FSA Consultation on applications for authorisation of miscellaneous regulated products: four novel foods, three food additives, removal of twenty-two food flavouring authorisations, and a proposal to set a limit for ethylene oxide in food additives

The FSA described: *"This consultation seeks stakeholders' views, comments and feedback in relation to the four novel food and three food additive applications, which have been submitted for authorisation; an application to remove the authorisation for twenty-two food flavourings; and a proposal to set a limit for ethylene oxide in all food additives considered in this document."*

Comments compiled by First Steps Nutrition Trust 28th March 2024 in response to applications for authorisation of RP549 lacto-N-fucopentaose I (LNFP-l) and 2' fucosyllactose (2'-FL) (Glycom A/S, Denmark) (new authorisation of a novel food) and RP1202 3-fucosyllactose (3-FL) (from strain of Escherichia coli K-12 DH1) (Glycom A/S, Denmark) (new authorisation of a novel food)

Questions asked in this consultation: Novel Foods:

Q1. Do you have any concerns about the safety of the novel foods with respect to the intended consumers?

Yes. We have concerns about the process used to determine the safety of human milk identical oligosaccharides (HMiOs) as novel foods added to infant formula, follow-on formula and infant milks for special medical purposes – commercial milk formulas - intended for consumption by infants and young children.

Concerns about the appropriateness of safety assessments

The safety assessments carried out by the manufacturer and assessed by the FSA conclude that the HMiOs tested are safe for use in infant and follow-on formula milks at levels that do not exceed their estimated intake in breastmilk. However because these ingredients are not classical "toxicants" the appropriateness of a traditional toxicologic testing and anthropometric studies approach to establishing the safety of their addition to infant and follow-on formula milks is limited (Kaneko et al, 2020). Furthermore, their addition is not supported by robust scientific literature on their long-term safety or benefits (Abrams and Daniels, 2018).

We also have concerns whether randomised controlled trials conducted by manufacturers in the course of product development are fit for purpose. The current situation permits the addition of novel ingredients based on data from clinical trials conducted by the manufacturer, with obvious conflict of interest and most of this evidence is poor quality (Helfer et al., 2021). More specifically, the randomised controlled trials that form the bedrock of product development for formula are biased by selective reporting – with the majority of trials never being published, and those that are published only reporting specific datapoints. Over 90% claim a favourable finding, and it was estimated that just 2% of formula trials report reliable findings (Helfer, et al., 2021).

Lastly, it is relevant to note that harms related to clinical trials of safety and efficacy of prebiotics, probiotics and synbiotics are not sufficiently well reported. "*Of 384 clinical trials, no harms-related data were reported for 106 trials (28%), safety results were not reported for 142 (37%), and the number of serious adverse events (SAEs) per study group was not given for 309 (80%). Of 242 studies mentioning harms-related results, 37% (n = 89) used only generic statements to describe AEs and 16% (n = 38) used inadequate metrics. Overall, 375 trials (98%) did not give a definition for AEs or SAEs, the number of participant withdrawals due to harms, or the number of AEs and SAEs per study group with denominators"* (Bafeta et al, 2018)

Concerns about microbiological safety

The manufacturers toxicology analytical data from six batches of LNFP-l/2'-FL confirmed the presence of very low levels of microbial endotoxins and residual proteins which were not considered to be a safety concern.

However, infants are particularly vulnerable to microbiological contaminants due to the immaturity of their gut. And whilst the level of endotoxins observed were not considered to be a safety concern, it is important to consider the impact of their proliferation in the context of storing and reconstituting powdered formula. Current NHS recommendations for the safe reconstitution and storage of powdered formula are that it should be made using water at a temperature of at least 70°C. Feeds should be made immediately prior to use and not stored. Surveys and studies indicate that PIF is often reconstituted and used at home in less than perfect conditions (Grant et al, 2023; McAndrew et al, 2012). In addition, popular preparation machines have been shown to use water at temperatures lower than the 70°C recommended by the NHS, giving any potential bacterial contaminants the opportunity to proliferate (Grant et al, 2023). Adding additional non-mandatory ingredients to powdered formula has the potential to increase the microbial load. We would consider this to be an unnecessary risk, particularly where there are no proven functional benefits for the novel ingredients added.

Q2. Do you have any comments or concerns on the impacts of authorising or not authorising the novel foods and, if in favour of authorisation, the terms on which the novel foods is authorised (as outlined in the FSA and FSS risk management recommendations)?

Concerns about authorisation

Yes. For context, it is unequivocal that the human milk oligosaccharides (HMOs) in human milk have functional health benefits for infants, however, the position in respect of artificially manufactured HMiOs added to infant and follow-on formula is much less clear. A review paper published by Vandenplas et al (2018), which included authors with significant affiliations to the infant formula industry, acknowledged that there are no established benefits for the addition of HMiOs to infant formula and that more prospective randomised trials in infants are needed to evaluate any clinical benefit of supplementing infant formula with HMiOs. This has been reiterated in several review articles since (Chouraqui, 2020; Wiciński et al, 2020) and it is clear that there is insufficient information to suggest a health benefit from the addition of artificially created HMiOs to commercial milk formulas.

There is ample evidence to show that manufacturers use the addition of non-mandatory ingredients in commercial milk formulas as the basis of misleading and poorly substantiated advertisements that imply health benefits (Cheung et al, 2023; WHO & UNICEF 2022; Hughes et al, 2017; Crawley and Westland 2016; Belamarich et al, 2016; IBFAN, 2004). Recent research

from a WHO multi-country study which included the UK shows how marketing plays an important role in influencing infant feeding decisions and this starts from pregnancy (WHO & UNICEF 2022).

Key findings from this research were:

- Formula milk companies distort science and medicine to legitimize their claims and push their product.
- Industry systematically targets health professionals – whose recommendations are influential – to encourage them to promote formula milk products.
- Formula milk marketing undermines parents' confidence in breastfeeding.

The impact statements for both RP549 lacto-N-fucopentaose I (LNFP-l) and 2' fucosyllactose and RP1202 3-fucosyllactose (3-FL) state that:

"The authorisation of these products should generally result in greater market competition, supporting growth and innovation in the sector."

"*The anticipated intake levels and the proposed use in foods and food supplements was not considered to be nutritionally disadvantageous and does not mislead consumers",*

Contrary to these conclusions, our perspective based on previous experience and existing product marketing, is that the authorisation of these products for use in infant and follow-on formulas provides scope for further misleading marketing such as the advertisement below. This advertisement for a 'premium' brand appeared in a supermarket magazine, and in a reel on social media: https://www.facebook.com/reel/393709163380220[1], It uses the addition of non-mandatory ingredients including prebiotic oligosaccharides to imply that it offers health benefits which other, less expensive products do not.

All families, regardless of how they decide to feed their infants, should be able to access impartial, accurate advice and information that is evidence based and free of commercial influence to enable them to make informed feeding decisions. Authorising the use of non-mandatory ingredients like HMiOs only serves to provide a tool for further misleading marketing and does not benefit the health of infants or their mothers.

[1] While currently adverts of follow-on formula are legal, parents/carers often perceive these ads to be adverts for infant formula, which are not legally allowed (Brown et al, 2020). This type of marketing is called cross-promotion (WHO/UNICEF (2019) Information Note Cross-promotion of infant formula and toddler milks).

Concerns surrounding the terms of authorisation

We would request that health and nutrition claims are not made in association with these novel ingredients, unless they are approved by a relevant body such as the UK Nutrition and Health Claims Committee.

We would also like to raise a concern relating to the additional labelling requirement for LNFP-l/2'-FL which states:

The labelling of food supplements containing lacto-N-fucopentaose I (LNFP-l) and 2'-fucosyllactose (2'-FL) mixture intended for infants under 12 months or young children aged 1 year to 3 years shall bear a statement that the supplements should not be used if breast milk or other foods with added lacto-N-fucopentaose I (LNFP-l) and/or 2'-fucosyllactose (2'-FL) are consumed on the same day.

and the additional labelling requirements for 3-fucosyllactose (3-FL) which states:

For infants under 12 months and young children aged 1 year to 3 years, food supplements are not intended to be used if other foods with added 3 fucosyllactose or breast milk are consumed on the same day.

We are concerned that labelling food supplements on the basis that they should not be used if breastmilk or other foods with added *LNFP-I/2'-FL* are consumed on the same day may undermine breastfeeding by suggesting that breastfeeding should be avoided if parents wish to use supplements. Careful consideration should be given to the wording of any such warnings to ensure that breastfeeding is not undermined or devalued.

The safety assessment for LNFP-I/2'-FL includes this statement:

Committee members noted that oligosaccharides are usually considered prebiotic and can cause bloating in high doses. Consequently, it was highlighted that risk managers may wish to consider whether there was a need for foods containing LNFP-I/2'-FL to be labelled on this basis.

It seems counter intuitive to add ingredients with no proven benefits to infant feeding products where it is acknowledged that they may cause bloating and therefore feeding discomfort for infants. Adding these ingredients to commercial milk formulas is not in the best interests of infants and they should not therefore be authorised for use in infant formula, follow-on formula nor formula milk for special medical purposes.

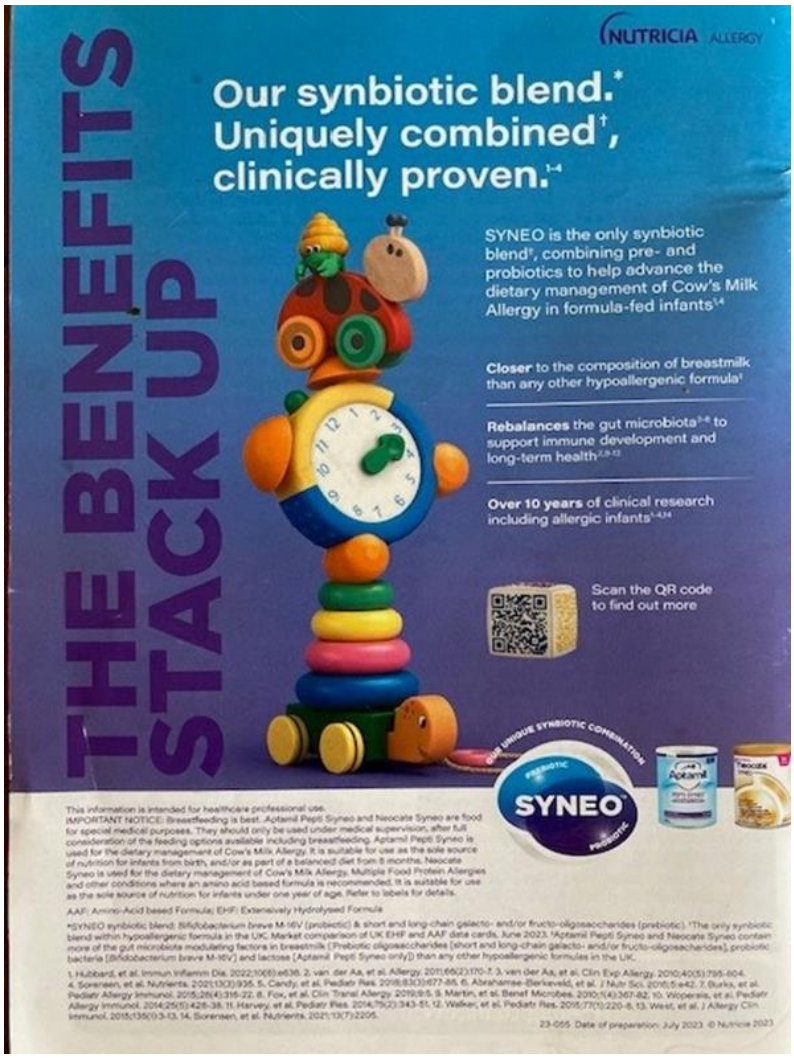
Q3. Are there any other factors that should be considered by Ministers that have not already been highlighted?

Misleading marketing of commercial milk formulas undermines breastfeeding

Public health recommendations of the World Health Organization (WHO and Unicef, 2003) and health departments across the world, including in the UK, are for exclusive breastfeeding for the first six months of life, and continued breastfeeding alongside complementary feeding up to the age of two years and for as long as the mother and baby wish thereafter (SACN, 2018). Evidence consistently shows that using commercial milk formula to replace breastmilk can have long term negative health implications for both infants and their mothers. Many mothers who can breastfeed and express the desire to breastfeed face barriers that undermine their breastfeeding aspirations. One key barrier is the inappropriate and misleading marketing of commercial milk formulas (Rollins et al, 2016, Victora et al, 2016).

There is an abundance of evidence that shows the extent to which parents are exposed to this type of marketing (WHO-UNICEF, 2022, Rollins et al., 2023, Baker et al, 2023; Pérez-Escamilla, et al., 2023*)* and how it diminishes the perceived value of breastfeeding and undermines women's confidence in their ability to breastfeed. Marketing plays on expectations and anxieties around feeding and positions commercial milk formulas as a better alternative to breast milk. *This aggressive promotion of formula milk can influence decisions to use formula milk in place of breast milk, health and nutrition claims are likely to contribute to this process by narrowing the perceived benefits of breast milk over formula* (Munblit et al, 2020).

One example of this type of marketing appears in an advertisement on the back cover of the Dec23/Jan24 edition of Network Health Digest, it undermines breastfeeding by positioning itself as closer to the composition of breastmilk on the basis of the inclusion of non-mandatory ingredients that are present in breastmilk, despite a lack of robust evidence for any health benefits.



Q4. Do you have any other feedback? Including consideration of any relevant provisions of assimilated law and other legitimate factors (other evidence further supporting clear, rational and justifiable risk analysis, such as consumer interests, technical feasibility and environmental factors).

Addition of non-mandatory ingredients has cost implications

The addition of non-mandatory (optional) ingredients increases the input (and therefore retail) cost of the product. Manufacturers of commercial milk formula use the strategy of premiumisation to segment brand ranges according to price and imply that premium priced products have more "innovative components/ ingredients" (Hastings, et al., 2020). This is despite the legal requirement for all infant formula to meet strict standards for nutrition composition, essentially meaning they are all nutritionally comparable and similarly able to support adequate growth and development. This marketing tactic works: Brown et al., (2020) reported that higher priced formulas were seen (by UK mothers) as more advanced, and despite unjustifiably high price rises for infant formula in recent years (First Steps Nutrition Trust, 2023)

there has been little evidence that parents/carers will 'trade down' to less expensive but nutritionally equivalent products (CMA, 2023).

Parents may make sacrifices (i.e. forgo paying other bills, borrow money, skips meals) to pay for premium infant formula even when they are on a tight budget and that families who are struggling to afford infant formula may resort to unsafe feeding practices which may have a detrimental effect on normal growth and development (APPGIFI, 2018)

Rather than encouraging further similar ingredient authorisations, we recommend revisiting legal permissible non-mandatory ingredients in infant formula: they do not confer health or nutrition benefits, the European Food Safety Authority (EFSA) acknowledges they place a burden on infant metabolism (EFSA, 2014), and their addition only adds to the price of the product and gives an opportunity for companies to differentiate their products including by increasing their price. Munblit et al (2020) makes recommendations which provide scope for innovation without new developments being used as the basis of claims, driving inappropriate price inflation and undermining public health efforts to promote and support breastfeeding.

Novel ingredients which have been independently shown by experts to be essential should be made mandatory for the nutritional composition of all infant formula rather than being used for 'improving' premium products. In addition, we suggest a review of standard, type and strength of evidence required to permit the addition of novel ingredients to infant formula, to reduce the number of ingredients added that are not supported by a robust evidence base for efficacy. Currently this is done internationally through Codex, but a more efficient process could be formation of a national committee to assess the validity of innovations with a view to mandating them (or more likely, rejecting them) as part of the compositional standards for infant formula.

In summary, permitting the addition of novel ingredients - including Human Milk Identical Oligosaccharides -based on limited evidence, including conflicted data from clinical trials conducted by the manufacturer, is not in the best interests of infants and may even be harmful, and serves only to drive further misleading marketing, which undermines breastfeeding and therefore the future health of infants and their mothers.

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