

a 5 percent difference in the proportions of symptoms between the olestra and triglyceride groups. The final number of participants to complete the study was 1,092,<sup>22</sup> which was fewer than planned. The rate of symptom reporting in the triglyceride group was 17.6 percent, which was higher than planned. Given the actual number of participants, and the actual rate of reports of symptoms in the triglyceride control group, FDA found that the study had an 80 percent chance of detecting a 7 percent difference between the test groups ( $p=0.05$ ) (Ref. 13).

FDA observed that 962 participants completed a post-movie interview within the 2 to 4 days goal of the study. Of the remaining 130 participants who were contacted, 124 participants were contacted in 5 to 10 days, 3 on the day of the movie, 1 within a day, and 2 within 23 days. FDA noted that P&G included data from these 130 participants in its analysis to enhance the sensitivity of its analysis.

FDA noted that in both the olestra and triglyceride groups, the most frequently reported GI symptoms were abdominal pain, diarrhea, and flatulence. These symptoms are also the symptoms most commonly reported to P&G's passive surveillance program. FDA agrees with the petitioner that in this study, there was no difference in the rate or severity reported for loose stools or abdominal cramps between subjects who ate olestra-containing chips and subjects eating triglyceride chips. FDA examined the percent of subjects reporting at different levels of chip consumption and found that reports of diarrhea increased for both the olestra and triglyceride groups with increasing consumption of chips, but there was no difference in the rate of reporting between the groups (Refs. 10 and 13).

### 3. Home Consumption Study

The Home Consumption Study<sup>23</sup> was designed to measure, under market use conditions, the effect of eating chips made with olestra on GI symptoms in adults and children over an extended period of time (Ref. 14). This double-blind placebo-controlled trial represented 1,138 households (3,181 individuals, ages 2 to 89) randomly assigned to either the olestra group or the control group. To be enrolled, at least half the members of the household had to have eaten corn or potato chips

at least four times in the previous month and all members of the household had to be willing to participate in the 6-week long study. A contact for each household was identified and was required to return to the study site once a week for 6 consecutive weeks. During each visit, the contact could choose from a selection of potato chips and tortilla chip products labeled as containing either olestra or triglyceride. The selection of snacks used in the study were products available in the marketplace presented in typical packaging. To encourage snack consumption, up to eight bags of chips (varying in weight from 5.5 to 9 oz) could be selected each week. For the households in the olestra group, the olestra-labeled packages contained olestra chips, but for the control group, the olestra-labeled packages contained triglyceride chips. For both groups, the triglyceride-labeled packages contained triglyceride chips. All olestra-labeled products displayed the olestra label statement.

At each weekly visit, the contact would also provide daily records kept by each member of the household regarding GI symptoms. The household contact assisted and/or completed the form for children. The record consisted of a check list of eight specific GI symptoms<sup>24</sup> as well as a field to write in any other symptoms. On each day a GI symptom was recorded, the subject was to rate the effect of those symptoms on daily activity using a scale ranging from "noticed but did not affect" to "missed all day at work/school." Medication use and physician visits were also to be recorded.

There were 1,620 subjects from 568 households in the olestra group and 1,561 subjects from 570 households in the control group. The groups were similar with respect to age, sex, and race. Subjects ate chips frequently throughout the study. The median number of days on which a subject consumed an olestra-labeled chip was 20 days of a possible 42 days for the olestra group and 21 of a possible 42 days for the control group. The length of the study and the large number of individuals per group resulted in a collective period of more than 30,000 "eating" days, making it possible to detect small differences in the reporting of GI symptoms. The median total amount of olestra-labeled chips eaten over the course of the study by the olestra group (25.2 oz) was slightly less

than that eaten in the control group (27.6 oz). During the 42-day study, subjects whose consumption was in the top 10 percent of the olestra group ate more than 59 oz of chips, while in the control group, the top 10 percent of the group ate more than 70 oz of chips. The petitioner presented data to show that the rates of olestra consumption achieved were beyond customary snacking by comparing the intake of olestra at the 90th percentile of consumption in this study (13.3 g/d) to Market Research Corp. of America (MRCA) preapproval estimates (6.4 g/d), and to data collected regarding "real-world" olestra consumption in the Active Surveillance Study (2.1 g/d). The petitioner concluded that the rates of consumption achieved in this study for both the olestra and triglyceride groups were higher than usual snack consumption.

The petitioner reported that for its original planned analysis for the study, which examined the percentage of eating days where GI symptoms were reported within 2 days, olestra-containing chips resulted in an increase ( $p<0.05$ ) in the GI symptoms of more frequent bowel movements, loose stools, and gas. There was no increase in reports of abdominal cramping or any of the other individual or total GI symptoms. The petitioner decided that this analysis could not be clearly interpreted because olestra labeled chips were eaten on numerous days of the study and therefore a particular GI event would be associated with 2 or 3 eating days.

The petitioner presented data from an analysis that compared the occurrence and frequency of GI symptoms between the olestra and control groups. The primary response variable was the percentage of individuals reporting a GI event. For all subjects who consumed olestra-labeled products, the petitioner found that there was no difference in the total percentage of subjects reporting a GI symptom between the olestra and control groups. Of the eight GI symptoms evaluated, the only difference was an increased number of reports of nausea for the control group. For those subjects who reported a GI event, the number of symptom days was also compared. When the petitioner examined the data by days on which subjects reported symptoms, there was a small increase in the olestra group in the number of days when more frequent bowel movements were reported (3.7 days for olestra compared to 2.8 days for controls;  $p=0.04$ ). The petitioner calculated that this increase was about one symptom day out of the 42 days of the study. The petitioner reported that

<sup>22</sup> Of the 1,742 individuals originally enrolled for the study, 1,123 kept their appointments. Thirty-one individuals could not be contacted for followup, leaving a total of 1,092 evaluable subjects.

<sup>23</sup> Dr. R. Sandler, Professor of Medicine, University of North Carolina, Chapel Hill, was the principal investigator for this study.

<sup>24</sup> The list of GI symptoms include the following descriptions: (1) Heartburn or indigestion, (2) nausea or queasiness, (3) vomiting, (4) gas, (5) bloating, (6) abdominal cramping or pains, (7) more frequent bowel movements, and (8) looser stool.