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## BABY MILK SUBSTITUTES

# Formula milk companies push allergy products despite flawed evidence

Europe has toughened its approach to formula milk products that claim to reduce allergy risks. But consumers elsewhere continue to be coaxed into buying products that make health claims without high quality evidence. **Melanie Newman** reports

Melanie Newman *freelance journalist*

For decades, the formula industry has claimed that certain breast milk substitutes can reduce the risk of allergies, but the science underlying these claims has been largely revealed to be fraudulent or flawed. Yet today, Nestlé and Danone are still advertising those claims in some countries with high rates of acute malnutrition, morbidity, and mortality and where how babies are fed is critically important.<sup>1</sup>

The World Health Organization has told *The BMJ* that governments should be scrutinising health claims on formula products more carefully. In a highly critical report on formula milk marketing last month, WHO said that the practice represented “one of the most underappreciated risks to the health of infants and children.”<sup>2</sup>

The health claims have been made for a type of formula milk called hydrolysed milk, including both partially hydrolysed and extensively hydrolysed formula (box 1).

### Box 1: What is hydrolysed formula?

There is no universally accepted definition of a partially hydrolysed formula (pHF) or extensively hydrolysed formula (eHF). Partially hydrolysed proteins are created using enzymatic processes to partially break the proteins into smaller fragments, or peptides. Extensively hydrolysed peptide based formula milks contain proteins that have been extensively broken down or hydrolysed, using pork enzymes.

pHF has been included in formula products intended to reduce the risk of allergic diseases and also to support other claims such as easy digestion. eHF is used in the management of formula fed infants who have cow's milk allergy or other less common intestinal issues such as pancreatic insufficiency or malabsorption.

After heavy campaigning, the UK, Europe, and the US<sup>3</sup> have taken steps to clamp down on unevidenced claims that hydrolysed milk products prevent or reduce the risk of allergies. Last year, in a move that the UK has followed, the European Commission prohibited the use of such allergy claims on infant formula unless manufacturers could prove the efficacy of each product. In one case Nestlé was prevented from claiming that a hydrolysed product reduced the risk of eczema in infants with a family history of allergy.<sup>4</sup>

But in other markets, including in China and Russia, consumers are being persuaded to buy expensive formulas that have little evidence of proven benefit

for healthy infants. So: what needs urgent attention, how should change be made, and what is the cost of the status quo?

### Flawed evidence

Over recent years researchers have gradually debunked most claims that infant formula reduces the risk of babies developing cow's milk allergy and eczema. Most significantly, the tide turned after the retraction in 2015 of a 25 year old study in *The BMJ*,<sup>5</sup> which had found that mothers with a history of allergy should feed their babies hydrolysed formula to reduce the risk of them developing an allergy to cow's milk. Ranjit Chandra, a Canada based researcher who was an author of the study, was investigated by his employer, which concluded that “scientific misconduct” had been committed. But before 2015 his work had been used by the formula industry to kick start a multimillion pound market for hydrolysed infant milks.

A year later, in 2016, the UK Food Standards Agency stated after a systematic review that hydrolysed formulas did not influence the risk of a child developing allergies.<sup>6</sup> At the same time a meta-analysis and systematic review in *The BMJ*<sup>7</sup> found no evidence to support the conclusion of a 2006 Cochrane review<sup>8</sup> that using hydrolysed formula instead of ordinary cow's milk formula could reduce allergies in babies and children.

In 2018 Cochrane updated its review<sup>9</sup> and found no evidence to support prolonged feeding with hydrolysed formula when compared with standard cow's milk formula for preventing allergic disease in infants. It also found “very low quality” evidence that short term use of an extensively hydrolysed formula compared with standard cow's milk formula could prevent infant cow's milk allergy. But it recommended further trials before implementing this practice.

Since then, Australia and the US are among the countries that have changed guidelines that previously recommended using hydrolysed formula to prevent allergies. Guidelines that have now dropped this recommendation include the Australasian Society of Clinical Immunology and Allergy<sup>10</sup> and the American Academy of Pediatrics.<sup>11</sup>

In a 2021 paper Robert Boyle, clinical reader in paediatric allergy at Imperial College London, UK, wrote, “Overall there is little evidence that hydrolysed

formula has any role in feeding healthy infants.”<sup>12</sup> The National Institute for Health and Care Excellence recommends specialist formula only for the treatment of suspected IgE-mediated cow’s milk allergy and only when the product is extensively hydrolysed.<sup>13</sup>

## Under-regulated markets

This growing consensus in the scientific community against the role of formula in allergy risk reduction has not, however, led to the withdrawal of products that make such claims elsewhere in the world.

In China, the largest and the most rapidly growing formula market in the world,<sup>14</sup> Nestlé heavily promotes its NAN HA product as one that will reduce the risk of allergies. The company’s website in China<sup>15</sup> currently advises pregnant women to take steps to reduce their baby’s allergy risk, including using partially hydrolysed formula when the baby is born. In 2021 the company teamed up with JD Health, China’s largest online healthcare platform, to provide information on formula and allergies through JD’s app, with content also provided by Chinese and overseas paediatricians.<sup>16 17</sup>

Nestlé’s press release for the initiative cites the German Infant Nutritional Intervention (GINI) study, which it says “confirmed that partially hydrolyzed whey protein formula not only reduces the risk of atopic dermatitis, but also has a protective effect on adolescent asthma.”<sup>16</sup> Boyle tells *The BMJ* that the key problem with the GINI study, which he analysed in his 2016 review, was that it selectively reported favourable datapoints.<sup>18</sup> In June 2021 the European Food Standards Agency rejected Nestlé’s evidence from the GINI study because of methodological limitations.<sup>4</sup> The agency was also uncertain about whether the formula investigated in the study was the same as the formula under evaluation.

On World Allergy Day 2019, senior Nestlé executives and the chief executive of the popular Chinese parenting website Babytree held an event<sup>19</sup> to promote Nestlé’s NAN HA “super energy” hypoallergenic formula. A Nestlé press release said that the “sensitive experience pavilion” taught parents how to prevent their child developing allergies and about the hydrolysis process. While the product pictured in the pavilion was NAN HA 3—a follow-on milk for children aged 12 months and over—research cited in the pavilion and in the press release referred to children aged 0 to 3.

In the same year, Babytree asked mothers to talk about using Nestlé’s partially hydrolysed formula in exchange for prizes. Mothers talked about how the formula apparently treated their babies’ allergies and eczema.

Nestlé said, “Allergy is a major concern for parents. Our aim is to use our research and innovation to provide them with infant formulas that can help prevent and manage allergies in babies. The efficacy of our partially hydrolysed infant formula in safely reducing the risk of atopic dermatitis is supported by more than 25 strong, independently run and peer reviewed studies. Furthermore, it has been on the global market for over 30 years and approved for use by the EU Commission.”

The company added, “We acknowledge EFSA’s [the European Food Standards Agency’s] opinion that, based on the evidence provided, no conclusion could be drawn on the efficacy of our product in reducing the risk of developing atopic dermatitis. This opinion does not reflect the GINI 20 year follow-up results, which were published following the submission of the dossier of evidence. These results further strengthen the evidence of efficacy of our partially hydrolysed infant formula.”

Boyle believes that the GINI 20 year assessment study suffers from similar issues of selective reporting to the other GINI study reports. “There is no trial registration, publicly available protocol, or statistical analysis plan describing the investigator plans,” he says. “In the 20 year report, the investigators describe evaluating atopic dermatitis by asking about symptoms, about treatment received, and about a doctor diagnosis of atopic dermatitis—yet they only report outcomes for doctor diagnosis, and we are left without information about self-reported atopic dermatitis symptoms or need for atopic dermatitis treatment.

“So, at least three atopic dermatitis outcomes were recorded, yet only one atopic dermatitis outcome is reported in the manuscript.”

Boyle adds that the 25 studies cited by Nestlé as evidence that its partially hydrolysed infant formula reduces the risk of eczema had been reviewed by comprehensive systematic reviews, including by the 2016 BMJ publication<sup>18</sup> and by Cochrane.<sup>9</sup> Both reviews found the studies wanting, he says.

Nestlé is far from alone in this. Danone is if anything even more vigorous in its promotion of partially hydrolysed formula for allergy prevention. A video on its Nutriclub.ru page on VK.com, Russia’s equivalent of Facebook, advertises the infant formula Nutrilon Hypoallergenic 1 with the tagline, “Helps to reduce the risk of allergies and in the development of the immune system.” An identical video advertisement appeared on its Facebook page. It also advertises Nutrilon 1 and 2 HA on women’s lifestyle websites in Ukraine. Danone’s 2018 policy for marketing breast milk substitutes says that it will not advertise or promote infant or follow-on formula for children under 12 months of age in higher risk countries such as Russia and Ukraine.

The International Code on Marketing of Breast Milk Substitutes states that there should be no advertising or any form of promotion to the general public of any breast milk substitutes, including infant formula (box 2). Although the code is meant to protect infants up to the age of 3 years, few countries have fully implemented the code into law, meaning that some form of breast milk substitute advertising to the general public is permitted in most countries, including Russia and China.

### Box 2: Brexit—an opportunity for the UK to become a global leader in responsible marketing

In February 2020, new rules came into force in the UK and the EU banning nutrition and health claims about infant formula.<sup>20</sup> The rules are not as strict for follow-on formulas, marketed for babies aged 6 to 12 months, but manufacturers are now required to make a clearer distinction in labelling, presentation, and marketing between these products and infant formulas. These changes initially excluded hydrolysed formula in the UK, but new rules came into force last month.

The rules tighten up the claims that can be made about hydrolysed formula milk. Manufacturers now have to provide evidence that claims about reduced allergy risk have been “scientifically evaluated by an authoritative or scientific body.”

Until very recently, Nestlé in the UK was promoting its SMA HA infant milk, a partially hydrolysed formula, which it says can “reduce the risk of developing allergy to cows’ milk proteins.” But in the run-up to the law change, Nestlé has discontinued the product in the UK market. The National Pharmacy Association has also taken down a Nestlé funded “learning module” for pharmacists that repeated claims that the product could prevent allergy and eczema in children.

For Robert Boyle, clinical reader in paediatric allergy at Imperial College London, Brexit gives the UK the opportunity to “get it right” regarding information provided to consumers about formula products, and he urged for the law to be further upgraded to better reflect the International Code of Marketing of Breastmilk Substitutes.

The code explicitly states that there should be no advertising or other form of promotion to the general public of any breast milk substitutes, including not just infant formula but any milks (or products that could be used to replace milk) specifically marketed for young children up to the age of 3 years.

Victoria Sibson, director of the First Steps Nutrition Trust, says, “The code is an international policy framework for protecting babies, young children, and their parents from marketing practices that commercialise infant feeding, mislead consumers, and threaten breastfeeding. The best way to put a stop to companies’ nefarious marketing practices would simply be to adopt ‘the code’ law, and Brexit affords the UK an opportunity to do this.”

Current UK regulation contains all sorts of loopholes that allow spurious nutritional claims to be made. These loopholes include the requirement for statements of intended use on formulas marketed as foods for special medical purposes (FSMPs), toddler milks, and follow-on formulas.

Of particular concern to Boyle is the marketing of FSMPs. “The science behind these milks is generally very weak,” he says. “Some do have an effect, but most claims are spurious—for example, products that claim to help colic and crying but with no evidence that they do that. They are meant to be given under medical supervision but are freely available online and in shops. The stated medical indication on FSMPs becomes another way that companies can effectively make claims for their baby formula products.”

In 2019 Danone opened a €240m (£201m; \$265m) production facility in the Netherlands focused on hydrolysed formula. Danone said, “Our baby formulas are based on peer reviewed, clinical research and are inspired by 40 years of breast milk research. Cow’s milk protein allergy is a complex medical condition. Many international guidelines have recommended using partially hydrolysed formula to prevent cow’s milk allergy.

“However, the science and understanding of how to reduce risk of allergies continues to evolve, which is why we continue to conduct research with external partners in this field. At the same time, regulations and guidelines in the EU relating to the use of partially hydrolysed formulas will change in 2022, and naturally Danone will comply with these new guidelines/regulations.”

It added, “To protect and promote breastfeeding, we report each year on our progress in implementing our strict, worldwide policy for the marketing of breast milk substitutes, and we welcome feedback on where and how we can continue to improve in implementing that policy.”

In Russia and Ukraine, Nutrilon HA stage 1 and stage 2 are designated by local legislation as “food for special medical purposes” and not breast milk substitutes, said Danone. “As such, these products are for patients who have been diagnosed with a medical condition, and are prescribed by a healthcare professional. In this communication, we make clear this information is for parents of children who have been diagnosed of being at risk of allergy,” it added, pointing out that this was spelt out in its videos on VK.com.

Nigel Rollins of WHO’s Department of Maternal, Newborn, Child and Adolescent Health says that childhood health disorders are commonly used to market products with claims based on weak evidence.

“Families are vulnerable—they are seeking to do the best for their child but do not have a knowledge base on which to form their judgments,” he says. “They are easily influenced by marketing that identifies a problem and provides a solution in the form of a product.

“There are many examples where products claim to be improving gut health, or immunity, sleep, or brain development, and the evidence used to support these claims is usually exceptionally poor

but presented in a way that is convincing. These are areas that governments should be scrutinising more carefully.”

For Victoria Sibson, director of the First Steps Nutrition Trust, only robust research should be used to evidence claims. “Breast milk substitute companies exploit regulatory loopholes to get away with making claims about their products which are not backed up by robust research,” she says. “Legal but inappropriate marketing misleads parents and healthcare professionals, who are unable to make informed decisions on which formulas to use, especially in the case of clinical need, whether this is perceived or real.”

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