H.A. Formula

**Key points**

H.A. formula is marketed as preventing eczema and cows’ milk protein allergy in babies from atopic families. It contains partially hydrolysed cows’ milk with 100% whey protein.

Nestlé has promoted an H.A formula, NAN HA, with the claim that it “helps to reduce the risk of atopic dermatitis in infants”. However, this claim was made using evidence from one trial and using statements from paediatric groups which may not reflect more recent evidence and opinion in this area. Neither the US Food and Drug Administration (FDA) nor the European Food Safety Authority (EFSA) has approved this claim.

A systematic review commissioned by The Food Standards Agency and published in the British Medical Journal in 2016 (Boyle et al, 2016) concluded that there was no consistent evidence that partially hydrolysed formula reduce the risk of allergic disease.

The NHS makes the statement: “Partially hydrolysed formulas aren't suitable for babies who have cows’ milk allergy.” (NHS, 2019).

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 to infants showing symptoms of cows’ milk protein allergy.

A recent study has raised the possibility of adverse effects from the use of partially hydrolysed whey protein in infant formula, and further information is required to investigate whether this has any clinical significance.

H.A infant formula is made from cows’ milk and is 100% whey based with lactose as the source of carbohydrate. The proteins in H.A infant formula have been partially hydrolysed which means that they have been partially broken down by enzymatic processes into smaller fragments. SMA H.A infant formula was launched in 2013 in the U.K. It is currently marketed as being ‘designed to reduce the risk of developing allergy to cows’ milk proteins’ and the manufacturer claims that it ‘reduces the risk of developing eczema by over 50% in the first year of life’.
Efficacy of H.A. formula

It is suggested that reducing exposure to intact allergens may prevent development of allergic diseases in infants and young children (Lowe et al, 2013) and many studies have examined the role of early infant feeding on atopic dermatitis (AD) outcomes, in particular whether hydrolysed protein in formula can reduce the incidence in infants and children with family history of allergic disease.

Most of the systematic reviews of evidence in this area highlight the lack of methodological rigour and consistency in study protocols in many of the trials that have been carried out, making clear conclusions difficult. A Cochrane review 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 cows’ milk formula reduces allergies in babies and children, including cows’ milk allergy. Concerns regarding quality of the evidence and consistency of the results indicates further studies are needed.” (Osborn and Sinn, 2006).

The key evidence used to support the use of partially hydrolysed whey-based formula in the reduction of allergy in infancy in children from atopic families used in some statements and by commercial companies comes from the German Infant Nutritional Intervention Study (GINI) (von Berg et al, 2003, 2008) which randomised formula-fed infants into four 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 AD in the first year of life, but it is important to note that the difference in the number of children who completed the study and who were diagnosed with 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. Also, 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 in the formula-fed groups were also receiving breastmilk, but this was not reported. 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 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 protein based (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 2013 a ‘review of systematic reviews’ looking at evidence in prevention and aetiology of food allergy considered 14 systematic reviews in this area 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.” (Lodge et al, 2013)

In the UK, public health guidance from the National Institute for Health and Clinical 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.” (National Institute for Health and Clinical Excellence, 2008).

When guidelines were reviewed in 2012, this guidance remained unchanged.

In 2012 the Food and Drug Administration (FDA) in the USA produced a revised recommendation. They 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.” (Chung et al, 2012)

The EFSA Scientific Opinion on the Essential Composition of Infant and Follow-on Formulae in 2014 stated that reducing the size of protein molecules cannot reduce the risk of allergy in infants from at-risk families (EFSA, 2014)

A systematic review, commissioned by the Food Standards Agency, into the evidence on diet and allergy in the first year of life also found no evidence that use of partially hydrolysed formula reduced the risk of allergy or autoimmune outcomes in infants at high risk (Boyle et al, 2016).

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.

The NHS makes the statement: “Partially hydrolysed formulas aren’t suitable for babies who have cows’ milk allergy.” (NHS, 2019)

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 to infants showing symptoms of cows’ milk protein allergy.

**Potential adverse effects from the use of partially hydrolysed whey protein based infant formula**

Data from a French longitudinal study of formula type and use has also highlighted potential risks of routine consumption of partially hydrolysed formula compared to exclusive breastfeeding or a non-hydrolysed formula. Despite some partially hydrolysed milks claiming that usage is associated with reduced risk of allergy, the study showed that use of a partially hydrolysed formula at two months of age was related to higher risk of wheezing at one year in at-risk infants and a higher risk of food allergy at two years of age both in at-risk and non-at-risk infants. Further studies looking at the risks associated with partially hydrolysed milks would be beneficial (Davisse-Paturet et al., 2019).

**Labelling and marketing of H.A infant formula**

H.A infant formula should comply with current regulations governing the composition, labelling and marketing of infant formula. The EU regulations changes in February 2020, which have been adopted by the UK, have meant that the claim that a hydrolysed infant formula can reduce the risk of cows’ milk protein allergy will not be allowed unless new evidence demonstrating efficacy is submitted to a relevant competent authority from which further consideration would be given to how to adequately inform parents and caregivers about that property of the product. H.A is a partially hydrolysed infant formula and as such, is not required to comply with the new regulations until February 2021.

You can find out more about regulations around infant milks by following the link to regulations at www.infantmilkinfo.org.
References


Davisse-Paturet C, Raherison C, Adel-Patient K et al (2019). Use of partially hydrolysed formula in infancy and incidence of eczema, respiratory symptoms or food allergies in toddlers from the ELFE cohort. Paediatric Allergy and Immunology, 30, doi: 10.1111/pai.13094


