



ChangeLab Solutions
Law & policy innovation for the common good.

2201 Broadway, Suite 502
Oakland, CA 94612
510.302.3380
changelabsolutions.org

October 14, 2016

Susan T. Mayne
Director, Center for Food Safety and Applied Nutrition
c/o Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket ID: FDA-2016-D-2241-0002

Re: Draft Guidance for Industry on Substantiation for Structure/Function Claims in Infant Formula Labels and Labeling

Dear Dr. Mayne:

ChangeLab Solutions is commenting to voice strong support for the Food and Drug Administration's *Substantiation for Structure/Function Claims Made in Infant Formula Labels and Labeling: Guidance for Industry*, drafted by the Infant Formula and Medical Foods Staff of the Office of Nutrition and Food Labeling in the Center for Food Safety and Applied Nutrition.

ChangeLab Solutions is a nonprofit organization that provides law and policy strategies to encourage healthy choices in communities across the country. We provide technical assistance to local, state, and federal public health officials and attorneys. We submit these comments for your consideration.

I. BACKGROUND

The Widespread Use of and Apparent Lack of Adequate Scientific Support for Structure/Function Claims on Infant Formula Products Warrant Strong Oversight

Infant formula products carry the most structure/function claims of all conventional foods. A 2006-2007 study of the prevalence of structure/function claims on conventional food labels found such claims on 68% of baby food products, which were mostly infant formulas; in comparison, overall, 5.5% of food labels bore such claims.¹ In January of 2011, the General Accounting Office (GAO) urged the FDA to reassess its approach to misleading labeling claims on foods.² The GAO noted that structure/function claims were a key area in need of additional FDA guidance.³ We strongly support the FDA for taking up this important issue and urge robust oversight.

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Commonly used infant formula structure/function claims have been found to be unsubstantiated. By law, all formula sold in the US must meet the FDA's "nutritional and quality standards."⁴ Claims about a particular product's ability to, for example, soothe infant colic, improve immunity, and reduce stomach upset are designed to position one product as superior to another in spite of the fact that all formulas are nutritionally adequate. By law, such claims must be truthful and not misleading. 21 U.S.C. 343(a)(1). However, a recent review of the actual evidence base for commonly used structure/function claims about infant formula products' ability to reduce colic, crying, and gastrointestinal upset in healthy infants found "a distinct paucity of evidence for the claims as written."⁵

II. PROVISIONS WE SUPPORT

We strongly support the following elements of the proposed guidance, in addition to our other recommendations described in detail below.

With respect to the need for guidance, we strongly support:

- As stated in the introduction to the Proposed Guidance, the statement that "[h]uman milk is the recommended source of nutrition for infants" and infant formula is a food product that simulates or substitutes for human milk.⁶
- The recognition that a clear substantiation standard is needed to prevent untruthful and misleading claims in the labeling of infant formula that are prohibited by law. 21 U.S.C. 343(a)(1).⁷

With respect to determining the meaning of structure/function claims:

- We strongly support equal application of the substantiation standard to express and implied structure/function claims.⁸
- We strongly support the statement that claims are to be analyzed in terms of their meaning "in the context of the labeling as a whole."⁹
- We strongly support the use of consumer testing to determine "consumer understanding of each claim in context...[w]hen all the statements and graphics in the labeling are considered together."¹⁰

With respect to identifying relevant studies, critical study elements, study quality and study strength:

- We strongly support the recommendation that substantiation rely on studies that "provide the most direct evidence for a cause-and-effect relationship" such as "infant feeding intervention studies that are randomized, double-blind, and parallel-controlled."¹¹
- We strongly support the following study criteria:
 - Substantiation of claims made for infant formula "intended for a particular population of infants (e.g., colicky infants) should derive from studies of that population of infants

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- because benefits observed in one infant population may not be generalizable to another infant population.”¹²
- “[A] structure/function benefit demonstrated for one constituent matrix (e.g., cow milk-based formula) may not be generalizable to other matrices (e.g., soy protein isolate-based formula)....”¹³ Therefore, studies are to use “the same form and amount of the constituent in the same or similar formula matrix as the infant formula that will bear the claim.”¹⁴
- The evidence base for claims of structure/function benefits that continue past infancy requires “[f]ollow-up studies” to meet the substantiation standard.¹⁵

In regards to document preservation:

- We strongly support the recommendation that “infant formula manufacturers and distributors retain in their files the documentation substantiating each of their claims.”¹⁶
- We strongly support the discussion of the Federal Trade Commission’s (FTC) concurrent authority over infant formula advertising and note that the FTC’s *Policy Statement on Advertising Substantiation* requires that firms substantiate all claims prior to dissemination and, by extension, must be able to adequately document such pre-claim substantiation.¹⁷

III. ADDITIONAL RECOMMENDATIONS

We provide the following additional recommendations for revisions needed to adequately protect the public from untruthful and misleading structure/function claims on infant formula labels.

a. Remove the Blanket Exclusion of Breast Milk Comparison Claims

Strike the blanket exclusion of breast milk comparison claims from the Introduction of the Proposed Guidance. The Proposed Guidance currently states: “We are aware that infant formula products may also bear labeling claims that suggest that the product contains constituents found in breast milk or that the product is ‘closer’ to breast milk than other formulas. These are not structure/function claims and are not addressed in this guidance”¹⁸ This statement should be stricken from the final guidance as it is overly broad and does not reflect the use of breast milk comparison claims on formula.

Statements about an infant formula product’s similarity to breast milk should be analyzed in the same manner as any other potential express or implied structure/function claim on infant formula labels. Breast milk is the “gold standard” for infant feeding, and contains myriad molecular and live tissue components such as secretory IgA, enzymes, lysozymes, hormones, macrophages and growth factors that are unique for each mother, cannot be manufactured, and are not found in breast milk substitutes.¹⁹ Comparisons to breast milk that expressly or impliedly claim that a formula confers the structure/function benefits of breast milk itself are structure/function claims in the same way that claiming a constituent like a prebiotic has a structure/function benefit in infants. As such, breast milk

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comparisons that implicate structure/function benefits in infants should be treated no differently than any other such claim.

As with all structure/function claims, breast milk comparisons can be express or implied. Infant formula labels now routinely pair express structure/function claims for a constituent with claims like “now closer to breast milk than ever” that imply the inclusion of the constituent or reformulation confers structure/function benefits found in breast milk (see Figure 1).

For example, Nestle’s Gerber Good Start Gentle product label (Figure 1) makes the express structure/function claim that the product is “Gentle” and “easy to digest” because it contains “Small easy-to-digest Comfort Proteins,” and the implied structure/function claim that the product is easy to digest because it is “Our [Gerber’s] closest to Breastmilk.”

FIGURE 1: Nestle, Gerber Good Start Gentle Product Label



As stated in the Proposed Guidance, structure/function claims include “not only...individual statements or phrases, but also...what effects on the structure or function of the body are being claimed when all statements being made for the product are considered together (i.e., in the context

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of the labeling as a whole).”²⁰ The Proposed Guidance further states that “it is equally important to substantiate the overall message conveyed when all statements and graphics in the labeling are considered together.”²¹

Gerber Good Start Gentle labels direct consumers to Gerber.com, where the overall message of the labeling claims is made clear in the following statements:

- “Modeled after the complete nutrition and gentleness of breastmilk for babies up to 12 months.”
- “Gerber® Good Start® Gentle formula is modeled after the complete nutrition and gentleness of breastmilk. It has Comfort Proteins®, small proteins that are easy for tiny tummies to digest.”²²

The overall structure/function message conveyed is that the product is easy to digest because it contains “Comfort Proteins” and because the product is similar to breast milk in how it is digested by infants. The Proposed Guidance should be revised to ensure breast milk comparisons that are used to make claimed structure/function benefits in infants are included.

Revise the Proposed Guidance throughout to clarify that express and implied claims that a formula confers the structure/function benefits of breast milk itself are to be substantiated by studies that use a control group of exclusively breastfed infants. A major error throughout the discussion section of the Proposed Guidance is the lack of even a mention of studies that include a control group of breastfed infants. The discussion of appropriate control groups only envisions studies involving a population of infants fed “a control formula” versus a “test formula.”²³ Yet, as described above, formula labels now pair express structure/function claims for a constituent with implied claims that the inclusion of the constituent confers structure/function benefits like those conferred by breast milk. Any and all such comparisons to breast milk should be supported by competent and reliable scientific evidence that includes properly conducted studies with control groups of exclusively breastfed infants. Studies should clearly define breastfeeding to prevent the use of mixed-fed control groups with results that are not generalizable to exclusively breastfed infants.

For example, Similac Pro-Advance and Pro-Sensitive labels are emblazoned with the term “Human Milk” to describe a prebiotic additive (that is not actually derived from human milk), and the claim that the additive is “For Immune Support” from “a prebiotic previously only found in breast milk” (Figure 2). Product labels direct consumers to Similac.com where the claimed structure/function benefit is described as follows: “Similac with 2’-FL HMO helps strengthen baby’s immune system to be more like the breastfed infant’s than ever before.”²⁴ Appropriate studies to substantiate such a claim should include a control group of breastfed infants since the structure/function benefit is as compared to outcomes for breastfed infants.

Figure 2: Similac Pro-Advance²⁵ & Similac Pro-Sensitive Structure/Function Claims on Product Labels and Similac.com



new!

Abbott
Complete Nutrition for Your Baby's First Year
Similac PRO-ADVANCE™
2'-FL HMO Human Milk Oligosaccharide* From human milk.
For IMMUNE SUPPORT a prebiotic previously only found* in breast milk.
OptiGRO
Brain DHA, Eye LUTEIN, Immune System VITAMIN E
POWDER MILK-BASED
NET WT. 23.2 OZ. (1.45 LB) (658 g)
Infant Formula with Iron

NON-GMO *Ingredients not genetically engineered

New Similac Pro-Advance™ & Similac Pro-Sensitive™

- What was once available just to breastfed babies is now available to formula fed infants.
- Did you know that 70% of your baby's immune system exists in the gut?
- Similac with 2'-FL HMO supports babies' developing immune system in the gut.
- Unlike other formulas, we have 2'-FL HMO, an immune-nourishing prebiotic that circulates throughout the body.



b. Clarify that Claims Related to Human Milk Supplementation and Replacement Are Structure/Function Claims

Infant formula affects the structure or function of two human bodies at the same time: lactating women and their infants. The Food Drug & Cosmetic (FD&C) Act expressly recognizes this fact by defining infant formula as “a food...for special dietary use solely as a food for infants by reason of its simulation of human milk or *its suitability as a complete or partial substitute for human milk.*” 21 U.S.C. 321(z) (emphasis added). Infant formula, therefore, can simulate human milk for women who cannot lactate and when human milk is otherwise unavailable, or completely or partially substitute for the human milk of a lactating woman. The complete or partial substitution of a lactating woman’s human milk supply with infant formula is included in the statutory definition of infant formula and undisputedly affects lactation—a basic bodily function of post-partum women.

Product claims relating to the structure/function of lactating women’s bodies should be included in light of the statute’s plain inclusion of language about human milk substitution. The proposed guidance limits its discussion to “claimed structure/function benefits in infants” by relying on a general case law interpretation of “food” instead of the highly unique nature of infant formula recognized in its statutory definition. *Nutrilab v. Schweiker*, 713 F.2d 335 (7th Cir. 1983), analyzed the FD&C Act’s general definitions of “food” to determine whether a novel weight loss product fell within the “other than food” exception to the definition of a “drug.”

In *Nutrilab*, the 7th Circuit noted that “[i]n the absence of clearcut Congressional guidance, it is best to rely on statutory language and common sense.” Unlike the weight loss product at issue in *Nutrilab*, infant formula has its own statutory definition that plainly includes products suitable “as a complete or partial substitute for human milk.” Structure/function claims related to the effect on lactation of complete or partial substitution of human milk with infant formula should be recognized in addition to claims that derive from infant formula’s character as a food used to nourish infants. *Nutrilab’s* general interpretation of articles otherwise undefined by statute should not supplant the specific statutory definition of infant formula.

Figure 3: Enfamil for Supplementing



The final guidance should clearly state that supplementation claims are structure/function claims. There are a series of infant formula products labeled as specially designed for “Supplementation” or “Supplementing.” Supplementation claims directly relate to the bodily function of lactation, and formula use affects lactation. For example, Enfamil has a product labeled “Enfamil for Supplementing” that directs consumers to the company’s website, www.enfamil.com, for more information. The website contains a page dedicated to “How Supplementing Helped These Moms Breast-Feed Longer” that makes the following claims about the impact of formula use on lactation:

- “Eight out of 10 new moms say supplementing with formula allowed them to breast-feed longer than nursing alone.”
- “Offering both breast milk and formula may help you stick with breast-feeding surprisingly longer than nursing alone.”
- “In most cases, the **optimal time to start supplementing** is after the first month so your milk supply gets established.”
- “Milk supply is based on demand. But when you replace just some feedings with formula, **your breast milk won’t disappear** overnight. It’s also possible to return to exclusive breast-feeding, if you want, by nursing more often and rebuilding milk supply.”²⁶

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These claims directly relate to the bodily function of lactation, and are for a food that is statutorily defined to include products that act as a complete or partial substitute for a lactating woman's human milk. The guidance should make clear that supplementation claims on infant formula will be analyzed as structure/function claims and require substantiation with competent and reliable scientific evidence.

c. Include Full Disclosure of Study Funding, Author Conflicts of Interest and Other Industry Engagement in the Study Evaluation Process and As a Critical Element and Quality Standard for Intervention Studies and Systematic Reviews

Funder bias and conflicts of interest by study authors greatly undermine study quality and can greatly compromise study findings. The proposed guidance should be revised to include the following additional steps in the "Recommended Process for Evaluating Scientific Evidence"²⁷:

- Eliminating studies with inadequate author conflict of interest disclosures.
- Eliminating studies that do not provide full disclosure of funding sources.

"Critical Elements for Intervention Studies"²⁸ should be revised to include an "Industry Engagement" section that references specific criteria for adequate ethical safeguards for nutrition research such as the International Life Sciences Institute (ILSI) North America Working Group on Guiding Principles' *Conflict of Interest Guidelines*.²⁹ Abbott Nutrition, Mead Johnson and Nestle are all ILSI members and should, at a minimum, be held to the basic conflict of interest guidelines set out by their own organization.

"Quality Considerations for Intervention Studies" should include a quality measure for full transparency of funding sources and require conflict of interest disclosures by study authors.³⁰ When not met, these quality measures should be used to exclude studies from systematic reviews. Disclosed conflicts of interest and steps taken to limit funder bias should be evaluated to determine the strengths and weaknesses of studies included in systematic reviews.

d. Engage in Formal Rulemaking to Adequately Address Infant Formula Labeling

Non-binding guidance documents are an important step in the process towards robust oversight of infant formula labeling claims. We applaud the current effort and fully support the Proposed Guidance as a useful step forward in the near term. We respectfully request that the FDA also pursue formal rulemaking on the issue of structure/function claims on infant formula. The FD&C Act grants the agency broad authority to efficiently administer the Act through regulations. 21 U.S.C. 371(a). Infant formula is a highly specialized product that is the sole source of nutrition for many infants. Infant formula labels are barred by the FD&C Act from containing false and misleading claims, and have been subject to the FTC Act's prohibition on false, deceptive and unfair trade practices and its Policy Statement for Advertising Substantiation, yet a recent analysis of structure/function claims on infant formula labels found widespread use of unsubstantiated claims.³¹

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The current Proposed Guidance is modeled after the Dietary Supplement Health and Education Act of 1994 (DSHEA). While some elements of the DSHEA may provide insight into infant formula labeling, the model proposed does not fully take into account the highly unique nature of infant formula. Moreover, a 2012 report by the Office of the Inspector General found that even after promulgation of structure/function guidance for the dietary supplements industry that included stricter criteria than those required by the present Proposed Guidance for infant formula (e.g. prior notification), structure/function claims on dietary supplements continued to fail to meet federal requirements.³² We hope that the Proposed Guidance marks the beginning of a concerted effort that includes formal rulemaking to ensure that families have the most reliable information when making crucial infant feeding decisions.

We are glad to serve as a resource if we can be of help as the FDA continues to work on this issue. If you have any questions or need any additional information related to our comments, please do not hesitate to contact us. Thank you for the opportunity to comment.

Sincerely,

A handwritten signature in black ink, appearing to read "Sabrina Adler". The signature is fluid and cursive, with a long horizontal stroke at the end.

Sabrina Adler
Senior Staff Attorney
sadler@changelabsolutions.org

ENDNOTES

¹ Shimakawa, T., & Ferguson, M. (2015). Prevalence of Structure Function Claims: 2006-2007 Food Label and Package Survey. *Procedia Food Science*, 4, 133-137.

² United States. *Food Labeling : FDA Needs to Reassess Its Approach to Protecting Consumers from False or Misleading Claims : Report to Congressional Committees*. Washington, D.C.: U.S. Govt. Accountability Office, 2011.

³ Id.

⁴ Huang, Y., Labiner-Wolfe, J., Huang, H., J. Choiniere, C., & Fein, S. B. (2013). Association of Health Profession and Direct-to-Consumer Marketing with Infant Formula Choice and Switching. *Birth*, 40(1), 24-31.

⁵ Belamarich PF, Bochner RE, Racine AD. [A Critical Review of the Marketing Claims of Infant Formula Products in the United States](#). *Clin Pediatr (Phila)*. 2016 May;55(5):437-42.

⁶ United States. *Substantiation for Structure/Function Claims Made in Infant Formula Labels and Labeling: Guidance for Industry (Draft Guidance)* (hereinafter "Proposed Guidance"). U.S. Dept. of Health and Human Services, Food and Drug Administration, Center for Food Safety and Applied Nutrition, 2016.

⁷ Id. at 4.

⁸ Id. at 6.

⁹ Id. at 13.

¹⁰ Id. at 6.

¹¹ Id. at 13.

¹² Id. at 11.

¹³ Id.

¹⁴ Id.

¹⁵ Id.

¹⁶ Id. at 13.

¹⁷ United States. (1987). *FTC policy statement regarding advertising substantiation*. Washington, D.C.: Federal Trade Commission. <http://purl.access.gpo.gov/GPO/LPS104180>.

¹⁸ Proposed Guidance at 5.

¹⁹ Walker M. Still selling out mothers and babies; marketing of breast milk substitutes in the USA. Weston, MA: NABA REAL 2007.

²⁰ Proposed Guidance at 6.

²¹ Id.

²² Nestle, Gerber, Stage 1 GERBER® GOOD START® Gentle Powder Infant Formula, <https://www.gerber.com/products/product/gerber-good-start-gentle-powder-formula> (last accessed Oct. 11, 2016).

²³ Proposed Guidance at 9.

²⁴ Abbott Laboratories, Similac, Similac Pro-Advance, <https://similac.com/baby-formula/pro-advance> (last accessed Oct. 11, 2016).

²⁵ Abbott Laboratories, Similac, Closest to Breast Milk, <https://similac.com/why-similac/closest-breast-milk> (last accessed Oct. 11, 2016).

²⁶ Mead Johnson Nutrition, Enfamil, How Supplementing Helped These Moms Breast-Feed Longer, <http://www.enfamil.com/articles-and-videos/how-supplementing-helped-these-moms-breast-feed-longer> (last accessed Oct. 11, 2016).

²⁷ Proposed Guidance at 6.

²⁸ Id. at 8.

²⁹ Alexander N., Rowe S., Brackett R.E., Burton-Freeman B., Hentges E.J., Kretser A., ... Mukherjea R. (2015). Achieving a transparent, actionable framework for public-private partnerships for food and nutrition research. *American Journal Of Clinical Nutrition*, 101(6), 1359-1363; Rowe, S., Alexander, N., Kretser, A., Steele, R., Kretsch, M., Applebaum, R., Falci, K. (2013). Principles for building public-private partnerships to benefit food safety, nutrition, and health research. *Nutrition Reviews*, 71(10), 682-691.

³⁰ Proposed Guidance at 10.

³¹ Belamarich PF, Bochner RE, Racine AD. [A Critical Review of the Marketing Claims of Infant Formula Products in the United States](#). *Clin Pediatr (Phila)*. 2016 May; 55(5):437-42.

³² United States. (2012). *Dietary supplements: Structure/function claims fail to meet federal requirements*. Washington, D.C.: Department of Health and Human Services, Office of Inspector General. <http://purl.fdlp.gov/GPO/gpo68583>.