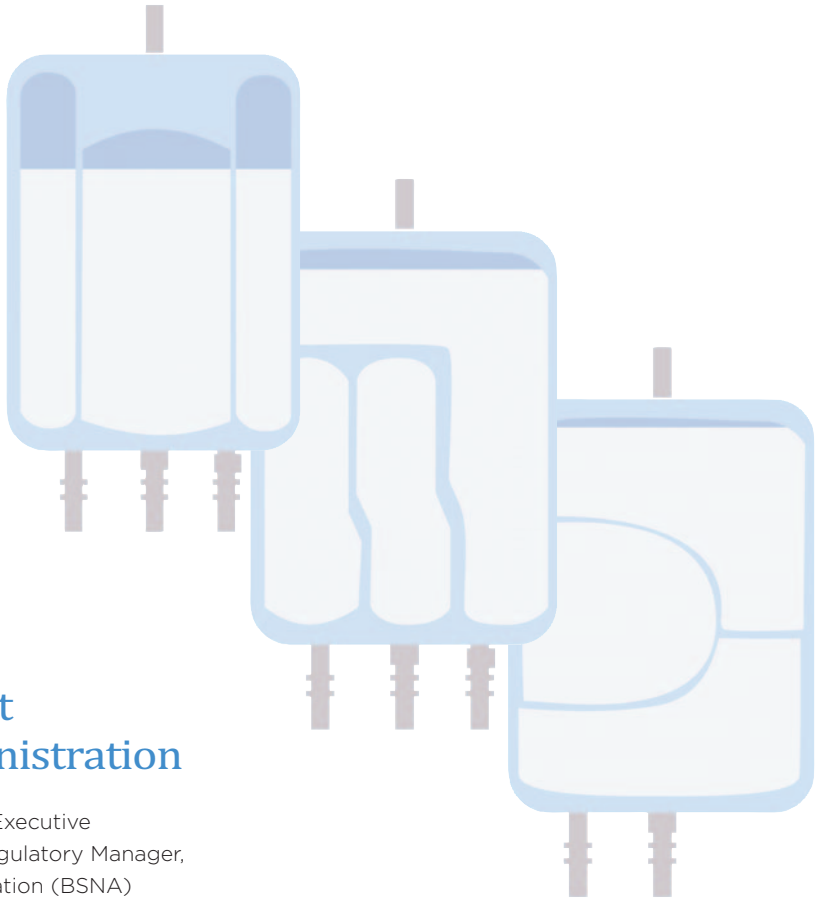

Parenteral Nutrition

Ensuring quality throughout preparation, supply & administration

Amber Knight, Medical Nutrition Executive
& **Naomi Brown**, Scientific and Regulatory Manager,
British Specialist Nutrition Association (BSNA)

The process of preparing Parenteral Nutrition (PN) is a complex one involving multiple, carefully controlled and regulated steps. These steps are essential to provide quality assurance of products during production, processing, delivery and administration.

PN is the provision of nutrition intravenously; when nutrients such as protein, carbohydrates, fats, electrolytes, vitamins and other trace elements are administered directly into the bloodstream, bypassing the normal digestive process of the gastrointestinal (GI) tract. It can play a vital role in preventing malnourishment and maintaining normal body function. It is recommended that healthcare professionals (HCPs) should consider PN for patients who are malnourished or at risk of malnutrition and have an inadequate or unsafe oral and/or enteral nutritional intake, or a non-functional, inaccessible or perforated GI tract.[1] PN may be used in both the home and hospital setting.

Clinically appropriate PN use is life-saving for many, helping to maintain hydration, metabolic activity and organ function when the oral route is either not viable or insufficient nutrients can be supplied to the body. As with any intravenous (IV) administered preparation, PN carries risks. To reduce these risks, manufacturers undertake a range of carefully controlled and regulated steps. Similarly, HCPs have a role in ensuring the safety and quality of products is maintained during storage and administration.

STAGE ONE: PREPARATION OF PARENTERAL NUTRITION

Regulating PN

PN is governed by pharmaceutical law (Medicines Act 1968) that relates to the creation, sale, distribution and use of such products. The Medicines and Healthcare Regulatory Authority (MHRA) is the UK body responsible for the authorisation, regulation and licensing of products and associated devices. This includes the individual components that PN is comprised of, and ready-to-use multi-chamber bags (MCBs). When PN is compounded from individual, licensed components or when licensed additions are made to a MCB, the result is an unlicensed product.

An unlicensed medicinal product is one that is manufactured without a Marketing Authorisation (MA) from the MHRA. Manufacturers of these products hold a Manufacturing Specials (MS) license issued by the MHRA and are subject to regulatory audits to maintain high quality standards and retain their license.

Stability & quality considerations

Aseptic techniques and processes are used during the manufacturing of PN to prevent contamination of pathogenic organisms by the manufacturing personnel, environment or equipment. Such techniques include:

- Sterile production facilities
- Sterile clothing
- Non-touch technique
- Environmental air filtration
- Automated compounding devices
- Vacuum filled chambers
- Gravity fill in appropriate sterile cabinets or isolations.

> Aseptic processing is the manipulation of sterile starting materials and components in such a way that they remain sterile and uncontaminated whilst being prepared for presentation in a form suitable for administration to patients.

PN is a complex mixture that can contain over fifty separate chemical entities. The complexity of such admixtures requires the careful consideration of factors that have the potential to affect stability. Key techniques are used to prevent destabilisation and slow down chemical reactions; manufacturers carefully consider the mixing sequence and maximum levels of each component to ensure stability and quality of the final product.

The bags in which PN is filled into influence the stability and quality of the final product. Many PN components are oxygen sensitive, oxygen barrier bags are frequently used to mitigate destabilisation via chemical reactions of PN components with oxygen in the air. MCBs provide a physical barrier between components to prevent adverse chemical reactions prior to manipulation, i.e. mixing and addition of vitamins and trace elements, offering a longer shelf life compared to compounded products. MCBs do not require refrigeration prior to aseptic manipulation, which includes but is not limited to activation and supplementation of electrolytes, vitamins and trace elements. Conversely, compounded PN is almost always refrigerated as part of an end-to-end cold chain process to slow down chemical reactions and ensure stability. Good Distribution Practice (GDP) ensures quality and integrity is maintained throughout the supply chain.

> Good Distribution Practice (GDP) describes the minimum standards that a wholesale distributor must meet to ensure that the quality and integrity of medicines is maintained throughout the supply chain.
> Compliance with GDP ensures that:
> - Medicines in the supply chain are authorised in accordance with European Union (EU) legislation;
> - Medicines are stored in the right conditions at all times, including during transportation;
> - Contamination by or of other products is avoided;
> - An adequate turnover of stored medicines takes place;
> - The right products reach the right addressee within a satisfactory time period, and;
> - This also includes tracing systems.

MCBs must undergo extensive stability and sterility testing before release into the market. For unlicensed products (compounded PN or compounded additions to MCBs), it is the responsibility of the compounding facility to ensure that adequate quality control measures are in place and carried out. The extent of local stability and sterility testing is dependent on the compounding unit and the shelf life of the product. Stability testing protocols may be included as part of regular MHRA audits.

Different resources are available to support stability testing and assessment of compounded PN. These include:

1. The NHS Pharmaceutical Quality Assurance Committee's Standard Protocol for Derivation and Assessment of Stability: Part 4 – Parenteral Nutrition.[2]
2. MHRA Guidance for Specials Manufacturers.[3]

"PN is a complex mixture that can contain over fifty separate chemical entities. The complexity of such admixtures requires the careful consideration of factors that have the potential to affect stability."

STAGE TWO: ADMINISTRATION OF PARENTERAL NUTRITION

Screening for nutritional status and assessment

All patients should be screened to allow early identification of malnutrition or risk of malnutrition.[1] There are multiple screening tools available, including the 'Malnutrition Universal Screening Tool' ('MUST').[4] It is recommended that HCPs use a validated screening tool recommended by their hospital.

Prior to commencing PN, it is essential that a member of the nutrition team carries out a detailed examination of metabolic, nutritional or functional variables. This detailed assessment ensures that an appropriate care plan, which considers optimum artificial feeding techniques, is devised for a patient.

Prescription

PN is a prescription-only medicine (POM) and must be legally prescribed by an appropriately qualified prescriber. The prescription must be clear, legible, complete and not open to interpretation; it must contain sufficient information relating to dose, duration and route of administration.

Administration

PN should only be administered by a suitably qualified professional. There are a number of considerations when providing PN:

- **Route of administration:** when administering PN there two different routes through which intravenous nutrition can be delivered: central and peripheral
- **Filtering:** PN delivered via an administration set that incorporates a filter is advocated
- **Light protection:** clinical data advocates covering PN bags with light protection at all times. The European Medicines Agency (EMA) has recently recommend that when delivering PN to neonates and children below 2 years of age, the PN bag and administration set should be protected from light exposure until administration is complete[5]
- **Care of lines:** Vascular access devices (lines) used for parenteral nutrition should be cared for in the same way as those used for other intravenous medication; handled in a clean way, using aseptic technique and according to locally approved protocols.

Monitoring

Ongoing monitoring of a new patient on PN is essential to minimise complications and to ensure the appropriate amount of electrolytes, nutrition and fluid are provided by the PN. As a patient's condition stabilises and improves, they may cease PN treatment or transition to other forms of nutritional therapy. The guidance for review of patients receiving PN varies depending on their condition and location of treatment.

Healthcare professionals should refer to '*NICE Guidelines: Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition (Clinical guideline CG32)*'.[1]

The BSNA have recently produced an animation and accompanying information sheet on *Parenteral Nutrition: ensuring high quality throughout preparation, supply and administration* – please visit the BSNA website: www.bsna.co.uk

References: 1. NICE (2006), Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition [CG32]. Accessed online: www.nice.org.uk/guidance/cg32 (Jan 2020). **2.** NHS Pharmaceutical Quality Assurance Committee (2016). A standard protocol for derivation and assessment of stability: Part 4 – Parenteral Nutrition. National Health Service. Accessed online: www.sps.nhs.uk/wp-content/uploads/2017/06/NHS-PQAC-YCD-Std-Protocol-Chemical-Stability-Part-4-Parenteral-Nutrition-1st-Edn-2016.pdf (9 Jun 2020). **3.** Medicines and Healthcare products Regulatory Agency (2015). MHRA Guidance for Specials manufacturers. MHRA. Acessed online: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/400232/Guidance_for__specials__manufacturers.pdf (Aug 2020). **4.** Malnutrition Advisory Group (MAG) (2003). Malnutrition Universal Screening Tool. Redditch: British Association of Parenteral and Enteral Nutrition (BAPEN). Accessed online: www.bapen.org.uk/pdfs/must/must_full.pdf (Jan 2020). **5.** Pharmacovigilance Risk Assessment Committee (PRAC) (2019). PRAC recommendations on signals. Amsterdam: European Medicines Agency. Accessed online: www.ema.europa.eu/en/documents/prac-recommendation/prac-recommendations-signals-adopted-8-11-july-2019-prac-meeting_en.pdf (18 Feb 2020).

The British Specialist Nutrition Association (BSNA) is the trade association which represents high quality specialist nutritional and aseptically compounded products. Our members produce infant formula, follow-on formula, young child formula, complementary weaning foods, medical foods for diagnosed disorders and medical conditions, parenteral nutrition and provide aseptic compounding services for chemotherapy, antibiotics and Central Intravenous Additive Services (CIVAS).

British Specialist Nutrition Association Ltd
bsna