

specifically stated that the prospective studies suggest that there may be other biological mechanisms by which *trans* fat contributes to CHD, in addition to the effects of *trans* fat on LDL-C and HDL-C. These comments therefore supported the possibility that the actual benefits of *trans* fat labeling may be greater than FDA's estimate using either Method 1 (LDL-C) or Method 2 (LDL-C and HDL-C).

Other comments, which were opposed to the November 1999 proposal or some of its provisions, questioned FDA's conclusions regarding the net health benefits of *trans* fat labeling. Some comments stated that the potential harm to the public remedied by *trans* fat labeling was not sufficient to outweigh the cost burden to specific industries. These comments suggested that, although *trans* fat was shown to increase LDL-C in some studies, the evidence was inconclusive on how to quantify the increase in LDL-C and CHD risk due to *trans* fat intake and on whether the increase in LDL-C and CHD risk due to *trans* fat intake were as large as those due to saturated fat. These comments suggested that FDA's estimate of health benefits of *trans* fat labeling was too high. One comment stated that it is premature to conclude that *trans* fat intake lowers HDL-C because many intervention studies showed that *trans* fat intake causes only a small decrease or has no effect on HDL-C. The comment implied that consumption of *trans* fat may not increase CHD risk by decreasing HDL-C. A few comments cited an FDA statement from the November 1999 proposal that no dose-response relationship had been demonstrated between *trans* fat intake and CHD (64 FR 62746 at 62752). The comments argued that, therefore, it is not possible to project quantitative health benefits due to *trans* fat labeling. One comment also stated that the health benefits estimate was inaccurate because it did not account for either other CHD risk factors, such as obesity, or other CHD prevention efforts.

A few comments questioned whether health benefits could result from *trans* fat labeling because the in the intervention studies the intakes of *trans* fat were very high and not representative of U.S. intakes of about 5.3 g/d (3 percent of calories). Some comments stated that, even if *trans* fat has adverse health effects at higher levels of intake, there is no clinical evidence that lower levels of intake, such as 0.5 g *trans* fat in a serving of a food product, has any adverse effect. These comments therefore questioned whether health benefits could result

from labeling of *trans* fat present in relatively small amounts in individual foods. Other comments suggested that the emphasis on *trans* fat in the proposed labeling regulations was out of proportion to the emphasis on saturated fat, because the overall amount of saturated fat in the diet is approximately five times that of *trans* fat. The comments stated that, therefore, decreased *trans* fat intake has much less potential for lowering CHD risk than does decreased saturated fat intake, and this should be considered when estimating the health benefits of *trans* fat labeling.

Regarding the comments that questioned whether the increase in LDL-C and CHD risk due to *trans* fat intake could be quantified and whether the increase in LDL-C and CHD risk due to *trans* fat intake were as large as those due to saturated fat, FDA stated in the review of the science in the 1999 proposal (64 FR 62746 at 62753) that the available studies did not provide a definitive answer about whether *trans* fat has an effect on LDL-C and CHD risk equivalent to saturated fat on a gram-for-gram basis. FDA noted that interpretation of the intervention studies is complicated because, in the individual studies, *trans* fatty acids replace other dietary fatty acids that also affect serum cholesterol levels (64 FR 62746 at 62751). This evaluation was based on a review and analysis of the individual studies, it was not done for purposes of an economic analysis. To overcome the difficulties in interpreting individual intervention studies, in the November 1999 proposal FDA used regression equations based on a meta-analysis of intervention trials to quantitatively estimate the relationship between *trans* fat and LDL (Refs. 62, 65, and 69) in its calculation of the health benefits of *trans* fat labeling (64 FR 62746 at 62768–62770). As noted in section IV of this document, and in the November 1999 proposal, the regression equations do predict a very similar increase in LDL-C with each one percent of energy increase in either saturated fat or *trans* fat. Thus, table 9 in this document shows that the change in LDL-C is negligible when one percent of energy from *trans* fat is substituted for saturated fat. Therefore, FDA disagrees with the comments that stated that the increases in LDL-C and CHD risk due to *trans* fat intake could not be quantified and were not as large as those due to saturated fat and that FDA's estimate of these health benefits of *trans* fat labeling was too high.

Regarding the comment suggesting that it is premature to conclude that *trans* fat intake lowers HDL-C, section

IV of this document states that Federal Government advisory groups (Refs. 88 to 90, 140) and an advisory group of health professionals (Ref. 91) have stated that substitution of *trans* fat for saturated fat lowers HDL-C. Specifically, the Dietary Guidelines 2000 Advisory Report states that *trans* fatty acids tend to lower a protective form of serum cholesterol (HDL cholesterol) (Ref. 88). NCEP 2001 states that randomized clinical trials show that when *trans* fatty acids are substituted for saturated fatty acids, HDL cholesterol levels are lower, with a dose response effect observed (Ref. 89). The IOM/NAS states that the preponderance of the data suggest that hydrogenated fat/*trans* fatty acids, relative to saturated fatty acids, result in lower HDL cholesterol concentrations (Ref. 90). AHA 2000 states that it has been established that dietary *trans*-unsaturated fatty acids can increase LDL cholesterol and reduce HDL cholesterol (AHA 2000, p. 2300) (Ref. 91). Therefore, FDA disagrees with the comment that it is premature to conclude that *trans* fat intake may lower HDL-C. As described in Section IV of this document, although FDA did not place primary reliance upon the relationships among *trans* fat intakes and adverse effects on HDL-C and CHD risk in deciding that nutrition labeling was warranted, FDA also recognizes this possible relationship, so concerns about possible adverse effects cannot be ignored. Therefore, we used changes in both HDL-C and LDL-C as a second method to quantify the effects of *trans* fat intake on CHD risk, with the noted qualification that the primary basis for the rule was the effect of *trans* fat on LDL-C (64 FR 62746 at 62769).

Regarding the comments discussing FDA's statement in the November 1999 proposal (64 FR 62746 at 62752) that no dose response relationship had been demonstrated between *trans* fat intake and CHD, this statement referred to the effect of *trans* fat on CHD risk in the observational studies, not to the effect of *trans* fat on LDL-C which was used to estimate the health benefits in Method 1 (LDL-C) and Method 2 (LDL-C and HDL-C). FDA's statement was a generalization regarding the observational studies overall, including both case control studies and prospective observational studies. However, the four large prospective studies did all show dose-response relationships between *trans* fat intake and CHD risk, but in two of the studies the dose-response relationship was not statistically significant in all analyses. In the Nurses Health Study, the dose response relationship at both 8 years