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28 September 2017

Food Standards Australia New Zealand
PO Box 5423
Kingston ACT 2604

Via email: submissions@foodstandards.gov.au

To Whom It May Concern:

Proposal P 1028 Regulation of Infant formula – Infant formula products for special dietary use

The Royal Australasian College of Physicians (RACP) welcomes the Food Standards Australia and New Zealand (FSANZ) call for submissions on Proposal P 1028 to consider the regulation of infant formula products specifically, infant formula for special dietary use.

The RACP has previously made submissions to FSANZ expressing concern over the regulation of marketing of infant formula in Australia, including labelling of infant formula products. The RACP has repeatedly highlighted the importance of expanding and strengthening regulation around marketing of infant formula in Australia.

For this consultation on the regulation of infant formula products for special dietary use, the RACP has consulted with members of our Paediatrics & Child Health Division and its Paediatric Policy & Advocacy Committee responding to the consultation questions in the enclosed submission.

The RACP will continue to advocate for effective means of safeguarding breastfeeding as the best infant feeding option for optimal health outcomes, and ensuring infant formula is safe for those who need to use it. Should you require further information or wish to discuss this further, please contact

Yours sincerely

Dr Sarah Dalton
President, Paediatric & Child Health Division

Enc RACP written submission to consultation

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FSANZ Consultation paper: Proposal P1028: Regulation of Infant formula – Infant formula products for special dietary use

Written submission (September 2017)

FSANZ Consultation paper: Proposal P1028: Regulation of Infant formula – Infant formula products for special dietary use

The Royal Australasian College of Physicians has consulted with members of our Paediatrics and Child Health Division and its Paediatric Policy Advisory Committee to provide the following comments:

Q1 Are there any other overseas regulations relevant to IFPSDU?

In 2011 PHARMAC NZ revised funding arrangements for these milk formulas in New Zealand.[1]

Q2 What are the advantages and/or disadvantages of these options, in particular creating an 'infant formula product for special medical purposes' subcategory? If you support creation of a separate category for IFPSMP, should pre-term products be included?

The RACP believes that retaining subcategories (2.9.1-13, 14 and 15) and narrowing their scope based on product use, highly specialised nature and risk may result in non-discriminant use in the community of infant formulas that have been developed on limited evidence.

There is limited research to show efficacy for formulas specifically designed to target constipation, colic and regurgitation and the evidence for partially and extensively hydrolysed protein to prevent allergic disease has shifted. A recent systematic review[2] reported that there was no consistent evidence to support a role for partially or extensively hydrolysed formula in the prevention of eczema, food allergy, asthma or allergic rhinitis in infants or children. The Australasian Society of Clinical Immunology and Allergy do not recommend hydrolysed (partially and extensively) infant formula for prevention of allergic disease, nor do they recommend partially hydrolysed infant formula for its management.[3] The RACP recommends that products designed for these conditions that are not underpinned by good evidence should not be marketed to health professionals such as pharmacists and general practitioners in Australia. Special health claims not underpinned by good evidence should be removed.

The RACP believes there is merit in having the regulatory classification of IFPSDU and two sub-categories for products, as per Figure 1 below. The RACP recommends that classification of a product into one or more of these two designated sub-categories should be dependent on their performance as being fit for purpose, assessed through clinical trial and standardised, measured outcomes. These trials should not be Industry-based, but rather funded through unconditional grants by industry to health care facilities that should ideally facilitate the conduct of ethical, robust, well-designed double blinded randomised trials with sufficient power to determine if new products are fit for purpose. We believe that such a system would enable infant formula products specifically designed to prevent allergic disease, or target transient gastrointestinal conditions such as constipation, colic and regurgitation to be classified into sub-category 2, if the evidence supported this classification.

The RACP recommends that products for premature or low birthweight infants should be inclusive of human milk fortifier and whey protein powder, as well as other nutritional products that are currently being used in feeding this subgroup of vulnerable infants, including energy supplements (carbohydrate and/or fat supplements) and food thickener. There should be provision in the Code to ensure that the same microbiological limits and processing standards that are applied to the manufacture of infant formula are also applied to these products. The RACP believes these measures will reduce the risk associated with using these products in preterm infants and suggests that Industry may be more likely to develop nutritionally appropriate and safe products for preterm and term infants if there is specific legislation to direct the manufacturing processes of these products.

[1] PHARMAC (2011): Special Foods - Notification of Funding and Access Changes from 1 April. Available at: http://pharmac.govt.nz/2011/02/28/2011-01%20Notification%20of%20Special%20Foods%20decisions.pdf (accessed 19 September 2017)
[2] Boyle et al. (2016): Hydrolysed formula and risk of allergic or autoimmune disease: systematic review and meta-analysis. BMJ 2016; 352 doi: https://doi.org/10.1136/bmj.i974 (accessed 6 September 2017)
[3] ASCIA (2016): Guidelines – Infant feeding and allergy prevention Available at https://www.allergy.org.au/health-professionals/papers/infant-feeding-and-allergy-prevention (Accessed 6 September 2017)

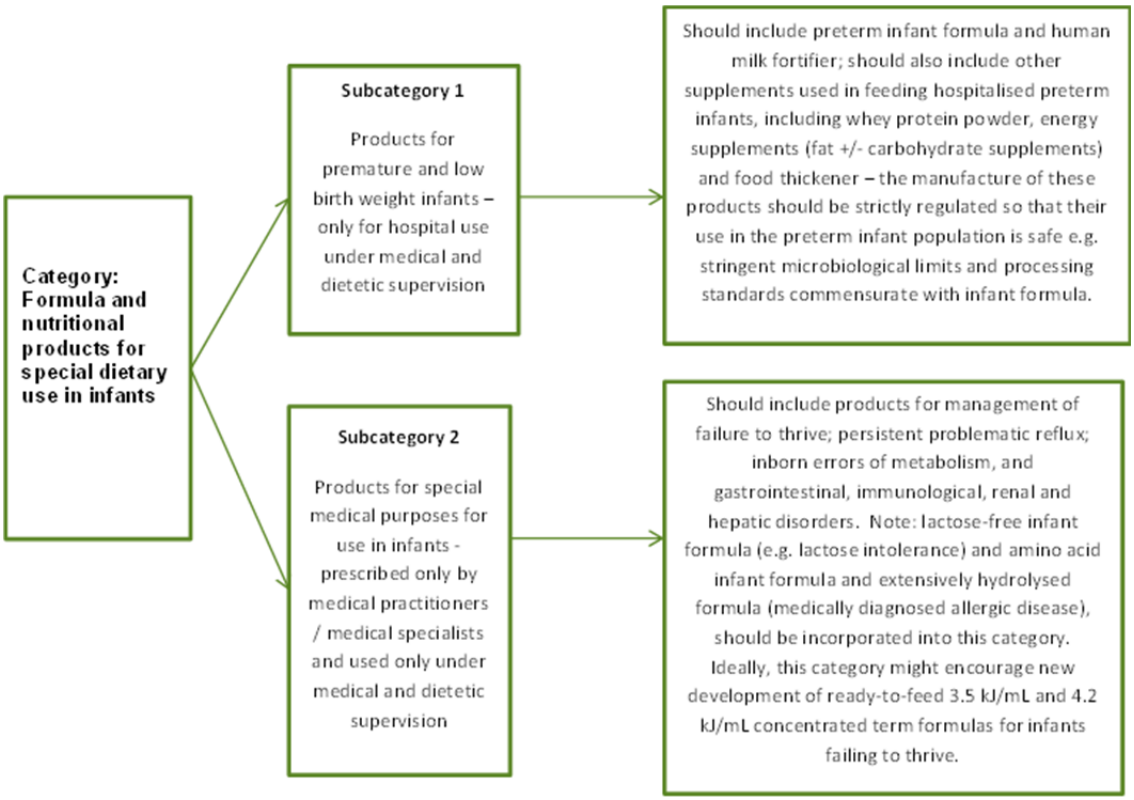

Figure 1: Possible new regulatory classification for IFPSDU

Q 3 Do you support inclusion of a category definition for IFPSDU in the Code? Why or why not? Is the proposed definition of IFPSDU appropriate; if not, what should it say?

Yes, the RACP believes that the inclusion of a category definition for IFPSDU in the Code is useful, but the definition should potentially be broadened to incorporate all nutritional products that are intended for use in infants (see Figure 1 above). The RACP believes that the definition for IFPSDU (Regulation (EU) No 609/2013) has greater capacity for such an interpretation and FSANZ should consider adopting it.

Q4 If you support including a subcategory definition for IFPSMP in the Code, is the proposed definition of IFPSMP appropriate; if not, what should it say?

Yes. The RACP believes that the inclusion of a subcategory definition for IFPSMP in the Code would be useful; however the proposed definition should incorporate the change suggested in our response to question 3. The definition should also be broadened to include infants who have a medically prescribed trial of thickened feeds (e.g. persistent, problematic GOR), concentrated feeds (e.g. failure to thrive), amino acid formula, extensively hydrolysed protein formula (e.g. cow's milk protein allergy) and modified macronutrient formulas, including extensively hydrolysed formula high in MCT's (e.g. short gut).

Q5 Are there any issues with the current definition for protein substitutes?

Yes. Please refer to the first paragraph of our response to question 2. While the RACP is aware that hypo-allergenic and extensively hydrolysed formulae may have been developed to reduce / prevent allergenicity and hypersensitivity, this is not supported by the latest emerging evidence. Boyle et al[4] in their systematic review reported that there was no consistent evidence to support a role for partially or extensively hydrolysed formulas in the prevention of eczema, food allergy, asthma or allergic rhinitis in infants or children. The Australasian Society of Clinical Immunology and Allergy also does not recommend hydrolysed (partially and extensively) infant formula for prevention of allergic disease nor does it recommend partially hydrolysed

[4] Boyle et al (2016)

protein formula for its management.[5] Therefore, the RACP does not agree with the current definition for protein substitutes.

Q6 Is there a benefit to defining one or more of the following in the Code:
- **Hypo-allergenic formula**
- **Partially hydrolysed formula**
- **Extensively hydrolysed formula**
- **Amino acid-based infant formula?**

If yes, what are the benefits of including these definitions? And what should be the key elements of each definition?

The RACP believes that there is a need to re-define partially hydrolysed (hypo-allergenic), extensively hydrolysed and amino-acid formula to ensure the degree of protein hydrolysis is mandated and defined for each, and to ensure that there is only inclusion in the definitions of health claims that are supported by the latest emerging evidence.

Q7 Are there any issues with the current definition for pre-term products?

Yes. As the nutritional needs of preterm infants vary, depending on age, the RACP recommends that the definition should differentiate preterm products according to the WHO classification for preterm infants. We believe that this would allow manufacturers to target their products to different gestational ages and weights. For example, feeding lower volumes of currently available preterm formulas to ensure lower protein intake for older preterm infants is not ideal, as this may not provide sufficient energy and other micronutrients for an infant and does not necessarily satisfy their hunger.

Q8 What, if any, are the benefits of including age and weight parameters in the regulatory definition for pre-term products?

Please refer to our answer to Q7.

Q9 What is the general composition of human milk fortifiers for premature or low birthweight infants? ….and composition and uses for groups other than premature or low birthweight infants?

Human milk fortifiers are used for preterm and low birth weight infants to add protein, energy, and micronutrients (especially bone minerals) to human milk to meet advisable nutrient intakes. The source of protein is usually cow's milk and the degree of hydrolysis in the various products available in Australia and New Zealand differs, depending on brand. Human milk fortifiers are generally not suitable for use in term infants. There is currently some interest in the commercialisation of human breast milk, including the development of human milk fortifiers.[6] This is likely to cross a number of regulatory regimens.

The RACP is concerned that one human milk fortifier product available on the Australian and New Zealand market has not had its formulation adequately reviewed for many years, despite updated nutritional guidelines in 2005, 2010 and 2014. We are also concerned that formula companies use different assumed compositions of human milk to demonstrate how each of their respective products achieves nutritional targets. The RACP believes that this is problematic and that it would be beneficial if FSANZ would standardise the preterm milk composition used by industry to calculate the capacity of their respective human milk fortifier products to meet advisable preterm nutrition targets.

The RACP recommends that the systematic review by Boyce et al.[7] should be used for standardising assumed macronutrient content of mature preterm milk. Until a better reference becomes available, the National Health and Medical Research Council (NHMRC) Nutrient Reference Values[8] should be used for standardising assumed micronutrient content.

[5] (ASCIA Guidelines – Infant feeding and allergy prevention 2016;)
[6] Steele, S et al (2015): Risks of the unregulated market in human breast milk. Available at http://www.bmj.com/content/350/bmj.h1485/rr-2 (accessed 19 September 2017)
[7] Boyce C, Watson M, Lazidis G et al. Preterm human milk composition: a systematic literature review. Brt J Nutr. 2016;116:1033-45. Available at: https://doi.org/10.1017/S0007114516003007 (accessed 19 September 2017)
[8] National Health and Medical Research Council (2006). Nutrient reference values for Australia and New Zealand. www.nrv.gov.au

The RACP is also concerned that currently no human milk fortifier product when added to breast milk meets protein needs for extremely preterm infants who are fluid restricted. Additional protein powder is often required for these infants. Other nutritional products that may be used for feeding preterm infants include energy supplements (fat emulsion and fat &/or carbohydrate powders) and food thickener. However, there is currently no provision in the Code to ensure the microbiological limits and processing standards employed in the production of any of these products renders them safe for feeding to preterm infants.

Q10 Is there a need to prescribe a name for IFPSDU – what are the implications for subcategories?

Yes. The RACP believes that the prescribed name for IFPSDU should be consistent with names suggested in Figure 1 in this document.

Q11 Is there a need to prescribe names for any the IFPSDU subcategories? If yes, what benefit would this provide?

Yes. As explained above, the RACP believes that prescribed names for the subcategories (if maintained) should be consistent with the names suggested in Figure 1 in this document.

Q12 Are any specific compositional requirements (energy/macronutrient etc) needed in the Code for formula intended for premature or low birthweight infants, or for those suffering metabolic etc. conditions? If so, what are they?

The RACP believes that formulations should be targeted to meet current advisable preterm nutritional intakes in volumes of 150 mL/kg/d or above. For example, IFPSDU formulations for preterm infants should target protein intakes of 4.5 g/kg/d in 150 mL/kg/d for infants weighing <1 kg and protein intakes of at least 3.5 g/kg/d in 150 mL/kg/d for infants weighing 1-1.8 kg.

The formulation of human milk fortifiers, when added to breast milk, should also target advisable intakes for preterm infants as above, adjusting formulations for increased frequency of breastfeeding as the infant ages.

Q13 Are any specific compositional changes needed in the Code for protein substitutes? If so, what are they and what is your justification for them?

Left blank.

Q14 Are any specific compositional requirements (energy/macronutrient etc) needed in the Code if a new subcategory of formula for special medical purposes were created? If so, what are they?
The RACP recommends that ready to feed infant formula products should be considered in the clinical setting over powdered products due to their sterility and alleviated risks associated with reconstitution of powdered infant formula. We therefore recommend that FSANZ encourages the development and use of ready-to-feed products for these categories in these settings.

The introduction of ready to feed formula at 1.25 and 1.5 times the strength of a standard term formula would alleviate the need in the hospital setting of making a concentrated formula from powdered formula for term infants and term corrected preterm infants failing to thrive. A ready-to-feed formula with a composition mid-way between a term and preterm formula may also benefit moderate-late preterm infants in the hospital setting – any new products would need to be clinically trialled and assessed against standardised outcome measures.

If food thickener specifically developed for infants is to be included in this category, the RACP strongly recommends that it meets all relevant legislative requirements that are applied to the processing of infant formula, including microbiological limits.

Q15 What benefit, if any, would the inclusion of a specific requirement for any IFPSDU to be demonstrated by generally accepted scientific data as: safe, beneficial and effective in meeting the specific nutritional requirements of intended infant subpopulation?

The RACP believes that the classification of a product into one or more of these two designated sub-categories must be dependent on their performance as being fit for purpose, assessed through clinical trial

and standardised, measured outcomes. The RACP recommends that any IFPSDU product trials must not be undertaken and funded solely by industry. Such trials should rather be funded through unconditional grants provided by industry to health care facilities that will facilitate (ideally) the conduct of ethical, robust, well-designed double blinded randomised trials with sufficient power to determine if new products are fit for purpose.

Such a system would enable infant formula products specifically designed to prevent allergic disease, or target transient gastrointestinal conditions such as constipation, colic and regurgitation to be classified into sub-category 2, if the independently derived evidence supported such classification.

Q16 Are there any issues with the current requirements for micronutrients and nutritive substances in IFPSDU products?

If companies choose to manufacture IFPSDU in the sub-category of products for preterm and low birth weight infants, and if the products classified under this sub-category are deemed fit for purpose (i.e. the nutrient content will meet advisable nutrient intakes for preterm infants within a volume of 150 mL/kg/d etc.), the RACP believes it would be helpful if legislation was in place to enforce timely review of the adequacy of the formulations of these products as and when new expert nutrition guidelines are released. Such regular reviews should also be undertaken for human milk fortifier products.

The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guideline for Vitamin D is 800-1000 IU/d.[9] The latest consensus guideline is 400-1000 IU/d.[10] The American Academy of Pediatrics guideline is 200-400 IU/d.[11] However, nutritional intakes are prescribed according to volume and weight (mL/kg/d).

The RACP is concerned that this translates to over and under-prescribing of Vitamin D for preterm infants, depending on amount of Vitamin D in a product, the weight of infant and volume/kg of feed prescribed. Of the three human milk fortifiers currently available in Australia and New Zealand, one product contains twice as much Vitamin D as the other two.

Q17 Do you have any information to support the inclusion of a minimum and maximum amount of chromium in IFPSDU? If yes, should this be considered only in relation to certain categories of IFPSDU?
Left blank.

Q18 Do you have any information to support the inclusion of a minimum and maximum amount of molybdenum in IFPSDU? If yes, should this be considered only in relation to certain categories of IFPSDU?
Left blank.

Q19 Could one category of IFPSDU be used for all additional food additives, or should additional or modified subcategories be devised (noting the possible four subcategories in section 2.2).

Please note the RACP refers only to food thickening agents in this response.
We believe that not all food thickening agents are suitable for use in preterm infants. The RACP is concerned that in Australia and New Zealand there is currently no food thickening product on the market that would meet the microbiological limits that are applied in the processing of infant formula in general. The RACP believes that industry should be asked to develop a food thickener intended for use only in preterm/term infants. We recommend that FSANZ legislates the Standard (including microbiological limits) for manufacturing such a product.

Q20 Do you support the proposed amendments listed in Table 7 for IFPSDU at the amounts shown?

[9] Agostoni et al. (2010): Enteral Nutrient Supply for Preterm Infants: Commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. Journal of Pediatric Gastroenterology & Nutrition: January 2010 - Volume 50 - Issue 1 - p 85–91doi: 10.1097/MPG.0b013e3181adaee0
[10] Koletzko B, Poindexter B, Uauy R (eds) (2014): Nutritional Care of Preterm Infants. Scientific Basis and Practical Guidelines. Basel, Switzerland: Karger AG
[11] Abrams, SA et al (2013): Calcium and vitamin d requirements of enterally fed preterm infants. In: Pediatrics. 2013 May;131(5):e1676-83 DOI: 10.1542/peds.2013-0420

The RACP cannot give its support for the removal of Guar gum as explained in our response below to question 21.

Q21 Can you provide information on suitable international safety assessment, a demonstrated history of safe use in the context of IFPSDU, and a technological justification for:

- **a) Calcium carbonates**
- **b) Calcium citrates**
- **c) Phosphoric acid**
- **d) Sodium alginate**
- **e) Xanthan gum**
- **f) Locust bean (carob bean) gum**
- **g) Pectins**
- **h) Sodium carboxymethylcellulose**
- **i) Sucrose esters of fatty acids**
- **j) Starch sodium octenylsuccinate**

The RACP is aware of case study reports in the literature suggesting an association between use of gum-based thickeners and gastrointestinal disorders in infants, including necrotising enterocolitis, which is a medical emergency in preterm infants.[12,13,14,15,16,17,18,19,20] Notably, carob bean gum and xanthan gum appear to have been the main thickening agents mentioned in the literature that have been associated with gastrointestinal disorders. Since there is a need at times for thickening agents to assist with managing persistent, problematic regurgitation in preterm and term infants, the RACP cannot support removal of guar gum as being a permissible thickening agent to infant formula.

However, the RACP recommends that FSANZ sets a maximum permissible amount (MPA) for addition of guar gum to formula and sets the microbiological limits that must be applied to the manufacture of any thickening agents which are intended for addition to infant formulas and/or for safe use in breast and formula fed infants, including those born preterm and low birth weight.

The RACP would like to note one company that manufactures a carob-based thickener sold in Australia and New Zealand and that actively markets their product as being suitable to add to breast milk and formula to assist in the management of regurgitation. Instructions on the can of this thickener for preparing thickened bottle feeds of expressed breastmilk (EBM) or infant formula exceeds FSANZ MPA for addition of carob bean gum to infant formula. The company also provides instructions for making a gel in concentrations that far exceed the MPA for the addition of carob bean gum in infant formula. The company suggests that the gel can be fed to infants before, during and after breastfeeding. The company also states on the can that failure to follow directions can be harmful to the infant, that the product should only be used under medical supervision and that it is not suitable for use in preterm infants. The RACP recommends that FSANZ consults with the formula manufacturer regarding its use of carob bean gum and its instructions and labelling of the product.

[12] Mercier JC, Hartmann JF, Cohen R, Tran H, Biriotti V, Kessler A. [Intestinal occlusion and enterocolitis caused by Gelopectose]. Archives francaises de pediatrie. 1984; 41(10): 709-10.
[13] Clarke P, Robinson MJ. Thickening milk feeds may cause necrotising enterocolitis. Arch Dis Child Fetal Neonatal Ed. 2004; 89(3): F280.
[14] US Food and Drug Administration (2011): FDA warns not to feed SimplyThick to premature infants; Last updated 18 September 2012.Available at http://www.fda.gov//ForConsumers/ConsumerUpdates/ucm256250.htm (accessed 6 September 2017)
[15] Beal J, Silverman B, Bellant J, Young TE, Klontz K. Late Onset Necrotizing Enterocolitis in Infants following Use of a Xanthan Gum-Containing Thickening Agent. J Pediatr. 2012.
[16] Lin J, Nafday SM, Chauvin SN, Magid MS, Pabbatireddy S, Holzman IR, et al. Variable effects of short chain fatty acids and lactic acid in inducing intestinal mucosal injury in newborn rats. J Pediatr Gastroenterol Nutr. 2002; 35(4): 545-50.
[17] Woods CW, Oliver T, Lewis K, Yang Q. Development of necrotizing enterocolitis in premature infants receiving thickened feeds using SimplyThick(R). J Perinatol. 2012; 32(2): 150-2.
[18] Mallett AK, Wise A, Rowland IR. Hydrocolloid food additives and rat caecal microbial enzyme activities. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association. 1984; 22(6): 415-8.
[19] Gunness P, Gidley MJ. Mechanisms underlying the cholesterol-lowering properties of soluble dietary fibre polysaccharides. Food & function. 2010; 1(2): 149-55.
[20] Trout DL, Ryan RO, Bickard MC. The amount and distribution of water, dry matter, and sugars in the digestive tract of rats fed xanthan gum. Proceedings of the Society for Experimental Biology and Medicine Society for Experimental Biology and Medicine (New York, NY). 1983; 172(3): 340-5.

Q22 Are there any technologically justified concerns with changing the permissions for citric and fatty acid esters of glycerol (472c) to:

a) MPL of 9000 mg/L for liquid products

b) MPL of 7500 mg/L for powdered products?

Left blank.

Q23 What is the technological justification for the use of diacyltartaric and fatty acid esters of glycerol (472e) in IFPSDU? Are there any technologically justified concerns with the removal of this permission?

Left blank.

Q24 Do you support retaining a maximum PRSL for any IFPSDU? Please provide your rationale.

Left blank.

Q25 To what extent is pre-term infant formula used following hospital discharge and how do caregivers access it (for example, by prescription)?

The RACP strongly supports that preterm infant formula is only available for use in the clinical setting and should not be accessible in the community such as, through pharmacies for example. The protein content and the content of some other micronutrients in preterm formula (and human milk fortifier) is too high for infants once they are old enough and well enough to be discharged and it's availability in the community lends itself to misuse and poses a medical risk for infants.

Q26 Would you support the requirement for a statement that the product must be used under medical supervision, where the wording is not prescribed (an approach which harmonises with the overseas and international requirements)? Please describe your reasons why you do/do not support.

The RACP strongly supports the requirement of a statement that preterm formula must be used under medical supervision only and that the product is not available after discharge. We recommend a statement along the following lines '*This product must only be consumed by preterm infants in hospital under medical and dietetic supervision'.*

Q27 Are there any specific FSMP labelling requirements that you consider applicable to a particular type of IFPSDU?

The RACP strongly recommends that any preterm formula products, including human breast milk fortifier, should require labels warning that their use should be under medical and dietetic supervision only and that they are only suitable for use in preterm infants. The use of preterm formula products in term infants or term corrected infants may pose a medical risk. The RACP also recommends that all products that are classified into proposed sub-category 4 in FSANZ Consultation paper: Proposal P1028, p 15 (Figure 1. Sub-category 2 in this document) should have labelling as per Codex requirements.

Q28 Are there any specific FSMP labelling requirements that should apply to all IFPSDU?

Yes the RACP recommends that the following labelling should be mandatory to apply to all IFPSDUs: "Must be medically prescribed and used under the supervision of a medical specialist or dietitian."

Q29 What specific labelling requirements for the safe preparation and use of IFPSDUs are being used that contradict the general requirements set out in subsection 2.9.1—19(3) of Standard 2.9.1?

The RACP notes that there are variations in recommendations for reconstituting infant formula by expert bodies such as the WHO, CDC, NHMRC, ESPGHAN. Formula companies appear to promote NHMRC and ESPGHAN recommendations.

The RACP notes that in neonatal and paediatric clinical settings, there is wide variation in practice – formula powder is reconstituted immediately before a feed, for 12 hours and for 24 hours, using the following options: boiled water cooled to not less than 70 degrees, and then blast chilled; lukewarm boiled water, then chilled; ambient sterile water, then chilled; chilled sterile water.

Q30 What evidence can you provide to support concerns regarding inappropriate access to any IFPSDU?

The RACP has provided references throughout this document. Please contact the RACP if you have any questions or should require further references.