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11/25/03

**SUPPLEMENTAL SUBMISSION TO  
PETITION FOR HEALTH CLAIMS:**

- CALCIUM AND ESSENTIAL HYPERTENSION.
- CALCIUM AND GESTATIONAL HYPERTENSION.
- CALCIUM AND PRE-ECLAMPSIA.

**SUBMITTED TO THE FOOD AND DRUG ADMINISTRATION  
NOVEMBER 24, 2003**

**PETITIONER:  
MARINE BIO USA, INC.**

2004Q-0098

SUPI

**Before the  
FOOD AND DRUG ADMINISTRATION  
Washington, D.C.**

In re: Petition for Health Claims: (1) Calcium may reduce the risk of essential hypertension; (2) Calcium may reduce the risk of gestational hypertension; (3) Calcium may reduce the risk of pre-eclampsia

Filed on: November 21, 2003

**SUPPLEMENTAL SUBMISSION**

Marine Bio USA, Inc. ("Petitioner") hereby supplements the record in the above-referenced health claim proceeding with the attached scientific references, consisting of the scientific articles cited by Michael John Glade, Ph.D., CNS, FACN in his report that were not available at the time of the initial filing with FDA on October 9, 2003<sup>1</sup>, and the PubMed search results requested by the agency. With those documents before you, petition processing should commence forthwith.

Respectfully submitted,

MARINE BIO USA, INC.,

By: 

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<sup>1</sup> Please note that the abstract for reference number 251 was originally submitted to FDA because a full article does not exist. Hence, we are not supplementing that abstract. Also, please note that reference number 322 contains information obtained from the World Congress of Hypertension in Pregnancy, Perugia, Italy, 1990, which was cited in another article submitted to FDA. There is no original publication of this material to submit to FDA; hence, we are not supplementing that information at this time.

# CALCIUM AND BLOOD PRESSURE CLAIMS SUPPLEMENT

## TABLE OF CONTENTS

### SECTION 1

#### Reference Number and Article Citation

3. Zhuang L, Peng JB, Tou L, Takanaga H, Adam RM, Hediger MA, Freeman MR. Calcium-selective ion channel, CaT1, is apically localized in gastrointestinal tract epithelia and is aberrantly expressed in human malignancies. *Lab Invest* 2002;82:1755-1764.
41. Schroeder HA. Relation between mortality from cardiovascular disease and treated water supplies: Variations in states and 163 largest municipalities of the United States. *JAMA* 1960;172:1902-1908.
61. David-Dufilho M, Pernollet M-G, Morris M, Astarie-Dekequer C, Devynck M-A. Erythrocyte Ca<sup>++</sup> handling in the spontaneously hypertensive rat. Effect of vanadate ions. *Life Sci* 1994;54:267-274.
62. Wells IC, Blotcky AJ. Coexisting independent sodium-sensitive and sodium-insensitive mechanisms of genetic hypertension in spontaneously hypertensive rats (SHR). *Can J Physiol Pharmacol* 2001;79:779-784.
65. Tisler A, Pierratos A, D'Arcy Honey J, Bull SB, Rosivall L, Logan AG. High urinary excretion of uric acid combined with high excretion of calcium links kidney stone disease to familial hypertension. *Nephrol Dial Transplant* 2002;17:253-259.
66. Resnick LM. Cellular calcium and magnesium metabolism in the pathophysiology and treatment of hypertension and related metabolic disorders. *Am J Med* 1992;93:11S-20S.
67. Perez-Castrillon JL, Justo I, Silva J, Sanz A, Igea R, Escudero P, Pueyo C, Diaz C, Hernandez G, Duenas A. Bone mass and bone modelling markers in hypertensive postmenopausal women. *J Hum Hypertens* 2003;17:107-110.
70. Hatton DC, Yue Q, McCarron DA. Mechanisms of calcium's effects on blood pressure. *Semin Nephrol* 1995;15:593-602.
71. Porsti I, Makynen H. Dietary calcium intake: Effects on central blood pressure control. *Semin Nephrol* 1995;15:550-563.
72. Nuglozeh E, Roberge AG. Dietary calcium supplementation and dopamine-beta-hydroxylase in spontaneously hypertensive rats. *Biochem Pharmacol* 1997;53:1867-1871.

73. Luft FC. Putative mechanism of blood pressure reduction induced by increases in dietary calcium intake. *Am J Hypertens* 1990;3:156S-160S.
74. Saito K, Sano H, Kawahara J, Yokoyama M. Calcium supplementation attenuates an enhanced platelet function in salt-loaded mildly hypertensive patients. *Hypertension*. 1995;26:156-163.
93. Evans GH, Weaver CM, Harrington DD, Babbs CF Jr. Association of magnesium deficiency with the blood pressure-lowering effects of calcium. *J Hypertens* 1990;8:327-337.
94. Hatton DC, McCarron DA. Dietary calcium and blood pressure in experimental models of hypertension. A review. *Hypertension* 1994;23:513-530.
95. Yuasa S, Sumikura T, Yura T, Takahashi N, Shoji T, Uchida K, Fujioka H, Miki S, Matsuo H, Takamitsu Y. Effect of low dietary calcium intake on blood pressure and pressure natriuresis response in rats: A possible role of the renin-angiotensin system. *Blood Press* 1996;5:121-127.
97. Lal KJ, Dakshinamurti K. The relationship between low-calcium-induced increase in systolic blood pressure and vitamin B6. *J Hypertens* 1995;13:327-332.
101. Butler TV, Cameron J, Kirchner KA. Dietary calcium supplementation restores pressure natriuresis responses in Dahl-S rats. *Am J Hypertens* 1995;8:615-621.
102. DiPette DJ, Greilich PE, Nickols GA, Graham GA, Green A, Cooper CW, Holland OB. Effect of dietary calcium supplementation on blood pressure and calciotropic hormones in mineralocorticoid-salt hypertension. *J Hypertens* 1990;8:515-520.
103. Porsti I, Arvola P, Wuorela H, Ilkka M, Saynavalammi P, Huhtala H, Metsa-Ketela T, Vapaatalo H. Effects of a high calcium diet and deoxycorticosterone on vascular smooth muscle responses in spontaneously hypertensive rats. *J Hypertens* 1990;8:835-841.
104. Makynen H, Kahonen M, Wu X, Arvola P, Porsti I. Endothelial function in deoxycorticosterone-NaCl hypertension: Effect of calcium supplementation. *Circulation* 1996;93:1000-1008.
105. Makynen H, Arvola P, Vapaatalo H, Porsti I. High calcium diet effectively opposes the development of deoxycorticosterone-salt hypertension in rats. *Am J Hypertens* 1994;7:520-528.
112. Lind L, Lithell H, Gustafsson IB, Pollare T, Ljunghall S. Calcium metabolism and sodium sensitivity in hypertensive subjects. *J Hum Hypertens* 1993;7:53-57.

119. Oshima T, Matsuura H, Matsumoto K, Kido K, Kajiyama G. Role of cellular calcium in salt sensitivity of patients with essential hypertension. *Hypertension* 1988;11:703-707.
126. Borghi L, Meschi T, Guerra A, Briganti A, Schianchi T, Allegri F, Novarini A. Essential arterial hypertension and stone disease. *Kidney Int* 1999;55:2397-2406.
134. McCarron DA, Pingree PA, Rubin RJ, Gaucher SM, Molitch M, Krutzik S. Enhanced parathyroid function in essential hypertension: A homeostatic response to a urinary calcium leak. *Hypertension* 1980;2:162-168.
136. Garcia-Zozaya JL, Padilla-Viloria M, Castro A. The relationship between low plasma rennin activity, low serum ionic calcium, and elevated systolic arterial tension in the normotensive elderly. *Am J Hypertens* 1988;1:393-396.
137. Strozecki P, Adamowicz A, Nartowicz E, Odrowaz-Sypniewska G, Wlodarczyk Z, Manitius J. Parathormon, calcium, phosphorus, and left ventricular structure and function in normotensive hemodialysis patients. *Ren Fail* 2001;23:115-126.
144. Cooper RS. Intracellular cations and hypertension in blacks. *Ethn Health* 1996;1:137-144.
160. Lijnen P, Petrov V. Dietary calcium, blood pressure and cell membrane cation transport systems in men. *J Hypertens* 1995;13:875-882.
190. Waal-Manning HJ, McMab M, Paulin JM, Simpson FO. Dietary interventions in treated hypertension (abstract). *New Z Med J* 1987;100:252.
206. Nichaman M, Skekelle R, Paul O. Diet, alcohol and blood pressure in the Western Electric Study (abstract). *Am J Epidemiol* 1984;120:469-470.
211. Hung J-S, Huang T-Y, Wu D, Yen M-F, Tsai S-H, Dahl HP, Neaton J, Dahl JC. The impact of dietary sodium, potassium and calcium on blood pressure. *J Formosan Med Assoc* 1990;89:17-22.
220. Zhou B-F, Wu X-G, Tao S-Q, Yang J, Cao T-X, Zheng R-P, Tian X-Z, Lu C-Q, Miao H-Y, Ye F-M, Zhu L-G, Zhu C, Jiang J-P, He H-Q, Ma F, Du F-C, Wang B. Dietary patterns in 10 groups and the relationship with blood pressure. *Chin Med J* 1989;102:257-261.
240. Feinleib M, Lenfant C, Miller SA. Hypertension and calcium (letter). *Science* 1984;226:384-386.

271. Suter PM, Sierro C, Vetter W. Nutritional factors in the control of blood pressure and hypertension. *Nutr Clin Care* 2002;5:9-19.
272. Garcia-Zozaya JL. Nutritional factors in high blood pressure. *J Hum Hypertens* 2000;14(Suppl. 1):S100-S104. \*\*\*This article is unavailable\*\*\*
274. Kristal-Boneh E, Green MS. Dietary calcium and blood pressure – A critical review of the literature. *Public Health Rev* 1990/1991;18:267-300.
276. Young EW, Bukoski RD, McCarron DA. Calcium metabolism in experimental hypertension. *Proc Soc Exp Biol Med* 1988;187:123-141.
281. Stein PP, Black HR. The role of diet in the genesis and treatment of hypertension. *Med Clin North Am* 1993;77:831-847.
290. Anonymous. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JCNVI). *Arch Intern Med* 1997;157:2413-2446.
291. Anonymous. The role of calcium in peri- and postmenopausal women: Consensus opinion of The North American Menopause Society. *Menopause* 2001;8:84-95.
329. Villar J, Repke J, Belizan JM, Pareja G. Calcium supplementation reduces blood pressure during pregnancy: Results of a randomized controlled clinical trial. *Obstet Gynecol* 1987;70:317-322.
332. Villar J, Repke J. Calcium supplementation during pregnancy may reduce preterm delivery in high-risk populations. *Am J Obstet Gynecol* 1990;163:1124-1131.
344. Hofmeyr GJ, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems (Cochrane Review). *Cochrane Database Syst Rev* 2000;(2):CD001059.
352. Malberti F, Surian M, Poggio F, Minoia C, Salvadeo A. Efficacy and safety of long-term treatment with calcium carbonate as a phosphate binder. *Am J Kidney Dis* 1988;12:487-491.
353. Moriniere P, Hocine C, Boudailliez B, Belbrik S, Renaud H, Westeel PF, Solal MC, Fournier A. Long-term efficacy and safety of oral calcium as compared to Al(OH)<sub>3</sub> as phosphate binders. *Kidney Int* 1989;36(Suppl. 27):S133-S135.
354. Tsukamoto Y, Moriya R, Nagaba Y, Morishita T, Izumida I, Okubo M. Effect of administering calcium carbonate to treat secondary hyperparathyroidism in nondialyzed patients with chronic renal failure. *Am J Kidney Dis* 1995;25:879-886.

355. Nolan CR, Qunibi WY. Calcium salts in the treatment of hyperphosphatemia in hemodialysis patients. *Curr Opin Nephrol Hypertens* 2003;12:373-379.

356. Clark AGB, Oner A, Ward G, Turner C, Rigden SPA, Haycock GB, Chantler C. Safety and efficacy of calcium carbonate in children with chronic renal failure. *Nephrol Dial Transplant* 1989;4:539-544.

357. Orwoll ES. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 1982;97:242-248.

360. Lagman R, Walsh D. Dangerous nutrition? Calcium, vitamin D, and shark cartilage nutritional supplements and cancer-related hypercalcemia. *Support Care Cancer* 2003;11:232-235.

361. Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. Dietary hypercalciuria in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 1994;60:424-429.

## SECTION 2

PubMed search results for all search terms cited in Glade Report.