

conclusion that FDA reached in its analysis of the study. The Acute Consumption Study was conducted to provide information relevant to whether olestra-containing foods should bear a label statement that informs consumers about the potential GI effects associated with olestra. FDA points out that the Acute Consumption Study was only one of several studies under consideration in this petition, and that the agency's decision on the petition is based on the totality of evidence in the record.

While the petitioner's Acute Consumption Study did not achieve the statistical power that P&G originally desired (80 percent power to detect a 5 percent difference between treatment groups), the study still provides meaningful information concerning the effect of olestra-containing foods on the GI system. FDA's scientific review determined that the study does have 80 percent power to detect a 7 percent difference between treatment groups (Ref. 13). The study showed that there was no difference in the rate or severity of loose stools or abdominal cramps between subjects who ate olestra-containing chips compared to those who ate triglyceride-containing chips.

The comment provides no evidence that the darkened theater or the method used to collect symptom data affected the outcome of the study. As discussed previously, the study protocol was designed to minimize the possibility of inaccurate measurements or subjects' sharing of chips. For example, study participants were instructed to be seated in the theater at least one seat away from other participants and not to share their chips or beverage with anyone else. The theaters were also monitored by several staff during the movie.

Similarly, the comment did not explain the effect on the study results, if any, from the 10-day period used to assess symptoms. After the movie, trained telephone interviewers contacted study participants and administered a recall questionnaire to collect information on any effects experienced since the movie. The study protocol specified that participants be contacted within 2 to 4 days of viewing the movie. The petitioner reported that 85 percent of study subjects (962 of the 1,092) were contacted within 2 to 4 days of viewing the movie, an additional 124 subjects were contacted in 5 to 10 days.²⁸

FDA agrees that the median chip consumption for the control group was greater than that for the olestra group.

As discussed previously, the Acute Consumption Study was designed to be an ad libitum study, allowing the investigators to examine the effects of customary or usual consumption. As an ad libitum study, it is possible that one group of subjects may consume more chips than the other. For example, the median consumption of chips made with olestra was 2.1 oz compared to 2.7 oz for chips made with conventional triglycerides. CSPI did not explain how the fact that one group of subjects ate more chips than the other affects the conclusions drawn from this study regarding the need for special labeling.

(Comment 7) A comment from CSPI to the current petition criticized the Home Consumption Study. CSPI's comment relies on its published letter²⁹ commenting on a published study that reports data from the Home Consumption Study (Ref. 14). The comment raises five issues: (1) The comment stated that some of the data relating to the highest decile of olestra consumers were overlooked; (2) the comment argued that it is important to focus on the small number of heavier consumers because most subjects ate relatively few olestra-containing chips; (3) the comment stated that in the highest decile of olestra consumers the incidence of more frequent bowel movements and loose stools was twice that of controls; (4) the comment stated that olestra consumers in the highest decile had symptoms on 18 percent of person-days, compared to 12 percent of person-days in the control group (table 4 in Ref. 14); and (5) the comment pointed out that olestra consumers missed some or all of their activities on 0.4 percent of days, compared to 0.2 percent in the control group.

Prior to publication of the article concerning the Home Consumption Study (Ref. 14), FDA conducted its own indepth analysis of the raw data from the Home Consumption Study (Refs. 15 and 16) and described this analysis at the 1998 FAC meeting in which CSPI participated. FDA's analysis included an estimate of the extra symptom-days experienced by subjects in both the 90th and 95th percentile of olestra-containing chip consumption (Ref. 15). Subjects at the 90th percentile ate 64 oz of olestra-containing chips over the course of the study while those at the 95th percentile ate 83 oz of olestra-containing chips over the course of the study. Although CSPI alleges that the subjects in the study ate relatively few olestra-containing foods, the petitioner presented data to show that, in fact, the

rates of olestra consumption achieved in the study were beyond usual snack consumption.

As part of the Home Consumption Study, the investigators considered the effect of GI symptoms on subjects' daily activities. In its comment, CSPI points out that olestra consumers missed some or all of their activities on 0.4 percent of days, compared to 0.2 percent in the control group, implying that this is significant. FDA disagrees.

CSPI does not explain how it calculated the percentage of days on which subjects missed some or all of their activities, nor does CSPI provide statistical analyses to assess whether these differences occurred by random chance (e.g., illness unrelated to olestra). FDA was able to replicate the numbers that CSPI presented and performed tests of statistical significance on the data. The actual number of days on which subjects in the highest decile missed some or all of their activities is very small (9 of 2,226 days in the olestra group versus 5 of 2,646 days in the control group). Five subjects in the olestra group and four subjects in the control group missed some or all activities at least 1 day. The number of subjects missing activities and the number of days missed by these subjects are comparable for the olestra and control groups, except for one subject in the olestra group who missed some or all activities on 4 days (Ref. 21).³⁰ From these data, it cannot be concluded that for the highest decile of consumers olestra consumption resulted in an increase in days in which consumers missed some or all activities. FDA believes that the Home Consumption Study, designed to examine the effects of "real life" olestra consumption, provides useful information relevant to the labeling of olestra-containing foods. CSPI does not show how their analysis would change FDA's conclusions.

(Comment 8) A comment from CSPI to the current petition criticized the petitioner's Stool Composition Study. The comment stated that this study does not negate and should not supersede the two preapproval 8-week studies or the preapproval Fecal Parameters Study. In its comment, CSPI cites a 1995 FDA memorandum discussing the Fecal Parameters Study (Ref. 22) and asserts that the memorandum says that several

³⁰ Sophisticated statistical models are impractical for such a small number of cases. However, a Fisher's Exact test showed that the proportion of subjects in the olestra group who missed some or all activity at least 1 day was not significantly different (p-value of 0.73) from the proportion of subjects in the control group who missed some or all activity at least 1 day.

²⁸ Of the remaining subjects, three were contacted on the day of the movie, one within a day, and two within 23 days (Ref. 13).

²⁹ CSPI's published letter was included in its comment as an attachment (Ref. 20).