



## Partially hydrolysed whey based infant formula and the prevention of allergy: A summary of current evidence and policy

### Summary

Exclusive breastfeeding for 6 months, and continued breastfeeding in the first year alongside complementary feeding should be recommended for infants from atopic families.

A review of current evidence and policy statements suggests that there is insufficient evidence to recommend that partially hydrolysed whey based infant formula can help prevent allergies.

Partially hydrolysed infant formula are not hypoallergenic and are therefore not suitable for infants and young children with diagnosed cows' milk protein allergy. We recommend very clear and bold labelling of any products available to minimise the risk to infants and young children if these products are used inappropriately.

Hydrolysed formula are created by using enzymatic processes to break proteins naturally found in a food into smaller fragments. It is suggested that reducing exposure to intact allergens may prevent development of allergic diseases in infants and young children (Lowe et al, 2013). The development of atopic dermatitis (AD) or eczema is one of the allergic outcomes that has been extensively studied in infants and children in the first year of life. There have been many studies which have attempted to consider the role of early infant feeding on AD outcomes, in particular whether hydrolysed protein in formula can reduce the incidence in infants and children with family history of allergic disease.

Partially hydrolysed whey based infant formula is cheap to manufacture and palatable to children compared to fully hydrolysed formula or partially hydrolysed casein formula (Lowe et al, 2011). Nestlé promote their NAN HA formula in 90 markets with the claim that it '*helps to reduce the risk of Atopic Dermatitis in infants*'<sup>1</sup>. This claim is however made using evidence from one trial and using statements from pediatric groups which may not reflect more recent evidence and opinion in this area. Neither the US Food and Drug Administration (FDA) or the European Food Safety Agency (EFSA) have approved this claim.

Most of the systematic reviews conducted reviewing evidence in this area highlight the lack of methodological rigour in many of the trials that have been carried out and the lack of

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<sup>1</sup> <http://www.nestle.com/asset-library/documents/investors/nis-2013-vevey/heiko-schipper-the-first-1000-days-nestle-leadership-in-infant-nutrition.pdf> [accessed Nov 7th 2013]

consistency in study protocols which make clear conclusions difficult. A Cochrane review (Osborn and Sinn, 2006) reported that

*'There is no evidence to support feeding with a hydrolysed formula to prevent allergy in preference to exclusive breastfeeding. In infants at high risk for allergy who are unable to be completely breastfed, there is limited evidence that feeding with a hydrolysed formula compared to a cow's milk formula reduces allergies in babies and children, including cow's milk allergy. Concerns regarding quality of the evidence and consistency of the results indicates further studies are needed'* (Osborn and Sinn, 2006).

In the UK, public health guidance from the National Institute of Health and Care Excellence (NICE) concluded from an extensive literature review that

*'There is insufficient evidence that infant formulas based on partially or extensively hydrolysed cows' milk protein can prevent allergies'* (NICE PHG11, 2008),

This public health guidance remained unchanged when the NICE guidance was reviewed in 2012.

A British Dietetic Association consensus statement in 2010 (BDA, 2010) recommended that partially or extensively hydrolysed *casein* based formula should be used in the first 4-6 months if babies are not breastfed and where there is family risk of atopic diseases, but they did not recommend hydrolysed *whey* based formula. This recommendation was based on clinical guidance in the journal of the American Academy of Pediatrics at that time (Greer et al, 2008), which states *'it is difficult to show that partially hydrolysed formulas have a very large effect on the reduction of atopic disease in infants who are formula fed'*. The BDA also quote statements from ESPGHAN (The European Society for Paediatric Gastroenterology, Hepatology and Nutrition) and the European Academy of Allergology and Clinical Immunology (EAACI) in support of their recommendation, although this joint statement was made in 1999 (Høst et al, 1999) and later recommendations from the EAACI only were only made in relation to extensively hydrolysed formula in terms of allergy prevention in non-breastfed infants (Muraro et al, 2004a, b, c). It is clear the BDA statement requires revision and updating.

The key evidence used to support the use of partially hydrolysed whey based formula in the reduction of AD in infancy in children from atopic families used in some statements and by commercial companies comes from the German Infant Nutritional Intervention Study (GINI) s (von Berg et al, 2003, 2008) which randomised formula fed infants into 4 groups and compared the incidence of a number of allergy symptoms. Data from this study is widely quoted as evidence that a partially hydrolysed whey based formula prevented atopic dermatitis (AD) in the first year of life, but it is important to note that the difference in number of children who completed the study with diagnosed AD at 12 months was relatively small (14.8% (n=38) in the cows' milk based formula group and 9.1% (n=22) in the partially hydrolysed formula group) and

that this study population had a high proportion of mothers exclusively breastfeeding in the first four months who were excluded from the study (42%). Some infants were also receiving breast milk in the formula fed groups, but this was not reported, and gender and family history are highlighted in this study as being of particular significance in AD development, suggesting that additional studies are needed to support these findings in other cohorts. In addition, the preferred analysis method of intention to treat analysis failed to show any benefit of partially hydrolysed whey based formula over cows' milk formula in this study (Lowe et al, 2011)

An Australian RCT published in 2011 (Lowe et al, 2011) considering the impact of a partially hydrolysed whey based formula (NAN HA), a standard infant formula (NAN) and a soy based formula (ProSobee) in infants who were formula fed, partially breastfed or who moved from breastfeeding to formula feeding in the first four months of life reported that there was no evidence that introducing partially hydrolysed whey based formula reduced the risk of allergic manifestations including eczema in infants from atopic families and they concluded *'that partially hydrolysed whey based formula should not be used as a preventive strategy for infants at high risk of allergic diseases'*.

In 2012 the Food and Drug Administration in the US (Chung et al, 2012) produced a revised recommendation also supported by the American Academy of Allergy, Asthma and Immunology (2011).<sup>2</sup>

The FDA concluded

*'There is little to very little evidence, respectively, to support a qualified health claim concerning the relationship between intake of partially hydrolysed whey based formula and a reduced risk of AD in partially breastfed and exclusively formula-fed infants throughout the first year after birth and up to 3 years of age'*.

In 2013 a 'review of systematic reviews' looking at evidence in prevention and aetiology of food allergy considered fourteen systematic reviews in this area (Lodge et al, 2013) and again concluded that:

*'There is insufficient evidence to conclude that the use of hydrolysed formula may reduce food allergy/sensitization when compared with standard formula in high atopy risk children'*

The UK Scientific Advisory Committee on Nutrition (SACN) has commissioned a systematic review of the evidence on diet and allergy in the first year of life through the Committee on Toxicology (CoT), however this will not report until October 2014. Until then, the NICE statement from 2008 remains policy in the UK.

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<sup>2</sup> <https://www.aaaai.org/global/latest-research-summaries/Current-JACI-Research/infant-formula-partially-hydrolyzed-whey.aspx>

## Safety issues related to partially hydrolysed whey based infant formula

There are safety concerns about partially hydrolysed whey based infant formula since they are unsuitable for the *treatment* of allergy in infants. The FDA requires the following warning statement be displayed to indicate to consumers that partially hydrolysed infant formulas are not hypoallergenic and should not be fed to infants who are allergic to milk or to infants with existing milk allergy symptoms.

*“Partially hydrolysed formulas **should not be fed to infants who are allergic to milk or to infants with existing milk allergy symptoms.** If you suspect your baby is already allergic to milk, or if your baby is on a special formula for the treatment of allergy, your baby’s care and feeding choices should be under a doctor’s supervision.”*

The FDA concluded that the use of bold type is necessary, in light of the significant public health risk that would be created by the feeding of these formulas to infants who are allergic to milk or to infants with existing milk allergy symptoms. Manufacturer claims of a relationship between the consumption of partially hydrolysed whey based formula and a reduced risk of developing AD could mislead consumers to think that these formulas are an appropriate choice for such infants.

NHS Choices currently makes the statement

*‘Infant formula with partially hydrolysed proteins is available in the shops, but this is not suitable for babies with a cow’s milk allergy’<sup>3</sup>*

Any new partially hydrolysed formula made available to parents in the UK should therefore be required to carry a clear and bold warning on the label to this effect. Any promotion of partially hydrolysed whey based formula milk products to health professionals must clearly warn of the risks associated with giving partially hydrolysed whey based formula to infants and children with diagnosed cows’ milk protein allergy or infants showing symptoms of cows’ milk protein allergy.

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<sup>3</sup> <http://www.nhs.uk/Conditions/pregnancy-and-baby/Pages/types-of-infant-formula.aspx#close> [accessed Nov 7<sup>th</sup> 2013]

## References

British Dietetic Association (2010). *Practical Dietary Prevention Strategies for Infants at Risk of Developing Allergic Diseases*. Consensus Statement from the Food Allergy and Intolerance Specialist Group.

Chung CS, Yamini S, Trumbo P (2012) FDA's Health Claim Revised: Whey protein partially hydrolysed infant formula and atopic dermatitis. *Pediatrics*, **130**: e408-e414.

Høst A, Koletzko B, Dreborg S, et al. (1999) Joint Statement of the European Society for Paediatric Allergology and Clinical Immunology (ESPACI) Committee on Hypoallergenic Formulas and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition. Dietary products used in infants for treatment and prevention of food allergy. *Arch Dis Child*: **81**:80– 84

Greer FR, Sicherer SH, Burks W (2008) Effects of early nutrition interventions on the development of atopic diseases in infants and children. The role of maternal dietary restrictions, breastfeeding, timing of introduction of complementary foods and hydrolysed formula. *Pediatrics*, **121**:183-191.

Lodge CJ, Allen KJ, Lowe AJ, Dharmage SC (2013) Overview of evidence in prevention and aetiology of food allergy: A review of systematic reviews. *Int J Environ Res Public Health*, **10**: 5781-5806.

Lowe AJ, Hosking CS, Bennett CM, Allen KJ et al (2011) Effect of partially hydrolysed whey infant formula at weaning on risk of allergic disease in high risk children: A randomised control trial. *J Allergy Clin Immunology*, **128**: 360-365.

Lowe AJ, Dharmage SC, Allen KJ, Tang MLK, Hill DJ (2013) The role of partially hydrolysed whey formula for the prevention of allergic disease: evidence and gaps. *Expert Review of Clinical Immunology*, **9**: 31-41.

Muraro A, Dreborg S, Halken S, et al. (2004a) Dietary prevention of allergic diseases in infants and small children. Part I: dietary prevention of allergic diseases in infants and small children. *Pediatr Allergy Immunol*; **15**:103–110

Muraro A, Dreborg S, Halken S, et al (2004b) Dietary prevention of allergic diseases in infants and small children. Part II: evaluation of methods in allergy prevention studies and sensitization markers. Definitions and diagnostic criteria of allergic diseases. *Pediatr Allergy Immunol*; **15**:196–205

Muraro A, Dreborg S, Halken S, et al (2004c). Dietary prevention of allergic diseases in infants and small children. Part III: critical review of published peer-reviewed observational and interventional studies and final recommendations. *Pediatr Allergy Immunol*; **15**:291–307

NICE (2008) *Improving the nutrition of pregnant and breastfeeding mothers and children in low income households*. Public Health Guidance 11. Available at: <http://guidelines.nice.org.uk/PH11>

Osborn DA, Sinn JKH (2006). *Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants*. Cochrane Database of Systematic Reviews Issue 4. Art. No.: CD003664. DOI: 10.1002/14651858.CD003664.pub3

von Berg A, Koletzko S, Grubl A, et al.(2003) The effect of hydrolysed cow's milk formula for allergy prevention in the first year of life: the German Infant Nutritional Intervention Study, a randomized double-blind trial. *J Allergy Clin Immunol*, **111**: 533–540

von Berg A, Filipiak-Pittroff B, Kramer U, Link E, Bollrath C, Brockow I, et al.(2008) Preventive effect of hydrolyzed infant formulas persists until age 6 years: longterm results from the German Infant Nutritional Intervention Study (GINI). *J Allergy Clin Immunol*, **121**:1442-7