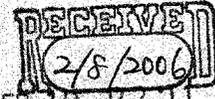




ROSS PRODUCTS DIVISION • ABBOTT LABORATORIES



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February 7, 2006

Barbara O. Schneeman, PhD  
Director  
Office of Nutritional Products, Labeling, and Dietary Supplements  
Center for Food Safety and Applied Nutrition  
BLDG CPK1/Room 4C096/HFS-800  
College Park, MD 20740

cc: Vincent de Jesus, MS, RD

Dear Dr. Schneeman:

Ross Products Division, Abbott Laboratories submits these comments to inform you of new information as well as additional information pertaining to the petition for a Qualified Health Claim (QHC) received by the Agency on 20 June 2005 from Nestle USA, Inc.

*"Breast feeding 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.*

*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."*

**Present Knowledge of Food Allergy Research:**

In light of new information described herein (CBC News 2006; Attachment 1), Ross has reviewed the proposed QHC and advertising materials related to the filing of the proposed QHC, and finds the proposed QHC to be a misinterpretation of the scientific evidence. The advertising materials associated with the proposed QHC may thus lead health care professionals (HCP) and consumers to interpret incorrectly that simply using the formula (without any other interventions) will significantly reduce an infant's risk of developing any food allergy (including peanut, tree nuts, egg, seafood, etc). In studies submitted by Nestle in support of the proposed QHC introduction of solid foods was often restricted until at least 4 to 6 months, major food allergens such as cow's milk, egg and peanut were withheld for 6 months to 3 yrs, prolonged breastfeeding was encouraged, and, in some studies, inhalant allergen controls were included.

The proposed QHC purports to reduce the risk of food allergy symptoms, but the studies cited are related to cow milk protein allergy (CMA) and do not support such broad "food allergy" claims. Food allergy is allergen specific, i.e., to become sensitized to egg one

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must be exposed to egg. The prevalence of food allergy has increased significantly in recent years, but the incidence of CMA appears to have remained stable at approximately 2.5% of all infants (Sampson 2004). Nearly all infants who develop CMA develop it during the first year of life and approximately 60% of these experience IgE-mediated reactions (Sampson 2004). Although atopic dermatitis (AD) is one of the most common IgE-mediated manifestations of food allergy in children, only about 35% of children with moderate-to-severe AD have IgE-mediated food allergy (Eigenmann et al 1998), making it very important in clinical prevention studies that the etiology of this outcome be confirmed.

The studies submitted in support of the proposed QHC were primarily controlled to prevent all exposure to intact cow's milk protein from birth through the intervention periods. Ross is not aware of any data to support the proposed QHC claims for infants who receive even a few feedings of milk-based formula (such as in the nursery or at day care) during the first 4-6 months of life. The reality is that most infants are exposed to intact protein formula or food in the first 4 to 6 months of life. The proposed QHC fails to consider this important clinical reality.

Ross has reviewed the most pertinent studies submitted to support the proposed QHC. Table 1 provides a summary of factors affecting interpretation of the clinical study data and why these studies should not be considered in support of the QHC. FDA should also review published independent reports which have reviewed a number of these studies as well (Schoetzau et al 2001; Zeiger 1997; Muraro et al 2004). Additionally, in just the last week, the Canadian Broadcasting Corporation broadcasted a three-part exposé seriously questioning the scientific validity of work published by Dr Ranjit Chandra (CBC News 2006). In particular, the Nestle supported allergy prevention study (Chandra et al 1997; Chandra and Hamed 1991; Chandra et al 1989), considered a primary study supporting the proposed QHC, was specifically questioned. Taken together, the submitted studies do not provide sufficient support of the proposed QHC under consideration.

Partial whey hydrolysate (commonly marketed as "HA") formulas like the one described in the proposed QHC now comprise a significant percentage of the formula usage in many European countries like Germany. Contrary to Nestle's proposed QHC, Ross is not aware of any reported decrease in the rate of CMA or allergic disease in those countries; this questions whether the proposed QHC translates into meaningful consumer benefits under real life situations of usage. In fact, recent reports have suggested that the rate of atopic eczema has actually increased in young children in Italy (Glassi et al 2006) and Germany (Maziak et al 2003) at the same time that the allergy prevention message associated with HA formula has been strongly promoted in these markets.

#### **Risk of Improper Usage:**

HCPs and consumers may misinterpret Nestle's proposed QHC to include a reduction in all allergy symptoms of any etiology. At present there is no clinically demonstrated means to prevent development of all allergic diseases. However, numerous clinical studies suggest that avoidance of common food allergens during vulnerable periods can, in many cases, reduce the likelihood of antigen-specific sensitization and, thus, development of food allergy, the most common allergy in early childhood. Zeiger et al (1992) have stated *"It is myopic to believe that isolated food allergen avoidance in the*

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*absence of attention to other critical environmental and genetic risk factors will exert any prolonged preventative effect on the development of atopy". Regarding the results of his study submitted in support of the Nestle QHC, Vandenplas (1992) has stated "The difference is due entirely to the postponement effect or decreased incidence of atopy during the first 6 months of life. Once the diet has become normal without restriction, both groups progress in a similar fashion – there is no difference if the groups are compared from 6 months on rather than from birth on." Thus, it appears clear that at the present time the feeding of no one formula alone can result in significant reductions of allergic disease without other concurrent interventions.*

Lastly, Ross has serious concerns that a claim of reduced allergy risk on the product label may mislead the HCP or consumer to believe that the product is suitable for use by a cow's milk allergic child. Indeed, a recent consumer article from *Bundle Magazine* (Jan 2006) incorrectly suggests to consumers that Nestle Good Start Supreme is indicated for babies allergic to milk-based formula and interprets the proposed QHC stating "*Good Start Supreme actually prevents the risk of common food allergies*" (Attachment 1).

**Conclusion:**

The petition submitted should be denied based on the poor quality of scientific evidence provided in the petition in support of the proposed QHC, the potential for HCPs and consumers to misinterpret the QHC, and the possible health risks to the infant if the product is inappropriately fed to a milk allergic infant. Ross respectfully thanks you for your consideration of this letter.

Sincerely,



Pamela Anderson, PhD, RD  
Director, Regulatory Affairs  
Ross Products Division  
Abbott Laboratories

**Table 1. Factors Affecting Interpretation of Data Submitted in Support of Nestle's Proposed Qualified Health Claim (June, 2005).**

Study	Not peer reviewed	Not double-blind	Methods Score <sup>1</sup>	Additional diet intervention <sup>2</sup>	Environmental control/advice	Confirmation of allergic symptoms by controlled challenge <sup>3</sup>
Baumgartner (1998)	X	X <sup>4</sup>	5,6	X		No <sup>7</sup>
Chan (2002)		X	-	X		No
Chan-Yeung et al (2000); Becker et al (2004)			-	X	X	No
Chandra (1989; 1991;1997) <sup>8</sup>			2	X		No <sup>8</sup>
de Seta et al (1994)		X	0	X		No
Exl et al (1998; 2000)		X	-	X		No
Marini et al (1996)	X	X	2	X	X	No
Osborn and Sinn (2003)	X	X <sup>4</sup>	- <sup>5</sup>	X		No <sup>7</sup>
Schmidt et al (1995)	X	X <sup>9</sup>	Excluded-no randomization	X		No
Tsai et al (1991)		X	-	X		-
Vandenplas et al (1992; 1995)			4	X		Unknown <sup>10</sup>
von Berg et al (2003)			-	X		No <sup>11</sup>
Willems et al (1993)		X	Excluded-included infants without family history	X		No

<sup>1</sup> As evaluated and reported by Schoetzau et al (2001) with a range of scores from 0-7 (higher scores better). Randomization, double-blinding, description of dropouts, and description of non-compliance assessed.

<sup>2</sup> Includes delay of solid food introduction, avoidance of food allergens, recommendations for exclusive breastfeeding, and/or pregnancy/lactation diet restrictions

<sup>3</sup> As evaluated and reported by Muraro et al (2004)

<sup>4</sup> Meta-analysis included studies that were not double-blind

<sup>5</sup> (-) Not evaluated by the authors

<sup>6</sup> Meta-analysis included studies reviewed and excluded by Schoetzau et al (2001) or with Method Scores <4

<sup>7</sup> Meta-analysis not evaluated by Muraro et al (2004) but included studies that had no confirmation of allergic symptoms by controlled challenge

<sup>8</sup> Serious questions regarding the scientific validity of this study have been raised (Canadian Broadcasting Corporation, 2006). No immunologic or food challenge confirmation mentioned until 1997 paper; no explanation for why these important data were not presented with the original results.

<sup>9</sup> Parents selected their infant's feeding group

<sup>10</sup> Method not described (i.e. blinding, placebo)

<sup>11</sup> Controlled elimination/challenge procedures only performed in cases of suspected food allergy with gastrointestinal manifestations