

Supporting document 1 (at Final Assessment)

Risk Assessment – Proposal P274

Review of Minimum Age Labelling of Foods for Infants

Executive summary

The appropriate timing for the introduction of solid foods to infants, also termed complementary feeding, is considered to be an important aspect of meeting an infant's nutritional requirements in the first year of life. Infants should be introduced to solid foods when breastfeeding (or infant formula) no longer provides sufficient nutrients and when developmental cues indicate a readiness to receive solid food. However, the ideal time period to introduce solid foods in terms of various long and short term health outcomes has been debated over the past few years.

A number of international expert bodies including the World Health Organization (WHO), the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), and the European Food Safety Authority (EFSA) have reported views on timing of introduction of complementary feeding. The National Health and Medical Council (NHMRC) and New Zealand Ministry of Health (NZ MOH) have also issued recommendations stating that introduction of solid foods should occur when an infant is 'around 6 months' of age. This recommendation differs from the current requirements in Standard 2.9.2 – Foods for Infants which refers to '4 months' as the minimum age for labelling infant foods.

Therefore, the main purpose of this assessment is to determine whether any food-related safety risks would be associated with the introduction of solid foods at 'around 6 months' relative to 'from 4 months'.

Long- and short-term health outcomes that have been examined in relation to the timing of commencement of complementary feeding include nutritional adequacy (including energy intake), growth and overweight, developmental effects (including food preferences), renal function, infectious morbidity and allergic diseases or syndromes. Because of the many differences and variables in study designs, it is difficult to link the specific timing (i.e. defined in months of age) to a health outcome. The strength of evidence for many of these associations is inconclusive due to studies where interpretation is complicated by study objectives which are separate to complementary feeding, such as duration of breastfeeding.

Because of the increase in the numbers of children observed with food allergy, sensitisation and anaphylaxis seen over the past 10-15 years, the association between allergic diseases and the timing of solid food introduction is of much current interest. In 2008, FSANZ reviewed the risk of allergy and other immune-mediated diseases in relation to timing of introduction of solid foods and concluded that, although preliminary information suggests that a window may exist between 4 and 7 months to minimise allergy risk, conclusive evidence was still lacking. In 2009, reports published by EFSA and ESPGHAN gave similar conclusions.

The risk assessment was therefore revised by FSANZ in 2013 to review the evidence for the appropriate timing for solid food introduction, focussing on reports and data published since 2008.

The main objectives of the 2013 assessment were to identify adverse health outcomes associated with timing of solid food introduction relevant to the proposed change for the labelling of infant foods as appropriate for infants 'around 6 months'. Food allergy risks were reviewed in detail because of current concerns, which are particularly relevant to the time periods covered in this proposal, and also due to the availability of new research in the area.

The main conclusions of this assessment are summarised as follows:

- Solid foods introduced at 'around 6 months' compared to 'from 4 months' effectively means that introduction of solid foods could be delayed by as much as up to 2 months. Based on several key review articles, there are no health effects that are clearly linked with adverse outcomes if solid food is introduced from 4 months compared to delaying until 'around 6 months' of age. Allergy risk appears to be associated with solid foods introduced to infants at less than 4 months based on several cohort studies. This association supports the current ESPGHAN and EFSA recommendations that 'from 4 months' is the appropriate minimum age at which solid foods are introduced.
- Since 2008, there is increasing evidence that the timing of solid food introduction may be related to the development of food-related allergy. The critical period to minimise the risk of allergy development seems to be between the ages of 4 and <7 months. However, because of unclear and inconsistent definitions of age categories, measurement bias in many studies and the contribution of various other factors in the development of allergic disease, the evidence is not conclusive. Currently, there are randomised controlled trials (RCTs) underway which aim to determine whether exposure to food allergens, and not avoidance, is critical during this period to minimise the risk of developing food-related allergy and to determine the optimal timing for introduction of solid foods.

Therefore, FSANZ concludes that there is a window from 4 to <7 months for introducing solid food which carries a low risk of adverse health outcomes.

Health surveys conducted in Australia (2010) and New Zealand (2011/2012) show that no more than 10% of infants are introduced to solid foods before four months of age. Of the mothers who introduced solids to infants before four months of age the proportion was highest among New Zealand Maori, young Australian mothers (<25 y) and the lower socio-economic groups in Australia. There appeared to be no association between the introduction of solids and cessation of breastfeeding.

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1 Introduction

Proposal P274 – Review of Minimum Age Labelling of Foods for Infants concerns a proposed amendment to Standard 2.9.2 – Foods for Infants that sets the labelling requirements for solid foods intended for infants.

The revised Australian Infant Feeding Guidelines, launched by the NHMRC in February 2013, recommended that solid foods be introduced to infants at ‘around 6 months’ (NHMRC 2012a). This recommendation is unchanged from the previous guideline issued in 2003 (NHMRC 2003). Likewise, the New Zealand Food and Nutrition Guidelines for Healthy Infants and Toddlers also recommended introduction of solid foods at ‘around 6 months’ (New Zealand Ministry of Health 2008). The timing for the introduction of solid foods in both guidelines is centred on ensuring adequate nutrient intake to infants when breast milk (or infant formula) may no longer be sufficient.

1.1 Objective of the assessment

This assessment provides an update of risk assessment work completed in 2008 and published as part of the Preliminary Final Assessment Report (PFAR) associated with Proposal P274 (FSANZ 2008) in relation to the timing of solid food introduction to infants. This assessment aims to:

- summarise the key conclusions of the PFAR
- summarise reviews or reports of international expert panels which have considered timing of complementary feeding for infants
- review published scientific data (particularly since 2008) that underlies Australian and New Zealand national infant feeding guidelines with emphasis on the induction of food allergy and/or gluten intolerance.

1.2 Scope of the assessment

Infant as defined under Standard 2.9.2 means a person up to the age of 12 months. Infant feeding practices up to the age of 12 months include breastfeeding, formula-feeding and, at an appropriate age, solid foods. Proposal P274 is relevant to the labelling requirements of foods intended for infants and this assessment will be directed at health effects associated with the time period over which solids are first introduced. The health benefits of breastfeeding (exclusive or mixed with formula-feeding) for infants up to 6 months of age are well recognised and will not be addressed. Similarly, the inadvisability of introducing solids before 4 months of age is well recognised and will not be addressed.

Previously, FSANZ considered whether delaying solid food introduction to around 6 months of age would have an adverse impact on a range of nutritional and developmental outcomes for infants (see Section 2.1) (FSANZ 2008). This assessment applied a tiered approach to determine whether there was recent research that might alter the previous conclusions. We considered several reviews of a broad range of health outcomes that were claimed to be linked to the timing of solid food introduction (see Section 2.3) and concluded that most were related to the introduction of solids before 4 months or were related to the use of infant formula. Only the risk of developing allergic diseases was identified as an area where newly available literature might change previous conclusions made in 2008. The literature was reviewed to update the previous consideration of this topic (See Section 3).

1.3 Risk assessment questions

The risk assessment question addressed in this assessment (covered in Section 3) is:

What conclusions can be drawn from the evidence on the association between the age of introduction of solid food and the development of food-related allergies and/or gluten intolerance in children?

It also describes the age at which solids are introduced in Australia and New Zealand and considers whether this is associated with cessation of breastfeeding (Section 4).

1.4 Definitions

The following definitions apply to this risk assessment:

Atopy A child with atopy produces IgE antibodies after exposure to common environmental allergens. The atopic diseases (eczema, asthma and rhinoconjunctivitis) are clinical syndromes each defined by a group of symptoms and signs (Gold and Kemp 2005).

Complementary feeding is defined as the gradual introduction of solid food and fluids along with the usual milk feed (breast milk or infant formula) to an infant's diet (New Zealand Ministry of Health 2008).

Exclusive breastfeeding refers to the WHO recommended definition which is breastfeeding with no additional liquid or solid foods other than vitamins and medications (Binns et al. 2009).

Food allergy (or food-related allergy) refers to food-mediated adverse reactions that involve the immune system resulting from oral exposure to food (Hayder et al. 2011).

Food sensitisation is an immune response to food allergen exposure which precedes development of food allergy.

2 Background to this risk assessment

2.1 Previous FSANZ assessment

The previous Proposal P274 nutrition assessment (FSANZ 2008) examined the following nutritional and developmental outcomes if introduction of solid foods were delayed to 'around 6 months':

- the potential for displacement of human breast milk and/or infant formula, any changes in energy intake, and whether growth outcomes are adversely affected
- the capacity of infant kidneys to deal with the higher solute load of solid foods prior to 6 months of age
- the impact on iron and zinc status, particularly in pre-term infants
- the influence of feeding practices during infancy on later food preferences.

The assessment concluded that in terms of infant growth, kidney function, and iron/zinc status, it is unlikely that there are differences in the nutritional and developmental outcomes for infants that receive solids at an early (close to 4 months) versus a later (close to 6 months) age.

In addition, the relationship between age of introduction of solid foods and the development of allergies was assessed. Conclusions in this assessment, however, were more uncertain with some evidence suggesting that the delay in the introduction of solid food to infants' diet may contribute to the risk of developing allergy and other immune-mediated diseases. FSANZ noted in the 2008 report that this was an active area of research that, once published, was likely to increase the confidence around the optimal age for complementary feeding.

2.2 Recommendations of expert panels and committees

Recommendations on the appropriate age for the introduction of solid foods to infants have been issued by the World Health Organization (WHO) and several international scientific panels including the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) and the European Food Safety Agency (EFSA). The views of these expert panels are based on consideration of several health outcomes and consensus on the benefits of breastfeeding for the first 6 months¹. However, recommendations are somewhat inconsistent for starting complementary feeding where timing of solid food introduction varies from 4 months compared to 'around' or 'at' 6 months of age (Table 1). These are subtle differences but may be important for certain health outcomes (addressed in Section 2.3).

Table 1: Comparison of recommendations for age of complementary feeding from Expert Panels and Committees

Expert Body	Recommendation
WHO (2003)¹	Recommends infants start receiving complementary foods at 6 months of age in addition to breast milk
ESPGHAN (2009)	Complementary feeding should not be introduced in any infant before 17 weeks and all infants should start complementary feeding by 26 weeks.
EFSA (2009)	Complementary food introduced between the age of 4 and 6 months is safe and does not pose a risk for adverse health effects.
NZ MOH (2008)	Recommends that infants be fed exclusively on breast milk to around six months of age, at which time complementary foods can be introduced with continued breastfeeding.
NHMRC (2013)	Recommends introduction of solid foods at around 6 months of age.

The NHMRC recommendation is based on systematic reviews (NHMRC 2011) conducted as part of the review for the Australian Dietary Guidelines. The findings of the systematic reviews were used to inform the 2013 NHMRC Infant Feeding Guidelines which were published at the same time (NHMRC 2012a). A detailed summary of the evidence base of the NHMRC guidelines is provided at Attachment 4.

¹ The WHO defines complementary feeding as foods or liquids that are provided along with breast milk and thus, infant formula is categorised as a complementary food. The intention of the WHO definition is to encourage exclusive breastfeeding until 6 months, particularly in developing countries where risk of infection from unsanitary food and water is significant (WHO 2003). In contrast, ESPGHAN and EFSA and others define complementary foods as all solid food and liquid foods other than breast milk or infant formula and follow-on formula. This assessment follows the ESPGHAN/EFSA definition.

The initial literature search for the Australian Dietary Guidelines revealed evidence on the relationships between age of introduction of solid foods and development of overweight and development of allergic symptoms.

Subsequent systematic reviews on these two relationships indicated that:

- (1) Overweight or obesity in children younger than 7 years of age, based on limited information (1 systematic review and 2 cohort studies; Grade D evidence²) showed “no relationship between the age of weaning and development of infant or child overweight”.
- (2) Development of allergic disease, based on limited information (1 systematic review, 2 RCTs, and 4 cohort studies; Grade D evidence), may be associated with the risk of allergic disease with some evidence that delaying the introduction until after 6 months may increase the risk of certain allergies. Details on the NHMRC review covering allergic syndromes is summarised in Section 3.

The NHMRC Infant Feeding Guidelines recommend introduction of solid foods at around 6 months based on the nutritional sufficiency of breast milk until 6 months of age, development of feeding behaviour to allow chewing and swallowing and maturity of the digestive system (see Attachment 4).

2.3 Summary of health effects associated with timing of the introduction of solid foods

ESPGHAN and EFSA published comprehensive reviews on timing of complementary feeding in relation to a number of potential health effects (Agostoni et al. 2008; EFSA Panel on Dietetic Products Nutrition and Allergies (NDA) 2009). In addition, Hornell et al recently published a systematic review on infant feeding practices and covering similar health effects (Hornell et al. 2013). Attachment 1 lists the key findings from each review. Specific health outcomes examined included nutrient adequacy (including energy), growth (including obesity and overweight), allergic diseases and infectious morbidity. The combined findings of these reviews indicate that:

- Deficiency of iron or zinc is unlikely if solid foods are introduced in the period of 4-6 months. However, data are lacking on nutrient intakes and hence nutritional status if solids are introduced after 6 months.
- Age at which solid food is introduced does not have a strong impact on growth rates (weight or length) but data are lacking for solid foods introduced after 6 months. Interpretation of studies is complicated by differences in growth that result from changes in dietary composition (e.g. different complementary foods or increased milk protein).
- The evidence is insufficient to demonstrate that the timing of solid food introduction affects the risk of obesity or overweight. A subsequent systematic review on the timing of complementary foods and obesity risk concluded that there is no increased risk if foods are introduced at 4–6 months or >6 months but that there is some evidence that very early introduction (before 4 months) may increase the risk of childhood overweight (Pearce et al. 2013).

² Appendix E of the Australian Dietary Guidelines states that Grade D indicates that the evidence was limited, inconclusive, or contradictory. These Grade D relationships were not used to inform the development of the Guidelines.

- Solid food introduction before 6 months of age is a significant risk factor for infectious diseases in developing countries. In developed countries this association has been examined in terms of non-exclusive breastfeeding rather than introduction of solids. An association with introduction of solids to infants less than 4 months of age has been observed in one cohort study conducted in Belarus (Kramer et al. 2003) but not in a study conducted in the UK (Quigley et al. 2009).
- Increased risk of allergic syndromes (food allergy, atopy, gluten intolerance and/or celiac disease, and asthma) may be associated with the timing of complementary feeding, particularly if solid foods are introduced outside the 4–6 month period.

For the purposes of Proposal P274, analysis of studies on links between infant feeding practices and certain long- and short-term health outcomes is not straightforward. Studies frequently consist of double-barrelled questions and/or definitions so that health effects may be related to more than one issue. For example, studies focussed on determining the optimal duration of breastfeeding are important for understanding numerous infant health issues. However these same studies do not necessarily reveal the appropriate age for the introduction of solid foods. Very few studies have assessed the timing of complementary feeding as an independent risk factor. Specific factors contributing to definitional problems in studies examining the timing of solid food introduction include the classification of formula as a complementary food, studies conducted solely on breastfed infants with no comparison with formula-fed infants, and extrapolation of evidence from studies in developing countries to developed countries.

As an example of such definitional problems, the current WHO infant feeding guidelines are based in part on the 'PROBIT' observational cohort study which found lower gastrointestinal rates infection in infants exclusively breastfed for at least 6 months (Kramer et al. 2003). However, in relation to solid food introduction, the 'PROBIT' study only examined two populations: infants exclusively breastfed for 6 months and solid food introduced thereafter compared to infants exclusively breastfed for 3-4 months then solid foods and/or formula introduced. The incidence of gastrointestinal infection in infants who were introduced to solid foods at 3–4 months **while continuing to be breastfed** or after adjusting for the use of breast milk versus formula was not determined in this study. Therefore it is not possible to separate the effect of solids from the effect of formula on gastrointestinal infection incidence in the group with shorter breastfeeding duration in the PROBIT study.

By contrast, the UK Millennium Cohort Study examined hospitalisation rates for gastrointestinal and lower respiratory tract infections separately for age of introduction of solids and from use of formula (Quigley et al, 2009) and adjusted the analyses. The results show lower hospitalisation rates are associated with breastfeeding compared to use of formula, but there is no association with age of introduction of solids for the two conditions studied. The authors reported:

*We assessed the independent effects of solids and breastfeeding on the risk of hospitalisation for infection in term, singleton infants in the Millennium Cohort Study (n=15,980). For both diarrhoea and lower respiratory tract infection (LRTI), the monthly risk of hospitalisation was significantly lower in those receiving breast milk compared with those receiving formula. **The monthly risk of hospitalisation was not significantly higher in those who had received solids compared with those not on solids** (for diarrhoea, adjusted odds ratio=1.39, 95% CI: 0.75-2.59; for LRTI, adjusted odds ratio=1.14, 95% CI: 0.76-1.70), and **the risk did not vary significantly according to the age of starting solids**. (Quigley et al, 2009, emphasis added).*

FSANZ has not identified any data that can be examined to determine if there is a difference in gastrointestinal infection rates in Australia and New Zealand according to whether infants were introduced to solid foods from 4 months or around 6 months of age.

Such data would be difficult to interpret in any case, as it would be confounded by other factors, such as infants in this age group moving into childcare. FSANZ believes that the data from the UK Millennium Cohort Study are likely to be more relevant to prevailing conditions in Australia and New Zealand than data from Belarus.

Apart from the potential links to allergic diseases, the three reviews covered in Attachment 1 indicate that there are no new data to change the view that there are no health effects clearly linked with adverse outcomes if solid food introduction is delayed to ‘around 6 months’ compared to from 4 months of age (see Attachment 1). There are new studies and reviews (Palmer and Prescott 2012) examining the potential association to allergic diseases published since the 2008 FSANZ assessment (FSANZ 2008). As this is an area of active research with new data which might alter previous conclusions, a more detailed analysis of this health effect is addressed in Section 3.

3 Solid food introduction and allergy

Allergy is an abnormal immune response to a variety of exogenous proteins such as pollen, insect venom and food proteins. The development of allergic diseases is complex and depends on interactions between a variety of environmental factors and the genetic susceptibility of the individual. For food allergy³, avoidance of potentially allergenic foods was originally considered to be important for susceptible individuals. Scientific evidence no longer supports this approach and oral tolerance (suppression of orally-induced immune responses in the gut) and timing of introduction and dose of potential food allergens are thought to be critical factors (Brandtzaeg 2010).

Common allergenic foods are cows’ milk protein, egg, soya, wheat, nuts and fish. Food allergy is an IgE-mediated immune response which is characterised by clinical outcomes or diagnoses such as atopic eczema (atopic dermatitis), allergic rhinitis and asthma. Food protein sensitisation precedes development of food allergy but does not always lead to an allergic disease for a given food.

For example, eczema is also a clinical symptom of food sensitisation, usually appearing in the first 18 months of age, which infants may outgrow in later childhood. Allergies to proteins in milk and egg increase risk of sensitization to pollen and development of asthma so that these health outcomes are also considered as food related.

The relationship between allergic disease and infant feeding has been covered in several recent reviews papers (Prescott et al. 2008, Prescott and Nowak-Węgrzyn 2011, Lack and Penagos 2011, Fewtrell et al. 2011, Palmer and Prescott 2012). The prevalence of allergic diseases and syndromes in children has increased substantially in the past 10–15 years. The cause of this increase is not known but exposure to food proteins is considered to be an underlying risk factor, with the type of food protein, exposure through the maternal diet and the timing of exposure to specific food proteins under investigation. In addition, infants exposed to food proteins too early may develop allergic disease due to inefficient digestion of food proteins, undeveloped gut permeability and degree of gut bacterial colonization (Shreffler and Radano 2011).

³ Food-related allergy includes gluten intolerance which is an immune-mediated response to proteins in gluten and can give rise to celiac disease and Type 1 Diabetes Mellitus (FSANZ 2008).

3.1 NHMRC review on age of introduction of solid foods and allergies

The relationship between development of allergies and appropriate timing for the introduction of solid foods was addressed within both the NHMRC Infant Feeding Guidelines (NHMRC 2012a) and the Australian Dietary Guidelines (NHMRC 2013). The underlying scientific data supporting these guidelines was described in the Literature Review (NHMRC 2012b) for the Infant Feeding Guidelines and the Evidence Report (NHMRC 2011) for the Dietary Guidelines.

The Literature Review for the Infant Feeding Guidelines considered the relationship of breastfeeding and formula-feeding to the prevention of atopic diseases and not timing of solid food introduction. However, the views and recommendations of various expert groups on the relationship between allergies and solid foods were also reviewed. Final comments suggested that there is no reason to restrict the introduction of any particular foods or groups of food to infants to prevent allergy or promote tolerance.

The Evidence Report for the Australian Dietary Guidelines was based on systematic reviews addressing specific targeted questions on food, diet and disease/health relationships, including whether the age of solid food introduction in children is associated with the development of allergic syndromes (NHMRC 2011). The literature searches identified seven studies of which only four cohort studies and one RCT, all published between 2006 and 2008, were judged to be of suitable quality. Only two of the five studies examined introduction of solid foods in the 4–6 month time period and the other three involved introduction of solids after 6 months. The review concluded that the data suggests that delaying solid food introduction until after 6 months may increase the risk of certain allergies but acknowledged that the conclusion is based on a limited number of studies (Grade D evidence).

3.2 FSANZ analysis on the potential association between the age of solid food introduction and allergy

The analysis of review papers shown in Attachment 1 indicated that the age of introduction of solid foods is potentially associated with the development of allergic disease. This potential link was also identified in the FSANZ assessment conducted in 2008 (FSANZ 2008) and is consistent with recent published reviews (Palmer and Prescott 2012). Current concerns about food allergy risk are also particularly relevant to the time periods covered in Proposal P274. Therefore, a more detailed analysis of the evidence for this association is described below.

Sources of data, search strategy

Primary research (cohort study or RCT) was selected according to the PICO⁴ method and included the following study characteristics:

- (1) Breastfed or formula-fed infants of normal allergy risk or at-risk of allergic disease (parental history, allergic symptoms).
- (2) Various solid foods or specific allergenic foods (but not infant formula) introduced from 4 months of age.
- (3) Depending on the study, age of solid food introduction was compared to another specified age (e.g. introduction at 4 months compared to 6 months) or a non-allergenic food (e.g. egg compared to rice powder).

⁴ PICO defined as population (P), intervention (I), comparison (C) and outcome(s) (O).

- (4) Outcomes were clinical diagnoses in infants and children up to age 10 years of food-related allergic diseases or symptoms: asthma, atopy or atopic disease, allergic rhinitis, allergic sensitisation, coeliac disease; Type 1 diabetes mellitus; eczema; food allergy, food sensitisation, and wheezing.
- (5) Studies or specific analyses within studies that examined the duration of breastfeeding and association with allergic diseases were excluded.

The following strategy was used to source primary research:

- (1) Studies cited by reviews conducted by expert bodies (EFSA, ESPGHAN, the American Academy of Pediatrics (AAP), NHMRC). These mainly covered the period up to 2008 when these reports were completed or published.
- (2) Studies cited by Palmer and Prescott (2012) which covers the period from 2008 to 2012.
- (3) Studies identified by searching PubMed database using search terms infant feeding, allergy, solid foods, complementary feeding plus related terms for the period 2008 to July 2013.
- (4) Include only primary studies; position or consensus statements and review articles (apart from Palmer and Prescott, 2012) were excluded.

Studies identified through this approach are listed in Attachment 2. In summary, 27 studies covering the period of 1981–2013 were reviewed. Most were prospective cohort studies including infants of normal or increased allergy risk. The studies measured numerous allergic disease outcomes in infants and children spanning 1–10 years of age. The search of the PubMed database identified four additional studies published in 2013 not included in the other reviews (Palmer et al. 2013; Frederiksen et al. 2013; Nwaru et al. 2013a; Nwaru et al. 2013b).

One systematic review on the association of complementary feeding with the development of allergy was included in Attachment 2 (Tarini et al. 2006). The review's conclusions were based on some of the primary research cited in this assessment plus several earlier publications. Allergy outcomes in relation to duration of breastfeeding have also been covered in several recent large systematic reviews (Kramer and Kakuma 2002; Kramer and Kakuma 2012) but, as mentioned in section 2.3, definitional issues mean that these reviews have limited use for Proposal P274.

Results

Comparing studies is complicated by the variety of foods, timing of solid food introduction, allergy risk, different allergy outcomes and age at assessment of outcome. To simplify analysis of these studies and address the question about the appropriate timing of solid food introduction, studies in Attachment 2 are grouped according to outcome:

- (1) Evidence that introduction before 4 months increases risk of allergic disease compared to introduction after 4 months.
- (2) Evidence shows no association (protective or adverse) between the timing of solid food introduction and risk of allergic disease.
- (3) Evidence that introduction of solid foods at around 6 months (i.e. after 4 months and before 7 months) is associated with decreased risk (or no increased risk) of allergic diseases compared to outside this age range.

Introduction of solid foods before four months increased the risk of eczema in six cohort studies conducted from 1981 to 1994. These studies were mostly small cohort studies and most were also centred on the protective effects of exclusive breast feeding.

These results are difficult to interpret because exclusive breastfeeding is often encouraged for at-risk infants (e.g. family history of allergic diseases) and so the results could reflect reverse causation (Zutavern et al. 2006).

The evidence that allergy risk appears to be associated with solid foods introduced to infants at less than 4 months combined with evidence that risk of infectious morbidity (based on evidence of protective effects of breastfeeding) is also increased with this time period, continues to support the current recommendations from ESPGHAN, EFSA, AAP and NHMRC that 4 months of age is the appropriate minimum age at which solid foods are introduced.

Seven studies carried out from 1983 to 2011 showed neither protective nor adverse effects related to the age of solid food introduction and the risk of allergic disease. The lack of association was measured across various allergic diseases or symptoms and included one systematic review of 13 cohort studies (Tarini et al. 2006) showing association between the introduction of solids before the age of 3–4 months and development of eczema. However, little data were available to support an association between early introduction of solid food and other allergic conditions. A comparatively large cohort study (Chuang et al. 2011) showed that solid food introduction before 4 months, between 4–6 months, and after 6 months was not related to the risk of atopic disease in infants up to 18 months of age. Given the number of participants, this study provides strong support that the timing of solid food introduction across the period of ‘around 6 months’ does not influence the development of atopic diseases. The study recruited participants from the general population of newborn infants but excluded those with physician-diagnosed atopic dermatitis in the first 6 months of life to eliminate contribution of reverse causality. The inclusion of children with apparent normal allergy risk, however, may mean that immune-mediated food sensitisation, which underlies development of allergy, may not have occurred in these infants. These issues indicate the complexities in designing and interpreting studies on the development of allergies linked to dietary factors.

A number of studies (12 as listed in Attachment 2) published more recently (2006 to present) suggest growing evidence that exposure to allergenic foods between 4–6 months and/or before 7 months may decrease the risk of allergic diseases. As previously highlighted, mainly prospective, cohort studies have been conducted involving various time points, types of foods, and allergenic outcomes. These studies also support the view that avoidance of food allergens does not prevent allergic disease and that exposure to food in the period between 4 and 7 months may actually result in ‘tolerance’ rather than allergy.

The main conclusion from the 2013 assessment was that, aside from the question of allergy, there were no adverse health effects that are clearly linked if solid food introduction is delayed to ‘around 6 months’ compared to ‘from 4 months’. Based on FSANZ’s review of primary research that was published between 1981 and 2013, the critical period for introduction of solids, to minimise the risk of allergy development, seems to be between the ages of 4 and <7 months. However, there are increased risks of allergy with solid foods introduced to infants less than 4 month. There may also be increased risk of allergy development when solids are introduced at 7 months or later. This latter conclusion is consistent with the NHMRC evidence statement “Delay in the introduction of solid foods until after the age of 6 months is associated with increased risk of developing allergic syndromes. (D)” (NHMRC 2011). The additional studies included in the FSANZ update might even increase the rating of this statement to C (suggestive) from D (inconclusive).

3.3 Studies currently under way (RCTs)

Prescott and Palmer (2012) highlight the main issues with conclusions based on observational cohort studies conducted to date. Many studies on timing of complementary feeding do not account for 'reverse causation' which arises when an allergy outcome influences the exposure.

For example, the children of allergic parents or infants showing early signs of allergy (eczema, for example) may be prescribed specific feeding practices (e.g. delayed solid food introduction) that are then interpreted as causative for increased risk of allergenic diseases measured at later time points (Zutavern 2006).

Most recent observational studies attempt to correct for reverse causation (e.g. Chuang et al, 2011) but numerous other factors are also not tested or controlled including timing of specific foods, quantity and quality of solid foods, influence of maternal exposure or environmental factors, and other routes of early allergen exposure that contribute to oral tolerance (Shreffler and Radano 2011; Lack and Penagos 2011). Several randomised controlled trials are now currently underway which will examine some of these factors and test the hypothesis that 'early' regular exposure to food allergens induces oral tolerance and reduces the risk of allergic disease (Palmer and Prescott 2012; Metcalfe et al. 2013). Interventions involve introduction of various foods in the range of 3–8 months but with a clear focus on the 4–6 month period. Mostly results are yet to be published. In support of the early exposure hypothesis, recent results from a small RCT showed that the incidence of egg allergy at one year was reduced in sensitised infants fed egg protein from 4 months compared to infants on a normal diet with egg introduced at 8 months (Palmer et al. 2013).

3.4 ASCIA recommendation on timing of solid food introduction

The Australasian Society for Clinical Immunology and Allergy (ASCIA) issued a position statement on allergy and infant feeding based on systematic review of relevant papers and recommendations by other expert panels (ESPGHAN and AAP) (ASCIA 2010). Based on current evidence, ASCIA concluded that there is little evidence that delaying introduction of solid foods beyond 6 months reduces the risk of allergy and current expert reviews support the recommendation that solid foods should be introduced from around 4–6 months. The ASCIA statement also suggests that delays in solid food introduction beyond 6 months may actually increase the risk of allergy development but acknowledges that more research is needed to make conclusive recommendations about the timing of introduction of solid foods. ASCIA recommendations are based on primary studies and review articles as cited in their assessment.

3.5 Prevalence of food-related allergy

As Proposal P274 relates to infant foods which can be fed to all populations of infants, the specific question of effects on at-risk populations was not addressed. However, studies reviewed in SD1 (see Appendix 2 table) covered the association between the timing of solid food introduction and allergy risk in both at-risk (e.g. having allergic symptoms or at least one direct family member with allergic disease) and normal risk populations. Increased risk of allergies in relation to the timing of solid food introduction is found in both populations.

A recent paper from the HealthNuts research program (Osborne et al. 2011) measured the prevalence of food-related allergy in one-year old Victorian children, as assessed by the 'gold standard' oral challenge test, to be at least 10%.

Also from this research group, the population prevalence of physician-diagnosed eczema⁵ at 12 months was recently reported as 20% (Martin et al. 2013) At-risk infants are generally defined as having one immediate family member with a history of any allergic disease (Koplin et al. 2013) On this basis, prevalence of allergy among at-risk infants could be much higher (Su et al. 2012) although an accurate determination of this is difficult due to complex aetiology of allergic diseases.

Nevertheless, the development of food-related allergies in infants and children is a significant public health problem. As noted above, several RCTs that are currently underway aim to determine whether 'early' regular exposure to food allergens induces oral tolerance and reduces the risk of allergic diseases.

3.6 Summary

Overall the evaluation of the studies listed in Attachment 2 suggests that the risk of allergic diseases or syndromes in children and infants to food is mainly linked to introduction of solids before 4 months and, possibly, after 7 months of age. Based on available evidence, the introduction of solid food at 'around 6 months' does not appear to present a greater risk of subsequent food allergy, relative to the introduction of solid food 'from 4 months'. This conclusion is consistent with current advice and recommendations issued by several expert bodies. However, as concluded in the PFAR for Proposal P274 (FSANZ 2008), evidence continues to emerge that the period of 4–7 months may be the critical window for the prevention of food-related allergy. Most of the evidence is limited to observational cohort studies and current efforts are focussed on appropriate studies designed to address the specific questions of timing of complementary feeding in relation to allergy. These include several RCTs currently underway.

4 Introduction of solids in Australia and New Zealand

4.1 New Zealand national data

The New Zealand Health Survey 2011/2012 showed fewer infants were given solid food before 4 months of age (10%) than in 2006/07 (16%) (Ministry of Health 2012). In addition, the percentage of Maori children that were given solid food before 4 months of age had fallen from 22% in 2006/07 to 16% in 2011/12. The New Zealand Food and Nutrition Guidelines for Healthy Infants and Toddlers (Ministry of Health 2008) recommend that complementary foods be introduced at 'around 6 months' (they had previously recommended 4 to 6 months). The Guidelines also recommend that solid foods should be introduced when an infant is at the appropriate stage of development, which will vary from infant to infant.

4.2 Australian national data

The 2010 Australian National Infant Feeding Survey (Australian Institute of Health and Welfare 2011a) assessed the age of introduction of solid foods in two different ways (Table 2). First, when asked about the day before the survey, 9.7% of mothers with infants aged 3–<4 months had fed their infant solids (n=3,887 mothers). In the second method, when asked to recall the age of introduction, 4.3% of respondents with an infant aged 4 months or older reported having introduced solids before 4 months (time-to-event analysis using responses from all mothers).

⁵ Eczema is also known as atopic dermatitis, atopic disease or IgE-associated eczema and is an inflammatory, non-contagious, skin disorder which is linked to food allergy (Gold and Kemp, 2005)

Also shown in Table 2, solids were introduced at 3–<4 months of age in 15.2% of infants with a mother aged 24 years or younger and in only 2.8% of infants whose mother was aged 35 years or older. There was under sampling of low socioeconomic status (SES) respondents with infants and those with low maternal age. If the national average is re-weighted using the national SES and maternal age at birth data (see Table 3.1 in: (Australian Institute of Health and Welfare 2011b)), then FSANZ estimates that the revised prevalences of introduction of solids before 4 months is 4.7% (SES weighting) and 6.0% (maternal age weighting).

Variation by jurisdiction ranged from 5.9% in Queensland to 2.3% in the ACT. FSANZ has confirmed the interpretation of these results with the Australian Institute of Health and Welfare. Therefore FSANZ concludes that for the Australian population, the proportion of infants who were receiving solids before 4 months of age ranged from 4–10%, noting that within this range there was some variation according to maternal age and SES.

Data from the Queensland Infant Nutrition Surveys for 2003 and 2008 (provided by Queensland Department of Health) shows a decrease in the proportion of infants receiving solid food before 4 months of age (48.5% to 12.3%), over this time period – and also a decrease in the number of infants who were introduced to solids after 6 months of age (12.1 to 8.3%). Before 2003, the recommended age to introduce solids was 4–6 months and this changed to ‘around 6 months’ in 2003.

Table 2: Selected infant feeding data from the 2010 Australian National Infant Feeding Survey^a

<i>Proportion of infants introduced to solid foods by age (%)</i>							
<i>Among infants aged (months)</i>	<i>Age (completed months)</i>	<i>Proportion receiving any breast milk^{b, KM}</i>	<i>Proportion received solid foods in previous 24 hours^{c, X}</i>	<i>Proportion who had ever received solid foods^{d, KM}</i>			
Birth-<1	0 (< 1 month)	90.2	0.0	0.1			
1.0-<2	1	74.6	0.7	0.1			
2.0-<3	2	72.7	2.2	0.8			
3.0-<4	3	70.3	9.7	4.3			
4.0-<5	4	68.7	35.3	28.4			
5.0-<6	5	62.9	70.2	56.2			
6.0-<7	6	60.1	91.5	91.6			
<i>Proportion of infants introduced to solid foods by maternal age^c (%):</i>							
<i>Mother's/carer's age (years)</i>	<i>Infants age at which solid food was introduced (months of age)</i>						
	<1	1-<2	2-<3	3-<4	4-<5	5-<6	6-<7
24 or younger	0.3	0.4	3.1	15.2	54.6	71.9	94.1
25 – 29	0.1	0.2	1.0	6.0	34.4	63.4	93.4
30 – 34	–	0.1	0.5	2.9	26.6	57.0	92.2
35 or older	0.1	0.2	0.5	2.8	22.4	48.9	89.9
All ages	0.1	0.1	0.8	4.3	28.4	56.2	91.6

^a Source: (Australian Institute of Health and Welfare 2011a)

^b From: Table 2.1 Proportion of children receiving any breast milk, by age.

^c From: Table 2.4 Proportion of children who had received soft/semi-solid/solid food in the last 24 hours, by current age.

^d From: Table 3.13 Proportion of children who were introduced to soft/semi-solid/solid food by month of age.

^x Cross-sectional analysis of children of this age on the day of the survey.^{KM} Kaplan-Meier time-to-event analysis using data from all respondents.

4.3 Introduction of solids vs prevalence of breastfeeding

When examining this question it is important not to use the self-referential definition of exclusive breastfeeding. Exclusive breastfeeding is defined by the WHO as *no other food or drink, not even water, except breast milk (including milk expressed or from a wet nurse) (WHO 2014)*. Once solid foods are introduced, by definition, the period of exclusive breastfeeding is ceased.

However this does not mean that risks associated with replacement of breast milk with formula also apply to the addition of solids to the diet for infants consuming breast milk. The two reasons why exclusivity of breastfeeding might cease need to be assessed separately because they do not necessarily have the same risks. For the current proposal, only cessation of exclusivity due to introduction of solids is relevant. This section examines whether introduction of solids is associated with cessation of any breastfeeding (i.e. switching to using formula) which would be an indirect effect of introduction of solids on health.

Data on infant feeding practices in Australia indicate that there is little association between the introduction of solid foods and continuation of breastfeeding (Table 2). Between 4–6 months of age, the prevalence of any breastfeeding declines from 69% to 60% while the prevalence of feeding solids rises to over 90%. Similarly, before 4 months of age, the decline in the prevalence of breastfeeding is double the prevalence of introducing solids. Similar data was not available from the New Zealand children's health survey (Ministry of Health 2012).

4.4 Summary

In both countries, 10% or fewer infants are introduced to solids before four months of age. This proportion appears to have declined compared to earlier surveys. The proportion was higher in Maori in New Zealand (16%) and in lower socio-economic groups in Australia (23%) or for mothers aged less than 25 years. Adjusting the Australian data for lower response rates in the latter group does not alter the national prevalence. There is little association between the introduction of solids and cessation of breastfeeding in Australia.

5 Conclusions

Australian and New Zealand authorities (New Zealand Ministry of Health 2008; NHMRC 2012a) recommend introduction of solid foods to the infant diet at 'around 6 months' of age, largely based on assessment of the benefits of breastfeeding to this age.

A FSANZ review in 2008 found that there are unlikely to be differences in the nutritional and developmental outcomes for infants that receive solids at an early (close to four months) versus a late (close to six months) age. This is consistent with the updated assessment that there are no health effects that are clearly linked with adverse outcomes if solid food is introduced from 4 months compared to delaying until 'around 6 months' of age, across a range of health outcomes including infectious morbidity, growth and micronutrient intake.

The evidence in relation to age of introduction of solids and subsequent development of allergic disease is uncertain but, based on current evidence, there does not appear to be any difference in risk of allergic disease when solids are introduced at any time within a critical window of 4–<7 months of age. There is some evidence that introduction before 4 months of age, and possibly after 7 months of age, is associated with increased allergy risk. Ongoing research in this area may help to clarify this relationship, when the research becomes available.

Attachment 1: Health effects associated with age of complementary feeding

Table A1. Summary of the key findings and conclusions from three recent reviews on the timing of solid food introduction to infants and risk of adverse health outcomes. BF = breast feeding; EBF = exclusive breastfeeding; FF = formula-feeding; CF = complementary feeding.

KEY FINDINGS: EVIDENCE THAT SOLID FOOD INTRODUCTION AT 'AROUND 6 MONTHS' MAY CONTRIBUTE TO ADVERSE HEALTH OUTCOMES				
	ESPGHAN¹	EFSA (2009)¹	HORNELL ET AL (2013)²	CONCLUSION BASED ON COMBINED FINDINGS OF THESE REVIEWS
Review Type	Medical Position	Scientific Opinion	Systematic review	
Main focus	Complementary feeding	Complementary feeding	Duration of exclusive breast feeding	
Health effect:				
Energy intake	Age of CF not specifically addressed.	Insufficient data – age of CF in terms of energy intake needs to be decided for individual infant (larger infants have greater energy requirements).	Association to duration of EBF examined: EBF to 6 months meets energy requirements and does not compromise infant growth.	Either no association or insufficient data to indicate the energy intake is compromised by age of introducing CF.
Nutritional adequacy	Timing of CF not specifically addressed although concluded that nutritional deficiencies during CF period (defined as after 17 weeks and before 26 weeks) are unlikely.	Reviewed studies on whether EBF provides adequate nutrients to 6 months; concludes that some infants need CF at 4–6 months for Fe and Zn sufficiency.	Not addressed.	No association but some infants may require solid foods at 4–6 months for Fe and Zn sufficiency.
Growth	Minimal evidence that solid foods introduced at 4–6 months affects growth.	CF introduced before 6 months does not have strong impact on growth rate. Late introduction (after 6 months) may reduce length and weight gain.	EBF for 4 months gives similar growth rates compared to EBF for 6 months.	No evidence of association between CF introduced at 4–6 months and growth rate.
Neurodevelopment	No specific data on age of CF reviewed but limited evidence that low intake of LCPUFA (oily fish) and Fe may have adverse effect on neurodevelopment.	Insufficient data to make conclusion	Not addressed.	Insufficient data to make conclusion

KEY FINDINGS: EVIDENCE THAT SOLID FOOD INTRODUCTION AT 'AROUND 6 MONTHS' MAY CONTRIBUTE TO ADVERSE HEALTH OUTCOMES

	ESPGHAN¹	EFSA (2009)¹	HORNELL ET AL (2013)²	CONCLUSION BASED ON COMBINED FINDINGS OF THESE REVIEWS
Food preferences	Age of CF not addressed but CF without added sugars and salt recommended.	Insufficient data to make conclusion	Not addressed.	Insufficient data to make conclusion
Renal function	Evidence indicates that renal function is sufficiently mature to metabolise nutrients from CF by the age of 4 months.	CF introduced after 4 months does not impact on renal function.	Not addressed.	CF introduced from 4 months is not associated with adverse renal function
Obesity, cardiovascular disease (CVD), and/or Type II diabetes (T2D)	Reviewed data on energy-dense complementary foods and protein intake in relation to obesity risk. No convincing evidence that age of CF is related to obesity risk or CVD risk.	Insufficient evidence to show that age of introduction of CF impacts on risk of obesity; no evidence that age of CF has effect on risk for T2D.	Any BF (including EBF) for longer than 4 months is protective against overweight and obesity in childhood.	Insufficient data to make conclusion on age of CF and risk of obesity, CVD, T2D. Some evidence that BF has protective effect.
Allergy, atopic disease, and/or asthma	Some evidence but limited that delayed introduction of CF beyond 4–6 months reduces allergies in infants (both normal and high risk infants)	Few studies examining the age of CF as independent risk factor for atopic diseases. No conclusion on appropriate age for CF.	Increased risk of eczema if CF introduced at <4 months. Insufficient or limited evidence that risk of asthma and gluten intolerance are associated with timing of CF.	Yes, possible increased risk of allergy with introduction of solids outside the 4–6 month period.
Celiac disease (CD) and/or Type I diabetes mellitus (T1DM)	Introduction of gluten and other food allergens at 4–6 months (while breastfeeding) may have protective effects against CD and T1DM.	Progressive introduction of gluten between 4 and 6 months (while BF) may reduce risk of CD and T1DM.	Not addressed.	Yes, possible increased risk of allergy with delayed introduction of solids (i.e. later than 4–6 months)
Infectious morbidity: acute otitis media (AOM) and/or gastrointestinal	Age of CF not specially addressed. Infectious outcomes considered in terms of exclusive versus partial BF	Breastfeeding protects against infectious morbidity. Introduction of CF at 3 months or less may increase risk of infectious morbidity.	Any BF (including EBF) is protective against AOM	Insufficient evidence to make conclusion on association of CF and infectious disease. Evidence of association primarily based of protective effects of BF.

KEY FINDINGS: EVIDENCE THAT SOLID FOOD INTRODUCTION AT 'AROUND 6 MONTHS' MAY CONTRIBUTE TO ADVERSE HEALTH OUTCOMES

	ESPGHAN¹	EFSA (2009)¹	HORNELL ET AL (2013)²	CONCLUSION BASED ON COMBINED FINDINGS OF THESE REVIEWS
Dental health	No conclusions on risk of caries and age of CF	No evidence that age of CF is related to having caries.	Not addressed.	Insufficient data to make conclusion

¹ Both ESPGHAN and EFSA define CF as the period when complementary foods are given together with either human milk or a breast milk substitute.

² Atopic disease, asthma and allergy were the only health outcomes that were examined specifically in relation to introduction of CF (other health outcomes examined were in relation to duration of breastfeeding, as noted).

Attachment 2: Allergy and association with age of complementary feeding

Table A2.1 Summary of primary studies investigating the link between age of introduction of solid foods and risk of food-related allergy, allergic diseases and syndromes. Studies were selected as described in Section 3.2. Columns on far right indicate where study has been cited by major review publications. See References for citation details. BF = any breast feeding; EBF = exclusive breastfeeding; FF = formula-feeding; CF = complementary feeding.

Study (location)	Type & Population	N	Effect ¹	Age assessed	Exposure variable (foods introduced; time period)	Outcome	Cited by ²				
							ES	A	N	EF	FP
Evidence shows early (before 4 mo) increases risk of allergic disease											
1981 Fergusson (New Zealand)	Cohort ± parental history of atopy	1265	E	2 yr	Solid foods at before/after 4 mo in breastfed and formula-fed infants	Solid foods introduced before 4 mo increases risk of E in both breastfed and formula-fed infants					✓
1983 Kajosaari (Finland)	Cohort w/ history of atopy	135	E, FA	1 yr	Solid foods introduced at 3 mo compared to 6 mo to EBF infants	Early solid food introduction (3 mo compared to 6 mo) increases risk of E, FA					✓
1990 Fergusson (New Zealand)	Cohort; Normal allergy risk	1265	E	0-10 yr	Various foods at before/after 4 mo	Solids introduced before 4 mo increases risk of E	✓	✓			✓
1991 Kajosaari (Finland)	Cohort w/ history of atopy	135	AD, FA	5 yr	Solid foods introduced at 3 mo compared to 6 mo to EBF infants	At 1 yr, delayed solid foods to 6 mo (compared to 3 mo) reduces risk of E, FA but no difference at 5 yr.		✓			
1994 Kajosaari (Finland)	Cohort w/ history of atopy	135	E, FA	1 yr	Solid foods introduced at 3 mo compared to 6 mo to EBF infants	Delayed solid foods to 6 mo (compared to 3 mo) reduces risk of E, FA					✓
2004 Morgan (UK)	Cohort; pre-term infants	257	E	1 yr	Solid foods before 17 weeks compared to after 17 weeks in EBF, BF, and FF infants	Introduction of 4 or more solid foods before 17 weeks increased risk of E		✓			
Evidence shows no association (protective or adverse effects) between age of introduction and risk of allergic disease											
1983 Fergusson (New Zealand)	Cohort; Normal allergy risk	1110	A, W	0-4 yr	Solid foods before 4 mo compared to after 4 mo in EBF and BF infants	No association between solids introduced before 4 mo and risk of A; BF in first 4 mo does not reduce incidence of A.		✓			
2002 Schoetzau	Cohort; w/ history of	1321	AD	1 yr	Egg/milk introduced before 4 mo compared to after 4 mo	Age of introduction of solid foods was not associated with incidence of AD					✓

Study (location)	Type & Population	N	Effect ¹	Age assessed	Exposure variable (foods introduced; time period)	Outcome	Cited by ²				
							ES	A	N	EF	FP
	atopy										
2004 Zutavern (UK)	Cohort; Normal allergy risk	605	W, A, E	5.5 yr	Various foods at time points between 3 and 9 mo	No evidence that later introduction protects against W, A, E. Increased risk of E with eggs at > 8 mo.	✓	✓		✓	
2006 Zutavern (UK)	Cohort ± allergic symptoms	2612	AD, AS	2 yr	Egg and milk introduced before 6 mo compared to after 6 mo	No evidence that introduction of solids after 6 mo reduces risk of AD, AS	✓	✓			
2009 Kramer (Belarus)	Cohort	2951	AD	6.5 yr	EBF for 6 mo compared to EBF for 3 mo then introduce solids or milk	No association between EBF duration or age of solid food introduction and A				✓	
2011 Chuang (Taiwan)	Cohort; Normal allergy risk	1877 3	AD	18 mo	Solid foods before 4 mo, between 4–6 mo, and after 6 mo.	No association between age of introduction and risk of AD					✓
2006 Tarini	Systematic review	N/A	E, AS, W, FA, AR, AD	1-10 yr	13 cohort studies; some with family history of allergy	Evidence for risk of allergy with solids at < 4 mo is inconsistent (possible increased risk for E with solids at < 4 mo)				✓	
Evidence that introduction of solid foods at around 6 months (i.e. after 4 mo and before 7 mo) is associated with decreased risk (or no increased risk) of allergic diseases											
2006 Poole (USA)	Cohort; Normal allergy risk	1612	FA (wheat)	1-4yr	Wheat introduced before 6 mo compared to after 6 mo	Cereal grain/rice introduced after 6 mo increased risk of wheat allergy		✓			
2008 Snijders (Netherlands)	Cohort; Normal allergy risk	2558	AD, AS	2 yr	Solid foods introduced before 7 mo compared to after 7 mo	Solids introduced after 7 mo increases risk for E, AD, AS, but not FS			✓		✓
2007 Filipiak (Germany)	Cohort, ± allergy risk	4753	E	4 yr	Various foods introduced before 4 mo, during 5-6 mo and after 7 mo	Delayed introduction of solids after 4 months or, for highly allergenic foods (e.g. nuts) after 6 months of age decreases risk of E compared to introduction after 7 months.	✓		✓	✓	
2008 Zutavern (UK)	Cohort; ± allergic symptoms	2073	A, AR, AS	6 yr	Solid foods before 4 mo, from 4–6 mo, and after 6 mo. (“late introduction” means after 4 or 6 mo)	Solid foods introduced after 4 mo increases risk of FS, E. No association between solid foods introduced at 4–6 months and risk of A, AR.			✓		✓
2010 Koplin (Australia)	Cohort; Normal allergy risk	2589	FA	12 mo	Egg introduced 4–6 mo compared to after 6 mo	Introduction after 6 mo associated with increased risk of egg allergy					✓

Study (location)	Type & Population	N	Effect ¹	Age assessed	Exposure variable (foods introduced; time period)	Outcome	Cited by ²				
							ES	A	N	EF	PP
2010 Hesselmar (Sweden)	Cohort; Normal allergy risk	184	A, E	18 mo	Fish introduced over various ages in first year	16% increased prevalence of E for every 2 mo delay in fish introduction					✓
2010 Nwaru. (Finland)	Cohort; ± diabetes risk	994	AS	5 yr	Various foods introduced from 4 to 10 months	Late introduction of potatoes (>4 mo), oats (>5 mo), rye (>7 mo), wheat (>6 mo), meat (>5.5 mo), fish (>8.2 mo), and eggs (>10.5 months) increases risk allergic sensitisation.					✓
2010 Virtanen (Finland)	Cohort; Normal allergy risk	1293	A	5 yr	Various foods over first year; Oats introduced before and after 5.5 mo	Early introduction of oats (<5.5 mo) decreases risk of A compared to introduction after 5.5 mo					✓
2013 Nwaru (Finland)	Cohort; ± atopic risk	3781	A, AD, E	2 yr & 5 yr	Various foods from 3–7 mo.	Early introduction (time specific to each food) decreases risk of A, AD, E					
2013 Nwaru (Finland)	Cohort; ± atopic risk	3781	AS	5 yr	Various foods at 3–11 mo to EBF, BF and FF infants.	Early introduction (time specific to each food) decreases risk of AS					
2013 Frederiksen (USA)	Cohort; at-risk for T1DM	1835	D	From 9 months	Various foods introduced at <4 months and ≥6 months	Risk of T1DM was increased at early (<4 months) or late (≥6 months) exposure times compared to 4-5 months					
2013 Palmer (Australia)	RCT; with mild-severe eczema	86	FA	8 & 12 mo	Daily egg powder compared to rice powder fed between 4–8 months	Incidence of egg allergy lower with egg exposure from 4 months compared to 8 months.					
Evidence or age range for solid food introduction not applicable to P274 assessment											
2006 Kull (Sweden)	Cohort; Normal allergy risk	2614	A, AR, AS, E	4 yr	Fish at before 9 months (3–8 months) compared to 9 mo	3-8 mo group had reduced risk for A, E, AR, AS	✓		✓		
2009 Alm (Sweden)	Cohort; Normal allergy risk	4953	E, FA	12 mo	Fish introduced before 9 mo compared to after 9 mo	Early introduction decreases risk of eczema					✓
2011 Joseph (USA)	Cohort; ± allergy risk	594	AD, AS	2 yr	Solid foods before 4 mo compared to after 4 mo	For infants with parental history of allergy, peanut sensitisation and possibly egg was reduced in infants exposed at <4mo					✓

¹Effect abbreviations: A = asthma; AD = atopic disease; AR = allergic rhinitis; AS = allergic sensitization; At = atopy; C = celiac disease; T1DM = type 1 Diabetes Mellitus; E = eczema; FA = food allergy; FS = food sensitization; W = wheezing

²Review abbreviations: ES = ESPGHAN (2008); A = AAP (2008); N = NHMRC (completed 2008, published 2013); EF = EFSA (2009); PP = Palmer and Prescott (2012).

Table A2.2 Studies included in reviews or advice on the relationship between timing of solid food introduction and development of allergy^a

	Reviewed by ^b						
	<i>NHMRC IFG</i>	<i>NHMRC ADG</i>	<i>ESPGHAN</i>	<i>AAP</i>	<i>EFSA</i>	<i>ASCIA</i>	<i>FSANZ</i>
Review or advice published (year)	2013	2013	2008	2008	2009	2010	2013
Literature searched until (year)	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	2013
Latest study included in review (year)	2010	2008	2007	2006	2008	2008	2013
No. of studies on which conclusions are based:	10	7	11	7	11	7	33
Breakdown:							
Published < 2002	0	0	2	3	4	0	6
Published 2002-2008	7	7	9	4	6	7	13
Published >2008	3	0	0	0	1	0	14
No. that were not primary data	1	1	5	0	2	6	0

^a Noting that SD1 also summarised 3 reviews covering other health effects associated with the timing of solid food introduction. Development of allergies & allergic disease is the only health effect for which there appeared to be current debate and significant new research indicating risk.

^b Abbreviations: NHMRC = National Health and Medical Research Council; IFG = Infant Feeding Guidelines; ADG = Australian Dietary Guidelines; ESPGHAN = European Society for Paediatric Gastroenterology, Hepatology, and Nutrition; AAP = American Academy of Pediatrics; EFSA = European Food and Safety Authority; ASCIA = Australasian Society of Clinical Immunology and Allergy; N.S = not specified.

Attachment 3: Summary of issues considered in FSANZ risk assessments relating to the age of introduction of solid foods

Date of assessment	Issues considered	Conclusions
August 2008	Potential for displacement of breast milk and/or formula, any changes in energy intake, and whether growth outcomes are adversely affected	Intervention studies showed introduction of solids at three-four months of age reduced breast milk intake but does not significantly affect the rate of increase in weight and length of the infant
	Capacity of infant kidneys to deal with the higher solute load of solid foods prior to six months of age	Unable to identify any studies that directly assessed changes in renal solute load or water balance with introduction of solid food, but greatest risk of negative water balance is during illness. However, the capacity of infants to reduce intake of solid foods during illness is likely to mitigate potential risk
	Impact on iron and zinc status, particularly in pre-term infants	Evidence from 2 studies provides some indication that exclusive breastfeeding to 6 months does not increase risk of iron deficiency at a later age. Expected that the outcomes on zinc status would be similar to, and no worse than, those for iron, as infants have a better storage of zinc compared to iron in the first 6 months of life
	Influence of feeding practices in infancy on later food preferences	Emerging evidence suggesting that the timing of solid food introduction can influence later dietary outcomes and preferences, but it is too early to draw conclusions about the impact this might have on recommended infant feeding practices
	Risk of allergy and other immune-mediated diseases	Evidence regarding the timing of the introduction of solids and risk of allergy and other immune-mediated diseases, such as coeliac disease and Type 1 diabetes, is emerging and no firm conclusions can be drawn at this time. However, preliminary indications are that the risk of allergy may be minimised if breastfeeding is maintained throughout the period of introducing solids, whereas the risk may increase if the introduction of solids is delayed beyond seven months
	Conclusion	Delaying introduction of solid foods to around six months of age is unlikely to have any discernible positive or negative effect on the nutritional or developmental outcomes of infants.

Date of assessment	Issues considered	Conclusions
October 2013	Risk of iron and zinc deficiencies in preterm infants with delayed introduction of solids	Unable to identify any studies addressing this
	Allergy risk – less than 4 completed months (~17 weeks of age)	Allergy risk appears to be associated with solid foods introduced at < 4 months. This association, combined with evidence that risk of infectious morbidity is also increased with this time period (as related to the protective effects of breastfeeding), supports the current recommendations from ESPGHAN, EFSA, and NHMRC that from 4 months of age is the appropriate minimum age at which solid foods are introduced.
	Allergy risk – 7 months or above	Since 2008, there is increasing evidence that the timing of solid food introduction may be related to the development of food-related allergy. Critical period to minimise the risk of allergy development seems to be between 4 and <7 months. However, because of unclear and inconsistent definitions of age categories, measurement bias in many studies and the contribution of various other factors in the development of allergic disease, the evidence is not conclusive.
	Conclusion	‘Around 6 months’ as the appropriate age for the introduction of solid food to infants, would have minimal effect on the risk of adverse health outcomes, when compared to ‘from 4 months’ of age
January 2014	Proportion of infants being introduced to solids at <4 months	The Australian national average proportion of infants who were receiving solids before 4 completed months of age was 4–10%, noting that within this range there is some variation according to maternal age and SES (2010 Infant Feeding Survey). New Zealand data (2011/12) indicates that the proportion of infants introduced to solids before 4 months was 10%, which was lower than previous survey (2006/07) of 16%.
	Introduction of solids and cessation of breast feeding	Data on infant feeding practices in Australia indicates there is little association between the introduction of solid foods and continuation breastfeeding. Between 4–6 months of age, the prevalence of any breastfeeding declined from 69% to 60% while the prevalence of feeding solids rose from around 10% to over 90%. Similarly, before 4 months of age, the decline in prevalence of breastfeeding was double the prevalence of introducing solids (2010 Infant Feeding Survey) .

Date of assessment	Issues considered	Conclusions
	Conclusions	Current evidence indicates that in developed countries with generally hygienically prepared foods, there is no additional risk from delaying the introduction of solids until around 6 months or, conversely, from introducing solids closer to the 4 month end of the window, ie. between 4 and <7 months.
July 2014	Gastrointestinal infection	Large UK cohort study identified no association between age of introduction of solids and hospitalisation for gastrointestinal or respiratory tract infections in the first 8 months of life.
	Overall conclusion	In Australia and New Zealand, there is no overall difference in risk between introducing solids from 4 months of age relative to around 6 months of age (ie within window from 4 months to <7 months of age).

Attachment 4: Basis of NHMRC guidelines for infant feeding

FSANZ's risk assessment conclusion supported a window for introducing solids from 4–<7 months. This is consistent with the current labelling requirements and also with the infant feeding guidelines of 'around 6 months' in both countries. However, the minimum age labelling permission 'from 4 months', and the recommendations in the guidelines 'introduce solids at around 6 months' appear to be inconsistent with each other. Therefore, FSANZ liaised with the NHMRC in 2014 to identify commonalities in the assessments undertaken and to understand reasons for the apparent differences between the agencies' use of their respective assessments.

The New Zealand guidelines also recommend complementary food at 'around 6 months' but emphasise that developmental cues are a key indicator of readiness for solids and that the timing of this varies between individual infants. The New Zealand guidelines were released in 2008 (Ministry of Health 2008), whereas the NHMRC undertook a literature review including evidence up to 2010 (NHMRC 2012b) and FSANZ has also reviewed more recent evidence. Therefore, this discussion focuses on the evidence assessed by FSANZ and NHMRC, rather than the New Zealand guidelines.

The NHMRC advice for 'around 6 months' is a risk management conclusion that takes into account the food-health outcome evidence assessed, the development of infants, and the need to provide general population advice on the likely optimal feeding of infants, including the importance of continued breastfeeding. This is different to FSANZ's purpose which is to ensure the provision of adequate information regarding suitability e.g. consistency, of a packaged solid food, so that consumers can make an informed choice.

The summary of evidence statements below are excerpted from evidence base used to support the Infant Feeding Guidelines. In almost all cases, both the Infant Feeding Guidelines Advisory Committee and FSANZ interpreted this evidence in the same way. Statements with grades⁶ were based on a systematic review of the literature up until 2010. In some cases, additional material published subsequently was also referred to in the guidelines.

NHMRC evidence statements for ages relevant to the Proposal (i.e. 4–<7 months), were (NHMRC 2013, page 89):

"Infants, from either developing or developed countries, who are exclusively breastfed for 6 months or longer do not have deficits in growth compared to those who are not exclusively breastfed." (Grade B)

"There are no apparent risks in a general recommendation for exclusive breastfeeding for the first 6 months of life, in both developing and developed countries. However, infants should still be managed individually in order to achieve sufficient growth and minimise adverse outcomes." (Grade B)

"Infants who are exclusively breastfed for 6 months experience less morbidity from gastrointestinal infection than those who are mixed breastfed as of 3 or 4 months." (Grade B)

⁶ Grades for evidence statements were graded A to D according to standard NHMRC protocols. See page 5 of the NHMRC Dietary Guidelines (NHMRC 2013)

FSANZ agrees with the first two of these conclusions. The third conclusion is discussed below.

Additional food-health outcome relationships were examined by the Committee and these received a D grade.

“Evidence of an association between the age of introduction of solid foods and risk of overweight in children younger than age 7 years is inconclusive” (Grade D) (NHMRC 2012a, page 87)

“Delaying the introduction of solid foods until after the age of 6 months is associated with increased risk of developing allergic syndromes.” (Grade D) (NHMRC 2012a, page 90)

Other conclusions were reached from other evidence sources. Those that relate only to solid foods and not to breastfeeding versus formula feeding include (NHMRC 2012a, page 86):

“By around 6 months of age breast milk (or infant formula) no longer provides sufficient nutrients and energy for growth and development.”

“By around 6 months of age most infants are able to adapt to different foods, food textures and modes of feeding.”

“If solid foods are introduced while the tongue-extrusion reflex is still strong, the infant will reject the spoon (a hard object) – the mother might then feel that the infant is rejecting the food, when in fact he or she is rejecting the object in the mouth”.

There were a number of other conclusions based on these evidence sources. However, these were largely derived from studies comparing infant formula to breast milk or exclusive to non-exclusive breastfeeding. Hence the results cannot be extrapolated to the comparison of the effect of introducing solids from 4 months compared with ‘around 6 months’. Relevant conclusions were:

“Breastfeeding exclusively to around 6 months *is compatible with* achieving the lowest rates of allergic disease.” (emphasis added) (NHMRC 2012a, page 16)

“The introduction of complementary feeding (adding solid foods and liquids other than breast milk or infant formula) at around 6 months is consistent with introduction of solid foods during the probable ‘window of tolerance’ between 4 and 7 months. The majority of Australian infants have solids introduced during this period.” (NHMRC 2013, page 90)

“Animal and human studies suggest that breastfeeding during the period of antigen introduction facilitates the development of oral tolerance, with transforming growth factor-beta (TGFβ) a possible critical component in this process and protective against allergic asthma.” (NHMRC 2012a, page 16)

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