

fat sources (64 FR 62746 at 62753). FDA also concluded that these findings are consonant with findings from observational studies among free-living persons in the United States and other countries (64 FR 62746 at 62753).

In the November 1999 proposal, FDA also summarized the results of estimates of dietary intake of *trans* fatty acids in the U.S. population (64 FR 62746 at 62752). FDA noted that estimates of mean consumption of *trans* fatty acids in the United States ranged from about 3 g/day to about 13 g/day. Based on national food disappearance data, estimated mean values for the daily per capita consumption of total *trans* fatty acids were variable: 12.8 g/day (Ref. 24), 10.2 g/day (Ref. 39), and 8.1 g/day (Ref. 25). Based on a nationally representative sample of the U.S. population, the estimated mean intake of *trans* fatty acids was 5.3 g/day (2.6 percent of calories) and the 90th percentile intake was 9.4 g/day for individuals 3 years of age and older in the U.S. population (Ref. 12). Estimates of mean *trans* fatty acids intake were 4.4 g/day for men and 3.6 g/day for women in one observational study in the United States (Ref. 18) and 3.4 g/day for men in another (Ref. 23). Some studies presented mean or median intakes for quintiles of the population studied. Median intakes were 3.1 g/day for men and 3.0 g/day for women in the lowest quintile and 6.7 g/day for men and 6.8 g/day for women in the highest quintile (Ref. 18). Another study reported intakes of 1.5 g/day and 5.3 g/day, respectively, for the lowest and highest quintiles of male health professionals (Ref. 19). For female nurses in the United States, mean energy-adjusted intakes of *trans* fatty acids were 2.4 and 5.7 g/day, respectively for the lowest and highest quintiles of *trans* fatty acid intakes (Ref. 21). FDA concluded that, overall, the estimates of mean *trans* fatty acids intakes are similar to intakes of *trans* fatty acids in the U.S. intervention studies (the selected intervention studies used in this comparison were those in which *trans* fatty acid contents were determined by chemical analysis of duplicate portions of the diets and for which statistically significant increases in serum LDL-C were reported compared to diets containing *cis*-polyunsaturated fatty acids (Refs. 13, 34, and 82) or *cis*-monounsaturated fatty acids (Ref. 12)). The intakes of *trans* fatty acids for which the increases in serum LDL-C were statistically significant in the intervention studies ranged from 7.6 g/day to 13 g/day (Refs. 12, 13, 34, and 82). FDA stated that these levels are very similar to the

estimated intakes of the many individuals in the United States whose *trans* fatty acid intake is greater than the mean of 5.3 g/day (64 FR 62746 at 62753).

Subsequent to the November 1999 proposal, additional studies on the topic of *trans* fatty acid intakes and CHD risk have been published (Refs. 98 through 102). FDA reviewed the findings from these new studies to evaluate whether they differ significantly from the findings of studies included in the proposed rule. In general, the results from these recently published intervention and prospective studies are consistent with the results from the studies included in the November 1999 proposal in that they also found that diets containing *trans* fat increased LDL-C, and therefore, CHD risk (Refs. 98 to 101) and that, in free-living populations, consumption of *trans* fat was associated with increased risk of heart attack and death from CHD (Ref. 102). In addition, a cross-sectional observational study has been published (Ref. 93). This study, which was the subject of several comments, suggests no relationship between current intakes of *trans* fat in European countries and CHD risk. FDA has addressed this study in Comment 4 of this document.

(Comment 3) Many comments discussed the strength of the scientific evidence for establishing whether *trans* fatty acids adversely affect CHD risk by raising LDL-C levels. A number of comments found the evidence to be strong and supportive of *trans* fatty acid labeling on foods. Other comments questioned whether there was sufficient evidence to warrant labeling of *trans* fat content. Several comments stated that the health impact of the intake levels reported in population-based surveys and observational studies was minimal.

A few comments to the November 15, 2002, proposal to reopen the *trans* fat comment period questioned the scientific validity of the IOM/NAS report based on the underlying science and regression equations relied upon. The comments argued that one of the articles relied upon (Ref. 83) was an opinion essay and was not peer-reviewed by the *New England Journal of Medicine* (NEJM) where it was published.

Based on an evaluation of the scientific evidence, FDA concludes that the scientific evidence is sufficient to require nutrition labeling of *trans* fat. In the November 1999 proposal, FDA systematically summarized and reviewed the available individual human studies (64 FR at 62749–62754 and 62798 to 62821). In re-examining this review in light of the comments,

FDA finds no basis to alter its earlier conclusion that, in general, there is consistency in finding adverse effects of *trans* fat on CHD risk. Controlled intervention studies in different population groups in the United States and other countries consistently indicated that consumption of diets containing *trans* fat results in elevations of LDL-C, and therefore, increased risk of CHD (Refs. 7 to 15, 34, 36, and 82). In addition, positive statistical associations are consistently reported in observational studies between estimated *trans* fat intake in free-living populations and incidence of CHD manifested as heart attack or death from CHD (Refs. 16 to 22, and 38) or increased risk of CHD as assessed by higher levels of LDL-C (Ref. 23) (64 FR 62751 to 62753). Thus, FDA continues to find that a large body of the most persuasive types of evidence (i.e., intervention trials and prospective cohort observational studies) consistently show that *trans* fat intakes adversely affect CHD risk under both controlled trial conditions and in free-living populations following their usual dietary patterns. This consistency was seen across studies done: (1) In the United States and several European countries, (2) using a variety of test and control products and study designs, (3) using a range of intake levels for *trans* fatty acids (less than (<) 1 percent to 7 percent of calories), (4) by different investigators and research groups, (5) with different populations and selection/exclusion criteria, and (6) within different total dietary contexts. This relationship was also consistently found in comparisons of high vs. low consumers of *trans* fats in free-living U.S. populations consuming their normal diets. Thus, whether controlled intervention trials or among free-living U.S. populations consuming their usual diets, the adverse effects of *trans* fat intakes on CHD risk were consistently observed.

Moreover, FDA's conclusions were consistent with those of independent Federal Government expert panels that published dietary recommendations for U.S. population groups subsequent to publication of the November 1999 proposal (Refs. 87 and 89 through 91) that were cited in the **Federal Register** to reopen the comment period on November 15, 2002. These expert panels, reviewing the same scientific evidence as FDA described in the proposed rule, and given their knowledge of U.S. dietary patterns, consistently concluded that *trans* fat intakes are associated with increased CHD risk and recommended that U.S.