DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

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Ms. Melanie Fairchild-Dzanis
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Nutrition Division
800 North Brand Boulevard
Glendale, California 91203

RE: Qualified Health Claim Petition – 100 percent Partially Hydrolyzed Whey Protein in Infant Formula and Reduced Risk of Food Allergy in Infants (Docket No. 2005Q-0298)

Dear Ms. Fairchild-Dzanis:

This letter responds to the health claim petition dated June 20, 2005, submitted to the Food and Drug Administration (FDA or the agency), pursuant to Section 403(r)(4) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 343(r)(4)) and in accordance with the July 10, 2003 Task Force Final Report on the Consumer Health Information for Better Nutrition Initiative. The petition requested that the agency authorize a qualified health claim characterizing the relationship between the consumption of 100 percent partially hydrolyzed whey protein in infant formula and a reduced risk of food allergy in infants.

The petition proposed the following model health claim for infant formulas:

> Breastfeeding is the best way to nourish infants. For infants who are not exclusively breastfed, emerging clinical research in healthy infants with family history of allergy shows that feeding a 100% Whey-Protein Partially Hydrolyzed formula may reduce the risk of common food allergy symptoms, particularly allergic skin rash, when used instead of whole-protein cow's milk formula from the initiation of formula feeding.
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> While this formula may reduce the risk, it is not intended to treat existing allergy symptoms. If you suspect your baby is allergic to milk, use only under a doctor's supervision.[1]

1 The petition originally proposed a different second paragraph of claim language: "Partially hydrolyzed formulas are not intended to treat existing food 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 should be under a doctor's supervision." On March 29, 2006, the petitioner asked that this original paragraph be replaced with the language listed here.

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FDA informed you on May 18, 2005, that the agency was not able to acknowledge receipt of the petition and begin its preliminary review of the petition because the petition was not complete. In response, you supplied the needed information in a supplemental submission received by FDA on June 20, 2005. FDA acknowledged the petition in a letter dated July 5, 2005, which initiated FDA's preliminary review of the petition. In that letter, FDA also informed you that it would either file or deny the petition by August 4, 2005.

The petition refers to food "allergy symptoms" in the claim language but refers to food "allergy" as the disease or health-related condition elsewhere in the petition.[2] FDA considers a claim about reduction of symptoms of disease as a drug claim rather than a health claim.[3] Thus, the agency reviewed the petition as a health claim petition about reducing the risk of food allergy.

FDA filed the petition on August 4, 2005 as a qualified health claim petition and posted the petition on the FDA website for a 60-day comment period, consistent with the agency's guidance for procedure on qualified health claims.[4]

The agency received five comments which included three from health professionals, one from an individual consumer, and one from an infant formula manufacturer. Two comments supported the proposed claim, stating that partially hydrolyzed whey protein in infant formula has shown less allergic manifestations compared to intact cow milk protein formulas, and thus is an appropriate alternative to breast milk for allergy prevention in infants at risk. One comment stated that the proposed claim should be denied, given the deficiency in scientific evidence provided in the petition and the risks posed by the presence of the claim on the label for infants who are allergic to cow's milk. One comment stated that cow's milk is unsafe and unhealthy for infants to drink. One comment stated that it is difficult to understand how partial hydrolysate of whey is protective, while complete hydrolysate of whey is not, and suggested more research on this subject. FDA considered the relevant comments in its evaluation of this petition.

This letter sets forth the basis of FDA's determination that there is no credible scientific evidence to support the proposed qualified health claim relating the consumption of 100 percent partially hydrolyzed whey protein in infant formula to a reduced risk of the development of food allergy in infants and the reasons the Agency is denying the qualified health claim.

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[2] *See, e.g.,* Executive Summary, page 2 ("for primary prevention of allergy")

[3] *See Whitaker v. Thompson*, 353 F.3d 947, 950-51 (D.C. Cir.) (finding FDA's distinction between disease prevention claims, regulated as health claims, and disease treatment claims, regulated as drug claims, to be reasonable), *cert. denied*, 125 S. Ct. 310 (2004).

[4] "Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements" (July 10, 2003). [http://www.cfsan.fda.gov/~dms/nuttf-e.html]

I. Overview of Data and Eligibility for a Qualified Health Claim

A health claim characterizes the relationship between a substance and a disease or health-related condition (21 CFR 101.14(a)(1)). The substance must be associated with a disease or health-related condition for which the general U.S. population, or an identified U.S. population subgroup is at risk (21 CFR 101.14(b)(1)). Health claims characterize the relationship between the substance and a reduction in risk of contracting a particular disease.[5] In a review of a qualified health claim, the agency first identifies the substance and disease or health-related condition that is the subject of the proposed claim and the population to which the claim is targeted.[6] FDA considers the data and information provided in the petition, in addition to other written data and information available to the agency, to determine whether the data and information could support a relationship between the substance and the disease or health-related condition.[7] The agency then separates individual reports of human studies from other types of data and information. FDA focuses its review on reports of human intervention and observational studies.[8]

In addition to individual reports of human studies, the agency also considers other types of data and information in its review, such as meta-analyses,[9] review articles,[10] and animal and *in vitro* studies. These other types of data and information may be useful to assist the agency in understanding the scientific issues about the substance, the disease or health-related condition, or both, but cannot by themselves support a health claim relationship. Reports that discuss a number of different studies, such as meta-analyses and review articles, do not provide sufficient information on the individual studies reviewed for FDA to determine critical elements such as the study population characteristics and the composition of the products used. Similarly, the lack of detailed information on studies summarized in review articles and meta-analyses prevents FDA from determining whether the studies are flawed in critical elements such as design, conduct of studies, and data analysis. FDA must be able to review the critical elements of a study to determine whether any scientific conclusions can be drawn from it. Therefore, FDA uses meta-analyses, review articles, and similar publications[11] to identify

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[5] See *Whitaker v. Thompson*, 353 F.3d 947, 950-51 (D.C. Cir.) (upholding FDA's interpretation of what constitutes a health claim), *cert. denied*, 125 S. Ct. 310 (2004).

[6] See guidance entitled "Interim Evidence-based Ranking System for Scientific Data," July 10, 2003. [http://www.cfsan.fda.gov/~dms/hclmgui4.html]

[7] For brevity, "disease" will be used as shorthand for "disease or health-related condition" in the rest of this letter.

[8] In an intervention study, subjects similar to each other are randomly assigned to either receive the intervention or not to receive the intervention, whereas in an observational study, the subjects (or their medical records) are observed for a certain outcome (i.e., disease). Intervention studies provide the strongest evidence for an effect. See Guidance entitled "Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements" (December 22, 1999). [http://www.cfsan.fda.gov/~dms/ssaguide.html]

[9] A meta-analysis is the process of systematically combining and evaluating the results of clinical trials that have been completed or terminated (Spilker, 1991).

[10] Review articles summarize the findings of individual studies.

[11] Other examples include book chapters, abstracts, letters to the editor, and committee reports.

reports of additional studies that may be useful to the health claim review and as background about the substance-disease relationship. If additional studies are identified, the agency evaluates them individually.

FDA uses animal and *in vitro* studies as background information regarding mechanisms of action that might be involved in any relationship between the substance and the disease. The physiology of animals is different than that of humans. *In vitro* studies are conducted in an artificial environment and cannot account for a multitude of normal physiological processes such as digestion, absorption, distribution, and metabolism that affect how humans respond to the consumption of foods and dietary substances (IOM, 2005). Animal and *in vitro* studies can be used to generate hypotheses or to explore a mechanism of action but cannot adequately support a relationship between the substance and the disease.

FDA evaluates the individual reports of human studies to determine whether any scientific conclusions can be drawn from each study. The absence of critical factors such as a control group or a statistical analysis means that scientific conclusions cannot be drawn from the study (Spilker et al., 1991, Federal Judicial Center, 2000). Studies from which FDA cannot draw any scientific conclusions do not support the health claim relationship, and these are eliminated from further review.

Because health claims involve reducing the risk of a disease in people who do not already have the disease that is the subject of the claim, FDA considers evidence from studies in individuals diagnosed with the disease that is the subject of the health claim only if it is scientifically appropriate to extrapolate to individuals who do not have the disease. That is, the available scientific evidence must demonstrate that: (1) the mechanism(s) for the mitigation or treatment effects measured in the diseased populations are the same as the mechanism(s) for risk reduction effects in non-diseased populations; and (2) the substance affects these mechanisms in the same way in both diseased people and healthy people. If such evidence is not available, the agency cannot draw any scientific conclusions from studies that use diseased subjects to evaluate the substance-disease relationship.

Next, FDA rates the remaining human intervention and observational studies for methodological quality. This quality rating is based on several criteria related to study design (e.g., use of a placebo control versus a non-placebo controlled group), data collection (e.g., type of dietary assessment method), the quality of the statistical analysis, the type of outcome measured (e.g., disease incidence versus validated surrogate endpoint), and study population characteristics other than relevance to the U.S. population (e.g., selection bias and whether important information about the study subjects – e.g., age, smoker vs. non-smoker – was gathered and reported). For example, if the scientific study adequately addressed all or most of the above criteria, it would receive a high methodological quality rating. Moderate or low quality ratings would be given based on the extent of the deficiencies or uncertainties in the quality criteria.

Studies that are so deficient that scientific conclusions cannot be drawn from them cannot be used to support the health claim relationship, and these are eliminated from further review.

Finally, FDA evaluates the results of the remaining studies. The agency then rates the strength of the total body of publicly available evidence.[12] The agency conducts this rating evaluation by considering the study type (e.g., intervention, prospective cohort, case-control, cross-sectional), the methodological quality rating previously assigned, the quantity of evidence (number of the various types of studies and sample sizes), whether the body of scientific evidence supports a health claim relationship for the U.S. population or target subgroup, whether study results supporting the proposed claim have been replicated,[13] and the overall consistency[14] of the total body of evidence.[15] Based on the totality of the scientific evidence, FDA determines whether such evidence is credible to support the substance/disease relationship, and, if so, determines the ranking that reflects the level of comfort among qualified scientists that such a relationship is scientifically valid.

A. Substance

A health claim characterizes the relationship between a substance and a disease or health-related condition (21 CFR 101.14(a)(1)). A substance means a specific food or component of food, regardless of whether the food is in conventional food form or a dietary supplement (21 CFR 101.14(a)(2)). The petition identified 100 percent partially hydrolyzed whey protein in infant formula as the substance for the proposed health claims. Infant formulas are foods (Section 201(z) of the Act (21 U.S.C. § 321(z)) and partially hydrolyzed whey protein is an ingredient of infant formula, and thus a component of food; therefore, the agency concludes that 100 percent partially hydrolyzed whey protein in infant formula meets the definition of substance in the health claim regulation (21 CFR 101.14(a)(2)).

B. Disease or Health-Related Condition

A disease or health-related condition means damage to an organ, part, structure, or system of the body such that it does not function properly or a state of health leading to such dysfunctioning (21 CFR 101.14(a)(5)). The petition has identified "food allergy" as

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[12] See *supra*, note 6.

[13] Replication of scientific findings is important for evaluating the strength of scientific evidence (An Introduction to Scientific Research, E. Bright Wilson Jr., pages 46-48, Dover Publications, 1990).

[14] Consistency of findings among similar and different study designs is important for evaluating causation and the strength of scientific evidence (Hill A.B. The environment and disease: association or causation? Proc R Soc Med 1965;58:295-300); See also Systems to rate the scientific evidence, Agency for Healthcare Research and Quality [http://www.ahrq.gov/clinic/epcsums/strengthsum.htm#Contents], defining "consistency" as "the extent to which similar findings are reported using similar and different study designs."

[15] See *supra*, note 6.

the disease or health-related condition for the proposed claim. The term food allergy encompasses a group of disorders characterized by immunologic responses to food proteins.[16] Symptoms of allergic reactions to foods include hives, atopic dermatitis or eczema (i.e., a skin condition characterized by itchy, scaly, red skin), asthma symptoms (e.g., coughing, wheezing, or difficulty breathing due to narrowed airways), and gastrointestinal symptoms (e.g., vomiting, diarrhea and abdominal cramping, and a red rash around the mouth, itching and swelling of the mouth and throat, nausea, abdominal pain, and gas).[17] In severe cases, consuming a food to which one is allergic can cause a life-threatening reaction called anaphylaxis – a systemic allergic reaction that can be severe and sometimes fatal.[18] The agency concludes that food allergy is a disease or health-related condition because there is damage to an organ, part, structure, or system of the body such that is does not function properly, or a state of health leading to such dysfunctioning. Therefore, FDA concludes that the petitioner has satisfied the requirement in 21 CFR 101.14(a)(5).

C. Safety Review

Under 21 CFR 101.14(b)(3)(ii), if the substance is to be consumed at other than decreased dietary levels, the substance must be a food or a food ingredient or a component of a food ingredient whose use at levels necessary to justify a claim has been demonstrated by the proponent of the claim, to FDA's satisfaction, to be safe and lawful under the applicable food safety provisions of the Act.

It is not necessary for FDA to make a determination about the safety of 100 partially hydrolyzed percent whey protein in infant formula in this letter because the agency is denying the proposed claim for lack of credible evidence, as discussed in sections II and III.

II. The Agency's Consideration of a Qualified Health Claim

FDA has identified the following endpoints to use in identifying a reduced risk of a food allergy for purposes of a health claim: incident cases of food allergies. FDA identified no validated surrogate endpoints to use in assessing food allergy risk reduction. The diagnosis of a food allergy is based on a thorough history (medical and dietary), physical examination, diagnostic testing (skin prick test or food specific IgE antibodies), and double-blind food challenge (Sicherer, 2002; Sampson, 2003). No one of the above alone is sufficient for diagnosis of a food allergy. Skin prick tests and food specific IgE antibodies are markers of sensitization, but are not definitive tests to document cases of food allergy under normal circumstances (Sicherer, 2002; Sampson 2003). In cases of

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[16] Food Allergy, American Academy of Allergy Asthma & Immunology, http://www.aaaai.org/patients/gallery/Default.asp?topic=foodallergy

[17] Tips to Remember: Food Allergy, American Academy of Allergy Asthma & Immunology, http://www.aaaai.org/patients/publicedmat/tips/foodallergy.stm

[18] See *supra*, note 17.

allergy to egg, milk, peanuts, fish, and tree nuts, the diagnosis may also be made by history, physical examination and ImmunoCAP Specific IgE fluoroenzyme-immunoassay (FEIA). The ImmunoCAP System FEIA measures food specific IgE levels and has a high predictive value when compared to a double-blind, placebo-controlled food challenge for the specific foods listed in children (Sicherer, 2002 and Sampson, 2003).

The petition cited 216 articles/reports as evidence to substantiate the relationship for the claim. These data consisted of 25 review articles; four abstracts; one meta-analysis; four *in vitro* studies; five animal studies; 109 articles describing studies that did not provide 100 percent partially hydrolyzed whey protein in formula to subjects and/or attempt to measure food allergy in the study subjects, the substance and disease that are the subject of the proposed claim, (e.g., studies involving other types of infant formula or studies of family history and allergies); three federal reports/book chapters; eight letters to the editor; five website printouts; 16 articles in a foreign language with no translation; and 36 studies evaluating the consumption of 100 percent partially hydrolyzed whey protein in infant formula on food allergies (see docket number 2005Q-0298 for bibliography).

A. Assessment of Background Materials

"Background materials" here refers to review articles, meta-analyses, abstracts, book reviews, letters to the editor, federal reports, and website print-outs. Although useful for background information, these materials do not contain sufficient information on the individual studies that they reviewed and, therefore, FDA could not draw any scientific conclusions from this information. FDA could not determine factors such as the study population characteristics or the composition of the products used (e.g., food, dietary supplement). Similarly, the lack of detailed information on studies summarized in these materials prevents FDA from determining whether the studies are flawed in critical elements such as design, conduct of studies, and data analysis. FDA must be able to review the critical elements of a study to determine whether any scientific conclusions can be drawn from it. As a result, the background materials supplied by the petitioner do not provide information from which scientific conclusions can be drawn regarding the substance-disease relationship claimed by the petitioner.

B. Assessment of Animal and *In Vitro* Studies

FDA also uses animal and *in vitro* studies as background information regarding mechanisms of action that might be involved in any relationship between the substance and the disease, and they can also be used to generate hypotheses or to explore a mechanism of action, but they cannot adequately support a relationship between the substance and the disease in humans. FDA did not consider the animal or *in vitro* studies submitted with the petition as supportive information about the substance - disease relationship because such studies cannot mimic the normal human physiology that may be involved in the risk reduction of any type of food allergy, nor can the studies mimic the human body's response to the consumption of 100 percent partially hydrolyzed whey

protein in infant formula. Therefore, FDA cannot draw any scientific conclusions from the animal or *in vitro* studies regarding 100 percent partially hydrolyzed whey protein in infant formula and the reduction of risk of food allergies.

C. Assessment of the Intervention Studies

There were a total of 36 studies that evaluated the relationship between the consumption of 100 percent partially hydrolyzed whey protein in infant formula and a reduced risk of food allergy. FDA determined that scientific conclusions about the relationship between the consumption of 100 percent partially hydrolyzed whey protein in infant formula and a reduced risk of food allergies could not be drawn from these 36 studies for one or more of the reasons discussed below (see Appendix 1).

Three studies (see Appendix 1) used infants/children previously diagnosed with food allergies. Health claims characterize the relationship between the substance and a reduction in risk of contracting a particular disease.[19] These claims involve reducing the risk of a disease in people who do not already have the disease that is the subject of the claim. As a result, FDA considers evidence from studies in individuals already diagnosed with food allergies only if it is scientifically appropriate to extrapolate to individuals who do not have the disease. That is, the available scientific evidence must demonstrate that: (1) the mechanism(s) for the mitigation or treatment effects measured in the diseased populations are the same as the mechanism(s) for risk reduction effects in non-diseased populations; and (2) the substance affects these mechanisms in the same way in both diseased people and healthy people. Given that such evidence was not available, the agency cannot draw any scientific conclusions from these three studies.

One study (Vandenplas et al., 1989) was a republication of another study being evaluated (Vandenplas et al., 1988) for the substance and disease relationship. Since this republication provided no new data or information, the original publication was relied upon for review.

The thirty-two remaining studies did not demonstrate that any observed reduction in food allergy is attributable to the partially hydrolyzed whey protein in infant formula, because these studies did not properly control for the removal of casein as a confounding variable.[20] The petitioner proposed to attribute a reduction in food allergy to the 100 percent partially hydrolyzed whey protein contained in its infant formula (PHF-W) when compared to whole protein cow's milk formula (CMF). The two proteins in CMF are non-hydrolyzed (intact) whey and casein. CMF typically contains non-hydrolyzed (intact) whey and casein proteins in a 20:80 ratio or a 40:60 ratio, whereas the petitioner's PHF-W contains a 100 percent partially hydrolyzed form of whey protein and no casein.

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[19] See *supra*, note 3.

[20] Confounders are factors that are associated with the outcome in question and the intervention and prevent the measured outcome from being attributed unequivocally to the intervention (Epidemiology Beyond the Basics, page 190 Aspen Publishers, 2000)

A study comparing CMF to PHF-W cannot attribute a decrease in food allergy due to the partially hydrolyzed whey proteins, because any decrease in food allergy may be due to the elimination of casein proteins. Casein and whey proteins are the major allergens found in cow's milk (Allergy Report, American Academy of Allergy, Asthma, and Immunology, page 69). Therefore, eliminating one of the major allergens (casein) from a formula could reduce the incidence of food allergy when compared to the cow's milk formula that contains casein, notwithstanding any potential effect of the partial hydrolysis of whey protein on food allergy risk. To demonstrate a relationship between the consumption of partially hydrolyzed whey protein and risk of food allergies, studies would need to include a control group fed infant formula containing non-hydrolyzed (intact) whey protein and no casein. Including three formulas, CMF, 100 percent PHF-W, and a non-hydrolyzed (intact) whey protein formula without casein, would allow evaluation of whether any observed reduction in food allergy is attributable to the elimination of casein, the partial hydrolysis of whey protein (as the petitioner suggests), or a combination of these factors. None of the 32 studies included a control group which evaluated a formula containing only non-hydrolyzed (intact) whey protein formula without casein, therefore no scientific conclusions can be drawn about a relationship between the consumption of partially hydrolyzed whey protein in infant formula and a reduced risk of food allergies.

Twenty-nine studies (see Appendix 1) did not definitively diagnose food allergy incidence in the study's subjects, which, as explained above, is the appropriate endpoint for measuring the food allergy risk reduction that is the subject of the proposed claim. As discussed above, diagnosing food allergy requires several steps including a thorough dietary and medical history, physical examination, diagnostic testing (skin prick test or food specific IgE antibodies), and a double-blind food challenge (Sicher, 2002; Sampson, 2003). In cases of allergy to egg, milk, peanuts, fish, and tree nuts, the diagnosis may also be made by a dietary and medical history, a physical examination, and an ImmunoCAP Specific IgE fluoroenzyme-immunoassay (FEIA). For a study to measure food allergy incidence, the study must demonstrate that the double-blind food challenge or ImmunoCAP FEIA was positive in individuals with physical symptoms (asthma, atopic dermatisis, urticaria etc.) of food allergy for definitive diagnosis (Sicherer, 2002). Physical symptoms, skin prick tests, and/or serum IgE blood levels alone are not sufficient to diagnose food allergy (Sampson, 2003). Many of the studies evaluated by FDA used only symptoms of allergic disease (i.e., atopic dermatitis, wheezing) and/or skin prick tests or serum IgE levels. Since these studies did not definitively diagnose food allergies, no scientific conclusions can be drawn from them concerning the incidence of food allergy in the subjects.

Twelve studies (see Appendix 1) provided no information on the nutritional status of the infants in their studies that would indicate, for example, that these infants experienced normal physical growth during the study. An infant's immune system can be impaired when adequate nutrition is not provided (Cunningham-Rundles et al., 2005), thereby potentially altering any immune mediated response, and making an allergic reaction less

likely. Without information on nutritional status, such as measurements of physical growth for the infants in the studied populations or other assurances that infants were properly nourished during the study, it cannot be determined whether infants are consuming the cow's milk control formula or the intervention formula in the same quantity (e.g., because of potential differences in formula taste). If infants in one group become undernourished because of differing consumption rates, their immune systems become impaired, and observed incidence of allergic reaction may be attributable, not to the test formula or control formula, but to the impaired immune system of the subjects. Without nutritional status information, it is not possible to compare the incidence of food allergy between the intervention and control groups. As a result, no scientific conclusions about the relationship between PHF-W consumption and food allergy risk can be drawn from studies without accounting for this potential confounding factor.

Sixteen studies (Appendix 1) evaluated PHF-W and CMF consumption in infants who were partially breastfed during the studies. Consumption of breast milk may influence the development of food allergy in infants (Friedman and Zeiger, 2005). These sixteen studies did not document whether the duration and extent of breast and formula feeding was similar between the intervention and control groups. If the duration and/or extent of breastfeeding was different between the intervention group and control group, then it could not be determined whether the observed food allergy incidence was due to the test formula, the control formula, or the amount of breast milk an infant received. Therefore, scientific conclusions cannot be drawn from these studies about the relationship between PHF-W consumption and food allergy risk.

D. Assessment of Observational Studies

There were no observational studies that evaluated the relationship between PHF-W and risk of food allergies.

III. Strength of the Scientific Evidence

Below, the agency rates the strength of the total body of publicly available evidence. The agency conducts this rating evaluation by considering the study type (e.g., intervention, prospective cohort, case-control, cross-sectional), the methodological quality rating previously assigned, the quantity of evidence (number of various types of studies and sample sizes), whether the body of evidence supports a health claim relationship for the U.S. population or target subgroup, whether study results supporting the proposed claim have been replicated,[21] and the overall consistency[22] of the total body of evidence. Based on the totality of the scientific evidence, FDA determines whether such evidence is credible to support the substance/disease relationship, and if so, determines the ranking that reflects the level of comfort among qualified scientists that such a relationship is scientifically valid.

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[21] See *supra*, note 13.
[22] See *supra*, note 14.

As discussed in Section II, there were no intervention or observational studies from which scientific conclusions could be drawn about the relationship between the consumption of 100 percent partially hydrolyzed whey protein in infant formula and a reduced risk of food allergy. Based on its review of the totality of publicly available scientific evidence, FDA concludes that there is no credible evidence for a relationship between the consumption of 100 percent partially hydrolyzed whey protein in infant formula and a reduced risk of food allergy.

IV. Agency's Consideration of Disclaimers or Qualifying Language

We considered but rejected use of a disclaimer or qualifying language to accompany the proposed claim. We concluded that neither a disclaimer nor qualifying language would suffice to prevent consumer deception in this circumstance, where there is no credible evidence to support the claim. Adding a disclaimer or incorporating qualifying language that effectively characterizes the claim as baseless is not a viable regulatory alternative because neither the disclaimer nor the qualifying language can rectify the message conveyed by the unsubstantiated claim. *See, e.g., In re Warner-Lambert Co.*, 86 F.T.C. 1398, 1414 (1975), *aff'd*, 562 F.2d 749 (D.C. Cir. 1977) (pro forma statements of no absolute prevention followed by promises of fewer colds did not cure or correct the false message that Listerine will prevent colds); *Novartis Consumer Health, Inc. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 290 F.3d 578, 598 (3d Cir. 2002) ("We do not believe that a disclaimer can rectify a product name that necessarily conveys a false message to the consumer."); *Pearson v. Shalala*, 164 F.3d 650, 659 (D.C. Cir 1999) (the court stated that, where the weight of evidence was against the claim, FDA could rationally conclude that the disclaimer "The FDA has determined that no evidence supports this claim" would not cure the misleadingness of a claim). In such a situation, adding a disclaimer or qualifying language does not provide additional information to help consumer understanding but merely contradicts the claim. *Resort Car Rental System, Inc. v. FTC*, 518 F.2d 962, 964 (9th Cir.) (per curiam) (upholding FTC order to excise "Dollar a Day" trade name as deceptive because "by its nature [it] has decisive connotation for which qualifying language would result in contradiction in terms."), *cert denied,* 423 U.S. 827 (1975); *Continental Wax Corp. v. FTC,* 330 F.2d 475, 480 (2d Cir. 1964) (same); *Pasadena Research Labs v. United States,* 169 F.2d 375 (9th Cir. 1948) (discussing "self-contradictory labels"). In the FDA context, courts have repeatedly found such disclaimers ineffective. *See, e.g., United States v. Millpax, Inc.,* 313 F.2d 152, 154 & n.1 (7th Cir. 1963) (disclaimer stating that "no claim is made that the product cures anything, either by the writer or the manufacturer" was ineffective where testimonials in a magazine article promoted the product as a cancer cure); *United States v. Kasz Enters., Inc.,* 855 F. Supp. 534, 543 (D.R.I.) ("The intent and effect of the FDCA in protecting consumers from . . . claims that have not been supported by competent scientific proof cannot be circumvented by linguistic game-playing."), *judgment amended on other grounds*, 862 F. Supp. 717 (D.R.I. 1994).

V. Conclusions

Based on FDA's consideration of the scientific evidence and other information submitted with the petition, and other pertinent scientific evidence and information, FDA concludes that there is no credible evidence to support the qualified health claim relating consumption of 100 percent partially hydrolyzed whey protein in infant formula to a reduced risk of food allergy, and thus, FDA is denying the petition for the following proposed qualified health claim:

> Breastfeeding is the best way to nourish infants. For infants who are not exclusively breastfed, emerging clinical research in healthy infants with family history of allergy shows that feeding a 100% Whey-Protein Partially Hydrolyzed formula may reduce the risk of common food allergy symptoms, particularly allergic skin rash, when used instead of whole-protein cow's milk formula from the initiation of formula feeding.
>
> While this formula may reduce the risk, it is not intended to treat existing allergy symptoms. If you suspect your baby is allergic to milk, use only under a doctor's supervision.

Please note that scientific information is subject to change, as are consumer consumption patterns. FDA intends to evaluate new information that becomes available to determine whether it necessitates a change in this decision. For example, scientific evidence may become available that will support the use of a qualified health claim or that will support significant scientific agreement for a health claim.

Sincerely,

Michael M. Landa
Deputy Director for Regulatory Affairs

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Appendix 1

Please see the petition in Docket No. 2005Q-0298 for full citation.

Treating infants previously diagnosed with food allergies
Aanpreung et al., 2003
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Improper Controls
Akimoto et al., 1997
Becker et al., 2004
Chan-Yeung et al., 2000
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[23]Chandra et al., 1989
Chandra et al., 1991
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Valverde (Thesis)
Porch et al., 1998
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Tsai et al., 1991
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[23] The three publications by Chandra et al., 1989, 1991, and 1997 are under investigation for scientific validity and Nestle has requested that the Agency not rely on them for the scientific review of this petition (see docket 2005Q-0298, Letter from Nestle March 31, 2006, signed by José M. Saavedra, MD.)

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Not an acceptable diagnosis of food allergy
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