

fruit and vegetable consumption, and triglyceride savory snack food consumption by consumers. Demographic information was collected as well. A telephone survey was conducted in each of the study sites before olestra-containing snacks were marketed. Subsequent yearly surveys were completed after olestra-containing snacks were introduced to the market.

A random sample of participants in each telephone cross-section sample was recruited into the second component, a clinical cross-section. The clinical cross-section was an investigation of the relationships among nutrient intake, olestra consumption, and serum nutrients. Study participants visited a clinic to provide further information, including dietary information, medical histories, and blood samples. Followup telephone interviews included questions about usual fruit, vegetable, and snack food use during the previous month, a 24-hour dietary recall to measure co-consumption of fruits and vegetables with savory snacks, health symptoms and status, and a short household food inventory.

Within the clinical cross-section, information on olestra intake was used to select olestra users from non-users to be recruited into the third component of the Active Surveillance Study, *i.e.*, the clinical cohort study. The clinical cohort study was an investigation of the relationships among nutrient intake, olestra consumption, and changes in serum nutrients over time. Participants in the clinical cohort are a subset of those people who participated in the Year 0 clinical cross-section and were monitored annually over the course of the Active Surveillance Study. The clinical cohort was designed to have an over-representation of consumers of olestra-containing snack food. The design for the clinic visit and the information gathered is the same as for the clinical cross-section.

The study was conducted in four U.S. cities. As of the publication of this document, data are available only from the sentinel site, Marion County, IN, where test marketing began in 1997.³² The study began one year later in the other cities, because national marketing of olestra-containing foods in those areas began later.

The first component of the active surveillance is the population cross-section. A random-digit-dial telephone survey of Marion County, IN, residents was completed before olestra-containing

foods were marketed in that area (February 1997). This survey (Year 0) included 1,962 adults, aged 18 years and over. The second telephone survey was completed after olestra-containing foods were introduced to the local market (between August 1997 and January 1998). This survey (Year 1) included 1,525 adults, aged 18 years and over. Based on the Year 1 data, which are weighted to be representative of the Marion County population, 15.5 percent of adults reported eating olestra-containing snacks one or more times per month with the median frequency being three times per month. Ninety percent of adults reported eating one or more servings of fruits and vegetables per day, thus providing a basis for assessment of any effects on dietary carotenoid absorption. Intake of fruits and vegetables and intake of total snacks did not change in the population cross-section between Year 0 and Year 1. Olestra-containing snack food introduction was not associated with an overall increase in savory snack consumption or with a decrease in fruit and vegetable intakes. There was a modest decrease in consumption of reduced- and non-fat savory snacks at Year 1 compared to Year 0.

Blood sera from study subjects, in both the cross-sectional and clinical cohorts, were analyzed for vitamins A, D, E, and K, total cholesterol, high density lipoprotein (HDL) and triglycerides, and the six major carotenoids that represent more than 90 percent of the circulating carotenoids (alpha and beta carotene, lycopene, lutein, zeaxanthin, and beta-cryptoxanthin). The study investigators then compared these serum measures based on olestra intake. Four olestra consumption groups were defined: (1) None; (2) low (less than 0.4 g/d of olestra, which is less than the 60th percentile of consumption); (3) medium (between 0.4 and 2.0 g/d of olestra, which is between the 60th and 90th percentiles of consumption); and (4) high (greater than 2 g/d, which is greater than the 90th percentile of consumption).

Results from the cross-sectional study comparing 1,252 subjects in year 0, and 1,164 subjects in year 1, show that with increasing olestra intake, there were significant trends for an increase in vitamin K levels ($p = 0.013$) and a decrease in serum cholesterol ($p < 0.05$). There were no significant differences or trends found for other vitamins or for total carotenoid or individual carotenoids that could be associated with olestra consumption.

For the clinical cohort (477 study participants), the sponsor reported that

for the entire cohort from year 0 to year 1, there was a decrease in mean serum concentrations of total carotenoids, as well as in concentrations of retinol, 25-OH vitamin D, lycopene, lutein, and zeaxanthin, and an increase in beta-cryptoxanthin. Tests of association between olestra consumption and changes in serum concentrations of fat-soluble vitamins and carotenoids were based on regression models that included variables to characterize the four levels of olestra consumption. However, these changes were not related to the amount of olestra consumed. A trend was observed for increased vitamin K, but the change did not reach statistical significance ($p = 0.087$). There were no changes observed for the other vitamins.

The petitioner cautioned that the results discussed previously reflect data from only the first year that olestra products were marketed, and that data were available from only a single site. With these caveats, the petitioner reached the tentative conclusion that it appeared that the consumption of olestra-containing foods in the marketplace had little, if any, effect on the status of fat-soluble vitamins and nutrients as measured by serum concentration.

FDA notes that survey results show that the co-consumption of savory snacks (made with or without olestra) with a fruit or vegetable was relatively rare. Overall, less than 15 percent of total carotenoids were consumed with any savory snack. Olestra's effect on the absorption of fat-soluble carotenoids is greatest when co-consumed with the source of the carotenoid. Interference with absorption of carotenoids diminishes and then disappears as the time between eating an olestra-containing food and a carotenoid-containing product increases.³³

In the clinical cross-sectional sample, 217 of 947 individuals reported eating at least one olestra-containing food in the previous month with a median intake of 8.1 g of olestra per month. The 90th percentile consumption level was 64 g of olestra per month. Of the 402 clinical cohort participants who were considered consumers of olestra, only 139 reported eating any olestra-containing foods in the previous month. The median frequency of eating olestra-containing foods for this group of consumers was 1.01 times per month with a median intake of 11.9 g of olestra per month. The 90th percentile

³³ The precise length of time olestra interferes with absorption varies with the dose of olestra, and also varies somewhat from individual to individual, as GI transit time is variable among individuals (61 FR 3118 at 3144).

³² The other three cities in the Active Surveillance Study were Baltimore, MD, San Diego, CA, and Minneapolis, MN.