

#### IV. Review of the Science

##### *A. Reviews by the Federal Government and the Institute of Medicine (IOM)/National Academy of Sciences (NAS)*

In the November 1999 proposal, FDA reviewed reports published by the U.S. Federal government and the IOM/NAS. These reports, which were published between 1988 and 1995, showed that conclusions about the role of *trans* fat in raising LDL-C, the primary risk factor for CHD, and dietary recommendations were evolving as results from new studies became available (64 FR 62746 at 62749). For example, the 1988 Surgeon General's Report (Ref. 2) and the 1989 IOM/NAS Report (Ref. 4) found no adverse effects of *trans* fat. Later, the 1993 publication from the NCEP stated that "*trans* fatty acids raise LDL-C levels nearly as much as do cholesterol-raising saturated fatty acids" (Ref. 5). The fourth edition of Dietary Guidelines for Americans, a joint 1995 publication from the U.S. Department of Health and Human Services and the U.S. Department of Agriculture (USDA) stated that, "Partially hydrogenated vegetable oils, such as those used in many margarines and shortenings, contain a particular form of unsaturated fat known as *trans*-fatty acids that may raise blood cholesterol levels, although not as much as saturated fat" (Ref. 6).

Subsequent to the November 1999 proposal, new expert panels have been convened to update, in light of new scientific evidence, the conclusions and recommendations in the reports discussed previously. FDA has reviewed these new reports to evaluate whether their updated conclusions reversed or significantly altered its earlier conclusions.

The Dietary Guidelines 2000 (Ref. 87) makes the following statements regarding *trans* fatty acids and food sources of *trans* fat:

Foods high in *trans* fatty acids tend to raise blood cholesterol. These foods include those high in partially hydrogenated vegetable oils, such as many hard margarines and shortenings. Foods with a high amount of these ingredients include some commercially fried foods and some bakery goods. (Ref. 87, p. 28);

Aim for a total fat intake of no more than 30 percent of calories, as recommended in previous editions of the Guidelines. If you need to reduce your fat intake to achieve this level, do so primarily by cutting back on saturated and *trans* fats. (Ref. 87, p. 30);

Limit use of solid fats, such as ... hard margarines, ... and partially hydrogenated shortenings. Use vegetable oil as a substitute. (Ref. 87, p. 30).

In the report describing the basis for its recommendations, the Advisory Committee on Dietary Guidelines 2000 (Ref. 88) suggested that information be

provided to help the reader of the Dietary Guidelines 2000 distinguish among the different kinds of fats—saturated, *trans*, and unsaturated. The advisory committee summarized the scientific evidence on *trans* fatty acids as follows:

*Trans* fatty acids are included because a definitive body of recent experimental evidence indicates that *trans* fatty acids raise the concentration of the most dangerous form of serum cholesterol (LDL-cholesterol).

The advisory committee further states:

*Trans* fatty acids also tend to lower a protective form of serum cholesterol (HDL-cholesterol). Prospective epidemiological studies further note that higher intakes of *trans* fatty acids are associated with a higher incidence of coronary heart disease. (Ref. 88, p. 37).

Recent guidelines from the National Cholesterol Education Program (NCEP) (Ref. 89) provide an update to the 1993 NCEP report (Ref. 5). The 2001 NCEP report is an evidence-based report that extensively references the scientific literature. The expert panel concluded that:

*Trans* fatty acids raise serum LDL-cholesterol levels. Through this mechanism, higher intakes of *trans* fatty acids thus should increase risk for CHD. Prospective studies support an association between higher intakes of *trans* fatty acids and CHD incidence. (Ref. 89, p. V-15).

Based on these conclusions, the Expert Panel recommended for individuals at increased risk for CHD that:

Intakes of *trans* fatty acids should be kept low. The use of liquid vegetable oil, soft margarine, and *trans* fatty acid-free margarine are encouraged instead of butter, stick margarine, and shortening. (Ref. 89, p. V-15).

Lastly, a recent report of the IOM/NAS found "a positive linear trend between *trans* fatty acid intake and LDL cholesterol concentration, and therefore increased risk of CHD" (Ref. 140). The report summarized that this would suggest a Tolerable Upper Intake Level (UL) of zero, but because *trans* fats are unavoidable in ordinary diets and achieving such a UL would require extraordinary changes in dietary intake patterns that might introduce other undesirable effects and unknown health risks, a UL was not proposed. Instead, the report recommended "that *trans* fat consumption be as low as possible while consuming a nutritionally adequate diet."

In summary, the recently updated Dietary Guidelines (Ref. 87), NCEP (Ref. 89), and IOM/NAS (Ref. 140) reports, based on current scientific evidence, consistently find that *trans* fatty acids are associated with increased LDL-C levels and, therefore, that lower intakes of both saturated and *trans* fatty acids are important dietary factors in reducing

the risk of CHD in the general population and for those at increased risk for CHD. In addition, these new reports (Refs. 87, 89, and 140) either reversed previous scientific conclusions of no deleterious effects of *trans* fatty acids (Refs. 2 and 4), or strengthened previous scientific conclusions of an adverse effect of *trans* fat intakes on CHD risk (Refs. 5 and 6). Thus, based on the current body of scientific evidence, there is strong agreement among the expert panels that the available evidence is sufficiently compelling to conclude that *trans* fat intakes increase CHD risk. Accordingly, these expert panels recommended, in addition to their longstanding recommendations that Americans consume diets limited in saturated fat, that consumers also select food products that are low in *trans* fat. Although the expert panels' primary emphases remain on limiting intakes of saturated fat (which contributes on average about 11–12 percent of calories in U.S. diets), they also have recommended limiting intakes of *trans* fats (which contribute, on average, about 3 percent of calories in U.S. diets). These recommendations are made for the general population (Refs. 87 and 140) and persons at increased risk for CHD whose LDL-C is above goal levels (Ref. 89).

(Comment 1) Several comments on the November 1999 proposal questioned whether the conclusions regarding *trans* fat would be supported by pending scientific reviews. Some of these comments recommended that FDA not issue a final rule until after publication of Dietary Guidelines 2000. Other comments recommended waiting until the IOM/NAS completes work on a review of dietary reference values for macronutrients.

The Dietary Guidelines 2000 have been published (Refs. 87 and 88). While they do not mention *trans* fat in its broad guideline, "Choose a diet that is low in saturated fat and cholesterol and moderate in total fat," the recommendations from the Dietary Guidelines 2000 and the accompanying advisory committee review clearly state that foods high in *trans* fatty acids tend to raise blood LDL-C which increases the risk of CHD. Reductions in intakes of both saturated and *trans* fats are suggested for maintaining total fat to no more than 30 percent of calories. Substitutions of foods low in *trans* and saturated fatty acids (e.g., vegetable oils) for foods with higher levels of *trans* fatty acids (e.g., hard margarines, partially hydrogenated shortenings) are also recommended. Thus, in the Dietary Guidelines 2000, the recommendations to reduce *trans* fat intake are definitive,