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To Whom it May Concern:

My name is Dale E. Bauman and I am Liberty Hyde Bailey Professor in the Department of Animal Science at Cornell University. I am coauthoring this letter with Adam L. Lock, Post-Doctoral Research Fellow in my department. As members of the scientific community, we appreciate the opportunity to provide comment on *trans* fatty acids in nutrition labeling and we are writing to communicate scientific information about the health effects of naturally occurring *trans* fatty acids in the diet.

The majority (80-90%) of dietary *trans* fatty acids found in the U.S. diet originate from partially hydrogenated vegetable oils that are used in cooking and preparation of processed foods (1, 2). The remaining small percent are naturally occurring, coming from food products derived from ruminants (3, 4). The major *trans* fatty acid isomers found in ruminant meat and milk are 18 carbon monounsaturated fatty acids. Vaccenic acid (VA; *trans*-11 18:1) is the most common, accounting for 60-80% of the total (3,5). The second most common group of *trans* fatty acids in ruminant fat is conjugated linoleic acids with the *cis*-9, *trans*-11 isomer (CLA) being the major form representing 75-90% of total conjugated linoleic acids (6).

Unfortunately, little or no distinction is generally made between the biological effects of various *trans* fatty acid isomers. Although most of the available data examining variables associated with coronary heart disease relate to *trans* fatty acids from partially hydrogenated vegetable oils, these data have been broadly extrapolated to imply that high intake of any and all *trans* fatty acid isomers is associated with increased coronary heart disease. Whereas ruminant *trans* fat contains mainly VA, PHVO contains a Gaussian distribution of *trans* 18:1 isomers that centers on *trans*-9, *trans*-10, *trans*-11 and *trans*-12 (3, 4, 5). It is important to consider the significance of double bond positioning in *trans* fatty acids in terms of their biological effects. These structural differences relate to differences in metabolism and biological outcomes. For example, Hodgson et al. (7) found that while the intake of *trans*-9 and

trans-10 18:1 were positively correlated with heart disease, the intake of VA was not. We have shown that VA and CLA are both effective in reducing the risk of cancer in biomedical studies with animal models whether given as a chemically synthesized supplement or provided as a naturally enriched food component (butter) in the diet (8, 9, 10, 11).

A number of epidemiological studies have investigated the relationship between dietary intakes of *trans* fatty acids and coronary heart disease, and these are cited as strong evidence for the need to reduce the intake of *trans* fats (2,5). Again, structural differences among *trans* fatty acid isomers may be an important consideration in regard to their effect on coronary heart disease. Some epidemiological studies have provided data that allow a comparison of food sources, and our assessment of these studies indicates that the positive relationship between *trans* fatty acids and coronary heart disease risk is specifically related to the intake of *trans* fatty acids derived from vegetable fats (12-16). In fact, in three of these studies (12, 14, 16) there was a negative association between the intake of *trans* fatty acids of animal origin and the risk of coronary heart disease. For example, Willet et al. (12) found that as the intake of *trans* fatty acids from vegetable fat progressively increased, the relative risk of coronary heart disease also increased with a risk of 1.78 at the highest quintile; in contrast, risk of coronary heart disease decreased with increasing intake of *trans* fatty acids from animal sources. Based on the results from these epidemiological studies, we conclude that *trans* fat from ruminant fats differ in their relationship to the risk of coronary heart disease and suggest that this difference relates to the type of *trans* fatty acids, specifically the presence of VA and CLA.

In addition, investigations with both animal and cell models have clearly established that CLA is anticarcinogenic for many types of cancer. These anticarcinogenic properties of CLA extend to VA because a significant amount of VA (~20%) is converted to CLA in humans, thereby increasing the CLA supply to tissues (17, 18). In collaboration with scientists at Roswell Park Cancer Institute, we demonstrated that dietary consumption of VA/CLA enriched butter was effective in reducing the incidence of tumors in a rat-model of mammary carcinogenesis (8, 10, 11). During our initial studies, we made the unexpected observation that the tissue concentration of CLA was greater when the CLA was supplied by butter than for a comparable amount of the same chemically prepared CLA isomer (8). Further studies showed that this difference was related to endogenous synthesis of CLA from the VA present in the dietary supply of butter. Fatty acid analysis showed that the conversion of dietary VA to CLA resulted in a dose-dependent increase in the accumulation of CLA in the mammary fat pad and this was accompanied by decreases in both tumor incidence and tumor number (10). Furthermore, we showed that the predominant mechanism for the anti-cancer effects of VA is related to its conversion to CLA via the enzyme Δ^9 -desaturase (11). From these data, it is clear that both CLA and VA, the predominant *trans* fatty acids present in dairy and ruminant products, are anticarcinogenic.

Recent studies have shown that pure *cis*-9, *trans*-11 CLA provides protection against cholesterol-induced atherosclerosis in the rabbit model (19). Likewise, Toomey et al. (20) used Apo E(-/-) mice that had pre-established atherosclerosis and found that a dietary supplement of *cis*-9, *trans*-11 CLA not only retarded further development of atherosclerotic lesions, but also induced regression of the lesions in the aorta. We have recently extended these data using the hamster model of human lipoprotein metabolism and we found that feeding a VA/CLA-enriched butter increased tissue fatty acid concentrations of VA and CLA, resulting in significant reductions in total and LDL plasma cholesterol content and a reduction in the plasma LDL:HDL-cholesterol ratio, a common marker for risk of atherosclerosis (21, 22). Based on the typical relationship between VA and CLA in ruminant fat and the extent of conversion of VA to CLA in humans (17), Parodi (18) has suggested that multiplying the CLA intake from human diets by 1.4 provides an estimate of the effective physiological dose of CLA derived from ruminant products.

In summary, *trans* fatty acid isomers that occur naturally in beef and dairy foods are not harmful, and in fact there is growing evidence that they may be beneficial to health. For this reason, we believe that the naturally occurring *trans* fatty acids that occur in ruminant-derived food products should be exempt from *trans* fatty acid labeling. In Denmark, the Danish Veterinary and Food Administration has already recognized the critical distinction between man-made and naturally occurring *trans* fats and its orders specifically exempt naturally occurring the *trans* fatty acids that naturally occur in animal fats (5).

Thank you for your consideration.



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References:

1. U.S. Food and Drug Administration. 2003. Questions and Answers about *trans* fat nutrition labeling. Available at www.cfsan.fda.gov/dms/qatrans2.html.
2. Institute of Medicine. 2002. Letter report on dietary reference intakes for *trans* fatty acids. National Academy of Science Press. Washington, D.C.
3. Emken, E.A. 1995. Physiochemical properties, intake, and metabolism. *Am. J. Clin. Nutr.* 62:659S-669S.
4. Craig-Schmidt, M.C. 1998. World wide consumption of *trans* fatty acids. In: J.J. Sebedio and W.W. Christie (Eds.) *Trans Fatty Acids in Human Nutrition*. pp. 59-114. The Oily Press, Dundee, Scotland.
5. Stender, S. and J. Dyerberg. 2003. The influence of *trans* fatty acids on health. 4th ed. Danish Nutrition Council. Publ. No 34. Available at: [http://www.ernaeringsraadet.dk/pdf/Transfedt NETUK.PDF](http://www.ernaeringsraadet.dk/pdf/Transfedt_NETUK.PDF).
6. Bauman, D. E., B. A. Corl, and D. G. Peterson. 2003. The biology of conjugated linoleic acids in ruminants. In: J.-L. Sebedio, W. W. Christie, and R. O. Adlof (Eds.) *Advances in Conjugated Linoleic Acid Research, Volume 2*. pp. 146-173. AOCS Press, Champaign, IL.
7. Hodgson, J.M., M.L. Wahlqvist, J.A. Boxall, and N.D. Balazs. 1996. Platelet *trans* fatty acids in relation to angiographically assessed coronary artery disease. *Atherosclerosis* 120:147-154.
8. Ip, C., S. Banni, E. Angioni, G. Carta, J. McGinley, H.J. Thompson, D. Barbano, and D. Bauman. 1999. Conjugated linoleic acid-enriched butter fat alters mammary gland morphogenesis and reduces cancer risk in rats. *J. Nutr.* 129:2135-2142.
9. Banni, S., E. Angioni, E. Murru, G. Carta, M. P. Melis, D. Bauman, Y. Dong, and C. Ip. 2001. Vaccenic acid feeding increases tissue levels of conjugated linoleic acid and suppresses development of premalignant lesions in rat mammary gland. *Nutr. Cancer* 41:91-97.
10. Corl, B. A., D. M. Barbano, D. E. Bauman, and C. Ip. 2003. *cis*-9, *trans*-11 CLA derived endogenously from *trans*-11 18:1 reduces cancer risk in rats. *J. Nutr.* 133:2893-2900.
11. Lock, A. L., B. A. Corl, D. M. Barbano, C. Ip, and D. E. Bauman. 2004. The anticarcinogenic effect of *trans*-11 18:1 is dependent on its conversion to *cis*-9, *trans*-11 CLA by delta-9 desaturase. 6th Congress of the International Society for the Study of Fatty Acids and Lipids, Brighton, UK, June 27 to July 1, 2004.
12. Willet, W.C., M.J. Stampfer, J.E. Manson, G.A. Colditz, F.E. Speizer, B.A. Rosner, L.A. Sampson, and C.H. Hennekens. 1993. Intake of *trans* fatty acids and risk of coronary heart disease among women. *Lancet* 341:581-585.

13. Ascherio, A., C. Hennekens, J. Buring, C. Master, M. Stampfer, and W.C. Willett. 1993. A case-control study of *trans*-fatty-acid intake and risk of myocardial-infarction. *Circulation* 87:702.
14. BoltonSmith, C., M. Woodward, S. Fenton, and C.A. Brown. 1996. Does dietary trans fatty acid intake relate to the prevalence of coronary heart disease in Scotland? *Eur. Heart J.* 17:837-845.
15. Gillman, M.W., L.A. Cupples, D. Gagnon, B.E. Millen, R.C. Ellison, and W.P. Castelli. 1997. Margarine intake and subsequent coronary heart disease in men. *Epidemiology* 8:144-149.
16. Pietinen, P., A. Ascherio, P. Korhonen, A.M. Hartman, W.C. Willett, D. Albanes, and J. Virtamo. 1997. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. *Am. J. Epidemiol.* 145:876-887.
17. Turpeinen, A. M., M. Mutanen, A. Aro, I. Salminen, S. Basu, D. L. Palmquist, and J. M. Griinari. 2002. Bioconversion of vaccenic acid to conjugated linoleic acid in humans. *Am. J. Clin. Nutr.* 76:504-510.
18. Parodi, P. W. 2003. Conjugated linoleic acid in food. In: J.-L. Sebedio, W. W. Christie, and R. O. Adlof (Eds.) *Advances in Conjugated Linoleic Acid Research*, Volume 2. pp. 101-122. AOCS Press, Champaign, IL.
19. Kritchevsky, D. 2003. Conjugated linoleic acids in experimental atherosclerosis. In: J.-L. Sebedio, W. W. Christie, and R. O. Adlof (Eds.) *Advances in Conjugated Linoleic Acid Research*, Volume 2. pp. 293-301. AOCS Press, Champaign, IL.
20. Toomey, S., H. Roche, D. Fitzgerald, and O. Belton. 2003. Regression of pre-established atherosclerosis in the ApoE(-/-) mouse by conjugated linoleic acid. *Biochem. Soc. Trans.* 31:1075-1079.
21. Lock, A. L., A. M. Salter, M. Hurley, D. A. Dywer, and D. E. Bauman. 2004. Effect of a vaccenic acid (VA)/conjugated linoleic acid (CLA)-enriched butter on tissue CLA concentrations in the hamster. 6th Congress of the International Society for the Study of Fatty Acids and Lipids, Brighton, UK, June 27 to July 1, 2004.
22. Horne, C. A. M., A. L. Lock, M. Hurley, D. E. Bauman, and A. M. Salter. 2004. Effect of a vaccenic acid (VA)/conjugated linoleic acid (CLA)-enriched butter on plasma lipoproteins in the cholesterol-fed hamster. 6th Congress of the International Society for the Study of Fatty Acids and Lipids, Brighton, UK, June 27 to July 1, 2004.