

benefits for the implementation of the 1990 amendments (56 FR 60856 at 60869, November 27, 1991). Accordingly, FDA estimated: (1) The changes in *trans* fat intake that would result from labeling changes; (2) the changes in health states that would result from changes in *trans* fat intakes; and (3) the value of changes in health states in terms of life-years gained, number of cases or deaths avoided and dollar value of such benefits. The rule may generate other benefits, but we do not quantify them. For example, consumers who are aware of the risks associated with *trans* fat will more readily find information on the *trans* fat content of various foods. The value of the reduction in search time for those consumers is an additional benefit of this final rule.

1. Changes in *Trans* Fat Intake

FDA has estimated the current *trans* fat intake of the population and the estimated changes in *trans* fat intake. Based on comments received and on its own reevaluation, FDA revised its estimate of current *trans* fat intake, shown in table 1 (section IX.C) and its projected estimate for changes in *trans* fat intake due to labeling (table 2, section IX.C). The estimate projects quantitative decreases in *trans* fat intake with implementation of the final rule, and discusses the qualitative replacement of *trans* fat by other types of fat.

2. Changes in Health States

In the November 1999 proposal, FDA used two methods to estimate the potential decrease in CHD likely to result from decreased intake of *trans* fat in response to the labeling change.

a. *Method 1.* Decrease in CHD risk due to decreased serum concentrations of LDL-C.

b. *Method 2.* Decrease in CHD risk due to decreased serum concentrations of LDL-C and increased serum concentrations of HDL-C. FDA also reviewed the association of CHD risk with *trans* fat intake found in large prospective observational cohort studies.

As described in section IV of this document, in the November 1999 proposal FDA concluded that the effects of *trans* fatty acids on serum LDL-C should be the primary criterion for whether *trans* fatty acids influence CHD risk. In Method 1, FDA used changes in the primary criterion, serum LDL-C, to evaluate the effects of *trans* fat intake on CHD risk (64 FR 62746 at 62768). Additionally, 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, the economic analysis 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).

Section IV of this document notes that observational epidemiological studies can provide evidence of an association between a risk factor and a disease, but cannot establish direct cause and effect. Therefore, FDA considered the evidence from observational epidemiological studies, including large prospective (cohort) studies, as indirect evidence for a relationship between *trans* fat intake and CHD risk. In the November 1999 proposal, FDA found that the prospective studies of *trans* fat intake and CHD risk consistently reported a greater risk of CHD attributable to *trans* fat intake than would be accounted for by either Method 1 (changes in LDL-C) or by Method 2 (changes in both LDL-C and HDL-C) (64 FR 62746 at 62770 to 62771). The estimates in Method 1 and Method 2 are calculated using factors from regression equations summarizing the results of short-term feeding trials (intervention studies). In the intervention studies, *trans* fat is fed to people for a few weeks, changes in serum lipids are measured, and it is assumed that the CHD risk associated with *trans* fat intake occurs through the mechanism of changes in LDL-C and possibly HDL-C. In contrast, the prospective studies measure actual CHD occurrence in a large group of people over a period of years, and describe all CHD risk associated with *trans* fat intake, regardless of the mechanism of action by which *trans* fat intake may be associated with CHD. Thus, the results of the prospective studies suggest that there may be additional mechanisms by which *trans* fat contributes to CHD risk. Because prospective studies do not show direct cause and effect, and because the relative risks determined in observational studies are imprecise, FDA did not use the results of the prospective studies in quantitative estimates of changes in *trans* fat intake and CHD risk. However, FDA noted that, if there are additional mechanisms by which *trans* fat contributes to CHD risk, as suggested by the prospective studies, then the actual benefits may be greater than estimated using either

Method 1 (changes in LDL-C) or Method 2 (changes in LDL-C and HDL-C) (64 FR 62746 at 62771).

As described in the November 1999 proposal (64 FR 62746 at 62768 and 62769), the regression equations of Katan et al. (Ref. 62) and Zock et al. (Ref. 69) were based on five intervention studies that made, in total, six dietary comparisons between consumption of *trans* fat and cis-unsaturated fat (Refs. 7, 8, and 11 through 13). The regression equation for LDL-C showed that each additional percent of energy from *trans* fat was predicted to increase LDL-C by 1.5 mg/deciliter (dL) (0.040 millimol/liter) ($R^2 = 0.86$, $p = 0.0028$) when substituted for the same percent of energy from cis-monounsaturated fat, holding total energy intake constant. The regression equation for HDL-C showed that each additional percent of energy from *trans* fat was predicted to decrease HDL-C by 0.4 mg/dL (0.013 millimol/liter) ($R^2 = 0.88$, $p = 0.0019$), when substituted for the same percent of energy from cis-monounsaturated fat. The regression lines were forced through the origin because a zero change in intake will produce a zero change in lipoprotein concentrations (Refs. 62, 69, and 154). In carrying out the regression, differences between diets in fatty acids other than *trans* fat and cis-monounsaturated fat were adjusted for by using regression coefficients from a previous meta-analysis of 27 intervention studies (Ref. 65).

Sample calculations using Method 1 and Method 2 are summarized in table 8 in this document. The table illustrates a decrease in *trans* fat intake of 0.1 percent of energy (calories) and shows the factors FDA used to relate a given decrease in *trans* fat intake to a corresponding change in CHD risk. To estimate the change in CHD risk with change in *trans* fat intake, for each type of serum lipid, LDL-C and HDL-C, we multiplied the change in *trans* fat intake by three factors, representing: (1) the change in serum lipid with change in *trans* fat intake, (2) the change in CHD risk with change in serum lipid, and (3) an adjustment for regression dilution. Table 8 shows that, for Method 1, based on changes in LDL-C, replacement of 0.1 percent of energy from *trans* fat with the same percent of energy from cis-monounsaturated fat would decrease CHD risk by 0.147 percent (-0.1 percent of energy from *trans* fat \times 1.5 mg LDL-C/dL per percent of energy from *trans* fat \times 0.7 percent change in CHD risk per mg LDL-C/dL \times 1.4 adjustment factor for regression dilution = -0.147 percent change in CHD risk). Based on changes in HDL-C, replacement of 0.1 percent of energy from *trans* fat would decrease