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REPORT ON STRUCTURE/FUNCTION CLAIMS FOR STEVIA

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BACKGROUND:

Since Stevia is approved only for use as a dietary supplement, and not as a sweetener or flavoring agent, this document will provide substantiation for non-sweetener uses of Stevia in the Cold-Free product.

NON-SWEETENER COMPONENTS:

Stevia (*Stevia rebaudiana*) contains over 100 identified bioflavonoids and terpenes, separate from the steviosides and rebaudiosides (sweet flavor compounds). Compounds ubiquitous to plants, such as minerals, sterols, and bioflavonoids are present. A partial list includes:

Protein, calcium, phosphorus.

Viana AM, Metivier J. Changes in the levels of total soluble proteins and sugars during leaf ontogeny in *Stevia rebaudiana* Bert. *Annals Botany* 1980; 45:469-474.

Hierbas Medicales, Caa Jhee. Bulletin, Centro de Promocion de las Exportaciones, Ministerio de Industria y Comercio, Paraguay.

Caffeic acid, Chlorogenic acid, Scopoletin, Umbelliferone, Quercetin, Isoquercitrin, Avicularin, Polystachoside

Komissarenko NF, Derkach AI, Kovalev IP, Bublik NP, Chermeneva GA, Komov AG, Zinchenko VV. Diterpenoid glycosides and phenylpropanoids of *Stevia rebaudiana* Bertoni (Asteraceae) leaves. *Rastitel'nye Resursy* 1994; 30(1-2):53-64.

Caryophyllene oxide, Spathulenol

Tsanava VP, Sardzhveladze GP, Kharebava LG. Effect of some technological measures on composition of the volatile complex in *Stevia rebaudiana*. *Subtropicheskie Kul'tury* 1991; (3):64-70.

Tsanava VP, Sardzhveladze GP, Kharebava LG. Studies on the volatile compounds of *Stevia rebaudiana*. *Subtropicheskie Kul'tury* 1989; (3):73-77.

Martelli A, Frattini C, Chialva F. Unusual essential oils with aromatic properties. I. Volatile components of *Stevia rebaudiana* Bertoni. *Flavour and Fragrance Journal* 1985; 1(1):3-7.

Fujita SI, Taka K, Fujita Y. [Miscellaneous contributions to the essential oils of the plants from various territories. XLI. On the components of the essential oil of *Stevia rebaudiana* Bertoni]. *Yakugaku Zasshi* 1977; 97(6):692-694.

Chamazulene (also found in chamomille)

NOTE: *Stevia serrata* is a close relative of *Stevia rebaudiana*.

Roman LU, Mora Y, Hernandez JD. *Stevia serrata*, a source of chamazulene. *Fitoterapia* 1990; 61(1): 84.

Sterebins E, F, G, H (diterpenoids)

Oshima Y, Saito JI, Hikino H. Sterebins E, F, G, and H, diterpenoids of *Stevia rebaudiana* leaves. *Phytochemistry* 1988; 27(2): 624-627.

Centaureidin (5,7,3'-trihydroxy-3,6,4'-trimethoxyflavone) (bioflavonoid)

Amat AG. Flavonoids of *Stevia rebaudiana* Bert. *Acta Farmaceutica Bonaerense (Argentina)* 1982; 1(2):121-123.

Sterols (stigmasterol, β -sitosterol, campesterol)

D'Agostino M, De Simone F, Pizza C, Aquino R. [Sterols in *Stevia rebaudiana* Bertoni]. *Boll Soc Ital Biol Sper* 1984; 60(12):2237-2240.

CLINICAL USES OF STEVIA REBAUDIANA:

Hyperglycemia

White JR, Kramer J, Campbell RK, Bernstein R. Oral use of a topical preparation containing an extract of *Stevia rebaudiana* and the chrysanthemum flower in the management of hyperglycemia [letter]. *Diabetes Care* 1994; 17(8):940.

Hyperglycemia: 35% drop in blood sugar 6-8 hours after *Stevia* leaf extract

Oviedo CA, et al. Accion hipoglicemiante de la *stevia rebaudiana* Bertoni (Kaa-he-e). *Excerpta Medica* 1971; 208:92-93.

Glucose Tolerance (normal humans): aqueous extracts from 5 g of *Stevia rebaudiana* leaves were given every 6 hours for 3 days to 16 volunteers. *Stevia* extract improved glucose tolerance after a glucose tolerance test (plasma glucose levels significantly decreased both fasting and after glucose load). A control group given arabinose did not show the same effects.

Curi R, Alvarez M, Bazotte RB, Botton LM, Godoy JL, Bracht A. Effect of *Stevia rebaudiana* on glucose tolerance in normal adult humans. *Braz J Med Biol Res* 1986; 19(6):771-774.

Wound Healing: Traditional use and reports from doctors and individuals have noticed enhanced healing with less scarring of cuts, wounds, burns, acne, seborrhea, dermatitis, and psoriasis after topical application of aqueous *Stevia* extracts. Of importance was the finding that steviosides (the sweet principle of *Stevia*) did not have the wound-healing effect the herbal concentrate did.

Mowrey DB. *Life With Stevia. How Sweet It Is. Nutritional and Medicinal Uses.* 1992, p.9.

Blood Pressure: A preliminary report in humans found that *Stevia* herb lowered elevated blood pressure, but did not affect normal blood pressure. This report led to use of *Stevia* herb in South American countries for non-medical treatment of high

blood pressure.

Boeckh EA. *Stevia rebaudiana* (Bert.) Berton: Clinical evaluation of its acute action on cardiocirculatory, metabolic and electrolytic parameters in 60 healthy individuals. *Third Brazilian Seminar on Stevia Rebaudiana (Bert.)*, 1986, July, p.22-23.

Anti-Inflammatory: Chamazulene, a component of other *Stevia* species (and possibly of *Stevia rebaudiana*), is an inhibitor of leukotriene B4 formation, which may have potential anti-inflammatory effects.

Safayhi H, Sabieraj J, Sailer ER, Ammon HPT. Chamazulene: an antioxidant-type inhibitor of leukotriene B4 formation. *Planta Medica* 1994; 60(5):410-413.

SUMMARY:

Stevia, like many other herbs and plant foods, contains many compounds found in other plants. *Stevia* also contains some unique compounds listed above, that are closely related to compounds found in other plants. Presumably, these ubiquitous along with unique compounds other than steviosides account for the observed effects of *Stevia* to date. Not mentioned are in vitro antibacterial effects, caries preventive effects, subjective effects on digestion, and folk use for treating influenza. Of course, these latter uses are medical claims, and require serious investigation as to their veracity. For our purposes, valid structure/function claims for *Stevia* include the following:

Stevia contains compounds that affect the function of mitochondria, thereby affecting blood sugar levels.

Stevia contains compounds that affect the function of mitochondria, thereby affecting blood pressure.

Stevia contains chamazulene, an antioxidant-like compound which affects the function of enzymes (lipoxygenase) that generate inflammatory leukotrienes.

Therefore, inclusion of *Stevia* in Cold-Free is for purposes of dietary supplementation of the compounds listed above.