Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Baxter Healthcare Ltd.	Guideline	006	006	Recommendation 1.4: Agree with content, no specific comments	Thank you for your comment.
Baxter Healthcare Ltd.	Guideline	006	014	If starting parenteral nutrition more than 4 days after birth, should consideration be given to the risk of re-feeding syndrome particularly in IUGR babies with a lower upper limit for glucose (Refeeding syndrome in very-low-birth-weight intrauterine growth-restricted neonates, J.Ross et al, J Perinatol, 2013)	Thank you for your comment. The evidence review did not identify re-feeding syndrome as a reported outcome and the guideline committee decided that re-feeding syndrome is an uncommon event in this group and therefore did not specifically mention this. The cited publication was not included because it did not include a comparison of differing amounts of constituents. It therefore did not match the protocol.
Baxter Healthcare Ltd.	Guideline	006	016	Amino acids: Agree with content, no specific comments.	Thank you for your comment.
Baxter Healthcare Ltd.	Guideline	007	021	Lipid and lipid emulsions: Baxter strongly disagree with the recommendation 'For preterm and term babies with parenteral nutrition associated liver disease, consider giving fish-oil containing lipid emulsions'.The Cochrane citations presented in the evidence review does not support the recommendation that fish-oil containing lipid emulsions should be considered in preference to other lipid blends in babies with nutrition-associated liver disease. The Cochrane review did not undertake a distinct review of fish-oil containing lipid blends compared to non-fish oil containing blends. The aggregation of studies with both 100% soy and lipid	Thank you for your comment. This recommendation is specific to babies with parenteral nutrition-associated liver disease and therefore the evidence that informed this recommendation was taken from the subgroup of babies with cholestasis presented in the Cochrane review. All of this evidence compared either pure fish oil or a composite lipid emulsion containing fish oil against pure soybean lipid emulsion. The committee decided that it is unclear whether the benefit is due to the fish oil, or to including lipids other than soybean. They recognised that the evidence overall was not compelling but that the possible benefits would outweigh the harms of parenteral nutrition associated liver disease. The recommendation has been amended to 'For preterm and term babies with parenteral

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				blends in the control group may have influenced the result.In the analysis comparing fish oil lipid blend with an olive containing lipid blend there were no statistically significant differences in PNALD outcome measures (Najm 2017; Savini 2013).The low-quality evidence cited in the committee's discussion of the evidence used to support this recommendation appears to be from a variety of individual studies included in the Cochrane review although without citation it is not possible to comment specifically. From the description it would seem some using pure-fish oil lipid emulsion not a fish oil containing lipid blend, the comparator for all groups was 100% soy-based lipid emulsion. The evidence does not support the weight gain, head growth, PNALD resolution and mortality benefits of fish oil containing lipid emulsions over olive oil/soy lipid emulsions (Deshpande 2009; Savini 2013; Najm 2017; Deshpande 2014) and therefore the cost effectiveness statement could also be applied to olive/soy lipid emulsions.	nutrition-associated liver disease, consider giving a composite lipid emulsion rather than a pure soybean lipid emulsion. The rationale and impact section has been amended to reflect this change.
Baxter Healthcare Ltd.	Guideline	008	010	Ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids: Agree with content in general. Baxter are aware of some centres who achieve a fixed carbohydrate to lipid ratio through the use of 3in1 neonatal formulations.	Thank you for your comment.
Baxter Healthcare Ltd.	Guideline	008	020	Baxter believes that the evidence presented in the guideline document does not support the recommendation of an acetate free solution but does	Thank you for your comment. After further consideration the committee have removed this recommendation from the

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				support the consideration of a balanced solution.Baxter are concerned that this recommendation may result in the need to reformulate a significant number of existing compounded neonatal PN formulations. The conventional interpretation of cited evidence is that neonatal formulations should contain a balance of acetate and chloride salts in order to facilitate the provision of sodium, potassium and calcium.Baxter is the marketing authorisation holder for Numeta G13%E Preterm, a UK licensed neonatal PN formulation, which contains both chloride and acetate salts. Baxter are concerned that this recommendation as written will be used as justification not to use a licensed product.	guideline. Additional text has been added to the rationale and impact section to explain this change.
Baxter Healthcare Ltd.	Guideline	010	005	Fat- and water-soluble vitamins can also be included in 3in1 (containing lipid, glucose and amino acids) admixtures.	Thank you for your comment. The committee agrees that there are a range of products available that are applicable to the guideline The committee did not make a recommendation endorsing any particular formulation or product.
Baxter Healthcare Ltd.	Guideline	010	019	Recommendation 1.6Baxter would recommend that reference to MHRA document 'The supply of unlicensed medicinal products ("specials")' (MHRA guidance note 14, 2014) be included in this section.'An unlicensed medicinal product may only be supplied in order to meet the special needs of an individual patient. An unlicensed medicinal product should not be supplied where an equivalent licensed medicinal product can meet the special needs of the	Thank you for your comment. In such cases there is a standard footnote that is added to NICE guidelines. This has been added to the relevant recommendation. It states: 'At the time of publication (February 2020), not all parenteral nutrition formulations have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.'

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				patient.'This section should include some comment from the rationale for standardisation on pages 37/38. If this section is supporting batch manufacture to improve efficiency and product quality, then this should be stated with the rationale that batch production will allow for a wider range of end product testing and sterility assurance. A lower acquisition cost for a standard bag is not justification for its use if there is no product quality assurance gain.	
Baxter Healthcare Ltd.	Guideline	014	017	Section 1.6 Service DesignBaxter would expect there to be a statement on responsibility for infusion safety and regular reassessment of parenteral nutrition associated infusion risks to be included in this section.Baxter believe that mention of governance and responsibility for pharmaceutical quality of purchased parenteral nutrition solutions should be included in this section and that pharmacy should be responsible for this.	Thank you for your comment. The committee agrees that this is important and have therefore highlighted in recommendation 1.9.3 that the multidisciplinary team should be responsible for governance including agreeing protocol and policies, ensuring that policies and protocols are followed and audited and that clinical outcomes are monitored. The committee agreed that there are many facets of such policies and protocols to minimise risks and ensure the safety of babies receiving parenteral nutrition. A comprehensive list of the content of such policies and protocols was outside the scope of this guideline and would depend on local and regional service provision.
Baxter Healthcare Ltd.	Guideline	016	004	Baxter would like the definition of aseptically compounded and terminally sterilised to be added to the terms used in this guideline to inform clarity for additional text in section 1.6	Thank you for your comment. The 'terms used in this guideline' is a section that provides definitions of any particular words or phrases that are used in recommendations and which may not be clear to every reader. The terms 'aseptically compounded' and 'terminally sterilised' do not appear in the

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					recommendations. Therefore we have not added them to this section.
Baxter Healthcare Ltd.	Guideline	016	005	Individualised parenteral nutrition formulations definition requires revision to include the concept of 3in1 solutions which are also used in this patient group.	Thank you for your comment. These definitions are related to the concept of 'individualised parenteral nutrition' rather than how they would be administered. There would always be an aqueous and a lipid component regardless of whether they are in one bag or in different bags. The defining characteristic of an individualised bag is that it is tailor made for each baby rather than standardised. It was therefore decided not to revise this definition.
Baxter Healthcare Ltd.	Guideline	017	003	Standardised parenteral nutrition formulations definition requires revision to include the concept of 3in1 solutions which are also used in this patient group.	Thank you for your comment. These definitions are related to the concept of standardised parenteral nutrition formulations' rather than how they would be administered. There would always be an aqueous and a lipid component regardless of whether they are in one bag or in different bags. The defining characteristic of a standardised bag is that it is one formulation that can be used for most babies in the majority of cases rather than a specific tailor made version that is prescribed for each baby. It was therefore decided not to revise this definition.
Baxter Healthcare Ltd.	Guideline	020	023	A licensed parenteral nutrition solution is available on the UK market suitable for initial parenteral nutrition support via a central line. This product has a shelf life of 18 months from manufacture and does not require refrigerated storage. This solution may reduce the costs of early provision through timely solution availability and short dated compounded stock wastage reduction.	Thank you for your comment. The committee was aware that there are a number of products available with differing length of shelf life. They did not endorse any specific product.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Baxter Healthcare Ltd.	Guideline	022	013	As per recommendation from MHRA and EMA PRAC all PN solutions in children under 2 should be protected from light during administration, both bag and set.	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.
Baxter Healthcare Ltd.	Guideline	022	028	Filtration: The use of a terminal filter is recommended for compounded parenteral nutrition solutions due to the inherent concerns regarding their stability. The recent ESPGHAN guidelines on parenteral nutrition recommend the use of a filter during administration. C. Hartman et al. / Clinical Nutrition 37 (2018) 2418-2429. Based on published evidence, Ball PA. Intravenous in-line filters: filtering the evidence. Curr Opin Clin NutrMetab Care 2003;6:319-25.In line with ESPGHAN guidelines the recommendation to use a filter during administration is included in the Summary of Product Characteristics for Primene, an amino acid solution used in neonatal parenteral nutrition solutions.	Thank you for your comment. The committee decided that there was too much uncertainty around the benefits and risks related to terminal filters as well as additional costs to make a recommendation on using filters. Why they decided not to make a recommendation is described in the related rationale and impact section. The cited reference would not have been included as evidence because it is narrative review.
Baxter Healthcare Ltd.	Standard Question 1	N/A	N/A	Q. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.A. Baxter healthcare have no particular concerns regarding this question.	Thank you for your response.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Baxter Healthcare Ltd.	Standard Question 2	N/A	N/A	Q. Would implementation of any of the draft recommendations have significant cost implications?A. The guidance for light protection, both bag, syringe and sets will have significant cost implications, however in view of the EMA recommendations this cannot be removed from the guidance. The use of 3in1 parenteral nutrition solutions has been shown to reduce the consumables cost when compared to separate aqueous and lipid.	Thank you for your response. The committee agreed that there may be additional acquisition costs related to light protection but that this would be outweighed by the benefits of safer provision and that current medical legislation would need to be adhered to. The committee could not comment on specific individual products in relation to potential savings.
Baxter Healthcare Ltd.	Standard Question 3	N/A	N/A	Q. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)A. Baxter are aware of several centres using the licensed NumetaG13%E Preterm bag as contingency stock and starter regimen to reduce the reliance on compounding aseptic capacity and mitigating risk of expired short dated stock.	Thank you for your response. The committee would hope that centres order appropriate stock for their needs. However, this was outside the scope of the guideline and the committee could therefore not comment on this.
British Dietetic Association Neonatal Sub-Group	Guideline	003 - 004	007 - 011 001	We are concerned that the terminology 'sufficient progress' 'sufficient enteral feeding' needs to be quantifiable or have lower limits set to avoid ambiguity or run the risk of PN not being started early enough or avoided.	Thank you for your comment. The committee could not define what constitutes sufficient enteral feeding as the evidence on enteral nutrition was not reviewed as part of this guideline. This information has been added to the rationale and impact section for indications for neonatal parenteral nutrition.
British Dietetic Association Neonatal Sub-Group	Guideline	003 - 004	014 008	We are concerned that HIE/Cooled term infants haven't been included, nor is there a quantifiable lower limit of intake needed to avoid use of PN. Eg. 'If by day 5 <100mls/kg enteral intake has not been	Thank you for your comment. The list of examples is intended to be illustrative rather than exhaustive. The committee decided not to include a recommendation related to a quantifiable lower limit of intake needed to avoid parenteral nutrition. Avoidance of parenteral nutrition would fall

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				achieved then PN needs to be commenced' would be preferable.	into the remit of enteral rather than parenteral nutrition and evidence on enteral nutrition was not reviewed as part of this guideline. They also thought that specifying a specific quantity of enteral feeding may be misleading since reaching a specific volume may not by synonymous with making sufficient progress at this volume.
British Dietetic Association Neonatal Sub-Group	Guideline	004	015	I am concerned that suggesting peripheral PN as a short-term option without giving any further information on maximum osmolarity could be hazardous if the guideline is used by staff inexperienced with its use.	Thank you for your comment. The committee were not able to provide a recommendation on maximum osmolarity because the included study provided a wide range of concentrations. They were also concerned there was only one study and that the evidence had high levels of uncertainty (mainly due to imprecision in the measurement of effect). They were therefore not confident to provide a specific level of concentration based on this. Details of the committee's discussion on this are provided in the rationale and impact section of the guideline as well as the committee discussion of the evidence section of evidence review B. Additionally, the committee expect that individual units have appropriate training and information for staff involved in the care of babies receiving parenteral nutrition, and also they could not make recommendations on staff training as this was not in the scope.
British Dietetic Association Neonatal Sub-Group	Guideline	004	021	Please consider adding 'If concentration of PN solution is appropriate for use in a peripheral line.	Thank you for your comment. Whilst the committee agreed that the concentration would need to be appropriate for a peripheral line (and evidence report B addresses this), they decided that the evidence was not strong enough to make a statement about what the specific maximum concentration should be.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					They therefore did not want to use the suggested wording of 'appropriate' in the recommendation because it is not possible to specify what this would translate to in relation to osmolarity or other measures of concentration. The rationale and impact section for this recommendation has been revised to include a more detailed explanation of why the committee decided not to include a reference to the concentration of parenteral nutrition in the recommendation.
British Dietetic Association Neonatal Sub-Group	Guideline	005	011	We are concerned that some of the comments that were received from the wider Neonatal Dietitians Group showed concern about the differences between ESPGHAN and this draft guideline. This implies that it isn't apparent in the document as to how ranges have been derived without close scrutiny of the extensive references.On the first day of life of premature neonates, at least 45-55 kcal/kg/dayshould be provided to meet minimal energy requirements (strong recommendation) - ESPGHAN Guidance	Thank you for your comment. The committee decided based on the evidence and consensus that the wider range of 40-60 kcal/kg/day (which includes the ESPGHAN range) would be more appropriate since it provides greater flexibility to tailor energy provision to babies who may need a bit more or less energy. They also noted that the energy range needs to be consistent with other recommendations once they are converted into kcal/kg/day from the amino acid, glucose and lipid ranges. They therefore agreed that no change was required.
British Dietetic Association Neonatal Sub-Group	Guideline	005	015	Table 2.3 Energy requirements (kcal/kg/day) for parenteral nutrition in different phases of disease (ESPGHAN) for pre term.2016 Recovery phase (90-120) 2016 Acute phase (45-55)* * recommended energy intake during the first day of life	Thank you for your comment. The committee decided based on the evidence and consensus that the wider ranges of 40-60 kcal/kg/day and 75-120 kcal/kg/day (which include the ESPGHAN ranges) would be more appropriate since they provide greater flexibility to tailor the energy provision to babies who may need a bit more or less energy. They also noted that the energy range needs to be consistent with other recommendations once they are converted into kcal/kg/day

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					from the amino acid, glucose and lipid ranges. They therefore concluded that no change was required.
British Dietetic Association Neonatal Sub-Group	Guideline	006	002	Maybe use acute and recovery phase energy recommendations from ESPGHAN.	Thank you for your comment. The committee decided to divide this into starting and maintenance ranges to be internally consistent with the recommendations on glucose, amino acid and lipid ranges which together would result in these kcal/kg/day ranges. Therefore this was not divided into acute and recovery phase.
British Dietetic Association Neonatal Sub-Group	Guideline	006	015	Recommended parenteral glucose supply in (pre)term newborns in mg/kg per min (g/kg per day) (LoE 2+, RG B, conditional recommendation)Start day 1 preterm newborn with 4-8 (5.8-11.5). Increase gradually over 2-3days to target 8-10 (11.5-14.4) with min 4 (5.8); max 12 (17.3).Start day 1 term newborn with 2.5-5 (3.6-7.2). Increase gradually over 2-3days to target 5-10 (7.2-14.4) withmin 2.5 (3.6); max 12 (17.3).ESPGHAN PN Glucose guidance.	Thank you for your comment. The recommendations made within this guideline fall within the ranges of the available evidence. The ESPGHAN guideline does not cite any specific evidence for their values. Therefore, the recommendations in this guideline may not match ESPGHAN. Reasons why the committee recommended these ranges are provided in the related rationale and impact section of the guideline as well as in the committee discussion of the evidence section of evidence review D1 - glucose.
British Dietetic Association Neonatal Sub-Group	Guideline	007	001 - 005	Start at 1.5g/kg from day 1 of life for prem.Aim for 2.5-3.5g/kg AA from day 2 (ESPGHAN)Not more than 3.5g/kg unless part of clinical trials.	Thank you for your comment. For preterm babies the values 3 to 4 g/kg/day were based on available evidence. The maximal intake in the studies was 4.0 g/kg/day. There is a detailed discussion of the reasoning for this upper limit in the rationale and impact section. The committee reviewed their rationale and concluded that the reason for this maximal limit was comprehensively covered. They therefore concluded that no change was required.
British Dietetic Association	Guideline	008	009	Non-protein intakes >65 kcal/kg/d (ESPGHAN)	Thank you for your comment. The NICE guideline methodology is not identical to that of the ESPGHAN

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Neonatal Sub-Group					guidelines and the committees differ; as such the recommendations made do not necessarily match. However, if the amount of non-nitrogen energy is calculated (from recommendations 1.3 on total energy and 1.5.6) at either the upper or lower level of the recommendation, the value can be lower or higher depending on which end of the ratio range is used (between 50 to 90 kcal/kg/day). As such a lot of this range is above 65 kcal/kg/day which would be consistent with ESPGHAN. The committee preferred the flexibility of a wider range so that the nutritional composition could be used in a number of different standardised formulations as well as tailored to individual babies if bespoke parenteral nutrition is needed.
British Dietetic Association Neonatal Sub-Group	Guideline	011	009	It would be helpful if tables or algorithms for ease of use could be considered.	Thank you for your comment. The guideline already includes algorithms as separate files and these will be signposted and easier to navigate to, in the final web version of the guideline (this also contains tables). This algorithm is separated into an algorithm for preterm and another for term babies. There are additional tables with illustrative examples of standardised formulations (using the dosages given in all recommendations related to the constituents of parenteral nutrition) in appendix M of Evidence review E - standardised neonatal parenteral nutrition formulations.
British Dietetic Association Neonatal Sub-Group	Guideline	015	018	We are concerned that this section should include 'discussions if patient needs home PN and training and team that will manage the home PN' when long term PN is likely.	Thank you for your comment. Home parenteral nutrition is a specialist topic which is not covered in the scope of this guideline. The committee were therefore unable to comment on this.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

British Dietetic Association Neonatal Sub-Group	Guideline	043	017	We are concerned that this will be challenging to implement. 4 out of 5 responses to the BDA Neonatal Subgroup Committee stated that the individual dietitian didn't have any involvement with their units PN. If a Network or unit don't have a neonatal pharmacist and dietitian who could be consulted about PN, there will be a cost and manpower implication to provide this level of service within trusts and Networks.	Thank you for your comment. As stated in recommendation 1.9.3 the multidisciplinary team's responsibilities would be both in the area of governance and protocols, as well as in supporting delivery of parenteral nutrition. Once such policies and protocols are in place it would most likely not mean that the dietitian would have frequent involvement at the local level. However, the committee agreed that a dietitian has an important role in ensuring safe provision of neonatal parenteral nutrition and that the benefits of this role might be expected to outweigh implementation costs.
British Specialist Nutrition Association	Guideline	007	022	Amend "…consider giving fish oil-containing lipid emulsions." to "…recommend giving composite lipid emulsions with or without fish oil in preference to pure soybean lipid emulsions." This is in line with the ESPHAGEN guidelines on nutrition in liver disease.	Thank you for your comment. The recommendation has been changed to "For preterm and term babies with parenteral nutrition-associated liver disease, consider giving a composite lipid emulsion rather than a pure soybean lipid emulsion.". The rationale and impact section has been amended to reflect this change.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Algorithm	General	General	The algorithm is helpful but we are concerned that it is a little lengthy. Did the committee consider presenting the recommendations by day of PN? This would probably be more practical and useful for the clinical setting.It would be helpful to stress that this is designed for infants <28 days of age. Clarity in the 'Constituents of neonatal parenteral nutrition' regarding the target for energy would prevent misinterpretation.	Thank you for your comment. The algorithm has been split into two algorithms, one for preterm babies and one for term babies, to minimise the amount of information presented in one document. The heading in the bottom corner of each page has been amended to clarify the population the algorithm covers. The algorithm has been amended to present the starting range for the first day of NPN, information about increasing NPN and maintenance range for NPN in one table to make it clear that constituents should be increased over the first 4 days, not stay within the starting range. Other minor amendments have been

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					made to the algorithm for clarity and to reflect changes made to the recommendations in response to stakeholder comments.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Evidence review documents	General	General	Reference numbers in clinical evidence statements would be helpful	Thank you for your comment. It is not NICE style to provide references to studies in the evidence statements (see examples in Box 6.4 in Developing NICE guidelines: the manual). All references are listed after the 'committee discussion of the evidence' section in the evidence reviews. We have therefore not added references to these statements.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	004	004 - 008	Did the committee consider the results of the PEPaNIC study (Fivez, 2016) in the recommendations regarding when to start PN in a critically ill term neonate?	Thank you for your comment. The pre-planned subgroup analysis of critically ill neonates included in the PEPaNIC trial (van Puffelen 2018) has been added to evidence review A2. The committee have considered this evidence but agreed not to make a separate recommendation for critically ill term babies. The explanation for this decision has been added to the rationale and impact section for timing of starting parenteral nutrition (as well as the related 'committee's discussion of the evidence' section of evidence review A2).
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	005	006	The MHRA and European Medicines Agency state that you 'should' rather than 'consider' protecting the syringe and infusion set of both amino acid and lipid portion of PN from light (new recommendation Sept 2019).	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	005	011 - 016	Please could the committee provide clarification in the document as to whether the recommendations are non-nitrogen or total calories, whereas the recommendation should be reducing PN as a whole	Thank you for your comment. The ranges provided in recommendation 1.3.1 are total calories because it refers to babies 'who need total parenteral nutrition'. Recommendation 1.3.2 refers to babies who receive enteral feeds and therefore the energy from parenteral nutrition should be reduced as enteral feeds increase. The committee did not specify how this reduction should be made, but provided other recommendations about ratios of macronutrients and that they should be maintained (recommendations 1.5.6 and 1.5.7) when parenteral nutrition is altered.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	005	017 - 019	We are concerned that this recommendation implies reducing energy in isolation which is not possible.	Thank you for your comment. The committee agree that energy is sourced from the macronutrients provided. However, the resulting kcal/kg/day would usually be referred to as 'energy'. The committee decided that this would generally be understood and did not make a change to the wording of this recommendation.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	006 - 007	009 - 012	Current standard formulations may provide amino acids and glucose in excess of the recommendations and therefore reformulation costs will need to be considered.	Thank you for your comment. The recommendations in this guideline are based on the best available evidence, and provide a range of potentially relevant concentrations which can be used in standardised formulations, regardless of whether or not they match current formulations. Where appropriate, the committee have considered economic evidence. However, providing nutritional care which ensures optimum current and later developmental outcome for the baby is the key consideration. This consideration of outcomes for the baby determines whether or not a formulation is cost

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					effective rather than matching recommendations to current formulations so that no reformulation is needed.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline/Algorithm	006	009 - 015 and algorithm	Constituents of neonatal PN box in algorithm – glucose. This recommendation is not consistent with the guideline document regarding days to increase glucose – the algorithm is more prescriptive. Waiting to increase glucose to day 4 may be a challenging change in practice.	Thank you for your comment. The committee agreed that the algorithm could be misconstrued in this way and have revised this to highlight that the increase should be gradual rather than wait until day 4. This is then consistent with the recommendation.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	007	020	More clarity for the maintenance dose after starting from day 4 onwards as inconsistent with line 18 - presume this is starting range?	Thank you for your comment. This has been corrected because it was meant to be the maintenance dose of babies starting before 4 days after birth (3 to 4 g/kg/day).
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	007	021	We are concerned that the guideline on lipid does not comment on EFA deficiency. It would be helpful to include the minimum volume of lipid emulsion required to meet EFA requirements based on lipid source.	Thank you for your comment. The rationale and impact section for the set of lipid recommendations comments on why the committee recommended to start low and incrementally increase to a maintenance range citing possible reduced risks of retinopathy and hypertriglyceridaemia. Therefore, since it is incremented, a minimum dose would not be helpful. The doses given were informed by the evidence reviewed. The committee discussed the importance of essential fatty acid (EFA) deficiency for preterm and term babies, which can happen especially where lipids are withheld for more than 2-3 days. However, while the minimum amount of a soy only lipid

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					emulsion is well established, they agreed that the evidence for mixed lipid emulsions is more difficult to interpret. Based on their knowledge the committee noted that there is evidence to suggest that preterm babies given fish oil containing lipid emulsions, which may not meet daily requirements of omega-6 fatty acid linoleic acid and omega-3 fatty acid alpha-linoleic acid, do not develop EFA deficiency. This is possibly due to the fact that they contain preformed long-chain polyunsaturated fatty acid. The committee decided that it is therefore not possible, at the moment, to give minimum amounts required of the different mixed lipid emulsions that are currently on the market. We have added a comment related to essential fatty acid deficiency to the rationale and impact section of the guideline.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline and throughout evidence review D4	007	021	Do the committee think that we should use the phrase IFALD rather than PNALD?	Thank you for your comment. As the focus of this guideline is parenteral nutrition and this section is about intravenous lipid emulsions, the committee decided that it is more appropriate to use the term parenteral nutrition associated liver disease (PNALD), as intestinal failure associated liver disease (IFALD) is a broader term that includes causes other than parenteral nutrition.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and	Guideline/Algorithm	011	009	We acknowledge that this guideline only includes the first 28 days of life, however some acknowledgement of fat-soluble vitamin and trace element monitoring at this point would be helpful.	Thank you for your comment. The monitoring of vitamin and trace elements was outside the scope of the guideline and so the evidence in these areas has not been appraised. Therefore the committee was not able to comment on the monitoring of these constituents either within the 28 days' timeframe of the guideline or at the end of it.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

North Middlesex NHSFT					
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	012	014	Checking triglyceride levels daily whilst increasing lipid would be a significant change in practice for some units, increasing costs and frequency of blood tests.	Thank you for your comment. The committee decided that triglycerides should be monitored at these frequencies to improve consistency across clinical practice and ensure the safety of the baby. The committee acknowledged that there is variability in practice but that some units already monitor triglycerides whereas others do not. Their recommendations on frequency are meant to indicate the minimum intervals of monitoring so that the amount of lipid intake can be adjusted if babies do not tolerate the recommended levels that are provided in recommendation 1.5.4. Given the possible harms the committee felt strongly that this is needed for safety reasons. However, the factors identified in recommendation 1.7.1 (for example retrieving as much information as possible from each blood sample and coordinating the timing of blood tests to minimise the number of blood samples needed) would ensure that the baby does not receive too many tests but a sufficient number to balance benefits and harms of testing.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline/Algorithm	013	011	Could the committee give more specific advice on which liver function tests should be monitored eg. GGT is not included in the LFT order set at all hospitals. A broad recommendation about when to contact a tertiary liver centre would be helpful (because most infants would benefit from earlier referral).	Thank you for your comment. The focus of the evidence review related to these recommendations was the frequency of testing rather than which tests to use, how to interpret them or the management thereafter. However, the committee noted also that these measurements could be difficult to interpret and have acknowledged this in the related rationale and impact section and in the discussion section of evidence review F - monitoring neonatal parenteral nutrition.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	013	013	Could this section be entitled 'Weaning and stopping PN' as the points are relevant to both? Infants are particularly at risk of undernutrition during the weaning period from PN to EN (Vaidya et al). From parenteral to enteral nutrition: a nutrition-based approach for evaluating postnatal growth failure in preterm infants. JPEN 2014 May;38(4):489-97) The guideline should acknowledge this to alert healthcare professionals of this risk, particularly during prolonged PN weaning.	Thank you for your comment. The committee decided that the focus of the evidence review that led to these recommendations should be about when to stop rather than the process of weaning. They did this because the weaning process is more related to enteral feeding rather than parenteral nutrition. Therefore, they decided to give this section the title 'stopping' and agreed that adding 'weaning' to this title would create the wrong expectation about the content of this section. The publication that is referred to would therefore not have been included because it addresses weaning rather than stopping.
Combined Response: Chelsea & Westminster, Great Ormond Street, UCL and North Middlesex NHSFT	Guideline	014	001 - 005	Recognition that these volumes do not necessarily meet enteral nutritional requirements (depending on volume and type of milk) would be helpful.	Thank you for your comment. Enteral requirements and enteral feeding is outside the scope of this guideline. The committee therefore could not comment on this.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	003	005	The guideline states "For preterm babies born before 31+0 weeks, start neonatal parenteral nutrition." The current practice in our unit (and in many others) takes into account other risk factors including babies' weights. BAPM recommends giving TPN for babies up to and including 29 weeks and 6 days, and for all infants weighing < 1250 g at birth. Providing TPN for all babies < 31 weeks' gestation would place a significant strain on resources in some units and	Thank you for your comment. The committee agreed that including more than 1 parameter (gestational age and birthweight) may lead to uncertainty in deciding when to start parenteral nutrition so agreed to make a recommendation solely on the basis of gestational age (see the rationale and impact section for indications for neonatal parenteral nutrition in the guideline document). The committee agreed a gestational age of 31+0 weeks as a cut-off as babies born before this point are unlikely to tolerate sufficient enteral feeding due to immaturity of the gastrointestinal tract (see also

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				would require additional Pharmacy and Aseptics support.	the 'committee discussion of the evidence' section in evidence report A1). With regard to additional resources, the committee recommended the use of standardised bags. This means that most babies would be on a standardised bag already and continue with standardised bags. These would be available with little pharmacy input which would only be needed for babies on bespoke bags.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	004	005	Regarding starting TPN for term babies who are NBM for 48 hours or more: risk of longline complications needs to be weighed up against sequelae of fasting. TPN may not be most appropriate decision in every case, especially in units where TPN is delivered centrally at all times.	Thank you for your comment. This recommendation does not state that parenteral nutrition should be restarted in all babies who have not had enteral feeds for 48 hours, rather PN should be restarted if enteral feeds have been stopped for 48 hours and there is no prospect of making sufficient progress within another 48 hours. Alternatively, PN should be restarted if at the point of stopping it is unlikely they will be restarted within 72 hours (an addition to this recommendation to address other stakeholders' comments). The committee decided that the risks and potential long term consequences of accumulating nutritional deficits over these time periods would outweigh the risks of line complications.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	005	006	We would suggest that the following sentence is re-worded: "Consider protecting the syringe and infusion set of both aqueous and lipid parenteral nutrition solutions from light during administration." EMA state that this is a recommendation.	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	009	013	The recent paper "*Metabolic bone disease of prematurity: Causes, recognition, prevention, treatment and long-term consequences"* (by A Chinoy, MZ Mughal and R Padidela, published in Archives of Disease in Childhood Fetal & Neonatal Edition 2019) recommends that Calcium to Phosphate ratios of 1.3:1 to 1.7:1 should be used, rather than the 0.75:1 to 1:1 stated here.	Thank you for your comment. The article to which you refer is a narrative review. Additionally, it is relevant for enteral feeding and as such it would not meet the inclusion criteria to be considered for this guideline. This means that the committee did not consider this evidence to be relevant to the context of parenteral nutrition.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	012	004	For babies who are stable on longterm TPN, we believe twice weekly gases should not be required unless changes in composition of TPN are made.	Thank you for your comment. The committee decided that twice weekly gases should be taken for safety reasons. They also recommend in 1.7.1 to coordinate the timing of blood tests to minimise the number of blood samples needed as well as to retrieve as much information as possible from the sample to strike a balance between minimising distress to the baby (and parents) and obtaining enough information to guide clinical care. The committee decided that this was therefore unlikely to mean that there would be additional tests since for example glucose will be monitored at the time when a bag is changed and tests could then be coordinated to also cover blood gases.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	012	018	The guideline has not made recommendations regarding how to amend lipids or what actions to take if triglycerides are raised, but in a unit where babies often stay on long-term TPN due to complex surgical issues, this would be a helpful addition.	Thank you for your comment. The committee decided that triglycerides should be monitored at these frequencies to improve consistency across clinical practice and ensure the safety of the baby. The focus of the review was the frequency of monitoring rather than the level at which an action should be taken or management thereafter, so the committee could not

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					comment on this. Their recommendations on frequency are meant to indicate the minimum intervals of monitoring so that the amount of lipid intake can be adjusted if babies do not tolerate the recommended levels that are provided in recommendation 1.5.4. Given the possible harms the committee felt strongly that this is needed for safety reasons.
Greater Manchester University Hospitals NHS Foundation Trust – Newborn Services	Guideline	013	007	The guideline suggests that "For preterm babies on neonatal parenteral nutrition who are 28 days or older, monitor for iron deficiency and treat if necessary." There is no recommendation to monitor iron / ferritin in term babies, and we wonder if this would be a helpful addition as non-feeding term babies can also be at risk of iron-deficiency anaemia.	Thank you for your comment. Longer term iron status monitoring for term babies who are 28 days or older is outside the scope of the guideline and so the evidence in these areas has not been appraised. Therefore, the committee was not able to comment on this. However, in this instance the committee explicitly acknowledged this in the discussion section of evidence review F - monitoring neonatal parenteral nutrition. They noted: 'For term babies who are 28 days or older, the committee could not make a recommendation on intravenous supplementation of iron in PN, because these babies were not included in the scope of the guideline. However, they noted that term babies continuing on long-term PN may need iron supplementation, and this would then have to be considered on a case-by-case basis.'
Leeds Teaching Hospitals NHS Trust	Guideline	005	015	The rationale to start patients on full requirements after 4 days of birth seems based on patient fluid requirements, and not on metabolic requirements. Using this approach it might cause metabolic decompensation, acidosis and lipaemia in premature/term babies.	Thank you for your comment. To provide a rationale for the timeframe of approximate 4 days we have revised the rationale as follows so that it makes reference to metabolic factors: 'This timeframe was primarily selected because neonatal metabolic adaptation occurs in the early days of life, enabling the baby to metabolise the nutrients delivered. In addition, fluid volume allowances are commonly increased over the first few days of

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					life and this allows increasing amounts of nutrition to be given parenterally'.
Leeds Teaching Hospitals NHS Trust	Guideline	006	013	ESPGHAN guidelines 2018 recommend a maximum of 17.3g/kg/day, having a cut off at 16g/kg/day might compromise total energy requirements	Thank you for your comment. The ESPGHAN guidelines have a target range of up to 14.4g/kg/day, but state it should not exceed 17.3g/kg/day, so the recommendation of 16g/kg/day is higher rather than lower compared to their target. The ESPGHAN guideline does not cite specific evidence related to the value of 17.3 g/kg/day. Recommendations in our guidelines fall within the ranges used in the evidence that was identified. The committee therefore agreed that this would not compromise total energy requirements.
Leeds Teaching Hospitals NHS Trust	Guideline	007	003	ESPGHAN guidelines 2018 recommend nitrogen above 3.5g/kg/day should only be administered as part of clinical trial.	Thank you for your comment. For preterm babies the values 3 to 4 g/kg/day were based on available evidence. The maximal intake in the studies was 4.0 g/kg/day. There is a detailed discussion of the reasoning for this upper limit in the rationale and impact section. The committee reviewed their rationale and concluded that the reason for this maximal limit was comprehensively covered. They therefore concluded that no change was required.
Leeds Teaching Hospitals NHS Trust	Guideline	014	002	It might be challenging to use residual PN when planning to stop it, as some manufacturers recommend to change the PN bag every 24h. Using intravenous fluids should be considered when planning to stop PN to give total volume required without having to use a small amount of PN.	Thank you for your comment. The committee agree that the total volume is important, and within the recommendation there is reference to contribution of parenteral nutrition and enteral nutrition. The committee thought that the commonly utilised approach would be to use the parenteral nutrition in the bag that is currently running but stop the parenteral nutrition when that bag is due to be changed. Whether additional intravenous fluids are needed after parenteral nutrition is stopped is outside

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					the scope of this guideline and would need to be a local clinical decision as to whether that baby needed extra intravenous water, glucose or electrolytes on top of the fluid and nutrition being absorbed enterally.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	003	013	Should necrotising enterocolitis (NEC) be included on the list of indications? Perhaps it could be added to 'critical illness such as sepsis *or necrotising enterocolitis*'	Thank you for your comment. The list of examples is intended to be illustrative rather than exhaustive. So the committee decided to focus on the most common examples.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	004	005 - 007	The 48hr in line 5 plus the additional 48hr in line 7 is too long a period to wait in these babies. We don't think that the intention is to wait 96hr, but it could be (and has been) read as this. A clearer wording would help.If the need to withhold enteral feeding is clear (e.g. diagnosis of NEC is confirmed, bowel perforation) it seems reasonable to start parenteral nutrition within 24 hours of enteral feeding being stopped and there should be consideration of starting earlier than 48 hours after cessation of enteral feeds particularly if the experience of the primary team is that recovery from that illness or procedure usually takes >48 hours.	Thank you for your comment. The recommendation has been amended to clarify that parenteral nutrition should be started (without waiting 48 hours) for babies who are unlikely to restart enteral feeds within 72 hours of stopping. The committee discussion of the evidence section in evidence report A1 has been amended to reflect this change.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	004	006	What is meant by 'sufficient' progress? This is a vague term.	Thank you for your comment. The committee could not define what constitutes sufficient enteral feeding as the evidence on enteral nutrition was not reviewed as part of this guideline. This information has been added to the rationale and impact section for indications for neonatal parenteral nutrition.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	004	010 - 011	In a term neonate this should take into account the risks of starting parenteral nutrition after hours if there is a lack of specialist knowledge available - and if on balance there is no advice available from paediatric pharmacist/gastroenterologist/dietitian/specialist nurse, it could be delayed up to 24 hours until that advice is available. There will be centres which routinely see only term babies where this would be reasonable. Need to consider that outside of NICUs there may not be highly protocolised approaches appropriate for every situation – consider the differences in fluid requirements for example between a baby post-op after malrotation surgery on triple antibiotics and IV analgesia versus a post-op complex cardiac baby on inotropes.	Thank you for your comment. The time frame specified in 1.1.6 refers to when parenteral nutrition should be started once the indications for requiring parenteral nutrition have been met, not the time frame for deciding parenteral nutrition is needed and starting it. The rationale and impact section of the guideline explains that it may take longer to decide whether parenteral nutrition is needed in term babies. The committee believe that this timeframe is based on what is both achievable and safe for the baby. To safeguard for situations where advice is not available locally the committee made recommendations on service design (recommendations 1.9.1 to 1.9.3) that specify that neonatal parenteral nutrition services should be supported by a specialist multidisciplinary team whose responsibilities (amongst others) include agreeing protocols and providing advice. This would mean that a delay would only be due to the identification of whether sufficient progress is made on enteral feeds rather than due to advice not being available.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	004	016	Considering that the recommendation 1.1.6 states that parenteral nutrition should be started as soon as possible, and within 8 hours at the latest, should they ‘delay in starting’ parenteral nutrition be quantified so that this line states to prevent delay in starting parenteral nutrition beyond 8 hours?	Thank you for your comment. The committee decided that delays should not exceed the 8 hours specified in recommendation 1.1.6, but healthcare professionals will need to consider the risks and benefits of inserting a peripheral line if it is anticipated that a central venous catheter would be inserted sooner. Further information has been added to the rationale and impact section of the guideline related to venous access to clarify this.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	004 018	014 – 021 004 - 005	Could the criteria for use of peripheral access be clarified? Should a statement around the parenteral nutrition solution being an appropriate concentration for peripheral administration be included? Was there sufficient data to specify for example 900-1400mOsm?There will be centres which strongly discourage using peripheral access for neonates outside neonatal unit, because it is best practice that all babies and children should only receive parenteral nutrition centrally to avoid extravasation and ensure good calories are provided. Advocating the use of peripheral lines in this guideline may imply in a hospital also treating infants and older children that peripheral parenteral nutrition is a reasonable option. The wording here should be chosen carefully as to whether practice could or should be different in a dedicated neonatal unit or not.We welcome the research recommendation 4 on what overall osmolality in parenteral nutrition can determine whether to administer centrally or peripherally.	Thank you for your comment. Recommendation 1.2.1 provides criteria as to when peripheral access should be used, but the recommendation has been revised to provide greater clarity. The committee did not want to use the suggested wording of 'appropriate' in the recommendation because it is not possible to specify what this would translate to in relation to osmolarity or other measures of concentration. The rationale and impact section has been revised to say 'up to 1,425 mOsm/l' rather than a range which was derived from the evidence reviewed and based on clinical experience of the committee; however, the included study had a wide range in the actual concentration they used. Additionally, the evidence was limited in quantity and was considered low quality. As such the committee did not think it was appropriate to give an exact osmolality in the recommendations. The recommendations state that peripheral lines should only be used in specific circumstances, and as such we do not agree we are advocating use in all situations. We are glad you agree the research recommendation is important.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	005	004 - 007	The MHRA and EMA have recommended that during administration to neonates and children <2 years, parenteral nutrition products containing amino acids and/or lipids should be protected from light (containers and administration sets). As such, using the word 'consider' in section 1.2.4 is not in line with these recommendations.We would suggest removing section 1.2.4 and amending section 1.2.3 to state:'Protect the neonatal parenteral nutrition bag,	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				syringe and infusion set of both aqueous and lipid parenteral nutrition solutions from light during administration. Protect the neonatal parenteral nutrition bag from light during storage.'The guideline doesn't clearly acknowledge risks to baby relate to lipid peroxides, should it?	
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	006	004 - 006	In recommending standard parenteral nutrition should be concentrated there should be some comment about the safety of using parenteral nutrition alongside fluid infusions and Y-sited electrolytes to make up the patient's requirements. Is it the opinion of NICE that 3+ infusions to provide parenteral nutrition is the most safe and appropriate way to do this, or should the fluid and electrolyte needs be incorporated into parenteral nutrition? There is a lack of evidence in this area and guidance would be very useful.	Thank you for your comment. The safety of using parenteral nutrition alongside fluid infusions and Y-sited electrolytes was outside the scope of this guideline and so the evidence in these areas has not been appraised. Therefore the committee was not able to comment on this.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	007	019 - 020	It is unclear why a baby starting after 4 days of age doesn't have same maintenance dose as those started younger, this isn't well explained in rationale. Is there evidence for this?	Thank you for your comment. This has been corrected because it was meant to be the maintenance dose of babies starting before 4 days after birth (3 to 4 g/kg/day).
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	008	005 - 006	These ratios of non-protein energy carbohydrate:lipid were quoted in ESPGHAN 2005 guideline but in 2018 guideline was revised to maximum of 50:50 provided newer lipid emulsions are used (i.e. SMOF/equivalent from other companies, Clinoleic, Lipofundin etc). Is this the right ratio to be advocating?	Thank you for your comment. We were unable to locate the recommendation of a 50:50 ratio of carbohydrates:lipids in the ESPGHAN guideline. However, the ESPGHAN publication states (Lapillonne 2018 in the publication related to lipids) that 'Generally a lipid intake of 25-50% of non-protein calories is recommended in fully parenterally fed patients'. The ranges of

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					ratios were informed by the evidence and the committee felt that their recommendations were very close to those ranges suggested by ESPGHAN but decided against an upper limit of 50%. They decided that there should be an upper limit of 40% lipids. Even though there is no evidence available to firmly state the risks of higher lipid provision, the committee concluded that 40% would be safe and not risk fatty liver or raised triglyceride levels. This is described in the related rationale and impact section.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	008	016 - 018	Does iron deficiency need to be monitored for term babies who are 28 days or older on parenteral nutrition as well as preterm babies?	Thank you for your comment. Term babies who are older than 28 days are outside the scope of this guideline, so recommendations could not be made in this area. However, the committee commented on this in the 'committee discussion of the evidence' section in evidence report F stating: 'For term babies who are 28 days or older, the committee could not make a recommendation on intravenous supplementation of iron in parenteral nutrition, because these babies were not included in the scope of the guideline. However, they noted that term babies continuing on long-term parenteral nutrition may need iron supplementation, and this would then have to be considered on a case-by-case basis'.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	008	020 - 021	We acknowledge the lack of evidence regarding adding acetate to parenteral nutrition and the intent that acetate is not routinely added to parenteral nutrition solutions, but reserved for situations when other methods to reduce hyperchloraemia have been insufficient. However, the way recommendation 1.5.10 is phrased may be interpreted by some as	Thank you for your comment. After further consideration the committee have removed this recommendation from the guideline. Additional text has been added to the rationale and impact section to explain this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				acetate should not be included at all. Could this be rephrased?	
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	008	020 - 021	Is there sufficient evidence to specify a maximum chloride recommended per kg or per bag?	Thank you for your comment. Levels of chloride were outside the scope of this guideline and so the evidence in these areas has not been appraised. Therefore the committee was not able to comment on this.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	009	001 - 021	One member commented that the recommended calcium levels of 1.5-2mmol/kg with similar amounts of phosphate might be difficult to achieve in low volume/concentrated bags.More research is needed on stability with organic phosphate salts to help with this.	Thank you for your comment. The evidence supporting this recommendation came from studies with calcium and phosphate in these ranges. It also showed that higher amounts of calcium and phosphate were beneficial in reducing the incidence of rickets, fractures and hypercalciuria, and increasing bone mineral density. The committee concluded that these levels would be achievable and illustrative examples of formulations which contain these doses are included in appendix M of evidence review E.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	009	002 - 008	The calcium dose is very high for term babies compared to ESPGHAN 2018 recommendation. In a unit seeing only term babies, I don't think such high doses are needed. It would be pragmatic to take the high dose then review via bloods in a neonatal unit with term babies but possibly not in a centre routinely seeing term babies. It may preclude the use of a standardised parenteral nutrition formula that could potentially be used safely for neonates and infants.	Thank you for your comment. The evidence supporting this recommendation came from studies with preterm babies and the committee acknowledged in the rationale and impact section of the guideline that preterm babies may need more calcium than term babies. The evidence also showed that higher amounts of calcium and phosphate were beneficial in reducing the incidence of rickets, fractures and hypercalciuria, and increasing bone mineral density. This guided the committee to agree that higher amounts of calcium and phosphate are preferable for preterm and term babies. However, they highlighted that this will be indicated by monitoring. The committee therefore decided not to make a

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					change to this recommendation. The reason for this is explained in the related rationale and impact section. The committee were aware that there are standardised bags with starting dosages of calcium and phosphate lower than this (since they recommend lower dose and incrementation for babies in the first 48 hours of life). Therefore they thought that if it is indicated by monitoring it would not preclude the use of a standardised formulation.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	009	010 - 016	The phosphate dose is very high for term babies compared to ESPGHAN 2018 recommendation. In a unit seeing only term babies I don't think such high doses are needed. It would be pragmatic to take the high dose then review via bloods in a neonatal unit with term babies but possibly not in a centre routinely seeing term babies. It may preclude the use of a standardised parenteral nutrition formula that could potentially be used safely for neonates and infants. The committee were aware that there are standardised bags with starting dosages of calcium and phospate lower than this (since they recommend lower dose and incrmentation for babies in the first 48 hours of life). Therefore they thought that if it is indicated by monitoring it would not preclude the use of a standardised formulation.	Thank you for your comment. The evidence supporting this recommendation came from studies with preterm babies and the committee acknowledged in the rationale and impact section of the guideline that preterm babies may need more calcium than term babies. the evidence also showed that higher amounts of calcium and phosphate were beneficial in reducing the incidence of rickets, fractures and hypercalciuria, and increasing bone mineral density. This guided the committee to agree that higher amounts of calcium and phosphate are preferable for preterm and term babies. However, they highlighted that this will be indicated by monitoring. The committee therefore decided not to make a change to this recommendation. The reason for this is explained in the related rationale and impact section. The committee were aware that there are standardised bags with starting dosages of calcium and phosphate lower than this (since they recommend lower dose and incrementation for babies in the first 48 hours of life). Therefore they thought that if it is indicated by monitoring it would not preclude the use of a standardised formulation.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	009	010 - 016	Could the phosphate requirement be clarified as whether this is the total requirement (i.e. in both aqueous and lipid components) or is it just the phosphate in aqueous solution?	Thank you for your comment. This refers to the total requirement (i.e. both aqueous and lipid component) and we have added a sentence with this information to the 'committee discussion of the evidence' section of the evidence review to make this explicit.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	010	008 - 009	We are aware of one Trust whose starter bags have no/minimal sodium or potassium in as their guidelines are to avoid giving either electrolyte whilst the postnatal diuresis is occurring. Does the evidence base suggest that this is necessary? If so, does it need highlighting here?	Thank you for your comment. The committee discussed that there are daily maintenance needs for sodium and potassium but also noted that such levels may not only be related to parenteral nutrition. They highlight in the rationale and impact section that these levels would need to be checked because they depend on multiple factors. It is also highlighted that sodium and potassium can be given using an additional intravenous infusion. Therefore if a bag only contains minimal sodium and potassium it could be added without a need to change the whole starter bag as long as the formulation is consistent with the other recommendations related to constituents and their dosages.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	010	010 - 012	Does there need to be a reflection of the maximum total rates of potassium from all sources here? Not necessarily by giving a number, but just as a flag for safety?	Thank you for your comment. It is highlighted in the rationale and impact section for this recommendation that levels fluctuate and depend on multiple factors. Therefore, they would need to be checked and if required could be adjusted using an additional infusion. The committee agreed that this would be a safe strategy. Providing recommendations on all sources of potassium independent of parenteral nutrition would be outside the scope of the guideline.
Neonatal and Paediatric	Guideline	011	005 - 008	Do metabolic diagnoses need to be on this list where individualised parenteral nutrition is indicated? It's not	Thank you for your comment. The committee decided that metabolic diagnoses are quite varied and a specialist area

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Pharmacists Group (NPPG)				easily possible to give tailored amino acid solutions, so can end up with a relatively (overall) lower protein formula.	which was outside the scope of the guideline and so the evidence in these areas has not been appraised. Therefore the committee was not able to comment on this.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	011	017 - 020	What is the rationale for continuing to perform glucose monitoring every days or 2 days once the baby is on a stable parenteral nutrition prescription? After 5 days or so this may be unnecessary. Many term babies won't already be having blood gases done, is it essential to prick them for glucose monitoring?	Thank you for your comment. The committee agreed glucose should be monitored when starting parenteral nutrition and at every change of the bag, for safety reasons. They also recommend in 1.7.1 to coordinate the timing of blood tests to minimise the number of blood samples needed as well as to retrieve as much information as possible from the sample to strike a balance between minimising distress to the baby (and parents) and obtaining enough information to guide clinical care. The committee decided that the time when a bag is changed would be a critical time where hypoglycaemia or hyperglycaemia could occur and therefore agreed that this timeframe is needed to ensure the safety of the baby.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	012	012 - 022	We note that there is no explanation for why triglycerides are being measured, what the implications are for a level >2.8mmol/L, and what to do if the level is >2.8mmol/L (apart from monitor more frequently). We acknowledge that the SMOFlipid Summary of Product Characteristics recommends monitoring triglyceride levels, and suggests to consider the reduction of dosage or cessation of the lipid emulsion if serum or plasma triglyceride concentrations during or after infusion exceed 3mmol/L. Please clarify what actions need to be taken if the level is >2.8mmol/L. For example: If >2.8mmol/L and rising, look at the clinical scenario and review /	Thank you for your comment. The committee decided to remove the level of > 2.8 mmol/litre from the recommendation since frequency of monitoring rather than the cut-off level was the aim of the evidence review. Different cut-off levels were therefore not reviewed and the committee, in hindsight, decided that they could not comment on this. They also noted that other guidelines use different levels (for example the ESPGHAN guideline). However, they agreed that recommendations about the frequency of serum triglycerides would be useful because of current variability in clinical practice and that this would therefore improve consistency. They agreed that triglycerides should be monitored when increasing dosages of lipid, because they were aware of

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				consider cutting down If >4mmol/L, stop lipid parenteral nutrition and monitor	evidence that suggests that around 10% of babies do not tolerate recommended intakes of lipids. The committee also agreed that when a baby is unstable or the level of triglycerides is elevated (or a blood sample is lipaemic) triglycerides should be monitored more frequently to ensure the safety of the baby. This is described in the rationale and impact section of the guideline.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	013	013	Stopping parenteral nutrition in term babies might be appropriate when they are on 75% of their enteral calorie requirements (BAPM 2016), and some centres might possibly use other cut-offs. Recommendations seem to be focused on NICU practice, there are cardiac, medical and surgical neonates outside of NICU who would not need feed volumes like this to be able to stop parenteral nutrition as their feed target might be 120ml/kg or 150ml/kg.	Thank you for your comment. The committee agreed that recommendations 1.8.2 and 1.8.3 were worded in a very prescriptive way. These recommendations were intended to be taken in the context of recommendation 1.8.1 which lists a number of factors that should always be taken into account when considering stopping parenteral nutrition. This also includes 'the individual baby's particular circumstances' and these could be any complex needs (such as cardiac or surgical conditions). They have therefore decided to make the relationship between these recommendations explicit by adding 'taking into account the factors in recommendations 1.8.1' to 1.8.2 and 1.8.3 so that clinical judgment can be used when considering whether parenteral nutrition should be stopped at these enteral feed volumes.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline	014	006	The service design section seems very NICU-centred. Would it be worth adding a comment that recognises the needs of neonates outside of NICU in terms of accessing specialist neonatal advice? I'm more thinking of our cardiac or metabolic neonates who are in the children's hospital, not the neonatal unit and	Thank you for your comment. In recommendation 1.9.1 it is stated that the multidisciplinary team could be based locally or within a clinical network. As highlighted in recommendation 1.9.3 part of their responsibilities would also include provision of clinical advice and enhanced multidisciplinary team input.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				acknowledging the barriers associated with the different geography and teams.	This would have an impact on clinical practice regardless of whether the baby is located in NICU or elsewhere.
Neonatal and Paediatric Pharmacists Group (NPPG)	Guideline & Evidence Review F	012 and General	001 – 011 and General	We note that sodium levels are not included in the monitoring recommendations. Should it be included?	Thank you for your comment. Even though not directly recommended it is highlighted in the rationale and impact section related to electrolytes that sodium and potassium levels are likely to fluctuate and that these changes may not only be related to parenteral nutrition formulations. The evidence review on monitoring addressed the frequency rather than the level to be monitored and the committee decided not to include sodium in the protocol. They did this because sodium levels depend on multiple factors and decisions should be made by the local clinical team based on the overall clinical situation. They therefore could not comment on a particular frequency or level of sodium. However, some of this is described in the related rationale and impact section of the guideline to emphasise these points.
Neonatal Critical Care Clinical Reference Group	Guideline	003	014	Major cardiac disorders are not a contraindication for establishing early enteral feeding. We suggest this is reflected in the text by clarifying as, 'Circulatory instability due to major cardiac disorders'	Thank you for your comment. The committee agreed that major cardiac disorders may not always mean that progress cannot be made with enteral feeding. However, there may be factors related to cardiac disorders other than circulatory instability that cause problems with progressing enteral feeding. Therefore, they decided that this was not a clear illustrative example and could cause confusion. They therefore decided to remove it from the examples listed in the recommendation rather than amend as suggested.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Neonatal Critical Care Clinical Reference Group	Guideline	019	010	Major cardiac disorders are not a contraindication for establishing early enteral feeding. We suggest this is reflected in the text by clarifying as, 'Circulatory instability due to major cardiac disorders'	Thank you for your comment. The committee agreed that this example may be confusing and have therefore removed it from the recommendation as well as the related rationale and impact section.
NHS Greater Glasgow and Clyde	Algorithm	General	General	Light protection – change to must be protected in line with recent EMA guidance	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.
NHS Greater Glasgow and Clyde	Guideline	004	007	Consider central access after one week if not progressing on feeds.	Thank you for your comment. The type of access, including when to use it, is covered by recommendations 1.2.1 and 1.2.2. In these recommendations the committee decided that central access should be provided for longer term parenteral nutrition but to use peripheral lines in the short term. However, they defined short term as less than 5 days rather than a week. They decided that this would best balance the benefits and harms of the different methods of venous access. This is described in the rationale and impact section of the guideline.
NHS Greater Glasgow and Clyde	Guideline	005	020	This should apply to all babies, not just term babies	Thank you for your comment. The evidence related to the recommendation was restricted to term babies. The committee did not want to extrapolate this to preterm babies because the nutritional stores of these babies are lower and therefore providing energy at the lower end of the range may not be

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					appropriate. The related rationale and impact section has been revised to make this more explicit.
NHS Greater Glasgow and Clyde	Guideline	007	021	“For preterm and term infants with PNALD consider fish oil based lipid”. The justification for which is “no conclusive evidence of benefit in those without” which I would suggest should say “there is no good evidence one way or another in those without”.	Thank you for your comment. This sentence has been amended to "there was not conclusive evidence of either benefit or harms". In addition the committee revisited this topic and the recommendation has been amended to: ‘For preterm and term babies with parenteral nutrition-associated liver disease, consider giving a composite lipid emulsion rather than a pure soybean lipid emulsion. The rationale and impact section has been amended to reflect this change.
NHS Greater Glasgow and Clyde	Guideline	008	019	Chloride/acetate, it would be useful to have a level stated for the max. chloride recommended in the bags (or /kg)	Thank you for your comment. Levels of chloride were outside the scope of this guideline and so the evidence in these areas has not been appraised. Therefore the committee was not able to comment on this.
NHS Greater Glasgow and Clyde	Guideline	008	020	Seems to be totally lacking an evidence base	Thank you for your comment. There was some evidence but it was limited. After further consideration the committee have removed this recommendation from the guideline. Additional text has been added to the rationale and impact section to explain this change.
NHS Greater Glasgow and Clyde	Guideline	009	006	We note that these ranges are lower than previous guidance	Thank you for your comment. We are unclear which guidance this is referring to but the committee recommended a range of possible values with some of them likely to be consistent with previous guidance (such as ESPGHAN). They noted that the amounts of calcium and phosphate in the evidence reviewed were lower than those currently given in UK clinical practice. However, the evidence also showed that higher amounts of calcium and phosphate were beneficial in reducing the

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

					incidence of rickets, fractures and hypercalciuria, and increasing bone mineral density. This guided the committee to agree that higher amounts of calcium and phosphate are preferable for preterm and term babies. This is described in the related rationale and impact section.
NHS Greater Glasgow and Clyde	Guideline	013	007	The suggested measurements (ferritin etc) are acute phase reactants and can be difficult to interpret in an unstable baby	Thank you for your comment. The focus of the evidence review related to these recommendations was the frequency of testing rather than which tests to use, how to interpret them or the management thereafter. However, the committee noted also that these measurements could be difficult to interpret and have acknowledged this in the related rationale and impact section and in the discussion section of evidence review F - monitoring neonatal parenteral nutrition.
NHS Greater Glasgow and Clyde	Guideline	022	026	Light protection – change to must be protected in line with recent EMA guidance	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.
NHS Greater Glasgow and Clyde	Guideline	General	General	For babies starting PN after day 4 of life consideration should be given to incrementing of constituents	Thank you for your comment. The committee agreed that these babies could tolerate the maintenance dosage and decided that incrementing for these babies would not be necessary. This is described in the related rationale and impact sections.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

NHS Greater Glasgow and Clyde	Guideline	General	General	It would be useful to have more clarity on sodium administration in the first few days of life for the preterm population	Thank you for your comment. The details of sodium administrations were not included in the scope of the guideline and so the evidence in this area has not been appraised. Therefore, the committee was not able to comment on this.
NHS Highland	Guideline	004	017	Adding the words < 3 days would basically imply that all babies born at a GA ≤ 30 weeks will get central venous access, even those in whom increasing enteral feeds at a good volume e.g. 30 ml/kg/d are well tolerated. There is no evidence for the < 3 days. There is evidence of potential complications of central venous access. It should be decided on an individual basis, are there problems with central venous access, can feeds be increased without any problems. I know it says e.g. < 3 days but this can point people in my opinion to the wrong direction.	Thank you for your comment. This has been amended to "for example, less than 5 days".
NHS Highland	Guideline	004	021	If there is poor venous access there will be poor venous access for peripheral canula's usually as well.	Thank you for your comment. The example of 'poor venous access' has been removed from the recommendation.
NHS Highland	Guideline	005	006	As far as I am aware there is only evidence that it is essential to have the lines through which lipids runs protected from light. I am a bit concerned that amino-acid/ glc and lipid solutions are being mixed up with significant consequences.	Thank you for your comment. We have revised the recommendation to be consistent with the European Medical Association (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) guidance. This includes combining the two recommendations related to light protection into one which states that there should be light protection of the bag as well as the syringe and infusion set. The rationale and impact section has been amended to reflect this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

NHS Highland	Guideline	008	020	Should that not read hypocloraemic acidosis instead of just 'hypocloraemia'?	Thank you for your comment. After further consideration the committee have removed this recommendation from the guideline. Additional text has been added to the rationale and impact section to explain this change.
NHS Highland	Guideline	009	013	I would not know of any standard TPN solution available which is able to give 2 mmol/kg/d after 48 hrs (day3 of life in the preterms, often that day on a fluid intake of approx 120 ml/kg/d)). I should ask our pharmacist but I do not think it is possible either to add that amount to the standard bag. So I am concerned that this recommendation is not achievable in practice.	Thank you for your comment. The evidence supporting this recommendation came from studies with calcium and phosphate in these ranges it also showed that higher amounts of calcium and phosphate were beneficial in reducing the incidence of rickets, fractures and hypercalciuria, and increasing bone mineral density. The committee concluded that these levels would be achievable and illustrative examples of formulations which contain these doses are included in appendix M of evidence review E.
NHS Highland	Guideline	010	010	In our hospital they can also be added to the standard bag, probably good to add that that might be possible as well.	Thank you for your comment. The committee agreed that this would be a possibility but once added to the bag would be difficult to adjust. They highlight in the rationale and impact section that these levels would need to be checked because they depend on multiple factors. Given that changes to sodium and potassium could occur and that the baby may already be on a bag with a lower level than they need, the committee wanted to emphasise that these levels could be adjusted using an additional intravenous infusion rather than needing to change to a bag with a higher sodium and potassium level.
NHS Highland	Guideline	012	014	There is no evidence, and also in my experience well stable preterm infants do not have issues with hypertriglyceridaemia when lipid intake is still low (1-2 g/kg/d). To minimise blood sampling I would suggest	Thank you for your comment. The committee decided that triglycerides should be monitored at these frequencies to improve consistency across clinical practice and ensure the safety of the baby. However, they decided that the level of >2.8

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				that in well preterm infants only to check TG levels when intake of 3 g/kg/d is reached.	mmol/l should not stated in the recommendation and have removed it. The aim of the review was the frequency of monitoring rather than the level at which an action should be taken or management thereafter so the committee could not comment on this. Their recommendations on frequency are meant to indicate the minimum intervals of monitoring so that the amount of lipid intake can be adjusted if babies do not tolerate the recommended levels that are provided in recommendation 1.5.4. Given the possible harms the committee felt strongly that this is needed for safety reasons. However, the factors identified in recommendation 1.7.1 (for example retrieving as much information as possible from each blood sample and coordinating the timing of blood tests to minimise the number of blood samples needed) would ensure that the baby does not receive too many tests but a sufficient number to balance benefits and harms of testing.
Nottingham University Hospitals NHS Trust (NUH)	Guideline	003	017	Recommendation 1.1.4 “For preterm babies on enteral feeds, start parenteral nutrition if: enteral feeds are stopped for more than 24hours and here is no prospect of making sufficient progress with enteral feeding within a further 48hours”. The committee’s choice of the word ‘and’ is challenged as, following this recommendation would mean, for example, that preterm infants with proven NEC for whom a prolonged period of nil enterally will be required, would need to ‘wait’ for 24 hours before PN is started. During this period they would become catabolic as listed in the rationale for 1.1.4 and elsewhere for early introduction of PN. There is not evidence to suggest	Thank you for your comment. The recommendation has been amended to clarify that PN should be started (without waiting 24 hours) for babies who are unlikely to restart enteral feeds within 48 hours of stopping. The committee discussion of the evidence section in evidence report A1 has been amended to reflect this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				that witholding PN in these circumstances is correct clinical management and denying these infants PN/nutrition for 24 hours is a concern. This recommendation should be reworded.	
Nottingham University Hospitals NHS Trust (NUH)	Guideline	007	001	Recommendation 1.5.2 is controversial – alternative 'expert opinion' would state "give a starting range of 1.5 to 2.5g/kg/day" as setting a maximum of 2g/kg/day for up to 4 days (as the recommendation infers) would be widely regarded as a suboptimally low intake.	Thank you for your comment. The recommendation to start amino acids at 1.5 to 2g/kg/day was based on the ranges given in the evidence that was included in the review. The recommendation then goes on to state that amino acids should be gradually increased (for example, over 4 days). Therefore it is not intended that the baby should be kept on 2g/kg/day until day 4.
Nottingham University Hospitals NHS Trust (NUH)	Guideline	008	020 - 021	Recommendation 1.5.10 is limited and non-evidence based. Acetate use is more widespread than the committee appear to realise (from their given rationale) and an integral part of some amino acid preparations e.g. Aminoven Infant(R) . In this recommendation, the extreme preterm infant born at 23-26 weeks gestation, for example, has to 'earn' acetate through developing hypercholaraemia where the chloride load from other treatments (which the committee acknowledge) represents an predictable, unavoidable unphysiological chloride load. Units where acetate is used for these infants *prevent* hypercholoraemia by inclusion of acetate through the consequent reduction of chloride load. Not to be able to do so would be a concern for optimising metabolic milieau and preventing hyperchloraemia, the effects of which can be wide-ranging. In light of ongoing	Thank you for your comment. The committee agree that the evidence was very limited. This is made clear in evidence review D6 and highlighted in the rationale and impact section. However, after further consideration the committee have removed this recommendation from the guideline. Additional text has been added to the rationale and impact section to explain this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				practice and lack of evidence, this recommendation should be amended or removed.	
Nottingham University Hospitals NHS Trust (NUH)	Guideline	012	012	Recommendation 1.7.6 The use of 'should' in the rationale for this recommendation and the recommendation itself are also non-evidence based and raise concerns. There is an absence of evidence for triglyceride monitoring and an absence of evidence on what action to take for numerical values of triglycerides obtained in such measurements. The recommendation would be appropriate if it read that 'triglycerides should be measured when serum appears lipaemic and lipid infusion adjusted' rather than a recommendation for other repeated blood tests in this vulnerable group with absence of rationale for threshold at which any action might be undertaken and for the possible actions themselves.	Thank you for your comment. The committee decided that triglycerides should be monitored at these frequencies to improve consistency across clinical practice and ensure the safety of the baby. However, they agreed that the level of >2.8 mmol/l should not be provided and has been removed. The aim of the review was the frequency of monitoring rather than the level at which an action should be taken or management thereafter so the committee decided, in hindsight, that they could not comment on this. Their recommendations on frequency are meant to indicate the minimum intervals of monitoring so that the amount of lipid intake can be adjusted if babies do not tolerate the recommended levels that are provided in recommendation 1.5.4. Given the possible harms the committee felt strongly that this is needed for safety reasons. However, the factors identified in recommendation 1.7.1 (for example retrieving as much information as possible from each blood sample and coordinating the timing of blood tests to minimise the number of blood samples needed) would ensure that the baby does not receive too many tests but a sufficient number to balance benefits and harms of testing.
Royal College of Nursing	General	General	General	We are pleased to receive the draft guideline for review and appreciate the extensive work undertaken to produce them. From a nursing perspective, we need to highlight gaps in the content such as:- frequency of line change - the use of filters, as well as- the importance of a transparent dressing to	Thank you for your comment. Frequency of line change and type of dressing were not included in the scope of this guideline and so the evidence in these areas has not been appraised. Therefore, the committee was not able to comment on this. However, these issues have been highlighted to the

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				enable easy inspection of the site. We would urge that NICE development team give due consideration to addressing these areas as they are crucial in terms of reducing and monitoring for infection etc.	surveillance team in NICE to be considered for future updates if evidence emerges. The use of filters was discussed but the committee did not make a recommendation about this due to lack of consensus. This is explained in the rationale and impact section for 'administration of neonatal parenteral nutrition' and in the committee discussion in evidence report J - general principles.
Royal College of Paediatrics and Child Health	Guideline	003	005 - 009	Using solely the cut-off of gestational age will miss severely growth restricted babies in need of parenteral nutrition. They are at high risk of bowel pathology and feeding intolerance. A sole cut-off related to weight would be better as it would include AGA preterms as well as SGA/IUGR preterms. For example a female 32 weeker with a birthweight of 1.1 kg might tolerate feeds but not grow due to disproportionate nutritional and metabolic requirements, etc. I would suggest following the BAPM guidance of < 1.25 kg for all babies and dropping gestational as indicator to keep it simple.	Thank you for your comment. Recommendation 1.1.2 would cover small for gestational age babies and babies with intrauterine growth restriction born at or after 31 weeks that cannot tolerate sufficient enteral feeds. This would become apparent in the first 72 hours of starting because practically it can take some time to work out if babies tolerate their feed. If longer time is required to determine whether these babies may need parenteral feeding, then the committee decided that this would be something more related to enteral rather than parenteral feeding. It is outside the scope of this guideline to make recommendations about babies where enteral feeds are given for longer periods of time to determine tolerance. We have highlighted this in the related 'committee's discussion of the evidence' section of evidence report A1 to make this clearer.
St. George's University Hospitals NHS Foundation Trust	Guideline	014	003	I am concerned that this recommendation may imply that patients born before 28 weeks will be stopped on PN despite their tolerance if they reach a volume of 140ml/kg – 150ml/kg and instead a sentence that readsIn patients born before 28 weeks consider	Thank you for your comment. The committee agreed that the decision on stopping should always take into account the factors highlighted in recommendation 1.8.1. The intent was therefore that the particular volumes given in recommendations 1.8.2 and 1.8.3 would be put into the context

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				stopping parenteral nutrition within 24 hours once the patient tolerates an enteral feed volume of 140ml to 150ml/kg/day. Tolerance can be assessed by stool/ stoma losses and weight gain.	of recommendation 1.8.1 as an overarching recommendation in this section whenever considering stopping parenteral nutrition. However, they reflected on this and since recommendations may be read in isolation, they agreed that the relationship between these recommendations could be missed. They have therefore revised recommendations 1.8.2 and 1.8.3 to include a cross-reference to recommendation 1.8.1 so that these factors are always considered when stopping parenteral nutrition at these volumes.
University Hospital Southampton NHS Foundation Trust	Guideline	003	010	We are concerned that statement 1.1.3 is a little ambiguous and needs more detail/clarification regarding a cut off period when infants with congenital gut disorders should start PN. Some surgeons often recommend that some of these infants should be allowed some time to establish feeding depending on the defect or the surgery performed. A clear cut off for how long a baby should be nil by mouth in these situations would be helpful. The objective criteria are listed in the next section under ‘indications for starting parenteral nutrition if feeds are stopped’; but this still leaves room for interpretation and is perhaps a little ambiguous in relation to infants who have never been fed. Therefore, these clear indications should also apply to starting parenteral nutrition in cases where enteral feeds have never been started, and so ideally should be included or referred to in statement 1.1.3.	Thank you for your comment. The committee agreed that the wording 'who are unlikely to establish sufficient enteral feeding' could include babies where enteral feeds have never been started but it is foreseeable that they would not tolerate it. However, clarifications about length of 'nil by mouth' are outside the scope of the guideline because this is not directly related to parenteral nutrition or its administration. The committee decided that clinical judgement would be needed to determine situations where babies are 'unlikely to establish sufficient enteral feeding', tailoring this to each baby's particular circumstances and condition. The committee decided that no change to the recommendation was required since surgical babies may also fall into the remit of 1.1.4 and 1.1.5 (their feeds would have been stopped before surgery). However, to make this clearer an explanation has been added to the rationale and impact section of the guideline.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

University Hospital Southampton NHS Foundation Trust	Guideline	008	020	We currently use acetate as an alternative to chloride salts in our standardised and bespoke parenteral nutrition. We find it beneficial given that many premature infants have a degree of metabolic acidosis early in life. We are a little concerned by the committee's recommendation to 'only' use acetate in parenteral nutrition if the patient is hyperchloraemia, and after minimising chloride intake first. This would potentially be challenging to implement in practice as it would potentially compromise the stability of our standardised bags. Many commercially available standardised bags also contain acetate, so this has wider implication beyond our own practice. Furthermore, we are unclear as to why the committee have recommended to only use acetate in the specific situation of hyperchloraemia. In addition, in the 'rationale and impact' section the committee state that are trying to ensure acetate is not used routinely, but we do not feel they present a strong case as to why this is strictly necessary. From the available literature, there does not appear to be evidence of harm from using acetate instead of chloride, so we would prefer the statement 1.5.10 to modified to be less didactic regarding the use of acetate, unless there is good evidence that using acetate in standardised bags is harmful or has other detrimental effects. Changing it so say 'consider including acetate' rather than 'only consider' would be helpful in the first instance	Thank you for your comment. After further consideration the committee have removed this recommendation from the guideline. Additional text has been added to the rationale and impact section to explain this change.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

University Hospital Southampton NHS Foundation Trust	Guideline	012	016	We feel that the guidance regarding monitoring of triglycerides (1.7.6 and 1.7.7) would benefit from more detail, as at the moment it is perhaps a little vague. Firstly, it does not state what the normal range is that should be considered when doing this – whilst it uses >2.8mmol/l when considering whether to test more frequently, there is not recommendation for what the normal range or upper limit should be outside this situation. The guideline also offers no guidance what to do if the triglyceride level is high- in our practice we would reduce (but not stop the lipid infusion) if the serum triglycerides are >3mmol/l. This is in line with the recent EPSGHAN guidance. Having some guidance as to what to do with the triglyceride result may aid implementation of this recommendation, as many units in our network do not measure triglycerides routinely (or at all in some cases) and so might be more likely to do this if there is clear guidance about how to manage the results. Some brief explanation about the need to reduce lipid when it is not tolerated (together with a concurrent reduction in amino acid in order to maintain energy:protein ratios) might also help reinforce this.In relation the ESPGHAN guidance, this uses the cut off of 3mmol/l for triglycerides, and so we are unclear why the committee has chosen 2.8mmol/l (I believe this is the value form the older 2005 ESGHAN guidance). Could this perhaps be amended to 3mmol in the NICE guidance to bring it into line with ESPGHAN?	Thank you for your comment. The committee decided that triglycerides should be monitored at these frequencies to improve consistency across clinical practice and ensure the safety of the baby. However, they agreed that the level of >2.8 mmol/l should not be provided so this has been removed from the recommendation. The aim of the review was the frequency of monitoring rather than the level at which an action should be taken or management thereafter so the committee could not comment on this. Their recommendations on frequency are meant to indicate the minimum intervals of monitoring so that the amount of lipid intake can be adjusted if babies do not tolerate the recommended levels that are provided in recommendation 1.5.4. Given the possible harms the committee felt strongly that this is needed for safety reasons. However, the factors identified in recommendation 1.7.1 (for example retrieving as much information as possible from each blood sample and coordinating the timing of blood tests to minimise the number of blood samples needed) would ensure that the baby does not receive too many tests but a sufficient number to balance benefits and harms of testing.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

University Hospital Southampton NHS Foundation Trust	Guideline	013	014	We whole heartedly agree with the recommendations 1.8.1 regarding factors to take into account when deciding to stop parenteral nutrition, in particular considering the tolerance of enteral feeds and the amount of nutrition being delivered. Thinking about *nutrition* rather than *fluids* is key to optimising preterm infant nutrition. However, these recommendations in 1.8.1 are then a little undermined by the ones that follow in 1.8.2 and 1.8.3 which encourage practitioners to consider stopping parenteral nutrition based on a particular volume of fluid. Whilst we accept the committee has reviewed evidence that some of these volumes potentially support growth, surely the key issue here is that the nutrition delivered by a particular volume of feed will depend on what that feeds is. In fact, considering current nutrient intake recommendations for preterm infants (ESPGHAN 2010 and Koletzko 2014), on paper volumes of 120-150ml/kg/day of unfortified maternal breast milk are nutritionally inadequate to meet these. Given this guideline is about parenteral nutrition and not enteral feeding, we are not sure giving a range of feed volumes at which enteral nutrient intakes are felt to be adequate and parenteral nutrition no longer necessary is within the scope of this guideline. Giving some factors to consider when making the decision to stop parenteral nutrition as in 1.8.1 seems like a good start, but we are uncomfortable with this being followed by specific volume target ranges in the absence of clarity of what the feed type might be and	Thank you for your comment. The committee agreed that the decision on stopping should always take into account the factors highlighted in recommendation 1.8.1. The intent was therefore that the particular volumes given in recommendations 1.8.2 and 1.8.3 would be put into the context of recommendation 1.8.1 as an overarching recommendation in this section whenever considering stopping parenteral nutrition. However, they reflected on this and since recommendations may be read in isolation, they agreed that the relationship between these recommendations could be missed. They have therefore revised recommendations 1.8.2 and 1.8.3 to include a cross-reference to recommendation 1.8.1 so that these factors are always considered when stopping parenteral nutrition at these volumes.

Neonatal parenteral nutrition

Consultation on draft guideline - Stakeholder comments table
[06/09/19 to 18/10/19]

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

				what the nutritional targets are, and would suggest that 1.8.2 and 1.8.3 are omitted. Leaving these in could potentially increase the risk of nutritional deficits.	