

CHD risk by 0.140 percent (-0.1 percent of energy from *trans* fat x -0.4 mg HDL-C/dL per percent of energy from *trans* fat x -2.5 percent change in CHD risk per mg HDL-C/dL x 1.4 adjustment factor for regression dilution = -0.140 change

in CHD risk based on changes in HDL-C). For Method 2, based on changes in both LDL-C and HDL-C, the decrease in CHD risk would be 0.287 percent (-0.147 percent based on LDL-C plus -0.140 percent based on HDL-C = -0.287

percent based on LDL-C + HDL-C). FDA used these estimation methods to project the decrease in CHD risk in the November 1999 proposal (64 FR 62746 at 62767).

TABLE 8.—SAMPLE CALCULATION FOR CHANGE IN CHD RISK WITH SUBSTITUTION OF *Cis*-MONOUNSATURATED FAT FOR *Trans* FAT

Estimation Method	Change in <i>Trans</i> Intake (% of Energy)	Type of Serum Lipid	Factor for Change in Serum Lipids (mg/dL per 1% of Energy)	Factor for Change in CHD Risk (% per mg/dL)	Factor for Adjustment of Regression Dilution	Change in CHD Risk (%)
Method 1 LDL	-0.1	LDL	1.5	0.7	1.4	-0.147
Method 2 LDL + HDL	-0.1	LDL	1.5	0.7	1.4	-0.147
		HDL	-0.4	-2.5	1.4	-0.14
		LDL+HDL				-0.287

In the scientific literature, *cis*-monounsaturated fat is commonly used as a reference point in describing effects of *trans* fat intake. Therefore, FDA first estimated the effect on CHD risk by assuming that a given amount of *trans* fat would be replaced by the same amount of *cis*-monounsaturated fat in the diet (table 8 in this document and 64 FR 62746 at 62767). However, it is likely that *trans* fat in the diet would actually be replaced by a combination of *cis*-monounsaturated fat, *cis*-polyunsaturated fat, and saturated fat. Therefore, FDA also considered the changes in LDL-C and HDL-C associated with replacement of *trans* fat by different types of fatty acids or carbohydrate (64 FR 62746 at 62767 to 62770). Table 9 in this document summarizes the factors for changes in LDL-C and HDL-C with different macronutrients and combinations of macronutrients replaced by *trans* fat. The first four columns of data show the factors for substitution of *trans* fat for 100 percent of individual types of fatty acids or carbohydrate. We project that, due to *trans* fat labeling, *trans* fat will be replaced by combinations of different types of fatty acids or carbohydrate. By combining the factors in the first four data columns, we obtained the factors for substitution of *trans* fat for combinations of different fatty acids and carbohydrate, shown in the last three data columns.

We generated the factors in table 9 by combining the results of two sets of metaanalyses. Table 9 shows the result of linking: (1) The regression equation coefficients of Katan et al. (Ref. 62) and Zock et al. (Ref. 69), for substitution of *trans* fat for *cis*-monounsaturated fat and (2) the regression equation

coefficients of Mensink and Katan (Ref. 65), for substitution of saturated and *cis*-unsaturated fat for carbohydrate. The regression equations of Mensink and Katan (Ref. 65) were based on 27 intervention studies that made dietary comparisons for consumption of carbohydrate, saturated fat, *cis*-polyunsaturated fat and *cis*-monounsaturated fat. The regression equation for LDL-C included 57 dietary comparison data points from 24 studies, and showed that, holding total energy intake constant, when substituted for one percent of energy from carbohydrate, each additional percent of energy from saturated fat was predicted to increase LDL-C by 1.28 mg/dL (0.033 millimol/liter) ( $p < 0.001$ ), each additional percent of energy from *cis*-monounsaturated fat was predicted to lower LDL-C by 0.24 mg/dL (0.006 millimol/liter) ( $p = 0.114$ ) and each additional percent of energy from *cis*-polyunsaturated fat was predicted to lower LDL-C by 0.55 mg/dL (0.014 millimol/liter) ( $p = 0.002$ ). The regression equation for HDL-C included 59 dietary comparison data points from 25 studies, and showed that holding total energy intake constant, when substituted for one percent of energy from carbohydrate, each additional percent of energy from saturated fat was predicted to increase HDL-C by 0.47 mg/dL (0.012 millimol/liter) ( $p < 0.001$ ), each additional percent of energy from *cis*-monounsaturated fat was predicted to increase HDL-C by 0.34 mg/dL (0.009 millimol/liter) ( $p < 0.001$ ) and each additional percent of energy from *cis*-polyunsaturated fat was predicted to increase HDL-C by 0.28 mg/dL (0.007 millimol/liter) ( $p = 0.002$ ).

Comparison with the observed data showed that the predicted regression lines explained 64 percent of the variation in changes in LDL-C and 88 percent of the variation in changes in HDL-C. The coefficients of Mensink and Katan (Ref. 65) are expressed as substitution of each type of macronutrient for carbohydrate, but the coefficients of Katan et al. (Ref. 62) and Zock et al. (Ref. 69) are expressed as substitution of *trans* fat for *cis*-monounsaturated fat. For comparability with the coefficients for *trans* fat, we expressed the coefficients of Mensink and Katan in terms of substitution of each type of macronutrient for *cis*-monounsaturated fat. As stated in the November 1999 proposal (64 FR 62746 at 62769), when substituted for one percent of energy from *cis*-monounsaturated fat, saturated fat raised LDL-C by 1.52 mg/dL, *cis*-polyunsaturated fat lowered LDL-C by 0.31 mg/dL, and carbohydrate raised LDL-C by 0.24 mg/dL. When substituted for one percent of energy from *cis*-monounsaturated fat, saturated fat raised HDL-C by 0.13 mg/dL, *cis*-polyunsaturated fat lowered HDL-C by 0.06 mg/dL, and carbohydrate lowered HDL-C by 0.34 mg/dL. We then combined these coefficients with the coefficients for *trans* fat, to obtain the changes in lipoprotein levels with *trans* fat substituted for different macronutrients, as shown in table 9.

Table 9 also gives examples of changes in CHD risk with replacement of 0.1 percent of energy from *trans* fat by different macronutrients and combinations of macronutrients. Table 8 shows the general method and illustrates the calculation of estimated changes in CHD risk with replacement