assurance of the production process carried out by PN suppliers, and processes may vary from manufacturer to manufacturer. As a result, a degree of variation in the recommendation of filter use stipulated on labelling and packaging may be noted. In recent years; in order to ensure a stable supply chain, a degree of flexibility has been required in order to move supply from one manufacturer or bag type to another. To mitigate this risk, the use of a filter during administration would seem a justifiable approach to clinical risk management as end-users, and thus makes it difficult to differentiate advice for filter use between patient groups given the common use of compounding methods across cohorts.

The role of the PN filter

Filters used in PN administration are most commonly available with membrane pore sizes of 0.2 µm and 1.2 µm. These filters can be an integral part of the intravenous administration set (integrated filter) or can be added as a separate device to an administration set (add-on filter). Administration sets with an integrated filter do not require additional manipulation

(e.g. adding a filter to the set) thus potentially reducing infection risks. If a separate add-on filter is used it must be sited as close to the patient as possible, thus removing contaminants as the infusion enters the bloodstream. Filter membranes can have different characteristics and be made of different materials with different properties. Based on the properties of the filter membrane material used, filters can be classed as 24-hour (0.2 or 1.2 µm filters) or 96-hour endotoxin-retaining filters (0.2 µm filters only). The 96-hour filters have a positively charged filter membrane that is capable of retaining bacterial endotoxins during the infusion for up to 96 hours, due to binding to the negative charge of endotoxins.[3,12] Filters have various priming volumes and maximum recommended flow rates and might be classed as adult, paediatric or neonatal. Filters with smaller priming or hold-up volumes will also have a lower maximum recommended flow rate and are usually used in neonates and paediatric patients.

The 0.2 µm filters must not be used for the administration of lipid-containing PN as the range of lipid globules size in parenteral intravenous lipid emulsion (IVLE) is 0.1–0.8 µm in diameter, with a mean diameter of 0.2–0.3 µm (similar to naturally occurring chylomicrons), which could result in filter membrane blockage and disruption of the emulsion stability. A stable IVLE has a mean droplet size not exceeding 0.5 µm, with no more than 0.05% of droplets in the emulsion larger than 5 µm.[12,21] Therefore, a 1.2 µm filter should be used for the administration of lipid-containing PN and undiluted IVLEs, which will retain enlarged lipid globules (larger than 1.2 µm), particulate matter (e.g. plastic debris from syringes or extension sets; stripped silicone oil from the syringe barrel), sizable microorganisms (*e.g. Malassezia furfur, Candida spp*.) and air bubbles.[3,12,22-24]

The role of filters in PN administration is to protect the patient from the infusion of:

1. **Air** – protects the patient from air embolism and the harmful effects of infusing air bubbles, arising from e.g. outgassing (spontaneous release of dissolved gasses from liquids) during infusion warming up, incomplete priming, accidental disconnection or run-dry.[25-27]
2. **Particulate contamination** – arising from infusion systems (e.g. administration sets, extension sets, effect of IV pumps on the silicone insert of the IV tubing during infusion), PN components (e.g. additives), manipulations (e.g. particles introduced during manual or automated compounding or when connecting to the patient for administration) and precipitates due to physico-chemical interactions between nutrient components (during compounding, storage or administration) or co-administration of drugs.[3,12,17,26,28] Particles can be deposited in the microvasculature of the lungs and other organs and may have detrimental clinical consequences.[29,30] Gross precipitation in admixtures (e.g. calcium phosphate precipitation) has proved fatal and may be obscured by the presence of lipids.[9,31]
3. **Bacterial contamination** (and endotoxins if a 0.2 µm filter with positively charged membrane is used) – reducing the risk of infection due to inadvertent contamination (e.g. during aseptic compounding or connection of PN for administration).[3] The 1.2 µm filters will only offer protection from microorganisms larger than 1.2 µm in size (e.g. some pathogenic fungi).[23, 24]
4. **Enlarged lipid globules** (and free oil) – Lipid emulsions can with time become unstable, resulting in the formation of oversized droplets or even free oil, if not compounded, stored or administered appropriately.[3] A 1.2 µm filter will protect the patient from the infusion of lipid globules larger than 1.2 µm and destabilised emulsions.

Table 3. Outline of differences between filter types

	Filter type	
	0.2 µm filter	**1.2 µm filter**
Protection against	• Air infusion – preventing air embolism • Particulate contamination • Micro-organisms (except *Mycoplasma spp*. and viruses)	• Air infusion – preventing air embolism • Particulate contamination (> 1.2 µm in size) • Enlarged lipid droplets (> 1.2 µm in size) • Micro-organisms > 1.2 µm in size (e.g. pathogenic fungi like *Candida sp*. and *Malassezia furfur*)
PN type	• Aqueous (lipid-free) PN admixtures only	• Lipid-containing PN admixtures and undiluted IVLE
Filter shelf-life	• Change every 24 hours • Change every 96 hours – ***only*** endotoxin-retaining filters with a positively charged membrane	• Change every 24 hours

Summary

PN patients receive a large volume of parenteral fluid therapy over a prolonged period of time, and unless this is filtered, are at risk of unintentionally receiving large amounts of particulate material, which has no therapeutic use and is known to be harmful.[32] The omission of appropriate filters during PN administration can compromise patient safety and could lead to increased morbidity and mortality.[9,18,30,32] Based on the evidence and guidance currently available, the BPNG strongly advise that all PN is prepared and administered using appropriate filters to support patient safety, reduce exposure and prevent complications and detrimental effects related to the unwanted infusion of particulate matter, air and enlarged lipid globules. All PN admixtures should be administered via a filter with a pore size no greater than 1.2 µm (micron).

The guidance in the 2001 BPNG position statement remains valid and our guidance is unchanged.[3] Detailed advice on filtering PN needs to be included in national UK PN guidance such as that proposed by NICE, BAPEN or similar. For clarity, we also suggest manufacturers of PN and PN amino acid/lipid emulsions revise their SPCs to include appropriate advice on filtering, including details on recommended filter pore size for the administration of their products.

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References

1. Mistry P, Smith RH, Fox A. Patient Safety Incidents Related to the Use of Parenteral Nutrition in All Patient Groups: A Systematic Scoping Review. *Drug Saf.* 2022;45(1):1-18. doi:10.1007/s40264-021-01134-3.
2. Royal College of Nursing. Standards for infusion therapy. https://www.rcn.org.uk/clinical-topics/Infection-prevention-and-control-advice/Standards-for-infusion-therapy. Published 2018 (currently under review). Accessed 21/09/2024.
3. Bethune K, Allwood M, Grainger C, Wormleighton C. Use of filters during the preparation and administration of parenteral nutrition: position paper and guidelines prepared by a British pharmaceutical nutrition group working party. *Nutrition.* 2001;17(5):403-408. doi:https://doi.org/10.1016/S0899-9007(01)00536-6.
4. National Institute for Health and Care Excellence. Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition. Clinical guideline [CG32]. https://www.nice.org.uk/guidance/cg32. Published 2006 (updated 2017). Updated 2017. Accessed 22/04/2024.
5. National Institute for Health and Care Excellence. Neonatal parenteral nutrition [NG154]. https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#administration-of-neonatal-parenteral-nutrition. Published 2020. Accessed 21/09/2024.
6. UK Medicines Information. Medusa - The Injectable Medicines Guide. Adult Intraveous Drugs. Parenteral Nutrition (intravenous nutrition) https://www.medusaimg.nhs.uk/. Accessed 21/09.2024.
7. UK Medicines Information. Medusa - The Injectable Medicines Guide. Paediatric Intraveous Drugs. Parenteral Nutrition (intravenous nutrition) https://www.medusaimg.nhs.uk/. Accessed 21/09/2024.
8. Electronic Medicines Compendium. Summary of Product Characteristics. https://www.medicines.org.uk/emc. Accessed 21/09/2024.
9. Food and Drug Administration. Safety alert: hazards of precipitation associated with parenteral nutrition. *Am J Hosp Pharm.* 1994;51:427-428.
10. Christensen ML, Ayers P, Boullata JI, et al. Lipid Injectable Emulsion Survey With Gap Analysis. *Nutr Clin Pract.* 2017;32(5):694-702. doi:10.1177/0884533617719671.
11. The National Clinical Programme for Paediatrics and Neonatology Parenteral Nutrition Expert Guideline Development Group. Guideline on the Use of Parenteral Nutrition in Neonatal and Paediatric Units https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/. Published January 2024. Accessed 21/09/2024.
12. Worthington P, Gura KM, Kraft MD, Nishikawa R, Guenter P, Sacks GS. Update on the Use of Filters for Parenteral Nutrition: An ASPEN Position Paper. *Nutr Clin Pract.* 2021;36(1):29-39. doi:10.1002/ncp.10587.
13. Haute Autorité De Santé Parenteral nutrition in neonatology - Good practice recommendation. https://www.has-sante.fr/jcms/c_2859140/en/nutrition-parenterale-en-neonatologie-recommandation-de-bonne-pratique#toc_1_4_3. Published July 2018. Accessed 21/09/2024.
14. Puntis J, Hojsak I, Ksiazyk J, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Organisational aspects. *Clin Nutr.* 2018;37(6 Pt B):2392-2400. doi:10.1016/j.clnu.2018.06.953.
15. British Pharmacopeia. Quality Standards for Medcines. Appendix XIII A. Particle Contamination: Sub-visible Particles. https://www-pharmacopoeia-com.manchester.idm.oclc.org/bp-2024/appendices/appendix-13/appendix-xiii-a--particulate-contamination--sub-visible-particle.html?date=2024-07-01&text=particles. Published 2024. Accessed 26/09/2024.
16. The United States Pharmacopeia tr, and the National Formulary,. Chapter <788>Particulate Matter in Injections. USP 35. In: Rockville, MD.2013.
17. Tran T, Kupiec TK, Trissel LA. Quality-Control Analytical Methods: Particulate Matter In Injections: What is It and What are the Concerns? *Int J Pharm Compd.* 2006;10(3):202-204. Published 2006/05/01.
18. Puntis JW, Wilkins KM, Ball PA, Rushton DI, Booth IW. Hazards of parenteral treatment: do particles count? *Arch Dis Child.* 1992;67(12):1475-1477. doi:10.1136/adc.67.12.1475.
19. Ball PA, Bethune K, Fox J, Ledger R, Barnett M. Particulate contamination in parenteral nutrition solutions: still a cause for concern? *Nutrition.* 2001;17(11-12):926-929. doi:10.1016/s0899-9007(01)00708-0.
20. European Commission. The Rules Governing Medicinal Products in the European Union. Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use. Annex 1: Manufacture of Sterile Medicinal Products, at: . https://health.ec.europa.eu/system/files/2022-08/20220825_gmp-an1_en_0.pdf. Published 2022. Accessed 21/09/2024.
21. Gill M, Hirsch A, Wilson N. Filtering Out the Facts: Recommendations to Optimize Performance of In-Line Filters for Parenteral Nutrition and Injectable Lipid Emulsion Infusions. *J Infus Nurs.* 2022;45(3):137-141. doi:10.1097/nan.0000000000000464.
22. Davies AF, Vadodaria B, Hopwood B, Dexter T, Conn D. Efficacy of microfiltration in decreasing propofol-induced pain. *Anaesthesia.* 2002;57(6):557-561. doi:10.1046/j.1365-2044.2002.02602.x.
23. Leck AK, Puntis JW. Yeast infections on the neonatal unit: one cheer for parenteral nutrition admixture filters. *Nutrition.* 1998;14(4):400-401. doi:10.1016/s0899-9007(97)00495-4.
24. Robinson R, Ball P. Does the Pall TNA-1E parenteral nutrition admixture filter retain Malassezia furfur? *Nutrition.* 1998;14(4):363-365. doi:10.1016/s0899-9007(97)00489-9.
25. Myers GJ. Air in intravenous lines: a need to review old opinions. *Perfusion.* 2017;32(6):432-435. doi:10.1177/0267659117706834.
26. Dewan PA, Ehall H, Edwards GA, Middleton DJ, Terlet J. Plastic particle migration during intravenous infusion assisted by a peristaltic finger pump in an animal model. *Pediatr Surg Int.* 2002;18(5-6):310-314. doi:10.1007/s00383-002-0810-7.
27. Varga C, Luria I, Gravenstein N. Intravenous Air: The Partially Invisible Phenomenon. *Anesth Analg.* 2016;123(5):1149-1155. doi:10.1213/ane.0000000000001604.
28. Foroni LA, Rochat MH, Trouiller P, Calop JY. Particle contamination in a ternary nutritional admixture. *J Parenter Sci Technol.* 1993;47(6):311-314. Published 1993/11/01.
29. Schmitt E, Meybohm P, Herrmann E, et al. In-line filtration of intravenous infusion may reduce organ dysfunction of adult critical patients. *Crit Care.* 2019;23(1):373. doi:10.1186/s13054-019-2618-z.
30. Hill SE, Heldman LS, Goo ED, Whippo PE, Perkinson JC. Fatal microvascular pulmonary emboli from precipitation of a total nutrient admixture solution. *JPEN J Parenter Enteral Nutr.* 1996;20(1):81-87. doi:10.1177/014860719602000181.
31. McKinnon BT. FDA safety alert: hazards of precipitation associated with parenteral nutrition. *Nutr Clin Pract.* 1996;11(2):59-65. doi:10.1177/011542659601100259.
32. Ball PA. Intravenous in-line filters: filtering the evidence. *Curr Opin Clin Nutr Metab Care.* 2003;6(3):319-325. doi:10.1097/01.mco.0000068969.34812.5d.