



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

OCT 24 2003

Jonathan W. Emord, Esq.
Emord & Associates, P.C.
5282 Lyngate Court
Burke, VA 22015

Re: Health Claim Petition – Calcium and colorectal, colon, rectal, breast and prostate cancers and recurrent colon polyps

Dear Mr. Emord:

This letter concerns your health claim petition, received on October 9, 2003, submitted pursuant to Section 403(r)(5)(D) of the Federal Food Drug and Cosmetic Act (FFD&C Act) (21 U.S.C. § 343(r)(5)(D)) with respect to health claims for the relationship between calcium and 1) colorectal cancer, 2) colon cancer, 3) rectal cancer, 4) breast cancer, 5) prostate cancer, and 6) recurrent colon polyps. You submitted this petition on behalf of Marine Bio USA, Inc. We are not acknowledging the receipt of your health claim petition, within the meaning of 21 CFR 101.70(j)(1), because the petition is not complete.

Under 21 CFR 101.70(j)(1), FDA is to notify the petitioner by letter (the "acknowledgment letter"), within 15 days of receipt of the petition, the date that the petition was received. This acknowledgment letter is intended to inform the petitioner that the petition is undergoing agency review and that the agency will subsequently notify the petitioner of its decision to either file the petition for comprehensive review or to deny the petition. Under 21 CFR 101.70 (f), the petition is required to include, among other attachments, copies of any computer literature searches done by the petitioner, copies of articles cited in the literature searches, and all other information that the petitioner relies upon for the support of the health claim.

FDA is not able to acknowledge the receipt of your petition and begin its review of the petition because the petition is not complete. We have found the following deficiencies in your petition:

1. You have not included in your petition the references listed below (by number of reference as cited in the petition) that you cite as support for your proposed health claims:

Ref 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.

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LET 1

- Ref 171 Bostick RM, Potter JD, Fosdick L, Grambsch P, Lampe JW, Wood JR, Louis TA, Ganz R, Grandits G. Calcium and colorectal epithelial cell proliferation: A preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 1993;85:132-141.
- Ref 228 Wargovich MJ, Stephens LC, Gray K. Effect of two "human" nutrient density levels of calcium on the promotional phase of colon tumorigenesis in the F344 rat (abstract). *Proc Am Assoc Cancer Res* 1989;30:196.
- Ref 234 Adell-Carcellar R, Segarra-Soria M, Gilbert-Jerez J, Salvador Sanchis JL, Lazaro-Santander R, Escrig-Sos J, Ruiz-Castillo J. Inhibitory effect of calcium on carcinogenesis at the site of colonic anastomosis: An experimental study. *Dis Colon Rectum* 1997;40:1376-1381.
- Ref 235 Arlow FL, Walczak SM, Luk GD, Majumdar AP. Attenuation of azoxymethane-induced colonic mucosal ornithine decarboxylase and tyrosine kinase activity by calcium in rats. *Cancer Res* 1989;49:5884-5888.
- Ref 238 Hambly RJ, Rumney CJ, Cunningham M, Fletcher JM, Rijken PJ, Rowland IR. Influence of diets containing high and low risk factors for colon cancer on early stages of carcinogenesis in human flora-associated (HFA) rats. *Carcinogenesis* 1997;18:1535-1539.
- Ref 261 Appleton GV, Owen RW, Wheeler EE, Challacombe DN, Williamson RC. Effect of dietary calcium on the colonic luminal environment. *Gut* 1991;32:1374-1377.
- Ref 282 Pence BC. Role of calcium in colon cancer prevention: Experimental and clinical studies. *Mutat Res* 1993;290:87-95.
- Ref 289 Ahnen J. Are animal models of colon cancer relevant to human diseases? *Dig Dis Sci* 1985;30:103S-106S.
- Ref 292 Potten CS, Loeffler M. Stem cells: Attributes, cycles, spirals, pitfalls and uncertainties. Lessons for and from the crypt. *Development* 1990;110:1001-1020.
- Ref 350 Biasco G, Zannoni U, Paganelli GM, Santucci R, Gionchetti P, Rivolta G, Miniero R, Pironi L, Calabrese C, DiFebo G, Miglioli M. Folic acid supplementation and cell kinetics of rectal mucosa in patients with ulcerative colitis. *Cancer Epidemiol Biomarkers Prev* 1997;6:469-471.
- Ref 381 Almendingen K, Hofstad B, Vatn MH. Lifestyle-related factors and colorectal polyps: Preliminary results from a Norwegian follow-up and intervention study. *Eur J Cancer Prev* 2002;11:153-158.
- Ref 382 Baron AJ, Beach M, Mandel JS, van Stolk RU, Haile RW, Sandler RS, Rothstein R, Summers RW, Snover DC, Beck GJ, Frankl H, Pearson L, Bond JH, Greenberg ER. Calcium supplements and colorectal adenomas. Polyp prevention study group. *Ann NY Acad Sci* 1999;889:138-145.
- Ref 403 Kampman E, Giovannucci E, van't Veer P, Rimm E, Stampfer MJ, Colditz GA, Kok FJ, Willett WC. Calcium, vitamin D, dairy foods, and the occurrence of colorectal adenomas among men and women in two prospective studies. *Am J Epidemiol* 1994;139:16-29.
- Ref 471 Anonymous. The role of calcium in peri- and postmenopausal women: Consensus opinion of The North American Menopause Society. *Menopause* 2001;8:84-95.

- Ref 511 Vlajinac HD, Marinkovic JM, Ilic MD, Kocev NI. Diet and prostate cancer: A case-control study. *Eur J Cancer* 1997;33:101-107.
- Ref 516 Tavani A, Gallus S, Franceschi S, La Vecchia C. Calcium, dairy products, and the risk of prostate cancer. *Prostate* 2001;48:118-121.
- Ref 519 Ohno Y, Yoshida O, Oishi K, Okada K, Yamabe H, Schroeder FH. Dietary beta-carotene and cancer of the prostate: A case-control study in Kyoto, Japan. *Cancer Res* 1988;48:1331-1336.
- Ref 520 Tzonou A, Signorello LB, Laggiou P, Wu J, Trichopoulos D, Trichopoulou A. Diet and cancer of the prostate: A case-control study in Greece. *Int J Cancer* 1999;80:704-708.
- Ref 521 Zhang Y, Kiel DP, Ellison RC, Schatzkin A, Dorgan JF, Kreger BE, Cupples LA, Felson DT. Bone mass and the risk of prostate cancer: The Framingham Study. *Am J Med* 2002; 113:734-739.
- Ref 523 Giovannucci E, Rimm EB, Wolk A, Ascherio A, Stampfer MJ, Colditz GA, Willett WC. Calcium and fructose intake in relation to risk of prostate cancer. *Cancer Res* 1998;58:442-447.
- Ref 524 Chan JM, Giovannucci E, Anderson S-O, Yuen J, Adami H-O, Wolk A. Dairy products, calcium, phosphorus, vitamin D, and risk of prostate cancer. *Cancer Causes Control* 1998;9:559-566.
- Ref 525 Chan JM, Giovannucci EL. Dairy products, calcium, and vitamin D and risk of prostate cancer. *Epidemiol Rev* 2001;23:87-92.
- Ref 533 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.
- Ref 534 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)₃ as phosphate binders. *Kidney Int* 1989;36(Suppl.27):S133-S135.
- Ref 535 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.
- Ref 536 Nolan CR, Qunibi WY. Calcium salts in the treatment of hyperphosphatemia in hemodialysis patients. *Curr Opin Nephrol Hypertens* 2003;12:373-379.
- Ref 537 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.
- Ref 538 Orwoll ES. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 1982;97:242-248.
- Ref 541 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.
- Ref 542 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.

2. You have not included in your petition the references listed below that you cite as support for your proposed health claims. In addition, we note that these articles are not in English.

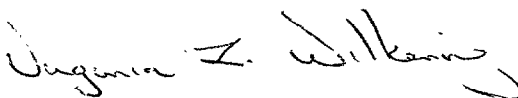
Under 21 CFR 101.70(a), all materials submitted in a foreign language must be accompanied by an accurate and complete English translation.

- Ref 288 Yu B, Wu J, Zhou X. [Interference of selenium germanium and calcium in carcinogenesis of colon cancer.] *Zhonghua Wai Ke Za Zhi* 1995;33:167-169.
- Ref 399 Yang G. [Relationship between colorectal cancer and ten inorganic elements.] *Zhonghua Yu Fang Yi Xue Za Zhi* 1993;27:282-285.
- Ref 400 Yang G, Gao Y-T, Ji B-T. [A case-contro study on colorectal cancer and dietary fiber and calcium of various sources.] *Zhonghua Yu Fang Yi Xue Za Zhi* 1994;28:195-198.

Please note that we have not evaluated at this time whether each claim cited in your petition represents a claim about a relationship between calcium and a disease or health-related condition. Our decision not to review your petition at this time is based on your failure to submit copies of the information on which you rely to support your petition, as required by 21 CFR 101.70. The comments in this letter cannot be considered a substantive review of your petition or a comprehensive list of all issues that may be identified in a complete review. If you wish FDA to review your petition, please resubmit it with the information required by 21 CFR 101.70.

If you have any questions please feel free to contact Lisa Lubin in the Division of Nutrition Programs and Labeling at 301-436-1694.

Sincerely yours,



for Christine L. Taylor
Director
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition