

QUALIFIED HEALTH CLAIM PETITION

**100% WHEY PROTEIN PARTIALLY HYDROLYZED
in Infant Formula and
REDUCING THE RISK OF ALLERGY IN INFANTS**

PRELIMINARY REQUIREMENTS

<u>SECTION CONTENTS</u>	<u>Page</u>
Introduction	2
100% Whey Protein Partially Hydrolyzed, when used in Infant Formula is a “Substance” under Section 101.14(a)(2).....	2
Allergic Disease is of Major Public Health Concern in the United States	3
100% Whey-Protein Partially Hydrolyzed Infant Formulas Contribute Nutritive Value to the Diet	7
100% Whey-Protein Partially Hydrolyzed Infant Formulas are Safe and Lawful	7
Dietary Considerations	8

INTRODUCTION

This Petition is being filed pursuant to Section 403(r)(4) of the Federal Food, Drug, and Cosmetic Act. Nestlé requests, however, that the Petition be reviewed as a qualified health claim and waives review under the Significant Scientific Agreement standard.

Petitions for health claims pertaining to a food or food component to be consumed at other than decreased dietary levels are required by 21 CFR § 101.70 to demonstrate that certain preliminary requirements are met:

that the object of the proposed claim conforms to the definition of a substance in Section 101.14(a)(2);

that the “substance” is eligible for a health claim according to Section 101.14(b) which specifies that the substance must be “associated with a disease or public health-related condition for which the general U.S. population, or an identified U.S. population subgroup ... is at risk ...”;

that the substance contributes taste, aroma, or nutritive value, or any other technical effect listed in 21 CFR § 170.3(o); and

that the substance is safe and lawful at the level necessary to justify the claim under the food safety provisions of the Food, Drug, and Cosmetic Act (the FDC Act).

Each of these points is discussed in turn, below – followed by a discussion of the more general dietary considerations regarding authorization of the proposed health claim.

100% WHEY PROTEIN PARTIALLY HYDROLYZED, WHEN USED IN INFANT FORMULA IS A “SUBSTANCE” UNDER SECTION 101.14(A)(2)

A “substance” is defined in Section 101.14(a)(2) as “... a specific food or component of food, regardless of whether the food is in conventional food form or a

dietary supplement that includes vitamins, minerals, herbs, or other similar nutritional substances.” Partially hydrolyzed whey protein, when used in infant formulas, is without question a component of food. And, 100% Whey-Protein Partially Hydrolyzed infant formula is a specific food in conventional food form. Because the data supporting the desired claim are all derived from studies involving 100% Whey-Protein Partially Hydrolyzed formulas – and because data suggest that how whey protein is processed and the matrix in which it is consumed are important considerations in assessing whether an allergy claim should accompany a formula – for ease of review and discussion the petition uses the collective term “100% Whey-Protein Partially Hydrolyzed infant formula” or “PHF-W” when referring to the “substance.” A detailed discussion and technical definition of the substance, including formulation requirements and analytical methodology that can be used to determine the eligibility of a given product to make the proposed claim, is presented in Section D: Analytical Data – Substance Characterization.

ALLERGIC DISEASE IS OF MAJOR PUBLIC HEALTH CONCERN IN THE UNITED STATES

The American Academy of Allergy, Asthma and Immunology (AAAAI) estimates allergies affect as many as 40 to 50 million people in the United States (AAAAI 2004a). Allergic diseases affect more than 20% of the U.S. population and are the sixth leading cause of chronic disease (AAAAI 2004a). And, all indications are that allergies are increasing. The World Allergy Organization (WAO 2004) reports that allergy and asthma in the western world have doubled or tripled in various populations over the last 40 years and have reached epidemic proportions. Allergic diseases affect people of all ages, as

evidenced by atopic dermatitis, asthma and food allergies being diagnosed in infants, children, and adults.

Such seemingly unrelated conditions are actually linked quite closely. Foods are among the most common of recognized allergens. Nearly 40% of infants with moderate to severe atopic dermatitis also have food allergies (Sicherer 1999). Estimates of the prevalence of food allergy vary widely, but one recent and conservative estimate is that four to six percent of children have *documented* food allergy (Zeiger 2003). Egg, cow milk, peanut, fish, nuts, wheat and soy are said to be the most likely to induce allergy in infants and children. Given current practices and recommendations for infant diets, it is not surprising that cow milk protein is the greatest cause of food allergy in formula-fed infants. According to Zeiger, at least 80,000 to 100,000 infants will develop cow milk allergy each year (1998).

One common sign of allergic disease in infancy, atopic dermatitis, is the most common chronic skin condition in children younger than 11 years of age (AAAAI 2004a). Recent studies in two different U.S. pediatric population cohorts revealed a prevalence of atopic dermatitis approximating 17% (Laughter 2000; Moore 2004). The study of Moore and colleagues looked specifically at the cumulative incidence of atopic dermatitis in the first 6 months of life. Similar, and even slightly higher results have been reported in European pediatric populations (Bergmann 1997; Wadonda-Kabondo 2003). Since the 1960s, the percentage of children diagnosed with atopic dermatitis has more than tripled. While atopic dermatitis is not life threatening, it is a condition with significant implications on the affected individuals. Considerable psychological, physical, social and financial

burdens have been associated with childhood atopic dermatitis (Chamlin 2004, Spergel 2003, Su 1997, Lapidus 1994). Using the Children's Dermatology Life Quality Index to assess the psychosocial effects of cutaneous disorders in children between the ages of 5 and 16, it was found that atopic dermatitis was second only to scabies among skin disorders adversely affecting the quality of life (Lewis-Jones 1995). As many as 66% of children complained that the itching associated with atopic dermatitis disrupts their sleep (Spergel 2003; Dahl 1995). Specifically in preschool children, more behavioral problems have been noted in those with atopic dermatitis than those without (Spergel 2003).

Even beyond the effects on the infant or child, family stress related to the *care* of children with moderate or severe atopic dermatitis includes sleep deprivation, erratic daily schedules, loss of employment, time taken for care of the disease and financial costs (Chamlin 2004, Kemp 2003, Spergel 2003, Bender 2002). The resulting family stress has been said to be greater than that associated with the care of children with type 1 diabetes mellitus (Kemp 2003). Financial costs for the family and community include not only the direct costs of medical and hospital treatments, but also the indirect costs associated with loss of employment (Kemp 2003, Spergel 2003). Lapidus and Honig estimated an annual cost of \$364 million to treat children with atopic dermatitis (Lapidus 1994). In the U.S., contact dermatitis and eczema accounted for 5.8 million annual office visits to a physician (Weiss 1994).

The effect of food allergy, in general, on quality of life has recently been investigated. Sicherer and colleagues evaluated the quality of life in families with children specifically documented as food-allergic (2001). These families reported significantly

more parental distress and worry and interruptions and limitations in usual family activities than families without food-allergic children. The stress experienced in the family of a food-allergic child can lead to built-up tension and possibly even reduced family income if a parent is unable to work due to complex care needs (Gowland 2001). Children with food allergy are reported to feel isolated due to interruptions and limitations placed upon them that are not applied to their *non*-food-allergic counterparts (Sicherer 2001). In addition to the social implications food allergy encompasses, it may also be a significant risk factor for life-threatening asthma in children (Roberts 2003).

In the year 2000 in America, there were approximately 10.4 million physician office visits for the treatment of asthma, of which over one-third were for patients under the age 18 (AAAAI 2004b). The Centers for Disease Control and Prevention report that asthma now affects nearly 5 million people younger than 18 years of age and is the third-ranking cause of hospitalization among those less than 15 years of age. In 2001, 6.3 million non-institutionalized children were diagnosed with asthma (CDC 2003). Direct health care costs for asthma in the U.S. total more than \$8.1 billion annually; indirect costs add another \$4.6 billion (AAAAI 2004b). The estimated cost of treating asthma in those younger than 18 years of age is \$3.2 billion per year. Beyond the economic costs is the social burden of the disease. Asthma accounts for 14 million lost days of school missed annually (CDC 2003). In addition, the psychosocial development of a child may be affected.

Atopic dermatitis, when diagnosed during infancy, has been associated with respiratory manifestations later in life, such as asthma (Spergel 2003). In fact, the

increased prevalence of atopic dermatitis is paralleled with the 75% increase in the prevalence of asthma since 1980. Approximately one-half of those with atopic dermatitis will go on to develop asthma (Boguniewicz 2003). The term “atopic march” has been defined as the typical progression of allergic manifestations occurring in an atopic individual. In this pattern, new predominant signs will emerge over time, and other signs, previously predominant, will wane. The most common and general pattern of symptom progression is that atopic dermatitis precedes allergic rhinitis and asthma, suggesting atopic dermatitis as the possible starting point for allergic disease (Spergel 2005).

100% WHEY-PROTEIN PARTIALLY HYDROLYZED INFANT FORMULAS CONTRIBUTE NUTRITIVE VALUE TO THE DIET

“Nutritive value” is defined in 21 CFR 101.14(a)(3) as “... a value in sustaining human existence by such processes as promoting growth, replacing loss of essential nutrients, or providing energy.” Partially hydrolyzed whey infant formulas clearly provide nutritive value and are eligible to be considered as a substance that is the object of a health claim.

100% WHEY-PROTEIN PARTIALLY HYDROLYZED INFANT FORMULAS ARE SAFE AND LAWFUL

The partially hydrolyzed whey protein infant formulas that are the subject of this petition have been marketed by Nestlé worldwide. Here in the United States the Company’s 100% Whey-Protein Partially Hydrolyzed infant formulas, NESTLE GOOD START SUPREME, NESTLE GOOD START SUPREME DHA & ARA, and NESTLE GOOD START 2 SUPREME DHA & ARA, have all been the subject of notifications filed pursuant to Section 412 of the Food, Drug, and Cosmetic Act and are safely and lawfully marketed in

this country. Moreover, both whey protein and the enzyme trypsin (essential for hydrolysis) are GRAS for the uses employed by Nestlé. 21 CFR 184.1979c covers whey protein, and 184.1914 covers trypsin. Both references are provided as appendices to Section D: Analytical Data – Substance Characterization.

DIETARY CONSIDERATIONS

Nestlé, like every infant formula manufacturer, recognizes that breastfeeding provides the ideal form of nutrition for infants. The labels for Nestlé USA formulas currently reflect this view and expressly state that breastfeeding is best for infants. The same will be true for the labels of the Company's formulas bearing the desired health claim – a claim that is carefully crafted to avoid sending a message that could affect current consumption patterns for breastfeeding.

The proposed claim is also carefully crafted to emphasize that the product bearing the claim is not intended for infants who already have exhibited allergic manifestations. Nearly half of the proposed wording of the claim is devoted to emphasizing that PHF-W formulas are not intended to treat existing food allergy symptoms, and to urging parents to consult a physician if they believe their baby is already allergic to milk.

It is foreseeable that authorization of the proposed health claim might result in the increased consumption of 100% Whey-Protein Partially Hydrolyzed infant formulas. In light of the fact that the proposed claim compares PHF-W formulas with standard intact protein cow's milk formulas, any such impact would come only at the expense of consumption of standard intact cow's milk formulas. It is important to note, therefore, that such a substitution would have no potential for dietary changes in nutrient intake or

adverse nutritional impact. This can be assured in two ways: first, all routine infant formulas by law must provide essentially the same nutrient intake; second, prior to the launch of any routine formula in the U.S., the FDA's Office of Nutritional Products, Labeling and Dietary Supplements conducts a thorough review of clinical data submitted by the manufacturer to ensure that the new formula demonstrates infant growth comparable to that seen on existing routine formulas. The Company's product was no exception to these rules and has been approved in the U.S. since 1989 for routine use in healthy infants.

Section 101.70(f) requests that a health claim petition address four specific questions:

1. Is there an optimum level of the particular substance to be consumed beyond which no benefit would be expected?

The question is largely irrelevant to the product category at issue: infant formula. The claimed benefit with respect to reducing the risk of allergy is related not to consuming more of PHF-W but rather to consuming PHF-W *instead* of intact cow's milk formulas in babies who are not exclusively breastfed.

2. Is there any level at which an adverse effect from the substance or from foods containing the substance occurs for any segment of the population?

Nestlé is unaware of any such level – and, in light of the extensive clinical testing of the Company's formulas, not to mention the millions of infant exposures on a daily basis to PHF-W formulas worldwide – the Company is confident that it would be aware of such a level if one existed.

3. Are there certain populations that must receive special consideration?

Again, specific PHF-Ws have been approved in the U.S. since 1989 for use in healthy infants. The only population that could generally fall within the contours of this question would be infants already diagnosed as allergic to milk. As noted above, product labeling clearly addresses that population.

4. What other nutritional or health factors (both positive and negative) are important to consider when consuming the substance?

Nestlé believes no other considerations are applicable: the proposed health claim would accompany only safe and wholesome infant formulas, designed for use in healthy infants and fully compliant with the rigorous federal regulations with respect to the safety, nutritional content, and quality of U.S. infant formulas.