

not tentative. Additionally, the recommendations in the Dietary Guidelines 2000 are reinforced by similar findings and recommendations from other recent expert panels (Refs. 89 through 91, and 140), including those of the IOM/NAS report on macronutrients (Ref. 140), which has also been published. The IOM/NAS report recommends that “*trans* fat consumption be as low as possible while consuming a nutritionally adequate diet.”

(Comment 2) One comment suggested that *trans* fat is a healthier choice than saturated fat, quoting 1994 and 1998 statements that it attributed to the American Heart Association (AHA) recommending that margarine be used instead of butter and that *trans* fats displace saturated fats in the diet. The comment suggested that, if AHA or others in the scientific community recommend margarine be used instead of butter, this establishes that hydrogenated vegetable oils and *trans* fat have health benefits, at least in comparison to saturated fatty acids. Several other comments stated that *trans* fats displace saturated fats in the diet, thus implying that they are healthful alternatives to saturated fats.

FDA disagrees with the comments' conclusions that the recommendations of the AHA and other scientific bodies that margarine be substituted for butter provides a basis for concluding that *trans* fat has health benefits or is a healthier choice than saturated fats. The recently updated 2000 AHA Guidelines (Ref. 91) recommend that intakes of foods with a high content of cholesterol-raising fatty acids (i.e., *trans* and saturated fats) be limited because both raise serum LDL-C levels, and consequently, increase CHD risk. Specifically, the AHA recommends limiting the intake of: (1) Foods rich in saturated fatty acids (e.g., full-fat dairy products, fatty meats, tropical oils), and (2) *trans*-fatty acids, the major contributor of which is hydrogenated fat (Ref. 91). Relative to *trans* fat, the 2000 AHA guidelines state that, “It has been established that dietary *trans*-unsaturated fatty acids can increase LDL cholesterol and reduce HDL cholesterol” (Ref. 91). Moreover, the AHA recommendations are consistent with the recommendations of the other scientific bodies described earlier in this document. All of these reports recommend substituting vegetable oils for animal fats; and, within the vegetable oil category, recommend selecting those products that are lower in or free of *trans* fat (e.g., liquid vegetable oils, soft margarines, and *trans*-free margarines) in place of more

hydrogenated oil products (e.g., stick margarines and shortenings). More recently, the IOM/NAS concluded that there is no evidence of health benefits associated with *trans* fat intakes, but that *trans* fat does increase LDL-C and, therefore, the risk of CHD (Ref. 140). Thus, the comment's premise that the current recommendations of the AHA and other scientific bodies support the conclusion that *trans* fat is a healthful alternative to butter and animal fats is not consistent with, nor supported by, the full context and intent of recommendations by the AHA and other scientific bodies.

Those comments that said *trans* fat is a healthful alternative to saturated fat also are not consistent with the recommendations of the AHA and other scientific bodies. These expert bodies all concluded that both *trans* and saturated fatty acids increase the risk of CHD by increasing serum LDL-C levels and, therefore, they recommended limiting intakes of both *trans* and saturated fatty acids.

It should be noted that recommendations to consume margarine instead of butter are based on the fact that the combined amount of cholesterol-raising lipids (*trans* and saturated fats) are lower in margarines than in butter (Ref. 92). Additionally, butter, unlike margarine, contains dietary cholesterol which also has cholesterol-raising effects (Ref. 139).

B. Published Studies

To evaluate the evidence that dietary *trans* fat increases the risk of CHD, FDA reviewed the scientific evidence cited in the petition and recent human studies from its own literature search. In the November 1999 proposal, FDA summarized its review of the findings of intervention and observational studies on the relationship between intakes of *trans* fatty acids and CHD (64 FR 62746 at 62749–62754). FDA considered the findings from human studies to constitute evidence that is more directly relevant and persuasive than findings from animal studies. FDA gave greater weight to results from dietary intervention studies than to observational (epidemiological) studies because of an intervention study's ability to provide evidence for a cause-effect relationship. FDA regarded results from observational studies as indirect evidence for a relationship between *trans* fatty acid intake and CHD risk. FDA also reviewed estimates of dietary intakes of *trans* fatty acids in the U.S. population (64 FR 62746 at 62752–62753).

In the November 1999 proposal, FDA evaluated results of 12 dietary

intervention studies (Refs. 7 through 15, 34, 36, and 82). FDA focused on the physiological measures of serum and plasma LDL-C concentrations to evaluate whether *trans* fatty acid intakes influence the risk of CHD because such measures are recognized as valid predictors of increased risk for CHD (Ref. 5). FDA concluded that controlled intervention studies, in different population groups in the United States and other countries, consistently indicate that consumption of diets containing *trans* fatty acids, like diets containing saturated fats, results in increased serum LDL-C (a major risk factor for CHD) compared with consumption of diets containing *cis*-monounsaturated or *cis*-polyunsaturated fat sources (64 FR 62746 at 62753). The agency also compiled reports of changes in serum total and high density lipoprotein cholesterol (HDL-C) and serum lipoproteins to present a more complete picture of serum lipid changes (64 FR 62746 at 62799–62821).

In the November 1999 proposal, FDA also reviewed nine publications that examined associations between *trans* fatty acids, serum lipids and CHD endpoints: Four publications describing three prospective cohort studies (Refs. 19 through 21 and 38), one publication describing an inter-cohort study (Ref. 22), three publications describing case control studies (Refs. 16 through 18), and one publication describing a cross-sectional study (Ref. 23). FDA stated that these epidemiological investigations of associations between dietary *trans* fatty acids and risk of CHD must be interpreted cautiously because of the imprecision associated with the dietary collection methodologies used, the difficulty of eliminating confounding factors, and because no dose-response relationship has been demonstrated in the studies (64 FR 62746 at 62752). FDA also stated that despite these generally recognized deficiencies in the observational studies, the repeated and consistent findings from these studies show that consumption of *trans* fatty acids is associated with adverse effects on CHD risk in humans, which supports the findings from intervention studies (64 FR 62746 at 62752).

Thus, in the November 1999 proposal, FDA concluded that controlled intervention studies in different population groups in the United States and other countries consistently indicate that consumption of diets containing *trans* fatty acids, like diets containing saturated fats, results in increased serum LDL-C compared with consumption of diets containing *cis*-monounsaturated or *cis*-polyunsaturated