

not submit data from the unpublished work that the comments asserted could provide an alternate explanation for the Ascherio et al. results. As noted in section IV of this document, the paper by Ascherio et al. is not the only information that the IOM/NAS used in concluding that *trans* fatty acid consumption should be as low as possible while consuming a nutritionally adequate diet (see comment 3). Additionally, the Ascherio paper is not the only information in the IOM/NAS report that supports a positive linear trend for *trans* fat intake and LDL-C and risk of CHD. For example, as mentioned previously in this section (see comment 39), the study of Lichtenstein et al. (Ref. 82), using six test diets at different levels of *trans* fat intake, found a positive linear trend for *trans* fat intake and LDL-C level. In discussing *trans* fat intake and HDL-C, the IOM/NAS report references work by Zock, Mensink, and Katan (Refs. 69 and 154). These papers pertain not only to HDL-C but also to LDL-C. The work of Zock and colleagues (Refs. 62, 69, and 154) gives one regression equation showing a positive linear trend between *trans* fat intake and LDL-C and another regression equation showing a negative linear trend between *trans* fat intake and HDL-C.

As noted in section IV and in this section of this document, FDA's primary rationale for *trans* fat labeling is the effect of *trans* fat intake on LDL-C. Additionally, the economic analysis uses 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 is the effect of *trans* fat on LDL-C. Therefore, as stated in the November 1999 proposal (64 FR 62746 at 62770), for purposes of economic analysis we used the equations of Zock et al. (Refs. 62 and 69) to estimate the effects of *trans* fat on LDL-C and HDL-C separately and did not use the equation of Ascherio et al. (Ref. 83), which estimates the positive linear trend between *trans* fat intake and the lipid ratio, LDL/HDL. FDA's Method 2, using the equations of Zock et al. (Refs. 62 and 69) for changes in both LDL-C and HDL-C, is different than the method of Ascherio et al. (Ref. 83), which uses changes in the lipid ratio, LDL/HDL. However, what FDA's Method 2 and Ascherio's method have in common is that they each provide a quantitative estimate of the adverse effects of *trans* fat on CHD risk using changes in both LDL-C and HDL-C.

As stated previously in this section (see comment 39), the regression equations of Zock et al. (Ref. 69),

showing a positive linear trend between *trans* fat intake and LDL-C, are consistent with newer regression equations in a study published in 2001 by Muller et al. (Ref. 130). Thus, there is a body of research, including the work of Ascherio et al. (Ref. 83), Zock et al. (Refs. 62, 69 and 154), Lichtenstein et al. (Ref. 82) and Muller et al. (Ref. 130), that supports the existence of a linear trend for *trans* fat intake and LDL-C levels, consistent with the conclusions of the IOM/NAS (Ref. 140). As discussed in the IOM/NAS report, the existence of a linear trend of saturated fat and LDL-C is very well-established, as shown by three sets of regression equations described in the IOM/NAS report (Ref. 140, Figure 8-3, pp. 8-47 to 8-48). Thus, the existence of a positive linear trend for *trans* fat intake and LDL-C, as shown by a body of research (Refs. 62, 69, 82, 83, 130, and 154) and recognized by the IOM/NAS (Ref. 140) is not unusual, considering that there is also a positive linear trend between saturated fat intake and LDL-C. Therefore, FDA is not convinced by the comments questioning the existence of linear trends between *trans* fat and lipid levels. FDA finds that, for the purposes of economic analysis, it is appropriate to quantify the health benefits of *trans* fat labeling using regression equations (Refs. 62 and 69) describing a positive linear trend between *trans* fat intake and LDL-C and a negative linear trend between *trans* fat intake and HDL-C.

(Comment 42) One comment stated that FDA's estimate of benefits of the November 1999 proposal neglected to account for the overall reductions of mortality and morbidity from heart disease that have been occurring in the United States for the past few decades. According to the comment, FDA should have projected the future reduction in heart disease that would be expected in the absence of labeling. With such a projection, the baseline for heart disease morbidity and mortality would be progressively lower over time, and the numbers of heart attacks and deaths avoided due to *trans* fat labeling would be commensurately reduced compared with FDA's estimate. One comment stated that an overall decline in CHD from 1970 to 1990 coincided with a decline in intake of fat and saturated fat. The comment stated that margarine intake (per person) was constant during this period. Therefore, the comment concluded that substituting margarine for high saturated fat and cholesterol products had proved beneficial in decreasing CHD.

FDA agrees that the rate of heart disease mortality and morbidity in the

United States has been decreasing for several decades (Refs. 132 and 133). For example, the age-adjusted death rate from CHD declined from approximately 290 per 100,000 in 1979 to 190 per 100,000 in 1996 (Ref. 133). However, because the risk of CHD is greater at older ages and the U.S. population is aging, the decline in the overall (crude) CHD death rate in this period was more modest, from approximately 225 per 100,000 to 180 per 100,000. Moreover, because of the increase in the total population, the decline in annual CHD deaths in this period was even more modest, from approximately 550,000 to 500,000, about a 10 percent decrease over 17 years. The number of deaths was fairly level during the period, 1992 through 1996. Thus, the baseline number of CHD deaths, as opposed to age-specific rates, has historically declined at a modest rate, and has been fairly level in recent years. Therefore, FDA did not correct for this in its projection of heart attacks and deaths avoided due to *trans* fat labeling. In response to the comment about correcting its estimate for overall reductions in heart disease over time, FDA acknowledges that, if the actual number of CHD deaths declines in the future, omitting this correction would result in a modest overestimate of the health benefits of *trans* fat labeling.

Regarding the comment about correlations of changes in dietary intake with declines in CHD from 1970 to 1992, information on *trans* fat intake is limited, as noted in section IV of this document. Therefore, although margarine intake was approximately constant, it is not known whether overall *trans* fat intake increased, decreased or remained the same during this period. Furthermore, the causes of the decrease in CHD over this time period have not been identified. Decreases in CHD risk factors, such as serum lipids, and decreases in saturated fat intake probably played a role, but the relative contributions of decreases in various risk factors and changes in medical care for heart attack patients are not adequately explained (Ref. 132). Therefore, FDA disagrees with the comment's conclusion that time trends in CHD incidence demonstrate a beneficial effect of margarine intake on incidence of CHD.

Based on the comments received and its own re-evaluation, FDA is not making any changes in the sample calculations for changes in CHD risk (table 8) or in the factors for changes in serum lipids and the examples of changes in CHD risk and the factors for changes in serum lipids with substitution of different macronutrients