DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 172

[Docket No. 2000F–0792]

Food Additives Permitted for Direct Addition to Food for Human Consumption; Olestra

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to remove the requirement for the label statement prescribed specifically for savory snack products that contain olestra. This action is in response to a petition filed by the Procter and Gamble Co.

DATES: The regulation is effective August 5, 2003. Submit written objections and requests for a hearing by September 4, 2003.

ADDRESSES: Submit written objections to the Division of Dockets Management (HFA–305), Food and Drug Administration, rm. 1061, 5630 Fishers Lane, Rockville, MD 20852. Submit electronic objections to *http://www.fda.gov/dockets/ecomments.*

FOR FURTHER INFORMATION CONTACT: Mary D. Ditto, Center for Food Safety and Applied Nutrition (HFS–255), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740–3835, 202–418–3102.

SUPPLEMENTARY INFORMATION:

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I. Subject of Petition

In a notice in the **Federal Register** of March 3, 2000 (65 FR 11585–11586), FDA announced that a food additive petition had been filed by the Procter & Gamble Co., 6071 Center Hill Ave., Cincinnati, OH 45224 (P&G, the petitioner) proposing that the food additive regulations be amended in § 172.867 *Olestra* (21 CFR 172.867) to remove the requirement for the label statement prescribed in § 172.867(e).

II. Background

In the **Federal Register** of January 30, 1996 (61 FR 3118, ''the 1996 final rule'') FDA announced the approval of olestra for use as a fat substitute in prepackaged ready-to-eat savory snacks. Olestra is the common name for a mixture of substances formed by chemical combination of sucrose with six, seven, or eight fatty acids. The fatty acids, bound to sucrose by ester bonds, are derived from edible fats and oils.

Olestra is essentially not absorbed or metabolized and passes unchanged through the gastrointestinal (GI) system (61 FR 3118 at 3125–3127). Therefore, olestra has the potential to affect GI physiology and function. Additionally, because of olestra's physical properties, fat-soluble nutrients present in olestra-containing foods [1] or other foods in the GI tract at the same time as olestra can partition into olestra and pass through the GI tract without being absorbed by the body. Therefore, FDA required the addition of fat-soluble vitamins A, D, E, and K, to savory snacks containing olestra to compensate for any inhibition of absorption by olestra (§ 172.867(d)).

At the time of the 1996 final rule, FDA concluded that, to avoid being misbranded within the meaning of sections 201(n) and 403(a)(1) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(n) and 343(a)(1)), olestra-containing foods would need to bear a label statement to inform consumers about possible effects of olestra on the GI system. The label statement also would clarify that the added vitamins were present to compensate for any nutritional effects of olestra, rather than to provide enhanced nutritional value. Therefore, the 1996 final rule required that foods containing olestra be labeled with the following statement in a boxed format: ''THIS PRODUCT CONTAINS OLESTRA. Olestra may cause abdominal cramping and loose stools. Olestra inhibits the absorption of some vitamins and other nutrients. Vitamins A, D, E, and K have been added.'' (§ 172.867(e)(1)). FDA included the term ''other nutrients'' because any nutrient that is as lipophilic as these vitamins would also be affected, although there was no known basis for adding such nutrients back. The agency also required that the statement be made in a standardized format that specifies, among other things, type style and type size, and that

[1] Olestra has only been approved for use as a fat substitute in savory snacks. Throughout this document, we refer to olestra-containing foods to include those savory snacks made with olestra as well as other olestra-containing foods used in the preapproval studies for olestra.

the label statement be surrounded by a box to ensure proper prominence. This requirement was established under section 409(c)(3)(B) of the act (21 U.S.C. 348(c)(3)(B)), which prohibits approval of a food additive if the proposed use would result in misbranding of food (61 FR 3118 at 3160). The legal authority and scientific basis that underlaid the requirement for this label statement are reviewed in detail in the next section of this document.

A. Basis for Requiring the Label Statement—1996 Decision

1. Legal Authority for the 1996 Label Statement

Under section 403(a)(1) of the act, a food is deemed to be misbranded if its labeling is false or misleading in any particular. Section 201(n) of the act amplifies what is meant by ''misleading.'' Section 201(n) of the act states that in determining whether labeling is misleading, the agency shall take into account not only representations made or suggested about the product, but also the extent to which the labeling fails to reveal facts material in light of such representations or material with respect to consequences which may result from use under the conditions of use prescribed in the labeling or under such conditions of use as are customary or usual (*see* 21 CFR 1.21). Thus, the omission of such material fact from the label or labeling of a food causes the product to be misbranded within the meaning of sections 201(n) and 403(a)(1) of the act.

2. GI Issues Associated With Olestra

As noted, olestra is not digested or absorbed, and it passes through the GI tract intact. The petitioner conducted a number of studies to address issues of potential concern with respect to the effect of olestra as it passes through the GI tract (61 FR 3118 at 3152–3159). For example, during studies designed primarily to assess potential effects of olestra on absorption of fat-soluble dietary components present in the gut at the same time, the petitioner also assessed the potential for olestra to elicit GI symptoms such as cramping, bloating, loose stools, and diarrhea-like symptoms by collecting reports from participants in the studies. In two human nutritional studies [2] (88 and 100 subjects respectively), the entire diet of the subjects was controlled during the length of an 8-week study period. The studies were parallel, double-blind, and placebo-controlled, with olestra dosages of 0 (placebo), 8, 20, and 32 grams per day (g/d).[3] The diets were formulated so that the total digestible fat (triglyceride) content was the same for all treatment groups. Triglyceride was added into the diets in the form of butter, margarine, or vegetable oil to compensate for the amount of fat replaced by olestra in the olestra-containing foods. Olestra was added to various food items by substituting olestra for triglyceride in recipes or in cooking oils. Therefore, the total amount of lipid-like material (digestible triglyceride plus olestra) increased with increasing olestra dose. Each meal contained olestra or the corresponding placebo (triglyceride). Subjects were questioned daily about changes in their health, including GI symptoms. To facilitate collection of GI symptom data, a questionnaire provided a list of common GI symptoms along with general definitions of each and was completed by each subject to capture data about the type, severity, and duration of symptoms experienced. As noted in the 1996 final rule (61 FR 3118 at 3152), the petitioner stated that the two 8-week studies were not intended to examine GI symptoms under real-life consumption conditions where snacks are not consumed every day with every meal and where people may moderate intake if they experience GI symptoms.

FDA's analysis of the data from the two 8-week studies (61 FR 3118 at 3152–3154) showed that there was a dose-response effect for olestra with respect to two endpoints, reported diarrhea/loose stools and fecal urgency. Reporting of diarrhea was based on subjects' perception of diarrhea. FDA found no evidence that study subjects experiencing olestra-related symptoms described as ''diarrhea'' also experienced significant fluid or significant electrolyte loss. The effect of olestra on stool consistency is similar to that produced by liquid petrolatum, which softens fecal contents. FDA recognized that the effect observed was not diarrhea in the clinical sense, but used that term in the 1996 final rule, and is using that term here, because it is the term used in the study report. FDA also found that these GI symptoms cease soon after olestra is no longer consumed.

The petitioner also conducted a study, the Fecal Parameters Study, designed to examine fecal composition of stools from subjects who reported diarrhea when consuming olestra (61 FR 3118 at 3155). The study consisted of two phases, a screening phase and a study phase. The screening phase was conducted to identify subjects who reported GI symptoms from olestra consumption. During the study phase, the identified subjects ate different amounts of olestra, and GI symptoms were recorded and fecal measurements were made. From the initial screening phase, eighteen subjects reported an increase in the frequency, severity, or duration of GI symptoms during the olestra period, relative to the placebo period. These 18 subjects were selected to take part in the study phase, and 15 completed the study. The study phase was a crossover, placebo-controlled, single-blind (subject) design with three treatment groups, 0, 10, and 20 g/d olestra. Each subject received each treatment for 7 days. The treatment periods were separated by 7-day washout periods. Subjects ate all treatment meals under supervision at the clinical site, and ate their habitual diets at home during the washout periods. Study subjects recorded GI symptoms daily. Total fecal collections were made the last 3 days of each treatment period. Daily stool collections were measured for wet weight, volume, and density, and the pooled three day samples were analyzed for water concentration, dry weight, olestra content, sodium (Na), potassium (K), chloride (Cl), total and individual bile salts, free fatty acids, triglycerides, and total lipids.

Measurements of the concentration of stool water and electrolytes (Na, K, and Cl) suggested that these parameters did not differ in the stools of persons reporting ''diarrhea'' during the olestra 20 g/d period from those in the nondiarrheal stools (during the placebo period) of the same persons. However, it was not possible to analyze stool electrolyte values by individual stools or by individual days because the stools were pooled from the 3-day collection period, as is normally done when measuring fecal parameters. FDA noted that there appeared to be an increased weight of stools in those subjects reporting ''diarrhea'' when eating 20 g/d olestra that is not completely accounted for by the presence of olestra in the stools. FDA concluded that the results of this study indicated that there is no difference in stool composition (*e.g.*, water and electrolyte content) when subjects consumed olestra versus placebo (61 FR 3118 at 3155).

FDA found that the number of subjects in the Fecal Parameters Study

[2] In evaluating olestra's nutritional effects, the petitioner conducted two 8-week clinical studies, the 8-week clinical dose response study (8-week DR), and the 8-week clinical vitamin restoration study (8-week VR)(61 FR 3118 at 3133–3134). In this document, when discussing the combined results of these studies, they will be called the two 8-week studies.

[3] By comparison, FDA concluded that the estimated lifetime-averaged daily intake at the 90th percentile of olestra consumption would be 7.0 grams per person per day (g/p/d) (61 FR 3118 at 3124).

who reported diarrhea increased with increasing dose of olestra (*i.e.*, 3 subjects (20 percent) in the placebo, 6 subjects (40 percent) who consumed 10 g of olestra, and 11 subjects (69 percent) who consumed 20 g of olestra). In addition, both the mean number of reported diarrheal bowel movements per subject reporting any diarrhea, and the severity of the reported diarrhea, increased with increasing olestra consumption. Although there was an increase in the number of subjects reporting loose stools with increasing olestra dose, this increase was not statistically significant. FDA concluded that these results were qualitatively similar to the results of the 8-week studies.

The agency concluded, based upon its evaluation of the data and information available at the time, that consumption of olestra causes GI effects such as loose stools, abdominal cramping, and diarrhea-like symptoms. Additionally, the agency concluded that while olestra caused these GI symptoms, there was no evidence that these effects represented adverse health consequences.

At the time of approval, the agency did not have information about the potential GI effects from usual or customary consumption of olestra in savory snacks. Nonetheless, FDA considered it prudent to rely on the available data in deciding whether a label statement about olestra's potential effects on the GI tract was necessary. Olestra had the potential to be consumed in relatively large quantities by every segment of the U.S. population. Additionally, because olestra had never before been available in the marketplace, consumers had no experience with it and were not familiar with it or its potential to cause GI effects. The agency believed that providing consumers label information about olestra's GI effects would preclude unnecessary concerns about the origin of GI effects, were they to be observed, and might also prevent unnecessary or inappropriate medical treatment of those symptoms (61 FR 3118 at 3161). Based on the weight of the evidence about olestra's potential to cause GI effects, as well as the agency's belief that consumers lacked familiarity with olestra and its potential to cause such effects, FDA concluded at the time of olestra's approval that the relationship between GI symptoms and consumption of foods containing olestra is a fact that is material in light of the consequences of consuming olestra, and therefore a label statement was required.

3. Nutritional Issues Associated With Olestra

FDA concluded that olestra inhibits the absorption of the fat-soluble components of the diet when these components are present in the GI tract simultaneously with olestra (61 FR 3118 at 3132–3147). Such components include the fat-soluble vitamins A, D, E, and K, and the lipophilic carotenoids. Based on the data from the nutritional studies, FDA concluded that addition of the four fat-soluble vitamins (A, D, E, K) to foods containing olestra would compensate for any decreased absorption due to the action of olestra, thus ensuring that consumption of an olestra-containing food would not alter the amount of vitamin available for absorption (61 FR 3118 at 3144–3147). The amounts of the vitamins to be provided are prescribed to ensure safe use (§ 172.867(d)). As required under section 403(i) of the act, these vitamins are declared in the ingredient listing.

The added vitamins were not to be considered in determining nutrient content of the food for the nutritional label or for any nutrient claims, expressed or implied. This is because the added vitamins simply compensate for the transient impaired absorption of vitamins A, D, E, and K, *i.e.*, they are added to ensure no change (neither increase nor decrease) in vitamin availability. Thus, the vitamins added to olestra do not contribute significant amounts of these nutrients to the diet (61 FR 3118 at 3161).

Labeling may be considered misleading not only if it fails to reveal facts that are material in light of consequences that may result from use of a food, but also if the labeling fails to reveal facts that are material in light of representations made. Therefore, to set the context for why vitamins A, D, E, and K were added, FDA required a label statement providing information both that vitamins A, D, E, and K had been added and that olestra inhibits the absorption of vitamins. Because FDA believed that consumers who see vitamins A, D, E, and K in the ingredient listing might incorrectly believe that the food was fortified with these vitamins, the agency required an explanatory statement on the label of olestra-containing foods to inform consumers that olestra-containing foods were not an enhanced source of vitamins A, D, E, and K. The statement indicated that olestra inhibits the absorption of vitamins and other nutrients to explain why they were added. FDA included the term ''other nutrients'' because any nutrient that is as lipophilic as these vitamins would also be affected, although FDA concluded that there was no basis for adding back nutrients other than vitamins A, D, E, and K. In this way, FDA sought to make clear to consumers the reason for the presence of vitamins A, D, E, and K in the ingredient listing.

Carotenoids are fat-soluble components in the diet, the majority of which are derived from fruits and vegetables. Data from the petitioner's two 8-week studies demonstrated that consumption of olestra inhibits absorption of carotenoids as measured by a decrease in serum carotenoid levels (61 FR 3118 at 3147–3149). Co-consumption of olestra and a carotenoid-containing food allows the greatest interaction between olestra and the carotenoid, thereby maximizing the potential for interfering with absorption of the carotenoid from the GI tract.

Beta-carotene is a provitamin A carotenoid that is a dietary source of vitamin A; provitamin A carotenoids are converted in the body into vitamin A. At the time of the 1996 final rule, FDA concluded that supplementing olestra-containing foods with vitamin A would compensate for olestra's effects on the provitamin A function of carotenoids.

In evaluating whether there is a scientific basis to require the addition of any carotenoids to olestra-containing foods, FDA consulted with scientists at the National Cancer Institute of the National Institutes of Health (NIH) and the National Eye Institute (NEI) of the NIH (61 FR 3118 at 3148–3149), and the agency's Food Advisory Committee (FAC) (61 FR 3118 at 3121). At the 1995 FAC meeting on olestra, experts with a range of views discussed whether carotenoids themselves have beneficial health effects, or whether it is some other substance in fruits and vegetables that provides the claimed health effects, in which case the carotenoids are serving solely as markers for fruit and vegetable consumption. Five different conferences or reviewing groups preceding the 1995 FAC meeting had examined the relationship between carotenoids and disease. All of these groups had concluded that there was insufficient evidence to recommend consumption of carotenoids, except to encourage the consumption of fruits and vegetables (61 FR 3118 at 3148). Although epidemiological studies showed an association between diets rich in fruits and vegetables (including those that contain carotenoids) and decreased cancer risk, there was no direct evidence that carotenoids themselves were responsible for or contributed in a significant way to that protective benefit. Therefore, at the time of the approval of olestra, the agency

concluded that the available data did not establish any identifiable nutritional or prophylactic benefits for carotenoids, either individually or collectively, aside from the provitamin A function (61 FR 3118 at 3147–3149).

Thus, FDA found no scientific basis for requiring the addition of any carotenoid to olestra-containing foods. The agency also found that the actual magnitude of olestra's effects on carotenoid absorption was likely to be within the range of the normal variation of such absorption due to diet and bioavailability, providing additional assurance that the effect of olestra on the absorption of carotenoids did not raise concern. Accordingly, FDA concluded that there was no basis for requiring a statement about carotenoids on the label of olestra-containing food.

B. Opportunity for Comment and Consideration of New Data

1. Request for Comments on the Label Statement Required by the 1996 Final Rule

Because section 409 of the act prohibits, among other things, approval of a food additive if doing so would cause misbranding, the agency concluded that the olestra label statement should be imposed as a requirement as part of the food additive petition process (§ 172.867(e)). The agency acknowledged, however, that the specific wording had not been tested or subject to an opportunity for comment. Thus, the agency requested comments on the label statement from interested persons on such issues as the need for labeling, the adequacy of its content, and the agency's current word choices (61 FR 3118 at 3160).

After the publication of the 1996 final rule, the agency received timely comments on the label statement,[4] as well as objections to the 1996 final rule.[5]

2. P&G's Commitment To Further Studies

In a letter to the agency dated January 24, 1996, the petitioner stated its intention to conduct focus group testing of the required olestra label statement, to establish a postmarket surveillance system, to conduct additional studies of olestra exposure (both amounts consumed and patterns of consumption), and to conduct additional studies regarding the effects of olestra consumption (61 FR 3118 at 3160 and 3168). FDA responded that P&G was to conduct the studies it had identified in its letter to FDA, consistent with the timetables identified in that letter (61 FR 3118 at 3168).

P&G did carry out the surveillance and studies outlined in its letter of commitment, and performed additional studies not mentioned in the January 1996 letter. After the publication of the 1996 final rule, P&G carried out its commitment to establish a system of passive surveillance to collect spontaneous reports of possible effects that consumers associated with the consumption of olestra-containing snacks. This system included establishing an outside panel of medical experts to review reports, followup on reports of serious illness, and provide FDA information about reports received.

P&G also carried out its commitment to conduct studies on the exposure and effects of olestra. The active surveillance program that P&G sponsored was designed to examine the impact of olestra consumption on endpoints such as serum concentrations of carotenoids and vitamins, olestra consumption patterns (including frequency and amounts), and GI symptoms.

These data and information were presented to the FAC in June 1998, and were eventually incorporated into the petition that is the subject of this rulemaking.

3. FDA's Commitment To Convene an FAC Meeting

In the 1996 final rule, FDA committed to review and evaluate any new data and information bearing on the safety of olestra and to present such information to the agency's FAC within 30 months of the approval of the use of olestra in savory snacks (61 FR 3118 at 3168–3169; § 172.867(f)).

FDA convened a meeting of its FAC within 30 months of the approval of the use of olestra in savory snacks. At an open public meeting, held June 15–17, 1998, new data and information concerning olestra, obtained since the 1996 approval were presented (Ref. 1). These new data, which comprise the majority of material that P&G subsequently submitted in its petition, are discussed in section III of this document. FDA, P&G, the Center for Science in the Public Interest (CSPI), and other interested members of the public made presentations to the Committee. After presentation of the new data, the FAC discussed the label statement specified in § 172.867(e). The complete set of transcripts of the June 1998 FAC meeting (''the transcript'' or ''transcript'') is publicly available through FDA's Division of Dockets Management and through FDA's Internet site.[6]

4. P&G's Petition To Remove the Requirement for the Label Statement

P&G submitted a food additive petition, dated December 1, 1999, to amend the food additive regulations in § 172.867 *Olestra* by removing the requirement for the label statement prescribed in § 172.867(e). This petition incorporated the studies and information that were performed after the publication of the 1996 final rule. As noted, much of that material was discussed by the FAC in 1998.

5. Comments Received

FDA received approximately 80 letters, each containing one or more comments, on the olestra label statement.[7] [8] Some of the comments were submitted in response to FDA's request in the 1996 final rule for comments on the olestra label statement. Other comments were submitted in response to the January 24, 1996, announcement of the approval of olestra for use in savory snacks. Because all of these comments addressed P&G's original petition, which was granted in 1996, in this document FDA refers to these comments as comments ''to the 1996 final rule.'' Comments were also submitted in response to publication in the **Federal Register** of the filing notice for the current petition (65 FR 11585, March 3, 2000); in this document, FDA refers to these comments as comments ''to the current petition.''

Comments were submitted by P&G, Frito-Lay, Inc. (Frito-Lay), and other members of the food industry, as well as from individual consumers, consumer organizations, academia, trade associations, and a member of Congress. Several comments were filed by CSPI. Several parties, including Frito-Lay and

[4] The comments received by April 1, 1996, included the results of P&G's consumer focus group studies on the label statement. Frito-Lay also submitted consumer perception studies on the olestra label statement. These studies are discussed in section III.F.1 of this document. The agency continued to receive comments on the label statement after April 1, 1996. In this document, FDA addresses comments received on the label statement regardless of whether the comments were received by April 1, 1996.

[5] Timely objections were to be filed by February 29, 1996. FDA's response to these objections and requests for hearing is published elsewhere in this issue of the **Federal Register.**

[6] The Internet site is located at *http://www.fda.gov/ohrms/dockets/ac/cfsan98t.htm#Food Advisory Committee* (choose June 15, 16, and 17).

[7] FDA notes that one of the objections submitted by CSPI concerns the label statement required by the 1996 final rule.

[8] Although not part of the petition being considered in the current rulemaking, FDA reviewed comments regarding labeling that were addressed to the 1998 FAC. These comments raised no substantive issue that was not already considered as part of the current food additive petition.

CSPI, submitted comments to both the 1996 final rule and the current petition.

Although section 409 of the act establishes no comment period for food additive petitions, and the agency generally does not solicit comments in notices announcing the filing of a food additive petition, it is FDA's practice to consider any relevant comments submitted prior to the agency's decision on a petition.[9] In this document, FDA separately discusses data from telephone surveys and passive surveillance regarding GI effects, new studies regarding GI effects, and active surveillance and other information regarding nutritional effects of olestra. As part of its discussion of these areas, FDA describes and responds to comments relevant to the topic. FDA discusses and responds to comments on other topics (such as the wording of the label statement, the prominence and placement of the label statement, and the need for a label statement) in a separate section (see section V of this document). In responding to the submitted comments, FDA has considered all of the data and information available in the record that bear on the olestra label statement, including the data and information in the 1996 final rule as well as the new information in the current petition.

III. Data and Information Since the 1996 Final Rule

A. Introduction

Olestra-containing snacks were introduced into test markets in April 1996, and national marketing began in February 1998. P&G established a system of passive surveillance to collect reports of possible effects that consumers associated with eating olestra-containing snacks. This surveillance system was in place when test marketing began. P&G has submitted reports to the agency, as well as analyses of such reports. P&G also established its program for active surveillance to monitor, among other things, possible nutritional impacts of olestra consumption.

P&G conducted studies concerning possible GI effects from consuming olestra-containing snacks in ''real-life'' situations. Specifically, P&G conducted four controlled studies concerning possible GI effects in humans and submitted reports about those studies to FDA.[10] The four controlled studies are described as follows:

- An Acute Consumption Study,
- A Six-Week Consumption Facilitated *Ad Lib* Study (also called the Home Consumption Study),
- A Rechallenge Study, and
- A Stool Composition Study.

In the current petition, P&G also submitted the following data and information:

- Reports and analyses of data collected through consumer focus group and perception studies,
- Surveys regarding GI symptoms,
- Updated literature reviews on carotenoids and disease, and
- A report and analysis of the first year of data collected in an Active Surveillance Study.

CSPI also submitted reports from individuals who attributed an effect to the consumption of an olestra-containing food (Docket No. 87F–0179). In some cases, CSPI obtained medical records from consumers and forwarded them to FDA for analysis.

Below, FDA describes in detail the studies and information submitted in support of this petition, comments to the 1996 final rule that discuss the labeling of olestra-containing foods, comments to the current petition, and other relevant information.

B. Surveys and Postmarket Passive Surveillance Regarding GI Effects

1. Telephone Surveys Regarding GI Complaints

a. *P&G.* P&G sponsored two telephone surveys to investigate the frequency and severity of GI complaints, to investigate the frequency of consumption of foods that consumers believe cause GI symptoms, and to determine knowledge about reported GI symptoms from olestra-containing foods. Both of these surveys were performed before olestra-containing foods were available for sale in those markets. The first survey was done in February 1997 in Indiana (in Marion County, where Indianapolis is located), which was later a test-market for olestra-containing foods. This survey also served as a pilot study for the second survey, which was a national survey of the U.S. population completed in September 1997. National marketing of olestra-containing foods began in February 1998.

The petitioner acknowledged limitations in the design of the first survey completed in Indiana. For example, because the first survey was also the pilot study, the study instrument had not yet been validated.[11] Also, the sample size was small and not shown to be representative of the general population surveyed. Despite these limitations, the petitioner concluded from the survey that GI symptoms were very common among the adult respondents polled. Asked about the previous three month period, respondents reported most frequently the GI symptoms of gas (34.6 percent), diarrhea (33.2 percent), and abdominal cramps (25.8 percent). Of those respondents who experienced one or more GI symptoms, 14 percent reported seeking medical attention because of the symptom. More than half of those who experienced a GI symptom said it was of moderate to severe intensity. The other result noted by the petitioner in this study was that there are a number of common foods (*e.g.,* beans, onions, spicy foods) that respondents said caused them to have GI symptoms, but more than 80 percent of these respondents said they continued to eat these foods. Approximately half of the respondents had heard of olestra and among that group, 18 to 28 percent associated olestra with a GI symptom such as abdominal cramping or diarrhea.

The second survey was a larger, national survey that was designed with a reliability check, and a portion of the survey was designed to be a truly random sample of respondents. In this survey, 40.5 percent of respondents reported having one or more GI symptoms in the previous month. Of those respondents reporting a GI symptom, 21.8 percent had abdominal pain or discomfort, and 26.9 percent reported diarrhea or loose stools. More than 65 percent of respondents rated each of their symptoms as moderate to severe in intensity, and 14 percent consulted physicians about their symptoms. When asked about specific foods, respondents reported having GI symptoms after eating foods such as beans (22 percent) or spicy foods (34.4 percent). Despite symptoms, approximately 80 percent continued to consume these foods. The petitioner also found that women were more likely than men to report GI symptoms, and that abdominal pain, discomfort, and bloating were more commonly reported by women. There was little difference between males and females for reports of diarrhea. More than half the respondents in this study had heard of olestra, and of those, a varying number associated olestra with different GI

[9] See discussion of comments in the filing notice for this petition (65 FR 11585–11586, March 3, 2000).

[10] A copy of the petition submitted by P&G, as well as copies of the studies, surveys, and other supporting materials listed here, can be found at the Division of Dockets Management, Docket No. 00F–0792.

[11] Data obtained from the first survey was used to validate the study instrument for use in the second survey.

symptoms (diarrhea (33 percent), loose stools (4 percent), cramps (11 percent), other GI problems (23 percent)).

FDA notes that in both these surveys, the percent of individuals reporting a GI symptom was high. FDA also notes that while the great majority of respondents in both surveys indicated that they consumed foods that caused them GI symptoms, the survey did not obtain information about the severity of these symptoms (Ref. 2).

b. *CSPI.* In 1996, CSPI commissioned a telephone survey in cities where olestra-containing foods were test marketed (Cedar Rapids, IA, Eau Claire, WI, and Grand Junction, CO), and submitted a report of the results to FDA.[12] The purpose of CSPI's survey was to determine how many people in the test market had tried olestra-containing snacks, and of those who had eaten olestra-containing snacks, how many had experienced GI symptoms. A random digit dialing sampling system was used, until a total of 506 telephone interviews were conducted in June and July 1996. CSPI said that 27 percent of individuals surveyed had tried the newly marketed olestra-containing chips, and of those, 20 percent reported experiencing GI symptoms characterized by CSPI as an adverse GI effect. Respondents characterized these events as mild (58 percent), moderate (23 percent), or severe (9 percent). CSPI also found that the majority of respondents (78 percent) had seen negative reports in the press about olestra, although only 28 percent said they were concerned about these possible effects. Based on this telephone survey, CSPI predicted that a large number of adverse events would be caused by the national marketing of olestra-containing foods. CSPI performed a separate survey of the original respondents who had not eaten olestra-containing chips but ate other chips to assess the frequency of GI events associated with consumption of conventional savory snacks and found that only 0.5 percent associated an adverse GI effect with eating a triglyceride savory snack.

CSPI commissioned a second survey, which was conducted in April and May 1997 in the Indianapolis area where olestra-containing foods were test-marketed. The purpose of the survey was to ascertain the consumption of olestra-containing foods and possible rate of adverse effects. CSPI submitted a report of the results to FDA.[13] CSPI reported that the majority of respondents said they had eaten savory snacks in the past 8 weeks (68.8 percent), and that a smaller portion of respondents (32.7 percent) said they had eaten olestra-containing foods. CSPI said that when respondents were asked whether they had eaten a specific brand of chips that contain olestra, they said yes, but when asked whether they had eaten olestra, these consumers responded that they had not eaten olestra. Of the group of respondents who had eaten an olestra-containing food, 8.3 percent reported experiencing what was characterized as an adverse effect after eating the olestra-containing food.

In its review of the data and information submitted by CSPI, FDA found that the studies provided information about the prevalence of use of olestra-containing foods, awareness of GI symptoms associated with olestra, and sources of information that consumers were using to learn about GI symptoms associated with olestra. FDA disagreed, however, that these studies could provide information about the cause of these GI symptoms. FDA found that the study design was inadequate to determine the cause of GI symptoms. Additionally, it is known from food-borne illness outbreaks that attribution biases can influence consumers and lead to the erroneous attribution of symptoms to a particular food. CSPI's survey does not allow for the evaluation of erroneous attribution of GI symptoms to consumption of olestra-containing chips, *i.e.,* other plausible causes for illness reports were not considered (Ref. 3).

2. Postmarket Passive Surveillance by P&G

P&G established a system of passive surveillance to collect consumer reports associated with the consumption of olestra-containing foods. Passive surveillance refers to the collecting of spontaneous, voluntary reports about a product. In its petition, P&G presents an overview of both the utility and limitations of data obtained from spontaneous, postmarket consumer reports. P&G characterized postmarket passive surveillance as a means of identifying and characterizing potential issues, including safety issues, once a product has entered the marketplace and been utilized by the population at large. The population experience with a product will be much broader than that derived during premarket testing because the number of individuals participating in premarket testing is necessarily limited. A reporting rate may be calculated based on the total amount of product sold and the number of reports received. P&G notes, however, that there are a number of limitations with passive surveillance reporting. For example, these data do not lend themselves to assessment of causality because of the lack of controlled conditions and various confounding factors, such as a high background incidence of reported GI effects. Voluntary reporting, such as that obtained in P&G's passive surveillance system, is also subject to a number of biases including the level of attention the subject is receiving in the news media. Because reporting is voluntary and subject to interpretation, and because the total number of ''exposures'' can only be estimated, a true incidence rate cannot be calculated from passive surveillance.

Reports to P&G under its passive surveillance program for olestra were, for the most part, collected via calls made by consumers to a toll-free telephone number displayed on olestra-containing foods. Such calls were taken directly by P&G via its own toll-free telephone number. Calls were also forwarded to P&G by other snack food manufacturers (specifically, Frito-Lay). In some cases, information from such calls (but not the calls themselves) was forwarded to P&G by other snack manufacturers. Information was collected from callers as to the product used, specific product code information (where available), amount consumed, the nature of the complaint, symptom onset and duration, recurrence, characteristics and treatment, concomitant medications, and physician or other health professional involvement. Where physician contact was involved, or a medically significant event was reported, the petitioner attempted to obtain more detailed information including release of medical records for evaluation.

Consumer reports were reviewed by trained medical affairs staff at P&G. Additionally, the petitioner established a committee (Olestra Postmarketing Surveillance Committee) of medical experts outside of P&G whose membership included specialists in GI disease (both adult and pediatric GI), epidemiology, and pharmacology to review the reports received, and to make recommendations about the implications, if any, of these reports on the safety of olestra. The petitioner submitted reports to FDA of complaints associated with olestra consumption beginning in April 1996 with the test marketing of snacks made with olestra.

The petitioner reported that there were peaks in the number of reports received after the test marketing and

[12] CSPI submitted this report to Docket No. 87F–0179.

[13] CSPI submitted this report to the Docket No. 87F–0179.

national introduction of olestra-containing foods. The petitioner found that while the absolute number of reports increased when olestra-containing foods were first introduced into test markets, the reporting rate (reports per amount of product sold) declined over time. The petitioner also found that over time the absolute number of reports declined and eventually reached a plateau. The greatest number of reports the petitioner received over a four month period was 4,951 in 1998 at the national introduction of olestra-containing snacks. The petitioner stated in its initial reports on passive surveillance that it is common to receive calls and complaints for products. At the start of national marketing the reporting rate was one report for approximately 100,000 servings sold, and 2 years later the reporting rate was one report for approximately 1 million servings sold.

The petitioner analyzed the data from its passive surveillance efforts and found no trend toward increased symptoms with increased consumption; no trend towards increased severity with increased consumption; and no difference in severity by age group or gender. The petitioner's Olestra Postmarketing Surveillance Committee reviewed reports using an algorithm developed to assess the likelihood that an effect was caused by olestra. Using this algorithm, P&G's committee concluded that many reports were not likely to be related to olestra and no serious reports could be attributed to olestra (Docket No. 00F–0792, submission dated March 3, 2000). Based on the nature of the complaints received, the petitioner designed subsequent studies to address, in part, issues arising from consumers' anecdotal reports after eating olestra-containing foods.

In the 1996 final rule, FDA determined that the use of olestra was safe based on results from the preapproval safety studies. FDA stated in the 1996 final rule (61 FR 3118 at 3168) that P&G's plans to continue to study the consumption and effects of olestra were both prudent and responsible. FDA expected, based on results of the preapproval studies, that some reports concerning GI upset, such as loose stools and abdominal cramping, would be collected through a system of passive surveillance. FDA also considered that postmarket passive surveillance had the potential to detect low frequency and unexpected events because postmarket passive surveillance involves the entire population that consumes a product.

FDA reviewed the reports of effects attributed to olestra and found that the majority of reports received concern GI effects such as loose stools and abdominal cramping. Other symptoms were reported at lower frequencies.

FDA recognizes that passive surveillance data such as those collected by P&G have utility but are limited in that they do not allow for the determination of a causal association between the product consumed (*i.e.*, olestra-containing foods) and effects reported. Such reports can, however, lead to hypothesis generation about why specific effects are occurring. This may then result in the development of studies used to test these hypotheses (Ref. 4).

FDA reviewed reports of effects associated with ingestion of olestra that led consumers to seek medical attention. Where possible, the agency reviewed medical records that were obtained directly from individuals who reported the effect or that were obtained through P&G and CSPI (Refs. 5 and 6). At the 1998 FAC meeting, FDA presented its analysis of the medical reports received up to that time. Among the reports discussed was a case where a consumer had undergone an appendectomy and associated this with consuming an olestra-containing food. The pathology diagnosis at the hospital noted that there were minimal inflammatory changes. FDA obtained a medical release from the patient in order to examine the pathology slides from the appendectomy, which were read independently by four FDA pathologists, all of whom confirmed the presence of inflammatory cells throughout the wall of the appendix meriting a diagnosis of acute appendicitis.[14] In many other of the medical records reviewed, physicians attributed patient symptoms to an etiology other than olestra, or did not provide an etiology. There were cases where physicians did attribute symptoms to olestra, but the limitations of passive surveillance make it difficult, if not impossible, to draw definitive conclusions about causality based on the review of individual medical records.

3. Postmarket Surveillance Reports From CSPI

CSPI has periodically submitted to FDA reports of effects allegedly associated with the consumption of olestra (Docket No. 87F–0179). The complaints were gathered initially in test markets by calls to an advertised toll-free telephone line, and gathered subsequently through CSPI's Internet site.

FDA analyzed the reports from CSPI and compared the information and analysis to the information and analysis of the reports submitted to FDA by P&G. FDA noted that the reports received by CSPI were very similar in nature, type of complaint, and amount consumed as the reports by P&G.[15] As discussed previously, passive surveillance has limited utility in determining causality.

4. Comments Regarding Consumer Reports

FDA received comments about reports of effects that consumers attributed to olestra. FDA considered these comments and responds in the following section of this document.

(Comment 1) One comment from an individual consumer to the current petition reported that a family member who had Addison's disease suffered gastric cramps and diarrhea, laid down, went into an Addisonian crisis, and died after consuming olestra-containing potato chips. The comment did not provide any further information regarding the death mentioned. CSPI forwarded to the agency the medical record of an Addison's disease patient who had reportedly consumed olestra-containing potato chips prior to death. The patient who died was diagnosed as having Addison's disease (adrenocortical insufficiency) and hypothyroidism in 1989. FDA believes, based on several factors, that the comment and medical record provided by CSPI refer to the same person.

FDA reviewed the medical record forwarded by CSPI. This patient collapsed suddenly after experiencing a bout of gastroenteritis, and reportedly consumed olestra-containing chips prior to the bout of gastroenteritis. An autopsy showed that the adrenal glands could not be identified and noted a finding of Hashimoto's thyroiditis. The medical record did not provide any information regarding the gastroenteritis experienced prior to death.[16] Due to the lack of information contained in the medical record, the agency was unable to determine whether the ingestion of olestra had any role in this patient's illness or death (Ref. 5).[17]

[14] Transcript, vol. 1, pp. 271–276.

[15] Transcript, vol. 1, pp. 258–270.

[16] The Certificate of Death lists acute cardiorespiratory arrest as the immediate cause of death with autoimmune adrenocortical deficiency syndrome as the underlying cause leading to the immediate cause of death. Other significant conditions contributing to death but not resulting in the underlying cause include mitral valve prolapse and Hashimoto's thyroiditis.

[17] FDA investigated the death mentioned in the comment. As part of the investigation, FDA spoke with the patient's spouse and the patient's co-

(Comment 2) A comment from CSPI to the current petition asserted that FDA has never conducted indepth investigations (beyond reviewing the medical records of a few individuals) of any of the anecdotal reports, including those reports involving rectal bleeding, hospitalization, and death. The comment further asserted that the agency has ignored all of the anecdotal reports and has said that there is no proof that any of the reports were due to olestra. The comment also stated that in some reports, a patient's physician attributed his/her symptoms to olestra. The comment also quoted FDA review memoranda (Refs. 6 and 7) stating that olestra may have been responsible for some of the effects reported.

FDA does not agree that it has ignored anecdotal reports. Nor does it agree that it must conduct further investigation of the anecdotal reports. FDA regularly reviews the reports forwarded to the agency by P&G and CSPI. The reports are analyzed and summarized using criteria such as sex, age, symptoms reported, duration of symptoms, and amount of olestra-containing food consumed. The agency also reviews any medical records forwarded with the reports. CSPI provided no evidence to support its allegation that anecdotal reports have been ignored. Nor has CSPI provided any reason to suspect that serious adverse health effects could have been caused by olestra. The agency will continue to monitor reports as they are forwarded to the agency.

As stated in the memoranda cited by the comment, some of the effects reported may have been caused by olestra. These reports were collected using passive surveillance. As noted previously, passive surveillance is useful in that it can lead to hypothesis generation about why specific effects are occurring. These hypotheses can then be tested in controlled clinical trials. For example, the reports received from consumers attributing their symptoms to olestra served as a basis for some of the hypotheses tested in the petitioner's most recent controlled clinical studies. However, while passive surveillance data have utility, such data are limited in that they do not allow for the determination of a causal association between the product consumed and effects reported. Thus, based on the passive surveillance data alone, it is not possible to determine whether the effects reported were caused by consumption of an olestra-containing food.

workers about the events leading up to the patient's death.

The agency has reviewed all of the medical records that it has received from CSPI and P&G about consumers who saw a physician for an effect attributed to the consumption of an olestra-containing food. In fact, FDA has conducted an investigation into the death mentioned in the previous comment. FDA has also obtained and examined the pathology slides of a patient who had undergone an appendectomy that the patient associated with consumption of an olestra-containing food. The agency has not found sufficient evidence to conclude that olestra is likely to have caused the symptoms that led the consumers to see a physician.[18]

(Comment 3) A comment from CSPI to the current petition stated that letters and electronic mail messages sent to P&G describing GI symptoms have not been included in reports that P&G submitted to the agency; therefore, the agency has not received all of the symptom-related reports. The comment recommended that the agency investigate whether it had received all reports.

FDA recognizes that not every report from a consumer will provide enough information for FDA to determine whether an effect was possibly related to olestra and that some judgement is needed in compiling data. In light of this limitation, the agency recognizes that P&G may not forward all reports it receives, such as those reports containing incomplete information, to the agency. While this may mean that less than 100 percent of reports are collected, the agency has no reason to believe that the complaints not forwarded to the agency constitute a unique data set or raise an issue not previously considered. Indeed, the reports gathered and forwarded independently to the agency by P&G and CSPI are consistent in terms of the nature of the complaints and the amounts of olestra consumed. CSPI's comment provides no specific information that would lead the agency to conclude that it has not received an accurate and representative sample of the effects reported to P&G or that such reports raise an issue not already considered. Thus, the agency finds that there is no basis for concluding that it should obtain and evaluate each and every report that P&G receives.

(Comment 4) A comment from CSPI to the current petition stated that the agency should obtain and disclose to the public the number of consumers (without identifying any particular individuals) who attributed their symptoms to olestra and reached an out-of-court settlement with the petitioner. The comment also asked for the number of consumers who, after attributing their symptoms to olestra, received or were offered reimbursement for their medical expenses. The comment requested that the agency consider this information in its rulemaking.

[18] Ref. 5 and Transcript, vol. 1, pp. 271–276.

FDA does not agree that it should obtain and disclose to the public the number of consumers who attributed their symptoms to olestra and reached an out-of-court settlement with the petitioner. Importantly, the comment does not demonstrate the relevance of the requested information to the question at issue: *i.e.*, whether FDA should continue to require special labeling for olestra-containing foods. Moreover, settlement of lawsuits may be reached for a variety of reasons, including improved public relations or avoidance of unnecessary conflict, and do not address any factual issues regarding whether olestra is capable of causing the effects claimed.

C. Studies Regarding GI Effects

1. Rechallenge Study

The petitioner submitted a report of a study designed to test whether individuals who complained of a GI effect after consuming olestra-containing snacks would have the same experience with subsequent exposure (Refs. 8 and 9). This test was designed to show whether the GI effect is consistently associated with consumption of the olestra-containing snack. The petitioner's study was a randomized, double-blind, placebo-controlled, four-period, within-subject crossover study. Subjects were recruited from consumers who had voluntarily called the snack manufacturer and reported GI symptoms associated with consumption of olestra-containing snacks. Each subject made four visits to the study site, at least 1 week apart, and was provided with 2 ounces (oz) of either potato chips containing olestra (olestra chips) or potato chips containing conventional triglyceride[19] (triglyceride chips). At each visit, subjects were to consume as much as they could of the 2 oz serving. Each participant was randomly assigned to receive olestra chips at two visits and triglyceride chips at two visits. Participants were contacted after each visit and asked whether they had

[19] In the various reports submitted by the petitioner, the terms triglyceride, full-fat, regular, and conventional were all used to describe the oil used in savory snacks. These terms mean the same thing. For consistency in this document, we use the word triglyceride.

experienced any GI symptoms within the week after eating the potato chip product.

The study was completed with 98 participants, the majority of whom had initially called to report that they had experienced diarrhea, loose stools, and/or abdominal cramping (61 percent, 16 percent, and 64 percent respectively). Approximately 48 percent of the participants described the symptoms that prompted their original call as severe. For nearly three-quarters of the participants, the amount of olestra chips consumed in the study was comparable to, or greater than, the amount associated with their initial call.

The petitioner found that during the study there were no significant differences following consumption of olestra chips, compared with consumption of triglyceride chips, in the frequencies of abdominal cramping (12 percent with olestra, 9 percent with triglyceride), diarrhea or loose stools (11 percent with olestra, 15 percent with triglyceride), gas (7 percent with olestra, 5 percent with triglyceride), or any other GI symptom (28 percent with olestra, 26 percent with triglyceride). Overall symptom severity ratings for all subjects were similar after consumption of olestra and triglyceride chips. The petitioner concluded that this study provided evidence that an episode that was initially reported to be an olestra-related effect was in all likelihood not olestra-related, and that there was no evidence of a population or subpopulation with a sensitivity to olestra. The petitioner suggested that these results indicate that initial calls made to the toll-free telephone line may reflect false attribution of symptoms to products made with olestra.

FDA found this study was adequately representative of the population who called the postmarketing surveillance system in terms of severity of initial symptoms and amount of olestra reportedly consumed prior to the initial symptom episode. FDA noted that while 98 participants were enrolled in the study, only 92 completed all 4 visits. The six dropouts were unrelated to olestra-related effects. Based on an analysis of the data in the study, FDA concluded that under the conditions of the study (two exposures of up to 2 oz of olestra-containing chips separated by at least a week), subjects eating olestra-containing chips were no more likely to report having had loose stools, abdominal cramps, or any other GI symptom compared to subjects eating an equivalent amount of triglyceride chips (Refs. 10 and 11).

2. Acute Consumption Study

P&G sponsored [20] a study to determine whether there was a difference in the nature or frequency of GI symptoms experienced by subjects eating olestra chips compared to those eating triglyceride chips, ad libitum on a single eating occasion (Ref. 12). The study was a randomized, placebo-controlled, double-blind study in which 1,092 adults and teenagers who were provided with a 13 oz bag of potato chips (either olestra chips or triglyceride chips) in a plain, unlabeled white bag, consumed as many chips as they desired while viewing a movie. Participants were also provided a 32-oz soft drink of their choice. Participants were told prior to the test that they might experience temporary dry mouth, thirstiness, or digestive symptoms (such as gas, cramping, or loose stools), as they might with salty or high fiber foods.

Participants were instructed to be seated in the theater at least one seat apart from other participants, to eat and drink as much or as little of their chips and beverage as they desired, and not to share with anyone else. The theaters were monitored by several study staff during the movies. At the conclusion of the movie, participants clipped their bags of chips shut; noted the approximate amount of beverage consumed; and completed a brief questionnaire about product acceptance, satiety, and sensory attributes. Participants turned in the completed questionnaires and bags with uneaten chips and were given a toll-free telephone number to call if they had any questions or problems. Bags of chips were subsequently weighed to determine the amount consumed by each subject.

Trained telephone interviewers contacted study participants and administered a recall questionnaire to collect information on any effect experienced since the movie. All subjects were specifically asked if they had experienced any GI symptoms during or since the movie, and to specify those symptoms including the severity and timing of any such symptoms. The study protocol specified that participants be contacted within 2 to 4 days of viewing the movie. The petitioner reported that 85 percent were contacted within 2 to 4 days and a total of 97 percent were contacted within a week of viewing the movie.

The petitioner reported that the median consumption of olestra chips was approximately 2.1 oz (approximately 16 g of olestra) [21] compared to about 2.7 oz of triglyceride chips. Overall chip consumption was similar across age groups, but males generally consumed more chips than females (median of 2.8 versus 2.1 oz, $p<0.01$). The overall palatability of the triglyceride chips was rated slightly higher than the olestra chips, with a mean score of 6.4 versus 5.6 on a 9-point preference scale ($p<0.01$). Regarding satiety, there were no significant differences between the groups as indicated by mean satiety scores of 5.9 versus 5.7 for triglyceride chips and olestra chips, respectively, on a 9-point scale, with 9 being ''extremely full'' ($p=0.07$). Nor were any differences seen in beverage consumption, choice of beverage, or time since last meal prior to the movie between the two groups.

The petitioner attributed the lower chip consumption in the olestra group to the slightly lower preference for olestra chips reported by study participants. The petitioner stated, however, that the median consumption (2 oz) was more than a typical single-serving snack size bag of chips, and that approximately 100 participants ate more than 4 oz of olestra chips (approximately 32 g of olestra).

The petitioner reported that the proportion of subjects who reported GI symptoms after consuming olestra chips was not different from that after consuming triglyceride chips (15.8 percent and 17.6 percent respectively). There were no differences between the olestra and triglyceride groups in the frequencies for 14 different self-reported GI symptoms (gas, diarrhea, pain, cramping, upset stomach, loose stools, nausea, bloating, indigestion, aftertaste, eructation, constipation, vomiting, bloody stool), overall symptom severity for any GI event, nor time to onset or duration of symptoms. The petitioner also reported that consumption levels did not correlate with the rate of symptom reporting in either the olestra or triglyceride group.

The petitioner planned to have 1,400 participants in the study and anticipated symptom reporting to be 10 percent for the triglyceride group and 15 percent for the olestra group. Using these assumptions, the study would provide 80 percent power for detecting

[20] The principal investigator for the study was Dr. L. Cheskin, Dept. of Gastroenterology, Johns Hopkins School of Medicine.

[21] In 1996, FDA estimated the probable life-time averaged intake of olestra at the 90th percentile to be 7.0 g/p/d. To evaluate subchronic conditions, FDA estimated that a ''high'' acute consumer of olestra (everyday for 12 weeks) would consume 20 g/p/d, equivalent to eating a 2 oz bag of potato chips every day, and the 99th-percentile single-day intake of olestra for the group consuming the highest level of savory snacks to be 45 g/d (61 FR 3118 at 3124).

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,[22] 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 [23] 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 [24] 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

[22] 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.

[23] Dr. R. Sandler, Professor of Medicine, University of North Carolina, Chapel Hill, was the principal investigator for this study.

[24] 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.

subjects' self assessments showed little or no impact of GI symptoms on subjects' daily life, and there was no increase in the percentage of reported severe impacts in the olestra group compared to the control group.

The petitioner also examined whether there were differences in the incidence of reported GI symptoms among the different age groups. The petitioner reported that there were no significant differences in total or specific GI symptoms between the olestra and triglyceride groups for children (2 to 12 years; n=885), teens (13 to 17 years; n=227), or the elderly (65 to 89 years; n=402), even among the highest consumers. This analysis showed that for adults (18 to 64 years; n=1667), there was an increased percentage in reporting the GI symptom gas in the olestra group compared to the control group. There was also an increase in the number of GI symptom days, and an increase in the number of more frequent bowel movement symptom days, among adult subjects eating olestra of approximately one symptom day out of the 42 days of the study.

Among adult females in the olestra group, compared to adult females in the control group, there was an increase of approximately one symptom day out of 42 days of the study with regard to more frequent bowel movements, gas, and any GI symptom. The only difference regarding reports of abdominal cramping was an increase in the control compared to the olestra group for adult males.

The petitioner concluded, based on the subjects' self assessments, that none of these reported increases in the number of symptom days were meaningful because there was no impact on subjects' daily activities. Based on its comparison of the percent of subjects who reported one or more GI events during the course of the study, P&G concluded that there were no meaningful or serious GI effects associated with eating olestra-containing chips.

At the end of the 6-week study, P&G asked participants which kind of chips they thought they were eating from the olestra-labeled bags. P&G reported that the percentage of subjects reporting GI symptoms was greater (approximately 50 percent) in those who believed they were eating chips made with olestra compared to those who thought they were eating triglyceride chips. This was true regardless of whether the participant was actually eating olestra or triglyceride chips.

FDA employed a number of statistical approaches to best address the different questions to be answered by the study, and while such differing approaches may yield different answers, this varied approach provides a more complete picture of the study results. FDA analyzed both the temporal relationship between consumption and symptoms, and summation data for the study (Refs. 15 and 16).

Examination of temporal data is important for evaluating an association between olestra intake and GI symptoms. Such an analysis is also important because in a study of this length, subjects can modify their eating behavior based on their experience with a product. FDA found that subjects in both the olestra and triglyceride groups modified their intake of chips as a result of experiencing more frequent bowel movements. FDA was able to conclude that consumers modify their behavior based on their experience with olestra chips by examining the amount of chips consumed the day before, the day of, and the day after a report of more frequent bowel movements. Chip consumption decreased after experiencing more frequent bowel movements, although consumption of chips did not cease.

In order to understand the temporal relationship between olestra consumption and GI symptoms, FDA examined the frequency of GI symptoms for numerous different patterns of olestra consumption over a period of several days.[25] In all these analyses, FDA found that for men, olestra consumption resulted in an increase in any GI symptom, gas, and more frequent bowel movements, and a decrease in nausea. For women, olestra consumption resulted in an increase in any GI symptom, gas, looser stools, and more frequent bowel movements. On the day that chips were eaten, the difference in the percentage of occasions that more frequent bowel movements were reported for the olestra chips compared to the triglyceride chips was 1.6 percent for males and 1.2 percent for females. These effects were seen on days of consumption of olestra chips but not on subsequent days on which olestra-containing chips were not eaten. When olestra chips were consumed on consecutive days there was some cumulative effect for the reports of these GI symptoms. This was particularly true for males. For example, the difference in the percentage of occasions that a report was made in the category ''any GI symptom'' for the olestra chips compared to the triglyceride chips increased from 0.9 percent on the first day to 1.7 percent on the second day, to 2.6 percent on the third consecutive day that chips were eaten and a complaint was recorded. There was also a trend for more frequent and recent consumption of olestra to result in a GI symptom. While increasing consumption of olestra and triglyceride chips both resulted in more symptoms, the effect of olestra was greater compared to triglyceride chips at all doses.

In examining the effect of olestra consumption on different age groups, FDA found that GI symptoms were primarily seen in the 18 to 64 age group. There were no olestra-related effects in the groups over 65 years or younger than 18 years.

In a separate statistical analysis, FDA focused on the sum total of symptom days and consumption of olestra-labeled chips over the course of the 42-day study (summation data). FDA analyzed the data for each GI symptom for both the entire study population, and for a population divided based on age and gender.

In the statistical analysis of the sum total of symptom days over the course of the 42-day study, FDA first examined the relationship between the reporting of particular GI symptoms and the consumption of olestra-containing foods by comparing the olestra group and the triglyceride group. FDA found that for all study subjects (males and females) over the course of the 42 day study, there was an increase of 0.28 more frequent bowel movement symptom days in the olestra group compared to the triglyceride group. FDA then examined the relationship between the reporting of particular GI symptoms and the consumption of olestra-containing foods by analyzing the olestra group and the triglyceride group separately by gender. FDA found for females in the olestra group, there was an increase in ''any GI symptom'' of 0.5 mean symptom days compared to the females in the triglyceride control. It was also observed that for females in the olestra group, there was an increase of 0.3 symptom days in more frequent bowel

[25] These included determining the percent of occasions for which GI symptoms occurred on the same day and the following 2 days of eating an olestra-labeled chip; comparing the frequency of occurrence of GI symptoms on days that olestra-labeled chips were eaten to days that chips were not eaten to determine a ''same day of eating effect''; determining the percent of days on which GI symptoms were reported for all non-eating days in order to evaluate possible delayed or continuing effects of olestra; comparing the percent of days on which GI symptoms were reported to the number of consecutive days eating olestra-labeled chips in order to examine possible cumulative effects; for various GI symptoms analyzing the pattern of consumption of olestra-labeled chips for the days prior to the GI symptom in order to examine how the most recent day of eating and the frequency of eating is related to the GI symptom; for various GI symptoms, determining the amounts of olestra-labeled chips consumed on the day the GI symptom occurred (Ref. 16).

movements over the course of the 42 day study compared to females in the triglyceride group. For males in the olestra group, the analysis showed an increase of 0.24 more symptom days for more frequent bowel movements compared to males in the triglyceride group.

FDA then examined the relationship between the amount of product consumed and symptoms reported for all study subjects (males and females), and found there were associations between olestra consumption and reports of ''any GI symptom'' (p=0.03), loose stools (p=0.006), and more frequent bowel movements (p=0.002). No such associations were observed between the consumption of the control chips (triglyceride chips labeled as olestra) and any measured symptom. When analyzed separately by gender, both sexes showed trends for an association between the consumption of olestra and loose stools (males p=0.001, females p=0.018), and more frequent bowel movements (males p=0.001, females p=0.042), but only males also showed a trend for an association between the consumption of olestra and ''any GI symptom'' (p=0.001).

FDA examined the relationship between the consumption of olestra-containing foods and reports of abdominal cramping. FDA found no difference in the frequency of reported abdominal cramping between the olestra group and the triglyceride group. FDA analyzed the olestra and triglyceride groups separately by gender for reports of abdominal cramping and found no difference between males or females in the olestra group as compared to the triglyceride group. FDA agrees with the petitioner that there was no observed difference in the incidence or association of reported abdominal cramps between the olestra group and the triglyceride group (Ref. 10).

4. Stool Composition Study

The Stool Composition Study was sponsored [26] by the petitioner as a followup to the preapproval Fecal Parameters Study (discussed previously in section II.A.2 of this document). The study was designed to establish whether consumption of olestra-containing foods is associated with changes in clinical measures of diarrhea (water and electrolyte loss), effects which may be harmful, or stool consistency alone, which may result from adding bulk to the stool and which is not harmful. In addition, the study was designed to determine the relationship between objective measures of clinical diarrhea (*e.g.*, stool water output and bowel movement (BM) frequency) and subjective reports of ''diarrhea'' from study subjects. The effects of olestra were compared to a placebo, triglyceride chips, and to sorbitol, an osmotically active sugar alcohol that was chosen as a positive control to ensure that the study methodology was adequately sensitive to detect increases in stool water output.

The study was a single-site, randomized, double-blind, placebo-controlled parallel clinical trial. Sixty-six subjects, ages 18 to 74, were housed on a metabolic ward for 12 days and consumed meals ad libitum. The meals conformed to the American Heart Association Step I diet guidelines (no more than 30 percent of calories from fat). Beverages were available ad libitum. All study subjects had to consume 5 oz of potato chips eaten as two afternoon snacks. A serving of potato chips was either olestra (test) or triglyceride (placebo). All subjects were also required to consume 1.5 oz of candy made either with sorbitol (test) or sucrose (placebo) as a morning snack. The first two days (study days 1 and 2) were a lead-in period during which subjects were acclimated to the living conditions and the diet, and consumed placebo snacks (triglyceride potato chips and sucrose candies). Stool samples were not collected during the lead-in period. The next 4 days (study days 3 to 6) comprised the baseline period, in which subjects continued to consume placebo snacks, and all stool samples, BM ratings, and GI symptoms were collected. For the final 6 days (study days 7 to 12), subjects consumed snacks according to their randomly assigned treatment group, and all stool samples, bowel movement ratings, and GI symptom reports were collected. There were two olestra test groups (20 g and 40 g olestra) and two control groups (positive control of 40 g sorbitol and placebo). The placebo group consumed two servings of placebo (triglyceride) potato chips and placebo (sucrose) candy. The positive control group consumed two servings of placebo potato chips and test candy (40 g sorbitol). The 20 g olestra test group consumed one serving of test potato chips (olestra), one serving of placebo potato chips, and placebo candy. The 40 g olestra group consumed two servings of test chips and placebo candy.

The petitioner noted that in the study the doses of olestra were threefold to sixfold more than the estimated daily intake, and 10 to 20 times more than the observed intake at the 90th percentile level in the Active Surveillance Study (see section III.D.1 of this document). The high dose, 40 g/d, was higher than the highest dose used in the preapproval nutrition studies (32 g/d) described previously in section II.A.3 of this document, in which the high dose group experienced an increase in GI symptoms, specifically in reported diarrhea/loose stools. In that preapproval study, FDA concluded that the reported diarrhea was not diarrhea in the medical sense because there was no evidence of subjects experiencing significant fluid or electrolyte loss (hemoconcentration, electrolyte imbalance; 61 FR 3118 at 3152-3154).

The petitioner concluded that with regard to the critical parameters that are medically relevant in defining diarrhea, the objective measures showed that olestra did not meaningfully change either the total stool output or stool water output, while sorbitol produced large effects on both parameters. Compared to baseline, mean stool water output increased 9 g/d and 37 g/d for the 20 and the 40 g/d olestra groups respectively, and 325 g/d for the 40 g/d sorbitol group. Stool water output decreased 28 g/d for placebo. The measured mean stool water content for the sorbitol group was nearly 10 times greater than the group consuming the highest level of olestra and the number of watery BMs was 140 in the sorbitol group, one in the 40 g/d olestra group, none in the 20 g/d, and one in placebo. While sorbitol significantly increased the severity of abdominal cramping compared to placebo, olestra did not. The petitioner found that olestra consumption did not result in any clinically meaningful increases in objective measures of diarrhea, namely, total stool output, bowel movement frequency, and stool water and electrolyte output. The mean number of BMs for the olestra 40 g/d group was increased compared to placebo but was not increased compared to the olestra 20 g/d group. Subject reports of ''watery, difficult to control diarrhea'' did not necessarily correlate with measured viscosity of the stool. Olestra did increase stool weight in proportion to the amount eaten, and daily consumption of olestra gradually softened stool in a dose-responsive manner. The sponsor found that there was increased reporting of ''diarrhea'' in the olestra treatment groups during the treatment phase without an increase in total water output outside the normal range, *i.e.*, the range observed during the baseline period and in the placebo group.

P&G concluded, based upon the study results, that the consumption of olestra

[26] The GI consultant to the study was Dr. R. Gianella, University of Cincinnati.

does not cause diarrhea, but simply adds bulk and softening to the stool.

FDA reviewed the data from this study and agrees with the petitioner's analysis, although some of the agency's analytical strategies differed from those of the sponsor (Ref. 17). FDA concludes that both comparisons of the mean after treatment and of changes from baseline showed dose responsive increases in stool characteristics (total output, water output, consistency, frequency and increases in water content) that were not clinically significant (Ref. 18).

Using a 7-point scale to rate consistency of bowel movements (1 = watery, diarrhea; 4 = normal; 7 = hard, constipation), subjective ratings of stool consistency showed that subjects who ate 40 g/d olestra perceived their stools to be looser (mean rating 2.4) compared to those who ate 20 g/d olestra (mean rating 3.1). By comparison, placebo subjects had a mean score of 3.9 whereas those subjects in the 40 g/d sorbitol group had a mean score of 1.5 (mean scores determined for days subjects consumed snacks according to their randomly assigned treatment group). When stool consistency was measured by peak force value for extrusion, both olestra groups had a lower mean stool consistency than placebo and the 40 g/d olestra group was lower than the 20 g/d group. These dose responsive findings seen among subjects eating olestra resulted from gradual stool softening effects observed after several consecutive days of olestra consumption. Although subjects characterized these viscosity changes as ''diarrhea,'' the changes were not associated with an increase in stool water.

FDA examined the percentage of symptom days for cramping and found that although the 40 g/d olestra group reported an increased incidence of abdominal cramping compared to those in the 20 g/d olestra group (35.8 percent compared to 9.8 percent), this difference did not rise to statistical significance. The percentage of subjects reporting abdominal cramping in the 20 g/d olestra group appeared to decrease when compared to baseline or placebo (9.8 percent compared to 20.5 percent or 18.3 percent). The 40 g/d sorbitol group had the highest percentage (69.8 percent) of reports of cramping. Subjects rated symptom severity on a scale of 0 to 5, with 0 representing none and 5 extreme. The severity of cramps reported by subjects in the olestra 40 g/d group was less severe than that reported by subjects in the 40 g/d sorbitol group (0.72 compared to 2.3). No significant olestra effects were found for GI symptom severity, although one individual in the 20 g/d olestra group reported severe urgency at a rating higher than any other report in any of the other groups (Refs. 10 and 18).

5. Comments Regarding the GI Studies

FDA received comments about the new GI studies. FDA considered these comments and responds in the following paragraphs. Comments regarding the label statement for GI effects will be discussed in section V of this document.

(Comment 5) A comment from CSPI to the current petition criticized the Rechallenge Study. The comment stated that the study subjects were not screened for sensitivity to olestra, as was done in the preapproval Fecal Parameters Study. The comment also asserted that the Rechallenge Study contained a strong likelihood of bias because only 10 percent of those contacted agreed to participate in the rechallenge and those that did participate consumed olestra on only 2 days, at least 1 week apart, which reduced the sensitivity of the study. CSPI asserted that the Rechallenge Study also assumed that those sensitive to olestra would respond to it 100 percent of the time. The comment contended that those experiencing adverse reactions may only do so under certain circumstances, not 100 percent of the time.

FDA does not agree that the selection of study subjects biased the Rechallenge Study nor does CSPI provide such evidence. FDA has determined that the subjects who participated in the Rechallenge Study were adequately representative of those persons who contacted the postmarketing surveillance system in terms of severity of initial symptoms and amount of olestra reportedly consumed prior to the initial symptom episode (Ref. 11). Further, CSPI provided no basis for its assertion that additional subject screening is necessary to accomplish the objectives of the Rechallenge Study.

CSPI states that the sensitivity of the Rechallenge Study was reduced because participants consumed olestra on only 2 days, at least 1 week apart. The conditions of the study were designed to be similar to the conditions under which the subjects originally reported effects that they attributed to consuming an olestra-containing snack. FDA found that for nearly three-quarters of the subjects, the amount of olestra consumed in the study was comparable to, or greater than, the amount associated with their initial symptom episode (Ref. 11). In addition, more than three-quarters of the subjects reported that their initial symptom episode occurred after a single eating occasion. Therefore, subjects were challenged with 2 oz of olestra chips on two occasions separated by a week, providing a dose and number of exposures comparable to, or greater than, those associated with many of the subjects' initial symptom episodes.

CSPI's comment did not reference where FDA or the petitioner assumed that those sensitive to olestra would respond to it 100 percent of the time, nor is FDA aware of anyone who has put forth such a position. Indeed, FDA agrees that even if an individual experiences a reaction to olestra, that individual may not experience such reaction after every exposure. The Rechallenge Study shows that subjects exposed to olestra containing-chips were no more likely to report GI symptoms than when exposed to an equal amount of triglyceride chips. Thus, the study subjects' reactions to olestra containing-chips are not so frequent that they can be distinguished from their reactions to regular chips under the conditions of the test.

(Comment 6) A comment from CSPI to the current petition criticized the Acute Consumption Study. CSPI's comment relies on its published letter [27] commenting on a published study (Ref 12.) that reports data from the Acute Consumption Study. CSPI stated that the study may have failed to detect the true incidence of GI effects due to a lack of statistical power or inadequate controls. For example, with the incidence of ''any GI event'' of about 15 percent, 550 subjects in each group would have provided only about a 50 percent probability of detecting a 5 percent actual increase in the treatment group. Along the same lines, diarrhea and loose stools were increased less than 1 percent in the olestra group compared to baseline levels of 2.6 percent and 1.1 percent, respectively. The comment asserted that maintaining 80 percent power to detect a 1 percent increase over a 2 percent baseline requires about 4,000 subjects per group. The comment also contends that the darkened movie theater may potentially cause exposure misclassification (some ''olestra eaters'' may have eaten few or none of their chips; some ''non-olestra eaters'' may have eaten friends' olestra chips). The comment also stated that it took up to 10 days after consumption to assess symptoms. CSPI also pointed out that non-olestra eaters consumed one-third more chips than the olestra eaters.

The criticism by CSPI of the Acute Consumption Study does not negate the

[27] CSPI's published letter was included in the comment as an attachment (Ref. 19).

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 letter[29] 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

[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).

[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.

subjects in the study experienced high rates of water loss through their stool. The comment also stated that the definition of diarrhea used in the Stool Composition Study was too narrow and is not consistent with the definition used by the Centers for Disease Control and Prevention (CDC; three or more loose stools in a 24 hour period). The comment asserted that self-reporting is usually considered sufficient to conclude that people experience diarrhea regardless of demonstrated loss of electrolytes.

In contrast to the Acute Consumption Study, the Home Consumption Study, and the Rechallenge Study, the Stool Composition Study was designed to extend the understanding of olestra's effect on stool characteristics that would potentially represent a safety concern. For this reason, the Stool Composition Study was conducted under conditions most likely to elicit GI effects. The highest dose of olestra provided in the Stool Composition Study (40 g/d) was greater than the 32 g/d used in the preapproval 8-week studies which was shown to cause an increase in GI symptoms (specifically in reported diarrhea/loose stools) and was twice as high as the highest dose given in the preapproval Fecal Parameters Study (20 g/d). Additionally, subjects' stool samples were collected for all 6 days of the treatment period in the Stool Composition Study, compared to only three days of the 7-day treatment periods in the Fecal Parameters Study. The Stool Composition Study does not negate the preapproval studies, but the results of the preapproval studies must be considered in light of those from the Stool Composition Study.

The results of the Stool Composition Study show that olestra consumption does not result in any clinically meaningful increases in the objective measures of diarrhea. Importantly, the Stool Composition Study assessed the effects of olestra consumption using objective parameters such as total stool output, bowel movement frequency,[31] and stool water and electrolyte output rather than a subject's subjective assessment of whether he or she experienced diarrhea. The use of objective measures of diarrhea is necessary to assess whether the ''diarrhea'' experienced by study subjects represents a safety concern.

[31] FDA notes that the mean bowel movement frequencies in the olestra-consuming groups were less than three bowel movements per day. The mean bowel movement frequencies were 1.6 ± 0.2 BM/d (mean ± standard error) in the 20 g/d olestra group and 2.0 ± 0.2 BM/d (mean ± standard error) in the 40 g/d olestra group (Ref. 18).

FDA was concerned with the potential for olestra to cause diarrhea because diarrhea of medical significance is associated with excessive water loss and electrolyte loss, which may raise safety concerns. The Fecal Parameters Study memorandum cited by the comment states that the stool water concentration of subjects who reported having diarrhea during the olestra 20 g/d period did not differ from that of their nondiarrheal stools during the placebo period. The memorandum also states that although the percent of water in the stools may not have differed, it is possible that absolute water loss was greater in subjects reporting olestra-associated diarrhea because of the greater mass (weight) of stool passed. FDA concluded in the 1996 final rule that the loose stools experienced in the preapproval clinical studies were not diarrhea in the medical sense because they were not associated with loss of water or electrolytes (61 FR 3118 at 3159). The agency also stated that even those subjects in the 8-week studies who experienced loose stools or diarrhea continuously for several weeks during olestra consumption did not show any evidence of fluid loss such as hemoconcentration or electrolyte imbalance. Thus, the agency determined that olestra-related GI effects were not adverse health effects (61 FR 3159). The results of the Stool Composition Study confirm the agency's 1996 decision that the GI effects resulting from olestra consumption do not represent adverse health effects, regardless of the terminology (diarrhea or otherwise) used to describe these effects.

D. A Study Regarding Nutritional Effects—Active Surveillance

As discussed previously in section II of this document, olestra is neither digested nor absorbed, and as such, passes intact through the digestive tract where it can interact with fat-soluble dietary components present in the gut at the same time. Fat-soluble nutrients and components tend to partition or dissolve into the olestra, thereby reducing the absorption efficiency of these substances (61 FR 3118 at 3144–3149). Olestra does not interfere with the absorption of macro-nutrients (protein, carbohydrates, and fats) or water-soluble nutrients (61 FR 3118 at 3149–3152). The clinical studies conducted in support of the 1996 final rule examining the effect of olestra on fat-soluble components of the diet were performed under conditions that maximized the interaction of olestra with these dietary components, *i.e.*, olestra was incorporated into foods eaten at every meal. These studies were not designed to examine effects from the usual or customary consumption of savory snacks made with olestra (*see* section II.A.3 of this document).

To compensate for the effect of olestra on the absorption of the fat-soluble vitamins A, D, E, and K, FDA required that these vitamins be added to olestra-containing foods. The level of addition was chosen to ensure that there would be neither a reduction in the absorption of fat-soluble vitamins from the diet, nor an increase in vitamin levels due to the presence of the added vitamins in the olestra-containing foods (see section II.A.3 of this document). Although FDA noted that olestra interferes with the absorption of carotenoids, FDA found no scientific basis for requiring the addition of any carotenoid to olestra-containing foods (61 FR 3118 at 3147–3149).

As outlined by the petitioner in its January 24, 1996, letter to the agency, P&G established a program of active surveillance. A report of this surveillance with results and analysis from the first year at the sentinel site was submitted to the agency on April 15, 1998. Additionally, the agency has continued to review and evaluate new data and information that bear on the safe use of olestra, such as new data and information on the health significance of carotenoids.

1. Active Surveillance Study by P&G

The petitioner provided funding to investigators at the Fred Hutchinson Cancer Research Center in Seattle, WA, to design and implement a multi-year, Active Surveillance Study to monitor patterns of use of olestra-containing savory snack products and to collect blood samples to measure nutrient status (Ref. 23). The study had three specific goals: (1) To monitor adoption and patterns of use of olestra-containing savory snack products in representative samples of the U.S. population; (2) to assess the association between the introduction of olestra-containing savory snacks and serum concentrations of carotenoids and fat-soluble vitamins in representative cross-sectional samples of the U.S. population; and (3) to assess the long-term association between consumption of olestra-containing savory snacks and serum concentrations of carotenoids and fat-soluble vitamins among a cohort of olestra consumers.

The study has three components corresponding to the three specific aims. The first component, called the population cross-section, was a telephone survey used to monitor the prevalence and patterns of olestra-containing savory snack consumption,

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

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

[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).

frequency of eating olestra-containing foods was six times per month with a 90th percentile intake total of 70.6 g of olestra per month.

FDA notes the infrequent and small olestra ingestion reported in the study. These reports are drawn from participants' ''real-life'' use of snacks made with olestra. FDA evaluated whether there were changes in serum levels of carotenoids and fat-soluble vitamins from year 0 to year 1 in the clinical cohort. FDA also evaluated whether olestra consumption was associated with changes in serum carotenoid status and fat-soluble vitamins. FDA noted the various changes in serum measures (a drop in total serum carotenoids as well as in concentrations of vitamins A and D, lycopene, lutein, zeaxanthin, and an increase in beta-cryptoxanthin) seen in the clinical cohort group from year 0 to year 1. FDA also noted that there is a lack of association in the clinical cohort between olestra ingestion and any nutrient changes, and therefore, the changes are unlikely to be caused by olestra consumption (Ref. 24).

2. Comments Regarding the Active Surveillance Study

FDA received comments about the Active Surveillance Study. FDA considered these comments and responds in the following paragraphs.

(Comment 9) Comments from CSPI and academia to the current petition asserted that P&G's Active Surveillance Study showing that olestra consumption produced no change in carotenoid levels provides little useful data because the subjects consumed only small amounts of olestra. CSPI stated that study subjects consumed no more than 2 g of olestra/day (approximately one-fourth to one-fifth of a serving of an olestra-containing snack per day) and only about 15 percent of adults in the study ate at least one olestra-containing snack per month. The comment from academia stated that any assumption about the effects of olestra on blood carotenoid levels should be based on the strong likelihood that at least some individuals will consume 1 to 4 oz of olestra-containing potato chips on a daily basis, the effects of which are addressed in the preapproval studies.

The Active Surveillance Study is only one piece of information in the current petition. It was designed to assess the effects of olestra consumption on serum carotenoids and fat-soluble vitamins under customary or usual consumption conditions. As such, it complements the preapproval studies, which were conducted using consumption scenarios designed to assess the safety of olestra's effects on serum carotenoids and fat-soluble vitamins. The highest dose of olestra consumed in the preapproval studies was 32 g/d, which is equivalent to eating approximately 4 oz of olestra-containing chips; in contrast to the Active Surveillance Study, in the preapproval studies olestra was consumed in a variety of foods for which it is not approved for use. FDA noted in the 1996 final rule that it was likely that olestra's effects on carotenoid absorption would be substantially less than those observed in the 8-week studies (61 FR 3118 at 3149). Under the conditions of the 8-week studies, which were designed to assess safety, FDA found supplementing olestra with vitamin A to compensate for the provitamin A function of beta-carotene addressed the possible safety concerns about carotenoid loss in olestra-containing foods. The comments provide no evidence to contradict FDA's 1996 conclusions.

FDA agrees that P&G's active surveillance did not identify high levels of olestra consumption. Importantly, however, the levels of olestra consumption identified in P&G's Active Surveillance Study provide information about customary or usual consumption which is relevant to the labeling issue raised by this petition.

E. Consultations and Literature Review Regarding Nutritional Effects

FDA considered data and information that became available after the 1996 decision in assessing whether the scientific understanding of the possible human health benefits of carotenoids has changed since FDA's 1996 decision, and whether new information should be reflected in the label statement.

The petitioner conducted a literature review of all peer reviewed articles published between January 1996 (when the 1996 final rule was published) and May 1998, just prior to the FAC meeting, concerning possible health effects of carotenoids. This review included more than 200 references to carotenoids and their possible role in human health (Refs. 25 and 26). The petitioner's conclusion was that the reviewed data did not establish that consumption of carotenoids confers protection from disease.

FDA considered data and information discussed at the 1998 FAC meeting. The petitioner presented its review of the scientific literature on carotenoids and human health. The petitioner sponsored a study that was presented to the FAC that found no significant association between macular pigment density with olestra intake. The researchers testified that the relationship between the carotenoid-rich macular pigment and the disease process was yet to be understood.[34]

At the FAC, the petitioner called upon Dr. Gilbert Omenn [35] to present results from intervention studies with beta-carotene.[36] These studies indicated that there was an association between beta-carotene intake and increased risk for lung cancer within the study groups.

During the open public hearing portion of the FAC meeting, a number of individuals that the petitioner invited as experts spoke about the potential role carotenoids play in human health and expressed the view that carotenoids do not explain the cancer preventive effect of fruits and vegetables.[37]

At the FAC meeting, CSPI, and the individuals they called upon as experts, asserted that a consensus had been developing among the scientific community that carotenoids are likely to reduce the risk of certain chronic diseases. For example, Dr. Graham Colditz of Harvard Medical School said that a low intake of carotenoids is associated with an increased risk of cardiovascular disease and certain cancers.[38]

Most members of the FAC expressed the view that epidemiological data show a decreased risk for certain chronic diseases and cancer with increased intake of fruits and vegetables. The increased intake of fruits and vegetables is associated with an increased serum level of carotenoids (which are a component of fruits and vegetables), but it is yet to be determined what, if any, specific role carotenoids play, and at what level they may be required in the diet.[39]

The Panel on Dietary Antioxidants and Related Compounds, Food and Nutrition Board, Institute of Medicine (IOM), National Academy of Sciences (NAS) published a report in 2000 (Ref. 27). The panel that produced the report considered dietary antioxidants and other compounds to assess the required daily intakes for these nutrients. The NAS panel noted that there is a considerable body of research relating blood levels of carotenoids with a lower risk for some chronic diseases. However, the NAS panel concluded that this evidence did not support a requirement for carotenoid intake because the observed effects may be due

[34] Transcript, vol. 2, pp. 197, 201, 210.

[35] At the time Dr. Omenn was Executive VP Medical Affairs and CEO, University of Michigan Health System and was a principal investigator for the CARET study.

[36] Transcript, vol. 2, pp. 154–160.

[37] Transcript, vol. 2, pp. 32–34, 42–44.

[38] Transcript, vol. 2, pp. 233–247.

[39] Transcript, vol. 3, pp. 102–174.

to other factors related to fruit and vegetable intake. Intervention studies designed to test whether carotenoids (specifically beta-carotene) had any direct protective benefits for health did not show any benefit compared to the control (placebo supplement), and indicated that there was an increased incidence in disease (lung cancer) for certain at-risk sub-populations (smokers). The panel did not propose establishing a dietary reference intake (DRI) for beta-carotene or any other carotenoid (Ref. 27).

FDA considered the NAS report on carotenoids and concluded that the evidence concerning carotenoids and the conclusions that could be drawn from the evidence about carotenoids and human health had not substantially changed since the 1996 decision. FDA acknowledges that investigations are continuing on carotenoids to better understand biochemical mechanisms and genetic controls of these substances, and what, if any, role carotenoids have in human health (Ref. 28).

In the fall of 2000, FDA consulted with the NEI for an update as to whether there had been a change in the understanding of the science regarding lipophilic carotenoids and eye health since FDA last consulted with NEI on this question prior to the 1996 final rule (Ref. 29). The NEI said that no specific vitamin or carotenoid had been established as protective against macular degeneration (Ref. 30). The NEI also said that the ongoing ''Age-Related Eye Disease Study'' (AREDS) includes a randomized clinical trial of an antioxidant combination (beta-carotene, Vitamins C and E) or zinc that is evaluating the effect of these nutrients on macular degeneration and cataracts.[40] Other investigations continue to explore the hypothesis that oxidative damage to the retina increases the risk of macular degeneration and that antioxidant nutrients and carotenoid pigments concentrated in the macula may protect against this damage (Ref. 30).

[40] Since FDA's consultation with the NEI in the fall of 2000, the ongoing AREDS study published a report of a randomized clinical trial of an antioxidant combination (beta-carotene, Vitamins C and E) or zinc evaluating the effect of these nutrients on macular degeneration and cataracts (Ref. 31). Results of the study showed that a combination of antioxidants (vitamin C, vitamin E, beta carotene) and zinc reduced the probability for the development of advanced age-related macular degeneration (AMD) in study subjects who were at high risk for developing AMD. The groups given only antioxidants, or only zinc, did not show this reduction in rates of at least moderate visual acuity loss.

F. Consumer Perception Studies of the Label Statement

P&G and Frito-Lay submitted data from studies designed to test consumer understanding of the label statement required by the 1996 final rule as comments to that final rule. Additional reports of testing, conducted after the original comment period for the label statement closed on April 1, 1996 (61 FR 3118 at 3160), were also submitted to the agency. These reports are discussed in the following paragraphs.

1. 1996 Consumer Studies

On April 1, 1996, P&G submitted consumer studies conducted on the label statement required on olestra-containing foods. These studies were completed before olestra-containing foods were available in the marketplace. The petitioner did both qualitative (focus group) and quantitative (mall intercept, detailed questionnaire) testing. The objective of the qualitative research was to determine how consumers comprehended the required label statement and to develop potentially more informative label statement(s) for use in subsequent quantitative research. The objective of the quantitative research was to understand how the required label statement and alternative label statements communicate to consumers, to understand issues raised by the various label statements, and to understand how the label statements affect consumers' understanding of olestra-containing snack foods.

In the qualitative research, three focus group sessions were conducted in each of three cities (total of nine focus group sessions) among adults or teens. Participants saw a realistic product package and several possible versions of the olestra label statement, and were told that a version of these statements might appear on product packages. Participants discussed their impressions of the product and the various label statements in their own words. The group went through each label statement line by line.

In the quantitative research, a detailed questionnaire was presented to 1,726 respondents, adults and teens, recruited at shopping malls at 40 different sites around the country. Respondents were randomly assigned to a group to assess one of four conditions for wording or presentation of the label statement. Respondents were shown the assigned information statement on a realistic product package that included a nutrition facts panel, ingredient list, and other product information. They then answered questions about the product, the information statement, and the effects of olestra.

The petitioner concluded from these studies that the required label statement did not communicate clear and understandable messages to consumers. The petitioner found that most participants in the studies were confused by label statements about both the GI effects and the nutrient effects.

The petitioner asserted that the data demonstrate that consumers, after reading the ''vitamins added'' portion of the required label statement, are left with the impression that eating olestra-containing foods will change their vitamin status. After reading the nutrient statements, some participants inappropriately concluded that olestra is not safe based on presumed vitamin effects. The petitioner stated that the qualitative research indicated that when participants understood that there are no net consequences on vitamins A, D, E, and K, the participants questioned the need for any statement or were suspicious of the statement. The petitioner stated that this study shows that consumers find the concept of nutritional effects and compensatory addition difficult to comprehend without extensive amounts of information. The petitioner concluded from the results of the quantitative studies that a simple label statement indicating that the vitamins in the ingredient statement do not provide a nutritionally significant source best communicates to consumers the fact that there would be no effect on their status of vitamins A, D, E, and K.

Also, the petitioner concluded that the term, ''other nutrients,'' appears to provide no meaningful information to consumers. The petitioner reported that a majority of participants concluded that there were no effects on other nutrients regardless of whether the label statement cited effects on ''other nutrients.'' For those participants who did notice the message, they incorrectly concluded that a variety of nutrients, some known not to be affected by olestra (for example, vitamins C and B) were, in fact, being affected.

The petitioner stated that results from the focus group study on the GI portion of the label statement showed that the currently required label statement may cause consumers to incorrectly attribute GI symptoms to the consumption of olestra, including GI symptoms that olestra does not cause and GI symptoms that are not listed on the label statement. The petitioner said that the research supports the conclusion that the label statement may cause consumers to wrongly attribute symptoms because participants

interpreted the label statement in the context of their experience with other foods that are not labeled. Because there are other foods that cause GI symptoms but are not labeled (*e.g.*, psyllium,[41] wheat fiber, and beans), consumers infer from the olestra label statement that olestra's effects must be worse. The petitioner characterized a typical participant reaction during the focus group testing to be, ''If it's like my other experiences, then why does it have this label?''

The petitioner found that a label statement with an explanation of why olestra might cause GI effects (''Because olestra is not digested, it may cause intestinal discomfort or a laxative effect.'') added significantly to participant understanding. When specific symptoms were mentioned, such as ''loose stools'' and ''abdominal cramping,'' more participants responded that they would expect those GI symptoms, compared to panelists who viewed statements that did not mention specific symptoms. The petitioner also found that general GI symptom terms, such as ''laxative effect'' and ''intestinal discomfort'' communicate the same expectations in GI changes as the specific terms for other GI symptoms, especially for the range of symptoms related to stool changes.

The petitioner also investigated consumer reaction to the boxed configuration of the label statement, and concluded that statements not boxed had less connotation of harm.

Frito-Lay, an interested party and producer of olestra-containing snack foods, also submitted to the agency results from consumer studies on the label statement conducted prior to marketing of olestra-containing foods (sent as comments to Docket No. 87F–0179, dated March 28, 1996, and March 29, 1996). The purpose of these studies was to test the effect and communication value of the required label statement and alternative statements developed by Frito-Lay. The same type of methodology described above for the quantitative assay was used to obtain responses from 1,183 individuals from 5 sites around the country. Respondents were shown a label statement and then asked, based on this label statement, whether they believed that products containing olestra were safe. Frito-Lay said that in response to all the tested label statements, including the required statement, most respondents were uncertain as to the safety of olestra (66 to 71 percent), or thought it unsafe (14 to 19 percent). Because none of the label statements Frito-Lay tested eliminated consumer misconception about safety (including a label statement declaring that olestra has been found safe for consumption by the FDA), Frito-Lay concluded that there should be no special label statement. Additionally, Frito-Lay found that 63 to 65 percent of respondents believed that some people would experience GI discomfort. About half of these respondents said that they would delay going to a doctor if they ate a product containing olestra and then experienced GI discomfort for which they would normally seek medical attention. Additionally, a majority of the respondents (68 to 71 percent) believed that olestra would decrease the level of vitamins A, D, E, and K in their bodies, and a majority believed that other nutrients are affected by olestra.

FDA reviewed the consumer perception studies submitted in 1996 by P&G and Frito-Lay (Ref. 32). FDA noted that the studies were an attempt to evaluate what the olestra label statement communicated to consumers regarding several issues. These issues include the following subjects: (1) The safety of olestra; (2) whether the portion of the label statement about GI effects communicates reasonable expectations about the severity, frequency and duration of potential symptoms, and whether alternate wording or presentations communicate more effectively; and (3) whether the portion of the label statement about the potential nutrient absorption effects of olestra effectively communicates the reason for the addition of vitamins A, D, E, and K, as well as the scope and potential severity of the consequences of eating olestra, and whether alternate wording or presentations communicate more effectively.

FDA found the mall intercept studies to be adequate in methodology and sample size to differentiate between the communication effectiveness of the statements tested, including such changes as alternate wordings, or separation of portions of the label statement. For example, in part of Frito-Lay's quantitative study, participants were asked about the safety of olestra before, as well as after, viewing the test label statement. This use of a question before viewing the label statement serves to measure the impact of the label statement on participants' opinions or whether that opinion was established prior to viewing the label statement. However, the studies were limited to some extent by the choice and wording of questions. For example, P&G's quantitative study did not include, as a control, a ''no information'' statement, so the communication value of simply having a statement on the product package cannot be evaluated.

Regarding the safety of olestra, FDA found that the results of the consumer perception studies conducted by the petitioner and by Frito-Lay show that the label statement is misunderstood by respondents and thought to be a warning about possible health consequences of olestra consumption. FDA notes that Frito-Lay's data demonstrate that there was an increase in the level of concern about the safety of olestra after participants read a label statement. Specific wordings or presentations contributed little to the level of expressed concern. Only when a label statement included wording that FDA has found olestra to be safe for consumption was some of the concern alleviated. FDA also noted that when participants were given the opportunity to respond to the question of whether olestra is safe by opting for ''uncertain,'' a majority chose this response to every label statement examined. When response options were limited to yes or no, the majority chose ''no'' (*i.e.*, not safe).

Regarding GI symptoms, FDA concluded that there was no indication from these studies that consumer expectations about the severity, frequency, or duration of GI symptoms was influenced by specific wording or qualifications on effects or by whether there were any directions about when to contact a physician. There also was no indication from these studies that consumers' expectations about the GI symptoms were influenced by whether the nutrient portion of the label statement was present. Participants tended to use the same words used in the label statement to describe potential symptoms (*i.e.*, loose stools, abdominal cramping), but alternate words to describe certain GI effects (loose stools, more frequent bowel movements, diarrhea) were all understood to mean the same thing. When asked what proportion of the population might experience symptoms, modifiers had little effect on respondents' answers.

Regarding the nutrient absorption portion of the label statement, FDA found that the results of the 1996 consumer perception studies show that the current label statement is not effective in explaining the rationale for and quantitative consequences of adding the four fat-soluble vitamins to

[41] FDA assumes that the term ''psyllium'' refers to the soluble fiber component of the psyllium husk that is the subject of the agency's regulation in part 101 (21 CFR part 101) authorizing a health claim for soluble fiber from certain foods and coronary heart disease (§ 101.81). FDA considers both ''psyllium seed husk'' and ''psyllium husk'' to be common or usual names for this substance, but uses the term ''psyllium'' where it was used by the petitioner or comments.

olestra-containing foods. Respondents' knowledge about olestra's ability to interfere with the absorption of fat-soluble components of the diet was not tested directly, so it is not possible to assess the role that prior knowledge has in respondents' interpretation of the label statement.

The studies demonstrate that consumers do not understand that the addition of the vitamins was intended to produce no *net* effect in the body. The studies also show that respondents tended to believe that the statement about the inhibition of absorption applied to many other nutrients, including those on which olestra has no effect.

Without the absorption statement, somewhat fewer respondents believed that vitamin A, D, E, and K levels would be changed by consuming olestra, but fewer respondents were also aware that olestra reduced the absorption of these vitamins. Even without an absorption statement, substantial fractions of respondents believed that consuming olestra-containing foods would change both fat-soluble and fat-insoluble vitamin levels, presumably because of prior beliefs about olestra. Variations on the wording of the portion of the label statement regarding vitamin absorption and addition made consumers more aware of the vitamin absorption effect of olestra, but none remedied the miscommunication.

FDA concludes, based on this work, that neither the current label statement nor the alternative label statements tested on product packaging clearly communicate to consumers the effect of olestra on vitamin absorption. Without more detailed information or familiarity with olestra, consumers drew inappropriate inferences about the scope and magnitude of the additive's effect on vitamin absorption.

2. 1999 Consumer Studies

In 1998 and 1999, the petitioner conducted quantitative consumer research using a detailed questionnaire, and submitted the study to the agency on April 22, 1999 (Docket No. 00F–0792). The petitioner's stated purpose for this study was to obtain quantitative data on consumer perceptions of the required label statement. Participants were asked to respond to a series of questions regarding safety and GI effects after reading the required label statement.

The petitioner reported that 61 percent of participants thought that the products bearing the required label statement were unsafe.[42] The same percentage believed that the label statement was the government's way of telling them that the product was unsafe. A majority viewed the label statement as a warning, and not as an information statement. After reading the label statement, 83 percent of respondents believed that they could experience symptoms after eating a handful of chips, and approximately a quarter of these respondents would attribute extremely serious symptoms to olestra (severe diarrhea lasting several days, bloody stools, or vomiting lasting up to several days). The petitioner noted that extensive clinical data on olestra show that the additive does not cause such symptoms. The petitioner concluded from the results of this study that the label statement is misleading and conveys messages to consumers that are not consistent with the total body of clinical data on olestra or with FDA's intention in requiring the label statement.

P&G also sought to assess consumer perceptions about the current and alternative label statements. Twenty alternative label statements were tested and rated on a scale of 1 to 9 for the degree of safety perceived from the label statement (1 is ''not at all safe,'' 9 is ''very safe''). For the GI portion of the label statement, P&G reported that respondents' perception of the degree of safety of olestra-containing foods after viewing the alternative GI statements ranged from 3.8 to 6.8. Alternative GI statements that provided a familiar frame of reference (comparison to beans, or onions for example), or that stated that GI symptoms were not a likely consequence, resulted in a greater perception of safety than those statements that provided generalized GI symptom data or context to qualify or describe GI symptoms. In this study, P&G found that the statements that elicited the lowest perception of safety were statements that specified GI symptoms, including those that are in the current label statement. For the nutrient portion of the label statement, P&G reported that more than 80 percent of study participants who read an ingredient declaration statement in which the vitamins A, D, E, and K were marked with an asterisk and accompanied with an explanatory phrase (''not a nutritionally significant source'') and that no longer had the phrase ''other nutrients,'' believed that levels of vitamins A, D, E, and K and other nutrients would not change after eating olestra-containing foods.

P&G also conducted research by a national tracking survey to measure consumer awareness of olestra and to determine whether consumers had concerns about olestra's potential GI effects (Docket No. 00F–0792). Survey results were obtained between January 1998 (just prior to the start of national marketing of olestra-containing foods) and May 1999. P&G reported that the results of the tracking survey showed that population awareness of olestra-containing foods increased substantially during this period (from 38 percent to well over 70 percent). The study also showed that respondents who were familiar with olestra-containing foods were quite concerned about possible GI effects. The percentage of ''aware'' consumers who were at least somewhat concerned about GI effects averaged 74 percent at the beginning of the tracking survey, and 70 percent after national marketing of olestra-containing food was fully underway.

Frito-Lay also conducted new studies on consumer perceptions of the olestra label statement to determine whether that statement was still capable of influencing consumer perception, as it did in 1996 (FAP 0A4708, exhibit 7 and August 13, 1999, Docket No. 00F–0792). Because the 1996 perception study was conducted shortly after FDA's approval of olestra but before availability of olestra in any product on the market, no participant in the 1996 study had eaten a product made with olestra. Frito-Lay therefore considers that the 1996 study showed the effect of the label statement on a ''naive'' population. Since the 1996 study, Frito-Lay points to numerous significant events involving olestra, including the nationwide availability of Frito-Lay products made with olestra, the FAC meeting held by FDA in 1998, and many national and local news stories about olestra. The new testing of the label statement was conducted with the protocol used in Frito-Lay's 1996 studies.

Frito-Lay reported that in its 1999 study, before seeing the required label statement, 64 percent of respondents were uncertain about safety, but only 6 percent said products made with olestra were unsafe. After viewing the label statement, the number of respondents who thought olestra products were unsafe more than doubled. No one who originally thought olestra products were unsafe changed their opinion after viewing the label statement. Frito-Lay presented results showing that only 24 percent of study participants concluded that products made with olestra do not affect the levels of vitamins in the body,

[42] By comparison, in the 1996 survey 45 percent of respondents, after viewing the required label statement, considered products containing olestra to be unsafe (Ref. 33).

and an approximately equal distribution of participants concluded that olestra did or did not affect the absorption of other nutrients.

Frito-Lay concluded from these studies that the olestra label statement did influence consumer perception, much like it did in 1996. Frito-Lay also concluded that consumers still did not understand the various parts of the label statement and viewed it incorrectly as a warning.

FDA reviewed the consumer perception studies of the label statement submitted by P&G and Frito-Lay in 1999 and found them to be similar to the 1996 studies in methodology and types of questions asked (Ref. 33). This set of studies concentrated on the GI portion of the required label statement and perceptions of safety about products made with olestra. As with the 1996 studies, the studies were limited by choice and wording of questions and did not include, as a control, a ''no information'' statement. FDA notes that it is difficult, without careful controls, to distinguish whether a label statement miscommunicates information, is ignored, or is ineffective. Another important limitation to this study is the lack of measurement of initial attitudes toward olestra. Testing of initial attitudes and preconceptions is needed in order to identify the direction of the label statement's effect (*i.e.*, whether the consumer is more accurately informed or not informed).

FDA concludes that P&G's tracking study showed that consumers became more aware of olestra-containing snack foods as products were introduced nationally, and that increasing awareness was accompanied by concern about possible GI effects caused by these products. However, FDA also concludes that the tracking survey does not establish the role (if any) the required label statement plays in consumers' association of olestra-containing foods and GI effects. It cannot be determined from this study whether the rise in product awareness and association with GI effects was due to news reports, advertisements, promotions, or reading the label statement.

FDA concluded that the 1998 and 1999 studies reinforced conclusions from the 1996 studies and support several new conclusions. The new conclusions include the following scenarios: (1) Consumers became more concerned about the safety of olestra-containing products between 1996 and 1998, prior to the introduction of olestra-containing food into national distribution; (2) consumers familiar with olestra-containing snack food (Olean brand name) are very likely to make an association between olestra and possible GI effects; and (3) consumers newly introduced to olestra-containing products by the introduction of Olean brand products into local stores and the accompanying advertising and promotion are just as likely to make the association between olestra and GI effects as those who already knew about Olean products.

FDA notes that the 1998 study gave respondents a choice of ''I don't know'' about safety. Given this option, 45 to 49 percent of participants in the 1998 study chose the response ''I don't know'' when asked about safety, and only 10 to 13 percent of participants in the 1998 study chose the response ''unsafe.'' In contrast, in the 1996 survey, when participants did not have an option to choose ''I don't know'' when asked about safety, 38 to 61 percent of participants chose the response ''unsafe.''

G. 1998 FAC Discussion of the Label Statement

The FAC discussed the required label statement on the last day of the 3-day meeting (June 17, 1998), after new data and information concerning possible GI and nutritional effects were presented and discussed. The FAC was to consider whether, in light of the new data and information concerning the consumption of olestra, the label of olestra-containing products should be changed in any way. The FAC was also asked to consider what factual information, if any, regarding the consequences of consuming olestra-containing products should be disclosed on the product label. FDA began the session by discussing the scope of the agency's authority, under the act, regarding labeling. The sponsor (P&G) made presentations to the FAC, followed by Frito-Lay, and CSPI. The FAC asked questions at the end of each presentation. Following this portion of the meeting, each FAC member was polled regarding the label statement.

Polling the individual members of the FAC about whether the label statement should be changed revealed a wide variation in opinions on the labeling issue.[43] A majority of members, however, did agree that the label statement should be modified in some way in order to make its messages more clear to the consumer. Several members stated that some labeling information about olestra was needed, based in part on their view that olestra-containing foods were still relatively new products and that consumers were not entirely familiar with these products. Some members of the FAC suggested there be a sunset clause on the label statement because after consumers became familiar with olestra, there would no longer be a need for a label statement.

Members made various suggestions for different wordings of the label statement to clarify to consumers the likelihood that olestra would cause GI effects and the nature of those effects. Other members expressed concern that consumers might confuse olestra's effect with more serious GI symptoms. Some members of the FAC concluded that olestra's GI effects did not warrant a special label statement, especially because consumers might mistakenly attribute more serious GI symptoms to the olestra. Other members thought a label statement should include information to tell the consumer to seek medical attention if symptoms persist. Several members said they believed that the current data did not support keeping the portion of the label statement on abdominal cramps.

A majority of the members of the FAC specifically agreed that the portion of the label statement regarding ''vitamins added'' should be removed and replaced with an asterisk following the vitamins in the ingredient listing and a footnote indicating that the added vitamins are not a nutritionally significant source or not nutritionally available. Both P&G and CSPI agreed that this approach was an acceptable and effective way to explain that the presence of the vitamins in the ingredient listing is not meant to imply that these foods are a source of these vitamins.[44]

A majority of members of the FAC agreed that there is no basis, at this time, for adding back any carotenoid, and that the role carotenoids play, if any, in human health is not yet understood. Members did say that the sponsor and the agency should be aware of the evolving understanding of the health effects of carotenoids, and consider that information and its bearing on the use of olestra. Some members expressed reservations about not having any statement on the label about olestra's potential to interfere with the absorption of fat-soluble nutrients such as carotenoids, and suggested that the statement about ''other nutrients,'' might be clarified by changing the phrase to ''nutrients found in fruits and vegetables.''

IV. FDA's Conclusions

A. The Applicable Legal Standard

Under section 409(c)(3) of the act, a food additive shall not be approved if

[43] Transcript, vol. 3, pp. 101–174.

[44] Transcript, vol. 3, pp. 92–93.

such approval would result in the misbranding of a food containing the food additive. Misbranding includes labeling that is misleading because it fails to reveal facts material with respect to consequences resulting from use of the additive under ''customary or usual'' conditions (sections 201(n) and 403(a)(1) of the act). Thus, the data and information of principal relevance to evaluating whether olestra must bear a label that discloses, for example, the possible GI effects of olestra, are those that evaluate the additive's effects when eaten at levels, and in patterns of consumption, that are customary or usual.[45] As the preceding discussion reflects, FDA has considered all of the evidence in the record and has considered the preapproval studies in light of the postapproval investigations reflecting customary or usual patterns of consumption.

FDA does not ordinarily require special labeling on a food that may have consequences of consumption (such as GI effects) when the available information shows that consumers are aware that such food cause the effects. Psyllium husk is an example of an ingredient that may cause GI effects. Consumers are aware of these potential effects because psyllium husk has been used as a laxative. However, FDA's health claim regulation for psyllium husk does not require a label disclosing these effects (§ 101.81). In those situations in which consumers understand the possible consequences of consuming a particular food, information describing those consequences is not new information for consumers and thus, such disclosure would not be material within the meaning of section 201(n) of the act. Thus, information about consumer knowledge of olestra and its potential to cause effects (such as GI effects) is relevant to determining whether labeling is required to prevent misbranding of olestra-containing food.

B. FDA's Conclusions Regarding Gastrointestinal Effects

1. Basis of the 1996 Final Rule—GI Effects

a. *Abdominal cramping.* In 1996, the agency concluded that olestra had the potential to cause abdominal cramping. FDA's conclusion was based primarily on two 8-week studies designed to assess olestra's safety in terms of its potential nutritional effects. These 8-week studies maximized participants' exposure to olestra in order to maximize the additive's possible nutritional effects. Although FDA estimated an intake of 20 g/d for the ''high'' acute consumer of olestra (every day for 12 weeks) (61 FR 3118 at 3124), the highest dose used in these studies (32 g/d) well exceeded this estimate. In addition, in these preapproval studies, olestra was incorporated into savory snacks as well as a variety of foods for which it is not approved for use, and these foods were eaten at every meal for 56 consecutive days. Finally, diets in these studies contained all the ambient levels of fat with no adjustment for the olestra added to the diet. As such, the 8-week studies were not designed to address the effects of customary consumption of olestra-containing snack foods. Based on the information available in 1996, the agency found that there were no safety concerns with the use of olestra in savory snacks.

Although FDA determined in 1996 that the 8-week studies did not reflect conditions of use that are usual or customary for the consumption of savory snacks, there were no other data or information available reflecting the usual or customary use of olestra-containing snack foods. Thus, FDA concluded that it would be prudent to rely on the available data that indicated that under some circumstances olestra had the potential to cause abdominal cramps. Because snack foods containing olestra were new, the agency further concluded that consumers would not know to associate abdominal cramps with these foods. Accordingly, FDA required that products containing olestra bear a label statement indicating that olestra may cause abdominal cramps. The agency imposed the requirement for this label statement because it concluded that consumers were not familiar with the newly approved food additive, olestra, and a label statement would allow consumers to associate GI symptoms they might experience with olestra and preclude unnecessary concern about such effects (61 FR 3118 at 3161).

b. *Loose stools.* In 1996, the agency also concluded that olestra had the potential to cause the GI effect ''loose stools.''[46] The studies on which this conclusion was based are the same studies discussed above on abdominal cramps, *i.e.*, the two 8-week studies. These studies were designed to measure the potential nutritional effects from consumption of olestra-containing foods, and were not designed to address potential GI effects from usual or customary consumption of olestra-containing savory snacks. Nevertheless, in the absence of more specific data, FDA relied on the data from the 8-week studies, which the agency concluded showed that at high doses, olestra increased the potential for loose stools. Accordingly, FDA required a label statement about the potential of olestra consumption to cause loose stools (61 FR 3118 at 3153). FDA believed that information on the label would enable consumers to associate olestra with any GI effects and preclude any unnecessary concerns about the origin of such effects. FDA evaluated the data available in 1996 and concluded that a label statement telling consumers that olestra may cause loose stools was necessary so that olestra-containing food products would not be misbranded within the meaning of section 201(n) of the act. In addition, FDA required the label statement about loose stools because at the time of the final rule, consumers were familiar neither with olestra itself, nor its potential to cause GI symptoms such as loose stools.

2. Data in the Current Petition—GI Effects

Three issues are relevant to determining whether the required statement concerning olestra's potential to cause loose stools and abdominal cramping should be modified: The additional data on olestra's association with these effects under customary or usual conditions of use; research concerning consumer understanding of this portion of the required label statement; and the evidence regarding the status of consumer knowledge of olestra and its potential to cause such effects.[47]

[45] This would be in contrast to the preapproval studies which were designed to assess safety.

In addition, it is critical to recognize that the issue presented by this petition is not whether olestra is safe for use in savory snacks; that issue was addressed in the 1996 final rule. Instead, the question before the agency is what labeling, if any, must be required for foods containing olestra to ensure that they are not misbranded (section 403(a)(1) of the act). Accordingly, the act's ''reasonable certainty of no harm'' safety standard in § 170.3(i) (21 CFR 170.3(i)), does not apply here.

[46] As noted previously, FDA concluded in 1996 that these effects are not adverse health effects.

[47] The agency also reviewed data from the petitioner's Stool Composition Study, which address the safety of olestra (*i.e.*, do the loose stools that olestra may cause constitute diarrhea that would be harmful from a health risk standpoint?). As noted, in 1996, FDA concluded that olestra was safe for use in savory snacks, specifically determining that loose stools caused by consumption of the additive were not ''harm'' within the meaning of the applicable safety standard (section 409(c) of the act; § 170.3(i)). The results of the Stool Composition Study confirm that

Continued

a. *Abdominal cramping.* In 1996, when FDA required the label of foods containing olestra to list the GI symptom ''abdominal cramping,'' it did so on the basis of data generated under conditions that were not customary or usual for savory snack use (see section 201(n) of the act). Since then, FDA has received and reviewed new data and information designed to evaluate olestra's effects under the customary or usual conditions of use for savory snacks. These new data provide no evidence of an increased frequency of abdominal cramps due to the ingestion of olestra in savory snacks. This lack of association is consistently found in several well designed, double-blind, placebo-controlled studies.

Specifically, the Home Consumption Study was conducted under circumstances that more closely reflect the usual and customary conditions of use for savory snacks. As noted, in this study, there was no evidence of an increase in reported abdominal cramping among subjects who ate olestra-containing foods compared to those who ate triglyceride-containing foods. Importantly, the Home Consumption Study had sufficient power to detect differences in the frequency of reported GI effects between the olestra and the triglyceride consuming groups, but such an effect was not found for abdominal cramping. Likewise, results from the Acute Consumption Study showed no difference in the rate or severity of abdominal cramps for the group consuming olestra compared to the group consuming triglyceride. Although CSPI has raised questions about the power of the Acute Consumption Study, the agency believes that the results of that study provide meaningful information that corroborates the findings of the more powerful Home Consumption Study. In addition, these results are confirmed by the Rechallenge Study. That investigation used a population of consumers who had previously reported a GI effect that they associated with eating an olestra-containing snack; in their initial symptom episode, the majority claimed to have experienced abdominal cramps. As noted previously, in the Rechallenge Study, there was no difference in the frequency of reports of abdominal cramps after eating olestra-containing chips when compared to triglyceride-containing chips. Finally, the results of the Stool Composition Study are consistent with outcomes of the foregoing three studies. In this study, although there was an increase in the percentage of symptom days for abdominal cramping, with increasing olestra dose, the difference was not significant. Accordingly, FDA concludes that consumers of olestra are no more likely to report abdominal cramping than are consumers of triglyceride chips under normal use conditions.[48]

FDA has also evaluated information about whether the current olestra label statement communicates effectively to consumers (*see* section III.F of this document). In general, evidence from consumer perception studies shows that after reading the required label statement, a majority of consumer participants did not correctly understand the nature, severity, or frequency of possible GI effects as a result of consumption of an olestra-containing snack. Although FDA's purpose in requiring the label was to provide information to consumers, most of those surveyed viewed the label statement as a warning and thus drew inaccurate conclusions about olestra's safety. Accordingly, FDA concludes that the required label statement is not an effective means of communicating accurate information to olestra consumers.

The new data and information that the agency has received since the 1996 final rule provide no evidence of an increased frequency of abdominal cramps when olestra-containing foods are consumed under the customary or usual conditions of use for savory snacks (*see* section 201(n) of the act). As discussed previously, this lack of association is consistently found in several well designed, double-blind, placebo-controlled studies. Accordingly, FDA finds that there is no scientific basis to support a statement on the label of foods containing olestra that olestra consumption may cause ''abdominal cramping.''

b. *Loose stools.* As noted, prior to the approval of the use of olestra for savory snacks and their subsequent marketing, consumers had little knowledge of, and no experience with, olestra. Since the 1996 decision, the agency has received additional data about olestra and the nature and frequency of loose stools; these new data better reflect the conditions of use that are customary or usual for savory snacks. FDA has found that olestra may increase the frequency of loose stools and bowel movements but that the magnitude of the increase is minor and the severity and impact of these effects on daily activity are not different from other foods that may cause an effect such as loose stools. In addition, the record before the agency shows that consumers are now familiar with olestra's potential to cause loose stools.

In particular, the Home Consumption Study found that consumers of olestra-containing chips experienced a small but measurable increase in more frequent bowel movements and loose stools compared to those who ate triglyceride-containing chips. Because of the number of subjects enrolled (3,181), and the length of time for the study (42 days), the study was able to detect small differences in the frequency of symptoms. Importantly, the absolute incidence of these reports was low, especially relative to the background rate of reported symptoms. Analysis of the reported incidence of severity did not show any difference between the olestra and triglyceride groups. The study showed no increase in the use of medications or physician visits associated with olestra consumption. FDA's analysis of the study showed that consumers who reported a GI event moderated their consumption of chips. Assessments by participants of a symptom's effect on the ability to carry out normal activities showed little if any impact on the daily life of subjects. There was no increase in the percentages of reported severe impairment in performing daily activities in the olestra group compared to the control group. There was no evidence that these effects (loose stools, more frequent bowel movements) were more severe or had any different impact on consumers' daily activities than those associated with similar foods made with fat.

Results from the Acute Consumption Study and the Rechallenge Study are consistent with the results from the Home Consumption Study. Specifically, the Rechallenge Study showed that under the conditions of the study, the incidence of reports of diarrhea or loose stools after exposure to olestra or to triglyceride chips did not differ. The incidence of diarrhea was 6 percent for the olestra group, 8 percent for the triglyceride group; the incidence of reports of loose stools was 5 percent for the olestra group, 7 percent for the triglyceride group. Subjects who had previously reported a GI effect (including loose stools and abdominal cramps) after consuming olestra were no more likely to report GI symptoms after eating olestra chips than those eating

olestra does not cause diarrhea but simply adds bulk and softens the stool.

[48] FDA reviewed a number of reports from passive surveillance of olestra consumers. As noted in the previous discussion, passive surveillance cannot establish cause and effect, although such information may be useful in supporting hypothesis generation. FDA has not relied upon information from the passive surveillance in reaching its conclusions about the current label statement.

triglyceride chips. Similarly, the Acute Consumption Study showed no difference in the frequency, nature, or severity of GI complaints (including loose stools) between the placebo (triglyceride) and olestra groups after a single, ad libitum eating occasion.

At the time olestra was initially approved and first marketed, consumers had limited awareness of olestra and its potential to cause GI effects. In contrast, evidence gathered in the postapproval consumer perception studies and the tracking survey show that there is currently a high degree of awareness among the public about olestra, including a high degree of awareness of olestra's potential to cause GI effects. Results from a postapproval tracking survey show that consumers became more aware of olestra as products were introduced nationally.

FDA does not have evidence to draw conclusions about the role played by the label statement in creating consumer awareness about olestra's potential to cause GI symptoms. However, as with other products that may cause GI effects but are not so labeled, awareness of the potential to cause GI effects is maintained in the population based on common knowledge and consumer experience. Consumers are accustomed to regulating their diets based on this knowledge and experience. FDA has no reason to conclude that the case for olestra-containing foods would be different.

As previously noted, FDA has evaluated consumer perception studies conducted with the olestra label statement and has concluded that while FDA's purpose in requiring the label was to provide information to consumers, a significant number of consumers perceive the label statement as a warning about possible health consequences of olestra consumption and consider olestra-containing foods to be unsafe.[49] This is contrary to FDA's determination that olestra is safe for use in savory snacks. Thus, the agency believes that the current label does not accurately communicate information to consumers about olestra's potential to cause loose stools.

Since the 1996 final rule, additional data about olestra and the nature and frequency of loose stools have become available. This information does not supersede the previous information, but rather, extends FDA's understanding of olestra under customary conditions of use and its potential to cause loose stools. FDA has found that olestra may increase the frequency of loose stools but the frequency of the increase is minor. FDA also has found that the severity and impact of this effect on daily activity are not different from other foods that may cause an effect such as loose stools.

In addition, the administrative record before the agency shows that consumers are now familiar with olestra's potential to cause loose stools. FDA believes that because there is currently an awareness among consumers about possible GI effects of olestra, and because the potential effects from customary or usual consumption of olestra-containing snacks are relatively insignificant, a label statement concerning loose stools for olestra-containing savory snacks is no longer needed to ensure that the product is not misbranded (sections 201(n) and 403(a)(1) of the act).

C. FDA's Conclusions Regarding Nutritional Effects

1. Basis of the 1996 Final Rule—Nutritional Effects

At the time of the 1996 final rule, FDA found that because olestra is a fat-like material that is not digested or absorbed, it may interfere with the absorption of fat-soluble components of the diet, including the fat-soluble vitamins A, D, E, and K. The agency had evaluated studies performed in humans and animals (61 FR 3118 at 3132–3252), and considered the available information concerning nutritional requirements for various fat-soluble components of the diet. FDA concluded that the addition of vitamins A, D, E, and K (§ 172.867(d)), to foods containing olestra would compensate for any inhibition of absorption of fat-soluble nutrients by olestra. The amount of vitamins added was intended to have no net effect (neither increase nor decrease) on vitamin status of olestra consumers. The agency required that the level of added vitamins be adequate to compensate for olestra's effects on absorption even if the olestra and fat-soluble vitamin are present in the gut simultaneously. Additionally, the agency set the amount of vitamins so that if there is no fat-soluble vitamin present in the gut with olestra, the level of added vitamin would not pose any safety concerns.

The added vitamins A, D, E, and K are required to be declared in the ingredient listing (section 403(i)of the act). In 1996, FDA concluded that this mandatory listing of vitamins A, D, E, and K could mislead consumers by implying that the food would provide significant amounts of these vitamins (61 FR 3118 at 3161). Thus, FDA required a label statement to explain why these vitamins were added and why the food should not be considered fortified, so that olestra-containing food would not be misbranded (sections 201(n) and 403(a)(1) of the act).

FDA required that the label include the statement ''Olestra inhibits the absorption of some vitamins and other nutrients. Vitamins A, D, E, and K have been added.'' FDA did not require a specific statement about carotenoids or any other fat-soluble components of the diet because such a statement could have falsely implied that their decreased absorption was known to be of significance.

2. Data in the Current Petition—Nutritional Effects

Three issues are relevant to determining whether the required statement as to olestra's effects on nutrient absorption should be modified: The additional data on absorption of the added vitamins A, D, E, and K obtained since the 1996 final rule; the current understanding of the nutritional importance of carotenoids and olestra's effect on their absorption; and the research evaluating consumer understanding of this portion of the required label statement.

As to the added vitamins A, D, E, and K, early data from the Active Surveillance Study confirm that, as the agency intended, there is no dietarily significant net loss or gain of vitamins A, D, E, and K due to the consumption of olestra-containing foods.[50]

The early data from the Active Surveillance Study also provide important information regarding olestra and carotenoids. First, these data show that consumption levels of olestra-containing foods are below FDA's original estimates and further, that co-consumption of any savory snack with a carotenoid-containing food is relatively rare. Second, although there are changes in serum measures of certain carotenoids, these changes are unlikely to be the result of consumption of olestra-containing foods because the clinical cohort data reflect no association between the amount of olestra consumed and the changes in serum levels of carotenoids.

As noted, FDA has considered the recent scientific literature pertaining to carotenoids and human health and concluded that the decreased risk of cancer is associated with increased

[49] In fact, these studies show that many consumers attribute certain serious GI effects to olestra, even though there is no evidence of olestra's potential to cause such effects.

[50] There was some indication from the Active Surveillance Study cross-sectional data of a small increase in vitamin K levels in the highest olestra consumers.

consumption of fruit and vegetables generally and that at the present time no specific role of carotenoids (other than the provitamin A function) has been identified.[51] The agency's conclusions are consistent with the recent NAS report (Ref. 27) that determined that there is no basis at present for setting dietary requirements for any carotenoid. Similarly, this conclusion is consistent with the results of recent intervention studies, which show no benefit from treatment with carotenoids over control.[52, 53]

FDA acknowledges that research is continuing and that the scientific community's understanding of the role of carotenoids in human health may evolve as new data emerge. The agency will review new information about the role of carotenoids in human health relevant to olestra use in savory snacks, and if necessary, take appropriate action. At this time, however, FDA concludes that no direct evidence demonstrates that the association between the consumption of diets high in fruits and vegetables and a decreased risk of cancer is due to any single carotenoid or group of carotenoids. Accordingly, FDA has determined that there continues to be no basis to require any label statement about olestra's effects on carotenoids or any other fat-soluble nutrient.

As discussed previously, FDA has also evaluated information about the effectiveness of the current olestra label statement to communicate about olestra's potential nutritional effects to consumers. In general, the evidence from consumer perception studies shows that after reading the required label statement, a majority of consumer participants did not correctly understand olestra's effect on the absorption of fat-soluble nutrients or why vitamins A, D, E, and K would be added to olestra-containing foods. Accordingly, FDA concludes that the required label statement is not an effective means of communicating to olestra consumers.

Although the currently required label statement may be misinterpreted by consumers, FDA still believes that because the presence of the added vitamins must be disclosed as ingredients of olestra-containing foods (§ 101.4(a)(1)), consumers may be misled and believe that such snacks are fortified with the added vitamins. Therefore, in order for olestra-containing foods not to be misbranded, the agency has determined that a statement about the presence of vitamins A, D, E, and K should be required. Accordingly, this final rule requires that the label of foods containing olestra use an asterisk following each of the added vitamins in the ingredient statement which would refer to a statement, ''Dietarily insignificant.'' Such a statement directly addresses the presence of the vitamins in the ingredient statement and closely links the message to the particular vitamin affected.[54] This format and configuration are familiar to consumers because such a configuration has been used previously in the nutrition facts panel. Likewise, as noted, the required wording, ''dietarily insignificant,'' is similar to wording used in other label statements, and thus, is familiar to consumers (§§ 101.60(c)(1)(ii), 101.61(b)(1)(ii), and 101.62(b)(1)(ii)).

FDA further concludes that there is no need for a contextual statement about olestra's effect on the absorption of the vitamins in order to avoid misbranding of olestra-containing foods. Indeed, information from consumer perception studies shows that the 1996 required label's contextual statement about ''some vitamins and other nutrients'' actually tends to mislead consumers and that contextual information is not necessary to understand that olestra-containing foods do not contribute significant amounts of vitamins A, D, E, and K to the diet. In addition, although olestra may affect the absorption of other fat-soluble components of the diet, such as carotenoids, there is no known basis for adding back carotenoids or nutrients other than vitamins A, D, E, and K to olestra-containing food. Finally, there is no representation made on the label about ''other nutrients'' that would require a specific statement about such nutrients. For these reasons, this final rule eliminates the requirement that the label for foods containing olestra include the sentence ''Olestra inhibits the absorption of some vitamins and other nutrients.''

In sum, having considered all of the evidence of record, FDA has determined that the olestra regulation, § 172.867, should be revised to require that vitamins A, D, E, and K listed in the ingredient statement be labeled with an asterisk (appearing as a superscript) following the listing of each of these vitamins, and that the asterisk reference the phrase, ''Dietarily insignificant,'' which shall appear immediately following the ingredient statement.

V. Response to Comments on the Label

In this section, FDA responds to comments not previously addressed in this document. FDA considered these comments and responds in this section of the document.

A. Label Statement for GI Effects

(Comment 10) In comments to both the 1996 final rule and the current petition, Frito-Lay recommended that the statement about the GI effects of olestra be eliminated. Frito-Lay based its recommendation on the results of studies, such as the petitioner's postapproval studies, showing that consumption of snack foods made with olestra produces no meaningful GI effects. Frito-Lay also cited a consumer perception study suggesting that consumers may attribute GI effects to olestra when their symptoms are caused by a more serious condition requiring medical attention. In that study, 58 percent of consumers said they would delay medical attention if GI changes occurred after eating products bearing the olestra label statement. A comment from P&G to the 1996 final rule argued that the label statement is inconsistent with data from the postapproval studies and has the potential to mislead consumers. P&G objected to the suggestion at the 1998 meeting of the FAC that the GI effects statement be amended and subject to a sunset clause, rather than dropped entirely, by arguing that discontinuing the GI effects portion of the label statement would be more consistent with the existing data and prevailing legal precedent.

In contrast, several comments to the 1996 final rule specifically stated that a GI effects statement was warranted but provided no factual evidence or rationale for their recommendation.

FDA agrees that the requirement for a label statement about olestra's potential to cause GI effects should be eliminated. As noted previously, P&G's postapproval studies show that customary or usual consumption of olestra in savory snacks causes only minor GI effects, and that the public is now aware of olestra's potential to cause GI effects. Therefore, the agency has no basis to require a label statement regarding olestra's potential to cause GI effects.

(Comment 11) A comment from CSPI to the current petition stated that instead of eliminating the label statement about GI effects, the statement should be amended to indicate that GI effects may occur in a ''small percentage

[51] The FAC reached the same conclusion in June 1998.

[52] This is true with respect to the NIH/NEI AREDS study, which showed no specific vitamin or carotenoid was protective of macular degeneration.

[53] Indeed, in at least one subpopulation (smokers), treatment with carotenoids was associated with an increased risk.

[54] This asterisk format is supported by P&G, CSPI, and a majority of the FAC members present at the 1998 FAC meeting.

of consumers.'' CSPI asserted that consumers need information on GI effects so that they can learn to associate olestra with possible symptoms and can avoid olestra in the future if such symptoms occur. CSPI also asserted that olestra's GI effects are material consequences that may result from customary consumption and that the label statement would be misleading without a statement about GI effects. CSPI asserts that P&G's two 8-week studies, together with a clinical study published in the *British Journal of Nutrition* [55] (Ref. 34), show an association between consumption of olestra (in the case of P&G) or sucrose polyester (in the case of the study published in the *British Journal of Nutrition*) and GI symptoms. CSPI also stated that the postmarketing studies provide some reassurance that no more than a small percentage of consumers experience GI symptoms.

FDA does not agree that olestra-containing foods should be required to bear a label statement indicating that GI effects may occur in a small percentage of consumers. The standard for determining whether this information must be required on the label is whether the labeling fails to reveal facts that are material with respect to consequences which may result under the conditions of use prescribed in labeling or advertising or under such conditions that are customary or usual (section 201(n) of the act). The fact that olestra-containing foods can cause GI effects under conditions such as those in P&G's two 8-week studies and the study published in the *British Journal of Nutrition* must be considered in light of the data from studies addressing the GI effects associated with customary or usual olestra consumption. As with other foods, GI symptoms may occur in a small percentage of olestra consumers, but the available data show that customary or usual consumption of olestra-containing foods does not cause GI symptoms with a frequency, severity, or impact on daily activity that are different from those from triglyceride snacks. In addition, the agency has determined that consumer perception studies and tracking surveys show that there is a high degree of public awareness concerning olestra and its potential effects. Based on the minor GI effects associated with customary or usual consumption of olestra-containing foods and the public's awareness of the potential for olestra to cause GI symptoms, the agency has concluded that olestra-containing foods should not be required to bear a label statement informing consumers of possible GI symptoms resulting from olestra consumption.

(Comment 12) Several comments to the current petition stated that the wording of the GI effects statement should be changed to indicate that symptoms may be ''severe.'' Many of these comments were from consumers who reported having GI effects that they attributed to olestra. Another comment supported the suggested change by citing consumers' GI effects reported to CSPI.

Comments from CSPI, individual consumers, and manufacturers of baked, fat-free snacks to the 1996 final rule stated that the wording of the GI effects statement should be changed to describe a greater number of potential side effects [56] and to indicate that the side effects could be ''severe.'' Several comments also suggested that the label statement should indicate that symptoms occur ''commonly.'' Some comments cited reports submitted to CSPI and P&G that report severe GI effects after olestra consumption as the rationale for the suggested labeling. CSPI asserted that if all pertinent symptoms are not identified, consumers might continue to eat olestra-containing foods even when GI disturbances are occurring, because many consumers will not make the connection between consumption of the fat substitute and symptoms not specified on the label statement. CSPI reported the results of a telephone survey that showed that 7.4 percent of consumers experienced GI effects or headache after an average of 4.8 exposures to olestra over a 2-month period. CSPI also stated that P&G's two 8-week studies showed that half of the subjects experienced diarrhea or other symptoms during the study. The comment also reported data from a study conducted by Frito-Lay that showed a 9 percent increase in anal oil leakage associated with olestra consumption.[57] CSPI compared the labeling for adverse effects caused by drugs to the labeling of olestra related effects, and argued that because olestra is consumed more widely, at greater amounts, and over longer periods of time than drugs, labeling for effects should be more complete and explicit.

In contrast, a comment to the 1996 final rule from P&G opposed a GI effects statement listing all GI symptoms that may possibly occur following olestra consumption. The comment stated that the clinical data show that the digestive effects of olestra are similar to the effects that consumers experience from eating certain other foods and food products (such as products that contain psyllium or wheat fiber) that are not specially labeled. The comment also stated that olestra's effects are similar to those of other foods that have no impact on daily activities and are not specially labeled.

FDA does not agree that olestra-related GI symptoms should be labeled as ''severe.'' FDA has no basis for concluding that the GI symptoms caused by olestra are severe when olestra-containing snacks are consumed under customary or usual conditions. Moreover, these comments provide no evidence that any severe symptoms were actually caused by olestra. As noted earlier (section III.B of this document), the reports of the type cited in the comments cannot be used to draw conclusions about cause and effect. Furthermore, the Home Consumption Study and the Acute Consumption Study demonstrate that the GI symptoms caused by customary or usual olestra consumption are not severe. In fact, the petitioner's postapproval studies show that customary or usual consumption of olestra in savory snacks causes only a minor increase in the frequency of loose stools.

FDA does not agree that the wording of the label statement should disclose a greater number of potential side effects. As described above, the postapproval studies show customary or usual consumption of olestra-containing foods causes only a minor increase in the frequency of loose stools and bowel movements, and no increase in the frequency of abdominal cramps. The results of the studies do not provide evidence that there are other GI symptoms resulting from customary or usual consumption of olestra-containing foods that warrant special labeling.

[55] FDA notes that this study was a double-blind, placebo-controlled, randomized, cross-over trial in which subjects consumed 20 to 40 g sucrose polyester or triacylglycerol per day. Each treatment was administered for three months. The study included measurements of the effect of each treatment on GI symptoms and plasma carotenoid concentrations. The article does not state whether the sucrose polyester used meets the specifications for olestra. Sucrose polyester was incorporated into chips, beefburgers, meat pies, sausages, sausage rolls, fruit pies, milk, margarine, salad cream, fruit dessert, processed cheese, biscuits, peanut butter, cake, crisps, chocolate spread, and chocolate bars.

[56] In its comments, CSPI suggested that symptoms such as diarrhea, loose stools, increased bowel movements, fecal urgency, nausea, gas, cramps, bloating, anal leakage, yellow-orange underwear staining, greasy bowel movements, yellow-orange discoloration of stools, and oil in toilet appear on the label statement.

[57] FDA believes that CSPI is referring to a marketing study conducted by Frito-Lay. Frito-Lay informed FDA that the execution of the study was flawed. FDA relied on data from the petitioner's safety studies to address the issue of anal oil leakage (61 FR 3118 at 3154–3155).

Based on the results of the postapproval studies, reviewed in light of the preapproval investigations, FDA has determined that there is no longer a basis to require special labeling for loose stools, abdominal cramps, or any other GI symptom.

(Comment 13) P&G stated in a comment to the 1996 petition that the GI effects statement is inconsistent with FDA's handling of psyllium-containing foods. The comment stated that the digestive effects that occur after eating psyllium-containing foods at levels necessary to support the agency's health claim are the same as for olestra, softer fecal contents and more frequent bowel movements, but are likely more pronounced than those that occur after eating olestra-containing foods. The comment stated that no label information related to GI effects is required on psyllium-containing foods.

As explained previously, FDA has concluded that olestra-containing foods should no longer be required to bear a statement about olestra's potential to cause GI effects. Therefore, whether the GI effects statement originally required in the olestra label is inconsistent with the labeling of psyllium husk-containing foods is no longer an issue.

(Comment 14) A comment from CSPI to the current petition objected to P&G's argument that the required labeling of olestra-containing foods is not consistent with the labeling of GI effects from psyllium-containing foods. CSPI argued that the GI effects of psyllium and olestra are different by citing FDA's published statements that psyllium would have no effect on the bowel other than to promote normal function by softening fecal contents and increasing fecal volume (63 FR 8103 at 8115, February 18, 1998) while olestra may cause bloating, loose stools, abdominal cramps, and diarrhea-like symptoms (61 FR 3118 at 3159). CSPI also states that psyllium's mild GI effects would not cause consumers significant discomfort, undue concern, or cause them to seek unnecessary medical treatment. CSPI points out that FDA does require disclosure of the material effects of psyllium consumption, the potential for esophageal blockage from not consuming adequate amounts of fluids. CSPI concludes that the requirement for disclosure of psyllium's material effects, the potential to cause choking, and the fact that disclosure of psyllium's nonmaterial mild bowel-normalizing effects, are not required to be disclosed is consistent with requiring disclosure of the material GI and carotenoid effects of olestra.

FDA determines the need for special labeling on a case-by-case basis. In this case, FDA must consider not only whether the potential GI effects of olestra-containing foods rise to the level that warrant special labeling, but also whether consumers are aware of the potential GI effects associated with the consumption of olestra-containing foods. Customary or usual consumption of psyllium husk-containing foods may cause stool softening effects and increases in stool volume and frequency of bowel movements (63 FR 8103 at 8115). Products containing psyllium husk are not specially labeled for GI effects because FDA believes consumers are aware that psyllium husk is dietary fiber and consumers know the effects of dietary fiber. Therefore, the labels of psyllium husk-containing foods are not required to disclose the stool softening effects and increases in stool volume and frequency of bowel movements associated with customary or usual consumption of foods containing psyllium husk. Based upon data and information obtained since the 1996 final rule, FDA believes that the GI effects of customary or usual consumption of olestra-containing foods are not significantly different from the stool softening effects and increases in stool volume and frequency of bowel movements associated with the customary or usual consumption of psyllium husk-containing foods.[58] In addition, FDA believes that there is now a high degree of awareness concerning olestra and its potential to cause GI effects. Based on the nature of the GI effects caused by olestra-containing foods and the public's awareness of such effects, the agency does not believe that olestra's potential to cause GI effects warrants special labeling.

(Comment 15) A comment from CSPI to the current petition stated that the olestra label statement should advise consumers to contact a health professional if GI symptoms persist because such symptoms may represent a problem more serious than those associated with the consumption of olestra-containing foods.

FDA disagrees with this comment. While FDA agrees that consumers experiencing persistent GI symptoms should contact a health professional because such symptoms may represent a condition more serious than those caused by olestra, a food label is not the proper place to provide medical advice unrelated to the product (61 FR 3118 at 3162). FDA notes, however, that the decision to delete the label statement requirement is consistent with the expressed concern that consumers may erroneously conclude that GI symptoms are related to olestra when, in fact, they are caused by something else.

(Comment 16) Assuming that the label statement would be retained, comments from P&G, Frito-Lay, academia, and several trade associations to the 1996 final rule stated that the wording of the GI effects statement should be changed to indicate that olestra causes a ''laxative effect.'' Comments cited focus group studies showing that the current statement creates unwarranted alarm and implies that the product is harmful. A comment from P&G reported research demonstrating that the phrase ''laxative effect'' was able to communicate the idea of loose stools and was more effective in communicating the range of other possible symptoms than the phrase ''loose stools.'' This comment also stated that the suggested changes are consistent with the views expressed by the FAC at its 1995 meeting. Other comments supported use of the term ''laxative effect'' by arguing that the current label statement is not consistent with the precedent set by the labeling of other food additives that cause similar effects, such as mannitol, sorbitol, and polydextrose.

In contrast, one comment opposed use of the term ''laxative effect'' because it puts olestra in the category of psyllium, and expressed the opinion that olestra does not belong in the same category as psyllium but provided no rationale for the opinion expressed. A comment from CSPI opposed a label statement indicating that olestra is similar to fiber because such a label statement would confuse the public. The comment asserted that although fiber and olestra cause similar GI symptoms, the appearance and disappearance of symptoms are so different that the label statement would be ''highly deceptive.''

FDA does not agree that olestra-containing foods should be required to bear a label statement indicating that olestra causes a ''laxative effect.'' Use of the term ''laxative effect'' in a label statement was discussed in the 1996 final rule. The agency chose not to use the term ''laxative effect'' in the label statement because such use may imply the therapeutic use of olestra as a laxative (61 FR 3118 at 3162). These comments provide no basis for the agency to change its position on this matter. Moreover, given the results of the postapproval studies, FDA believes that there is no longer a basis for requiring special labeling about the potential GI effects associated with customary or usual consumption of

[58] The published statement about olestra's GI effects referenced in the comment by CSPI represents effects seen under the consumption conditions associated with the petitioner's preapproval studies that were designed to demonstrate the safety of olestra.

olestra-containing foods. Therefore, the specific characterization of these GI effects by terms such as ''laxative effect'' is no longer an issue.

(Comment 17) A comment from CSPI to the 1996 final rule stated that olestra causes diarrhea and the word ''diarrhea'' should appear in the label statement. CSPI stated that olestra-related diarrhea meets the criteria established for ''clinical diarrhea'' discussed at the 1995 meetings of the Olestra Working Group (OWG) [59] and FAC. In support of its comment, CSPI quotes portions of the FDA memorandum that discusses data from the preapproval Fecal Parameters Study (Ref. 22). CSPI quotes portions of the memo discussing subjects' ability to distinguish between ''normal,'' ''loose,'' and ''diarrhea'' stool as well as portions of the memorandum discussing water loss through diarrheal and nondiarrheal stools. CSPI states that one of the criteria for ''clinical diarrhea'' discussed at the 1995 meeting of the OWG and FAC was increased water content of diarrheal stool compared to normal or loose stool. CSPI also asserted that in the petitioner's preapproval Oil Loss Study, bowel movements exceeded 3/d for subjects in all the study groups who consumed olestra potato chips while no such increase was reported for subjects who consumed chips with triglyceride. CSPI also reports that some subjects in the preapproval study of patients with inflammatory bowel disease reported an increased frequency of bowel movements. CSPI states that bowel movement frequency exceeding three per day was a criteria for ''clinical diarrhea'' considered at the 1995 meetings of the OWG and FAC. CSPI also quotes an FDA memorandum that reviews a preapproval study of the effect of olestra on intestinal micro flora (Ref. 35). CSPI quotes a portion of the memorandum stating that the projected means for fecal volume for the olestra-fiber consuming groups [60] in the study indicate diarrhea at 24 g of olestra if the strict definition of diarrhea used by research gastroenterologists (200 g/d) is applied.

FDA does not agree that olestra-containing foods should be required to bear a label statement indicating that olestra causes diarrhea. FDA considered the evidence presented by CSPI during the agency's review of the original petition for the use of olestra in savory snacks. Upon evaluation of all of the data considered in the original petition, FDA concluded that the ''diarrhea'' reported by study subjects was not diarrhea in the medical sense because it was not associated with objective measures of diarrhea (*i.e.*, the loss of water or electrolytes) (61 FR 3118 at 3159). Moreover, as discussed previously, data from the petitioner's Stool Composition Study support FDA's 1996 decision that consumption of olestra does not cause medical diarrhea. Therefore, FDA has no basis to require a label statement indicating that olestra causes diarrhea.

(Comment 18) A comment from CSPI to the 1996 final rule stated the group's opposition to any use of the phrase ''excessive consumption of olestra'' in the label statement because P&G's data show that consumption of even modest amounts of olestra can cause GI disturbances. CSPI also opposed labeling indicating that olestra's GI symptoms were ''usually minor,'' arguing that diarrhea is not a minor symptom and that some subjects experienced moderate or severe symptoms.

At the time of the 1996 final rule, FDA believed that it was prudent to rely on the data generated from the safety studies as a basis for requiring labeling to disclose potential GI effects of olestra-containing foods. The data generated from the safety studies did not provide a basis to characterize the frequency of GI symptoms or the consumption levels at which consumers would experience such effects under customary or usual consumption of savory snacks. Data and information obtained since the 1996 final rule examining the effect of customary or usual consumption of olestra-containing foods show that olestra causes only minor increases in the frequency of loose stools and bowel movements, and no increase in the frequency of abdominal cramps. Based on these findings, the agency believes that there is no longer a basis to require a label statement about the possible GI effects associated with the consumption of olestra-containing foods. Therefore, use of specific phrases such as ''excessive consumption of olestra'' and ''usually minor'' in the label statement are no longer at issue.

B. Label Statement for Nutritional Effects

(Comment 19) Comments from CSPI and Frito-Lay to the current petition suggested that the label statement regarding the addition of vitamins A, D, E, and K should be replaced with an asterisk and a phrase such as ''Not nutritionally significant'' because the current statement is confusing. Frito-Lay stated that the suggested labeling will ensure that consumers know the product has not been fortified to provide a nutritional benefit with respect to vitamins A, D, E, and K. Frito-Lay also stated that the vitamin statements should be eliminated from the olestra label because they are widely misunderstood and P&G's postapproval research shows that the added vitamins compensate for any absorptive effect of olestra.

Similarly, comments from P&G, Frito-Lay, trade associations, and academia to the 1996 final rule stated that the statements regarding added vitamins should be dropped from the label. Some of these comments asserted that the added vitamins should be labeled instead in the ingredient list with an asterisk directing consumers to a statement such as ''Not a nutritionally significant source.'' Arguments presented in support of this recommendation were summarized briefly as follows: (1) Consumer studies submitted by P&G and Frito-Lay arguably show that the current label statement is difficult for consumers to understand; (2) quantitative research submitted by P&G shows that the suggested labeling (use of an asterisk and referencing language such as ''Not a nutritionally significant source'') best communicates the fact that olestra will have no net effect on the status of vitamins A, D, E, and K; (3) the suggested label statement is consistent with the views expressed by the FAC at the 1995 and 1998 meetings; and (4) consumers are accustomed to seeing the suggested-type of labeling on the nutrition label for skim milk and some fat-free products; therefore, they are more likely to understand it.

FDA agrees with these comments. As discussed previously, by this final rule, a label statement that explains olestra's potential effects on the absorption of fat-soluble vitamins and other nutrients is no longer required, and information that informs consumers that olestra-containing foods have not been fortified with vitamins A, D, E, and K will be provided through an asterisk and the statement ''Dietarily insignificant'' that will follow the ingredient list of olestra-containing foods.

[59] The OWG was a subcommittee of the 1995 FAC functioning as a special working group on olestra. The OWG was made up of several members of the FAC as well as consultants and indepth review experts who represented scientific disciplines appropriate for the evaluation of a macro-ingredient fat substitute. The OWG met for 3 days (November 14–16, 1995) and reported its findings to the FAC in a meeting on November 17, 1995. The transcripts for the 1995 FAC meetings are available at the Division of Dockets Management (*see* **ADDRESSES**).

[60] FDA notes that subjects in the study were fed breakfast meals daily containing 7 g or 24 g of fiber with 24 g of either olestra or triglyceride for 28 days.

(Comment 20) Some comments to the 1996 final rule suggested specific language changes to the vitamin statements because the statements in the label are too vague or misunderstood by consumers. All of the suggested language changes indicated that olestra interfered with the absorption of vitamins A, D, E, and K and that these vitamins were added to compensate for potential losses.[61] A comment from P&G also suggested that, if the label statement is retained, it should explain why olestra has effects on vitamin absorption.

Based on consumer studies, FDA believes that the current label statement is not an effective means of communicating to consumers that olestra affects the absorption of fat-soluble vitamins or why vitamins A, D, E, and K are added to olestra-containing foods. As part of this rulemaking, the agency has concluded that a statement about olestra's effects on the absorption of fat-soluble vitamins is not needed in order to understand that olestra-containing foods do not contribute significant amounts of vitamins A, D, E, and K to the diet. Therefore, the agency believes that the label statement about olestra's effects on vitamin absorption should be eliminated, not simply re-worded. The agency does, however, believe that the label of olestra-containing foods must communicate that the vitamins A, D, E, and K added to such foods will not change consumers' vitamin status. Accordingly, this final rule requires the use of an asterisk and short explanatory phrase, ''Dietarily insignificant,'' a configuration that will communicate the intended message more clearly than the current statement. FDA notes that the petitioner concluded from consumer studies that the asterisk/statement configuration best communicates to consumers the fact that the vitamins A, D, E, and K added to olestra-containing foods would have no net effect on consumers' vitamin status. It is also a format and configuration familiar to consumers because it is used in the Nutrition Facts panel and is similar to language used in other label statements (§§ 101.60, 101.61, and 101.62).

(Comment 21) A comment from a trade association to the 1996 final rule stated that the vitamin statement should be eliminated because the statement is a nutrient content claim for added vitamins and therefore violates §§ 101.13, 101.54, and 101.9(c)(8)(ii). The comment stated that to satisfy a nutrient content claim for added vitamins, the product must provide an additional 10 percent of the reference daily intake (RDI) compared to a reference food. The comment claimed that vitamin addition to olestra would not always contribute an additional 10 percent of the RDI for the added vitamins; therefore, the vitamin statement violates §§ 101.13 and 101.54. The comment also argued that the label statement violates § 101.9(c)(8)(ii) because any claimed nutrient must be included on the nutrition label. Under the current policy, the vitamins added to olestra are not included on the nutrition label.

Because the olestra label statement will no longer be required to appear on the package of olestra-containing foods, whether the label statement contains a nutrient content claim is no longer an issue.

(Comment 22) A comment from CSPI to the 1996 final rule recommended that the label statement advise consumers not to consume olestra with meals or vitamin supplements because such consumption would maximize nutrient loss. In contrast, a comment from P&G opposed such a label statement. In its comment, P&G cited preliminary data from its Active Surveillance Study showing that consumption of olestra-containing food does not result in any meaningful decrease in serum carotenoids. P&G also stated that the compensation levels of vitamins A, D, E, and K required by the agency are based on data reflecting worst-case consumption scenarios. P&G also noted that the majority of members of the FAC concluded in 1998 that there were no new data showing that olestra will adversely affect health by interference with the absorption of fat-soluble vitamins or other lipophilic substances.

FDA does not agree that olestra-containing foods should be required to bear a label statement advising consumers against consumption of olestra with meals or vitamin supplements. FDA required the addition of vitamins A, D, E, and K to compensate for the known effects of olestra and established compensation levels that would be adequate for those individuals who consume olestra-containing snacks at meals. For carotenoids, FDA concluded in the 1996 final rule that there was no basis to require compensation of olestra-containing foods with specific carotenoids (61 FR 3118 at 3147–3149). Moreover, in its comments, CSPI provided no data to show that customary or usual consumption of olestra-containing snacks with meals or vitamin supplements causes nutrient losses that warrant a statement advising consumers not to consume olestra-containing snacks with meals or vitamin supplements.

(Comment 23) A comment from CSPI to the 1996 final rule stated that the olestra label statement should include information directed toward those using coumarin derivatives to control blood clotting because there are no clinical data in the olestra petition showing that the addition of vitamin K to olestra-containing foods would be safe and efficacious for people who use coumarin derivatives. The comment also suggested that the label statement include information directed toward those with hemophilia or ''other blood diseases.'' A comment from academia also requested that the label statement provide information directed at those taking coumarin derivatives and cited an article in the *New England Journal of Medicine* (Ref. 36) as support for a warning label statement. The comment asserted that olestra's inhibition of vitamin K absorption could result in extreme elevation of prothrombin time and that patients taking this medication would need a careful and more frequent monitoring system to regulate and adjust drug administration. The comment also asserted that safety studies with olestra should be performed in patients taking coumarin derivatives. Another comment requested that the label statement indicate that olestra could cause blood clots, but provided no data or rationale to support this assertion.

One comment opposed the use of ''hemophilia'' in statements directed toward users of coumarin derivatives, stating that vitamin K status is not a factor in hemophilia. The comment also opposed use of the phrase ''other blood diseases'' in any statement directed toward users of coumarin derivatives because it is too vague. The comment also stated that the routine monitoring by physicians of patients taking coumarin derivatives will result in alterations in drug dosing if major and persistent alterations of vitamin K-compensated olestra-containing food intakes are found to influence drug efficacy.

FDA does not agree that olestra-containing foods should be required to bear a label statement directed toward those using coumarin derivatives to control blood clotting. FDA concluded in 1996 that consumption of olestra would not significantly influence the rate or extent of absorption of drugs (61

[61] Two examples of wording suggested by the comments are: ''Because olestra interferes with your body from absorbing certain nutrients and the vitamins A, D, E, and K, these essential vitamins have been added to this product.'' and ''Olestra reduces the absorption of some nutrients, and vitamins A, D, E, and K have been added to compensate.''

FR 3118 at 3132). Further, FDA stated that it did not expect olestra consumption to have a significant effect on the absorption of Coumadin, the most commonly prescribed form of coumarin (61 FR 3118 at 3132). As part of the 1996 final rule, FDA required olestra-containing foods to be compensated with 8 micrograms vitamin K_1/g olestra so that consumption of vitamin K-compensated foods will have no net effect on vitamin K status (61 FR 3118 at 3167). FDA also concluded in 1996 that any change in vitamin K status due to consumption of vitamin K-compensated olestra would likely be within the normal range of dietary variation (61 FR 3118 at 3147). The comments do not provide the agency with any evidence that vitamin K-compensated olestra would cause changes in vitamin K status beyond the normal range of dietary variation or that olestra would affect the absorption of coumarin derivatives. Thus the agency has no basis to require labeling directed to those individuals using coumarin derivatives to control blood clotting.

(Comment 24) A comment from Frito-Lay to the current petition as well as comments from P&G, Frito-Lay, and academia to the 1996 final rule stated that the phrase ''other nutrients'' should be eliminated from the label because the health benefits associated with consumption of fruits and vegetables have not been specifically attributed to carotenoids and consumer perception studies show that consumers are confused as to its meaning. One comment added that current evidence does not show that inhibition of carotenoid absorption has any nutritional significance. One comment stated that this phrase creates a misperception of a lack of safety and serves no purpose because carotenoids are neither specifically mentioned nor added back. P&G and Frito-Lay both reported that data from consumer studies show that the phrase ''other nutrients'' is not informative and may be misinterpreted.

A comment from academia to the 1996 final rule criticized the focus group study submitted by P&G, stating that the participants were not adequately informed about the depletion of blood carotenoids and the evidence relating low blood carotenoids to risks of serious major health outcomes; therefore, this comment concluded that the results of the focus group study are ''specious.''

FDA agrees that the phrase ''other nutrients'' should be eliminated from the label statement. Information from consumer perception studies shows that the label's contextual statement about ''some vitamins and other nutrients'' tends to mislead consumers and the contextual information is not necessary to understand that olestra-containing foods do not contribute significant amounts of vitamins A, D, E, and K to the diet.

In the 1996 final rule, FDA did not require a specific statement on carotenoids because doing so could falsely imply that their decreased absorption is known to be of significance (61 FR 3118 at 3161). FDA determined in the 1996 final rule that the data and information available to the agency do not establish any identifiable nutritional or prophylactic benefits for carotenoids, with the exception of their provitamin A effects (61 FR 3118 at 3149). Thus, FDA does not agree that the results of the focus group studies are ''specious'' because participants were not informed of possible health consequences of decreased levels of blood carotenoids.

(Comment 25) A comment from CSPI to the current petition asserted that the olestra label statement should indicate that olestra consumption may reduce the absorption of carotenoids and that carotenoids may protect against certain chronic illnesses. Alternatively, the comment stated that FDA should require fortification of olestra-containing foods with the relevant fat-soluble carotenoids. The comment asserted that olestra's effect on carotenoid levels is a material consequence that may result from customary consumption and that the olestra label statement would be misleading without a statement about carotenoid loss. The comment cited P&G's two 8-week studies as well as two published articles describing human studies [62] conducted with sucrose polyester and asserted that all of these studies showed substantial decreases in serum carotenoids associated with olestra consumption. CSPI quotes statements from the two published studies conducted with sucrose polyester indicating that the effects of sucrose polyester on carotenoids are undesirable. CSPI also quotes from an invited commentary on one of the studies. The commentary states that the deleterious effects of sucrose polyester should be studied further before it is widely available for long-term consumption (Ref. 38). CSPI also stated that there is growing evidence that carotenoids provide a health benefit, citing studies reviewed by Dr. Graham Colditz at the 1998 FAC meeting and three other research articles submitted to the docket by another comment (Refs. 39 through 41). CSPI added that consumers need information concerning carotenoid absorption because they cannot monitor depletion of their carotenoids, and detection of health changes caused by carotenoid depletion may occur only after irreversible damage has taken place. Finally, CSPI stated that the agency should base its decision on the potential nutritional effects of daily consumption of olestra, as documented by the preapproval clinical studies.

Similarly, in its comments to the 1996 final rule, CSPI suggested that the phrase ''other nutrients'' should be expanded to advise consumers that olestra has been shown to decrease blood levels of carotenoids. The comment also stated that the label statement should include statements about the types of conditions that carotenoids may help prevent, such as cancer and blindness. The comment reported that the majority of carotenoid experts contacted by CSPI agreed that depletion of carotenoids is likely to pose hazards or risk of harm to health. The comment also cites the 1995 edition of the ''Dietary Guidelines for Americans'' issued on January 2, 1996, jointly by the Department of Agriculture and the Department of Health and Human Services. CSPI stated that the guidelines say that antioxidants such as carotenoids are of interest because they may have a beneficial role in reducing the risk of cancer and certain other chronic diseases. CSPI asserts that if evidence of carotenoids' value in protecting health is sufficient to warrant such a statement by the Department of Health and Human Services, it should be sufficient for FDA to inform consumers that olestra depletes carotenoids. CSPI also argued that depletion of carotenoids is a side effect that the public cannot monitor and the public needs information on side effects in order to decide whether to buy olestra-containing foods.

In contrast to CSPI's comments, a comment to the 1996 final rule specifically opposed use of the words ''causing cancer or blindness'' on the label statement because the words put olestra in the category of cigarettes and expressed the opinion that olestra did

[62] One of the articles cited by CSPI is described in section VI.A (Ref 34). The other article cited by CSPI describes two studies (Ref. 37). The first study was a double-blind, placebo-controlled crossover study in which subjects received, through margarine, zero or 12.4 g of sucrose polyester per day for 4 weeks. The second study was a double-blind, placebo-controlled parallel comparison study in which subjects received, through margarine, zero or 3 g of sucrose polyester per day for 4 weeks. Both studies measured the effect of the treatments on plasma carotenoid concentration. The article does not include information (such as specifications) to determine the similarity between the sucrose polyester tested and olestra.

not belong in the same category as cigarettes, but provided no factual information or rationale in support of the opinion expressed.

FDA does not agree that olestra-containing foods should be required to bear a label statement indicating that consumption of these foods may reduce the absorption of carotenoids and that carotenoids may protect against certain diseases, nor does FDA agree that it should require addition of specific carotenoids to olestra-containing foods. Current evidence supports the connection between the consumption of fruits and vegetables (many of which contain carotenoids) and reduced risk for certain diseases. The available data do not, however, establish any identifiable nutritional or prophylactic benefits specifically for carotenoids, either individually or collectively (61 FR 3118 at 3149) other than their provitamin A function. This position is consistent with the conclusions of the 2000 report of the IOM Panel on Dietary Antioxidants and Related Compounds which found no basis for establishing a DRI for beta-carotene or other carotenoids.[63] The 1995 ''Dietary Guidelines for Americans'' recommend healthy dietary habits, including eating fruits and vegetables, but do not present any new scientific information related to possible beneficial health effects specifically attributed to the consumption of carotenoids. Based on the lack of an identifiable nutritional or prophylactic benefit for carotenoids (other than their provitamin A activity), FDA has no basis at this time to require a label statement about carotenoids and their potential health effects or to require the addition of specific carotenoids to olestra-containing foods.[64]

FDA determined in its 1996 final rule that, based on the existing scientific evidence, including the 8-week studies examining the nutritional effects of daily olestra consumption, that there was no justification or need to require compensation of olestra-containing foods with specific carotenoids (61 FR 3118 at 3149). The data and information obtained since the time of the 1996 final rule do not change the agency's 1996 conclusion.

The issue of olestra's effect on carotenoids was discussed by the FAC in both 1995 and 1998. Most members of the FAC agreed in 1995 that the effect of olestra on the bioavailability of carotenoids is not a fact that is material in light of the consequences that may result from consumption of olestra-containing foods and therefore the effect does not warrant disclosure on the label of such foods (61 FR 3118 at 3162). Subsequently, in 1998, a majority of the FAC expressed the view that there were no new data to show that the potential effect of olestra on carotenoids represents a public health concern.[65]

(Comment 26) A comment from academia to the current petition stated that the issue of olestra, carotenoids, and chronic disease should be considered by an impartial body such as the NAS to determine whether there is reasonable certainty that reductions in carotenoid levels will not increase the risk of various diseases. The comment states that the approval process for olestra was flawed because in the first review, the committee did not include cancer or nutritional epidemiologists or other experts who are qualified to review the issue of carotenoid intake and its effect on risk of chronic disease. The comment also stated that in the second review, the committee did not consider evidence considered by the first committee, but only considered new evidence.[66] The comment asserted that since the June 1998 FAC meeting, there have been a substantial number of publications indicating that low carotenoid status may be linked to increased risk for certain diseases and included copies of three published articles on carotenoids.[67] The comment also states the results of a 1996 survey of 13 members of the NAS Committee on Diet, Nutrition, and Cancer who authored the 1982 review of Diet, Nutrition, and Cancer.[68] The survey asked the following questions: (1) ''Are you reasonably certain that carotenoids contained in fruits and vegetables are not related to the apparent benefits of these foods in reducing cancer risk?'' and (2) ''Are you reasonably certain that reductions in blood levels of carotenoids will not increase the risk of cancer?'' The comment stated that seven members answered ''no'' to both questions and that not one member could affirm that they could be reasonably certain that reductions in blood carotenoids would not increase cancer risk. Based on the results of the survey, the comment concluded that the FDA's conclusion of olestra's ''reasonable certainty of no harm'' is not supported by expert scientific opinion. The comment asserted that the effects of carotenoids are poorly understood and we cannot be reasonably confident that reduction in blood carotenoid levels will cause no harm. The comment also stated that the logic that we cannot be certain whether it is the carotenoids in fruits and vegetables that are protective against disease violates the precautionary principle and FDA's guideline of reasonable certainty of no harm because the burden of proof should be on the petitioner to show that carotenoids are not the protective factors in fruits and vegetables.

This comment raises the issue of whether olestra's use in savory snacks is safe (section 409(c) of the act), given the potential effects of olestra consumption on serum carotenoids levels. This issue is beyond the scope of the petition before FDA which concerns labeling. FDA notes that even if the comment is correct that olestra's use in savory snacks is unsafe due to the additive's effect on serum carotenoids, such lack of safety cannot be rectified through labeling. Indeed, as noted, in the 1996 final rule, FDA concluded that olestra is safe for use in savory snacks, a conclusion reached after a review of the evidence in the record concerning carotenoids and human health. If the comment wishes to have FDA consider this safety issue, they must file a citizen petition requesting such consideration, 21 CFR 10.30, not raise it as a collateral issue in this proceeding. FDA addresses the issue of labeling for olestra's effect on carotenoids in its response to the previous comment. FDA addresses the issues raised about the 1995 meeting of the OWG and FAC and the 1998 meeting of the FAC in response to comment 43 of this document.

C. Labeling for Special Populations

(Comment 27) Some comments to the current petition stated that the olestra label should include a statement that olestra-containing foods should not be given to children. One comment stated that olestra should be marketed in childproof containers or the food label should include the statement ''Keep out of reach of children.'' One comment expressed concern that there is a lack of testing and evaluation of olestra in young children, and that even small packages may be a relatively high dose in children when considered on the basis of grams of olestra per kilogram of body weight. Two comments reported

[63] FDA notes that in its report, the panel considered the 1999 research articles referred to by CSPI (Refs. 39 through 41).

[64] FDA notes that the addition of vitamin A to olestra-containing foods compensates for any provitamin A losses caused by the inhibitory effect of olestra on carotenoid absorption.

[65] Transcript, vol. 3, pp. 101–174.

[66] FDA assumes that the first review referred to by the comment is the 1995 meeting of the OWG and FAC and that the second review referred to by the comment is the 1998 meeting of the FAC.

[67] The publications submitted with the comment are the same as those discussed in the previous comment (Refs. 39 through 41).

[68] The survey was conducted in May 1996 by Drs. Walter Willett and Meir Stampfer of the Department of Nutrition, Harvard School of Public Health.

GI reactions of a child who had consumed an olestra-containing food.

CSPI submitted comments to the 1996 final rule requesting that the olestra label contain statements directed toward certain populations of consumers. In particular, CSPI stated that the label statement should contain special notification for children and for the elderly because olestra is poorly studied in children and there are inadequate data regarding the possible hazards of olestra consumption over both the long and short terms. The comment also quoted a 1995 FDA review memorandum of the petitioner's preapproval Fecal Parameters Study which expresses concern for two populations not represented in the study, the elderly and young children, because of the potential for increased water loss through the stool of subjects reporting olestra-associated diarrhea (Ref. 22). CSPI also stated that the label of olestra-containing foods should include statements directed toward pregnant women because there are inadequate data regarding the safety of olestra for use by pregnant women. CSPI suggested that the label statement indicate that those with inflammatory bowel diseases, irritable bowel diseases, and malabsorption disorders should contact a physician before eating olestra-containing foods because, in CSPI's opinion, the study of inflammatory bowel disease patients was too small and too brief to determine conclusively that olestra is safe for people with these illnesses.

FDA does not agree that the agency should require olestra-containing foods to bear a label statement directed toward special populations. In the 1996 final rule (61 FR 3118 at 3156–3157), the agency stated its conclusion that olestra was safe for use by children. Three studies submitted in support of the original petition reported GI symptoms in the young. FDA noted that GI symptoms seen in children were similar to those seen in the 8-week studies of adults. FDA concluded that the safety of olestra for use by children could be addressed by extrapolating the GI effects in adults to the young. This approach was fully consistent with the expert views provided by the OWG and the members of the FAC. Further, the petitioner's Home Consumption Study submitted in support of the current petition shows no olestra-related effects in the group of subjects younger than 18 years (Ref. 15). The comments provide the agency with no new data to show that olestra-containing foods should not be consumed by children, or should be specially labeled or packaged for children.

Similarly, FDA does not agree that olestra-containing foods should be required to bear a label statement directed toward the elderly. The agency is not aware of any safety issues specific to olestra-consumption by the elderly, nor does the comment provide evidence of such issues. Since submission of this comment, the agency has received several postapproval studies from the petitioner that have included subjects over the age of 65. These studies have not identified any concerns specific to the elderly that would require specialized labeling.

FDA does not agree with CSPI's conclusion that the agency's memorandum (Ref. 22), should drive the overall conclusion about the effects of consumption of olestra-containing food on children and the elderly. The agency considered this memorandum in its analysis of the original food additive petition on olestra (61 FR 3118 at 3155). In the 1996 final rule, FDA concluded that the Fecal Parameters Study showed there is no difference in stool composition (*e.g.*, water and electrolyte content) between those olestra-consuming subjects who reported diarrhea and those who did not (61 FR 3118 at 3155). In its overall conclusions on the effects of olestra on the GI tract, the agency stated that even those olestra-consuming subjects in the preapproval studies who experienced loose stools continuously for several weeks did not show any evidence of fluid loss, such as hemoconcentration or electrolyte imbalance (61 FR 3118 at 3159). Since publication of the 1996 final rule, P&G submitted the Stool Composition Study, which examined the effect of olestra on the water content of stools. The Stool Composition Study used a dose of olestra that was greater than the highest dose used in the Fecal Parameters Study and collected stools from study subjects for a longer period of time. As discussed previously, based upon the agency's evaluation of the Stool Composition Study, FDA has concluded that the GI effects observed are not clinically significant (Ref. 18), and that the stools study subjects characterized as ''diarrhea'' were not associated with an increase in stool water (Ref. 10).

In addition, FDA does not agree that olestra-containing foods should be required to bear a label statement directed toward pregnant women. FDA concluded in 1996 that olestra is safe for its intended use in savory snacks (§ 172.867). FDA has no basis to conclude that there are consequences associated with the consumption of olestra that are specific to pregnant women. Importantly, the comment provides no information to demonstrate that olestra-containing foods present a unique risk to pregnant women.

Finally, FDA does not agree that olestra-containing foods should be required to bear a label statement directed toward those with inflammatory bowel disease, irritable bowel disease, or malabsorption disorder. Once again, the comment provides no evidence to establish that there are consequences of olestra consumption specific to patients with inflammatory bowel disease, irritable bowel syndrome, or malabsorption disorder, that warrant special labeling. Moreover, FDA considered data regarding inflammatory bowel disease at the time of the 1996 final rule. In particular, P&G conducted a study to address concerns as to whether the presence of olestra in the GI tract exacerbates the disease state of patients with inflammatory bowel disease. FDA acknowledged that the study of inflammatory bowel disease patients was limited in size and duration (61 FR 3118 at 3155–56). The study does, however, provide reassurance that consumption of 20 g olestra/d for up to 31 days did not cause an observable effect in populations with inflammatory bowel disease. In addition to this human study, the petitioner conducted studies to assess the potential for increased absorption of olestra in guinea pigs with compromised GI tracts containing lesions similar to those seen in ulcerative colitis and Crohn's disease. The studies showed that the absorption of intact olestra is no greater in guinea pigs with compromised GI tracts than in guinea pigs with normal GI tracts (61 FR 3118 at 3126–3127).

(Comment 28) One comment from an individual consumer to the 1996 final rule expressed concern that it is important for diabetics to know that sucrose is part of the olestra molecule.

FDA disagrees with this comment. As discussed in the 1996 final rule, olestra is a chemical combination of sucrose with six, seven, or eight fatty acids (61 FR 3118 at 3118). While olestra is made from nutritive ingredients, only a minuscule amount of olestra is absorbed by the body (61 FR 3118 at 3120 at 3126–3127), and therefore, most of the sucrose present in olestra is not biologically available. Similarly, FDA noted that rats administered the formulation of olestra proposed for human consumption absorbed only 0.14 percent of the administered dose (61 FR 3118 at 3126). Thus, at most, only trivial amounts of sucrose could be obtained from the ingestion of olestra. FDA concluded in 1996 that all safety issues regarding olestra had been addressed

adequately and that the use of olestra in savory snacks is safe (61 FR 3118 at 3168). The comment provides no evidence that the small amount of sucrose potentially obtained from olestra is hazardous to diabetics or warrants disclosure on the food label. Therefore, FDA concludes that there is no basis for the agency to require that the label of olestra-containing foods disclose that olestra is made from sucrose.

D. Label Statement in Its Entirety

(Comment 29) Frito-Lay and P&G submitted comments stating that the olestra label should be eliminated in its entirety and that the added vitamins should be labeled in the ingredient list with an asterisk and a statement such as ''*Not a nutritionally significant source.'' The comment from P&G to the 1996 final rule reported the findings of an expert panel it convened to examine whether the label statement should be maintained. The comments from both Frito-Lay and P&G provided arguments for the elimination of the GI and nutritional effects statements. FDA responded to these arguments in the previous sections discussing comments on the GI and nutritional effects statements. Both comments argued that the current scientific evidence does not support retention of the label statement and that the label is misleading. Frito-Lay also pointed out that the sentence ''This product contains olestra.'' is not needed in the label statement because olestra is listed in the ingredient statement, and manufacturers that use olestra generally place the logo of the olestra brand name, Olean, on the front panel of olestra-containing foods.

In contrast, a comment from CSPI to the current petition supported the retention of a label statement. In its comment CSPI proposed the following label statement enclosed in a box:

THIS PRODUCT CONTAINS OLESTRA. Olestra may cause abdominal cramping and loose stools in a small percentage of consumers. If you experience adverse effects that may be caused by olestra, call 1–800–OLESTRA. If your symptoms persist or are severe, contact a health professional. Frequent consumption of olestra may reduce your body's absorption of fat-soluble nutrients (carotenoids). Carotenoids, found in fruits and vegetables, may protect you against certain chronic illnesses.[69]

CSPI argued that a nondescript declaration of the word ''olestra'' in the ingredient listing does not inform consumers of the side effects of consuming olestra, and unless consumers are aware of the potential side effects, they would have no reason to consult the ingredient list to determine if a food contains olestra. CSPI asserted that a similar concern was raised about the use of the terms ''pasteurized'' or ''unpasteurized'' in the preamble to the final rule requiring warning label statements for unpasteurized juices (63 FR 37030, July 8, 1998). CSPI pointed out that the final rule stated that some consumers do not know the significance of pasteurization and therefore would not be able to make an informed decision on whether to purchase and consume the products and that use of the term ''pasteurized'' or ''unpasteurized'' alone would not give consumers information about the risks presented by untreated juices (63 FR 37030 at 37034). CSPI noted that the final rule for labeling of unpasteurized juices argues that the presence of some pathogens that have been responsible for recent outbreaks of food borne illnesses associated with untreated juice products is a relatively new phenomenon. Therefore, consumers do not associate such pathogens and the risks they present with the consumption of untreated juice (63 FR 37030 at 37032–33). CSPI asserted that label statements for olestra are necessary to inform consumers of the unexpected, potential consequences of consuming foods that have long been consumed without adverse effects and that simply disclosing the presence of olestra in the ingredient statement does not inform consumers of olestra's potential side effects.

FDA agrees with the comments from Frito-Lay and P&G that olestra-containing foods should no longer be required to bear a label statement. FDA concluded in the 1996 final rule that olestra was safe for its intended use in savory snacks. As part of the 1996 final rule, FDA required a label statement to appear on olestra-containing foods. The label statement was required to inform consumers of the potential for olestra to cause GI effects and because consumers had no experience with this food ingredient. The label was also required in order to prevent consumers from erroneously concluding that the vitamins added to olestra-containing foods would contribute significant amounts to their diet when, in fact, these vitamins were added to offset any vitamin losses caused by the consumption of olestra-containing foods. The rationale used in the labeling of untreated juice products cannot be directly applied to the labeling of olestra-containing foods because untreated juice products were labeled to warn consumers of potential health hazards such as serious illness, while olestra-containing foods were labeled to inform consumers of potential effects that do not represent health hazards.

In determining the wording of the warning statement for unpasteurized juices, FDA determined from focus group research that most participants had a good understanding of what pasteurization was, but a significant number of participants did not (63 FR 37030 at 37034). The agency also concluded that use of the terms ''pasteurized'' or ''unpasteurized'' alone would not give consumers information about the risks presented by untreated juices (63 FR 37030 at 37034). In contrast, as discussed previously, postapproval consumer perception studies and tracking surveys show that there is currently a high degree of awareness about olestra and its ability to cause GI effects. Indeed, it appears that consumers are more likely to overestimate rather than underestimate the potential for olestra to cause GI effects. FDA does not typically require label statements for products that may cause GI symptoms when consumers are aware that such foods may cause such effects. As noted in the response to previous comments, FDA does not believe that the label of olestra-containing foods should be required to contain information about the effect of olestra on serum carotenoid levels. FDA will require that vitamins A, D, E, and K added to olestra be labeled in the ingredient list with an asterisk and the phrase ''Dietarily insignificant'' to prevent consumers from being misled to believe that the added vitamins contribute significant amounts to the diet.

(Comment 30) Many comments to the current petition specifically stated that olestra-containing foods should bear a label statement. Most of these comments were from consumers who reported experiencing GI reactions that they associated with consuming olestra-containing foods. One comment stated that the label statement was important in identifying the cause of their GI symptoms. Another comment expressed concern that there is insufficient knowledge about olestra. Another comment stated that a side effect such as severe abdominal cramping and diarrhea should be made known to

[69] FDA notes that since the 1996 final rule, CSPI has submitted several versions of a suggested label statement. The version presented is CSPI's most recent version. Previous versions are generally characterized as including a greater number of possible GI symptoms, statements about olestra's effect on the absorption of vitamins A, D, E, and K, statements that loss of carotenoids may increase the risk of certain health conditions, and statements directed toward special populations (such as children, patients taking Coumadin, and those with bowel disorders).

people who consume olestra, because such symptoms can have significant clinical effects on patients with many different medical conditions.

In addition, some comments to the 1996 final rule specifically stated that olestra-containing foods should bear a special label statement. One comment stated that the label statement required by the 1996 final rule is clear and should be retained. One comment supported the need for labeling by citing reports from a number of constituents who had consumed olestra-containing foods and had experienced severe GI reactions that they believe were caused by olestra. Other comments requested that olestra-containing foods bear a label statement so that these products can be avoided.

As explained previously, FDA has concluded that olestra-containing foods should no longer be required to bear a label statement. FDA does not agree that it should require special labeling for olestra-containing foods on the basis that consumers are not familiar with olestra and the potential GI symptoms it may cause. In reaching its decision on this food additive petition, FDA considered the public's awareness of olestra's potential to cause GI effects. As stated previously, the postapproval consumer perception studies and the tracking surveys show that there is currently a high degree of awareness about olestra and its potential to cause GI effects. FDA does not typically require special labeling of products that may cause GI symptoms when consumers are aware that such foods may cause such effects. FDA notes that, even in the absence of the label statement, consumers who wish to avoid olestra will still be able to identify olestra-containing foods because olestra is required to be declared in the ingredient list of such products.

The agency concluded in 1996 that olestra was safe for use in savory snacks and that olestra's GI effects were not adverse health effects (61 FR 3118 at 3159). The comments reporting GI reactions provide no basis to conclude that the GI symptoms reported are actually caused by olestra. The new data and information submitted by the petitioner show that customary or usual olestra consumption causes no increase in the frequency of abdominal cramps and only a minor increase in the frequency of loose stools and bowel movements and that these effects do not have a meaningful impact on daily activity. Moreover, the petitioner's most recent studies show that the label statement could be misleading and cause consumers of olestra to attribute serious problems to olestra when this is unlikely to be the case.

(Comment 31) Some comments from individual consumers to the current petition stated that olestra-containing foods should bear a label statement because the public has a right to know about the potential side effects of olestra-containing foods.

FDA notes that the act does not provide the agency with the authority to require labeling simply because consumers appear to want such information. (*See Stauber* v. *FDA,* 895 F. Supp 1178, 1193 (N.D.Wisc. 1995); *Alliance for Biointegrity* v. *Shalala,* 116 F. Supp 166, 179 (DDC Sept. 29, 2000).) FDA could require the suggested labeling if, without such labeling, the product labeling failed to reveal facts that are material in light of the consequences which may result from the conditions of use prescribed in the labeling or under conditions of use that are customary or usual.

(Comment 32) A comment from Frito-Lay to the 1996 final rule stated that the label statement should contain only a message directing consumers to a telephone number for more information instead of the current label statement. The Frito-Lay comment cited a consumer study showing that none of the label statements evaluated in the study eliminated consumer misperception and that consumers interpreted the current label statement as a safety warning. The comment concluded that this type of labeling, however worded, has a strong negative effect on the consumer's perception of the safety of olestra-containing foods. In a comment to the 1996 final rule, P&G stated that as an alternative to the nutritional effects statement or the labeling of the added vitamins in the ingredient list with an asterisk, the agency could consider requiring manufacturers to provide a telephone number for consumers to obtain nutritional information. In its comments to both the current petition and the 1996 final rule, CSPI stated that the label statement should include a telephone number for consumers to obtain more information or to report adverse effects.

FDA does not agree that it should require the labeling of olestra-containing foods to include a telephone number. As explained previously, FDA has concluded that olestra-containing foods should no longer be required to bear a label statement and that vitamins A, D, E, and K required to be added to olestra-containing foods should be labeled in the ingredient list with an asterisk that refers to the statement ''Dietarily insignificant.'' FDA is requiring this labeling to ensure consumers understand that such foods do not contribute significant amounts of the vitamins A, D, E, and K to the diet. FDA does not agree that it should require manufacturers to provide a telephone number in place of this information. FDA believes that there is no basis to require that the label for olestra-containing foods include a telephone number for consumers to obtain more information or report adverse effects, nor do the comments explain why such a number is necessary to prevent the misbranding of these foods. FDA recognizes that some firms voluntarily include telephone numbers on their food labels. For those products that do not contain a telephone number, consumers may obtain more information or report adverse effects by contacting the company using the company's name and address, both of which are required to appear on the food label in accordance with § 101.5.

E. Data and Information Considered in This Rulemaking

(Comment 33) A comment from CSPI to the current petition stated that the postapproval studies should be considered, but they should not supersede or override the preapproval studies. The comment asserted that the postapproval studies are not a reason to reject all the previous evidence that olestra can cause GI symptoms. The comment also asserted that the lack of adverse effects reported during P&G's postapproval studies may be due to the small doses of olestra consumed, relative to the preapproval studies, and that rules should be based on the possibility that a greater number of olestra-containing foods would be consumed more frequently in the future. CSPI also stated that the postapproval studies cannot disprove that olestra-containing foods cause adverse effects in a small percentage of consumers.

In deliberations on this petition, FDA has considered all evidence of record (including both preapproval and postapproval studies). The agency notes that the petitioner's postapproval studies are meant to complement, not supersede, the preapproval studies. The preapproval studies were designed to address safety while the postapproval studies were, with the exception of the Stool Composition Study, designed to address labeling.

FDA's 1996 decision to require special labeling of olestra-containing foods was based on preapproval studies which were designed to address the safety standard for food ingredients—reasonable certainty of no harm under the intended conditions of use (§ 170.3(i)). These studies examined the

effect of conditions of use that did not reflect expected intake and thus, do not provide information about the effects of olestra consumption under customary or usual conditions. In contrast, the petitioner's recent Acute Consumption Study, Home Consumption Study, and Rechallenge Study more closely address the factual predicate of the legal standard for requiring special labeling—facts that are material with respect to consequences which may result under the conditions of use prescribed in labeling or advertising or under such conditions of use that are customary or usual (section 201(n) of the act). Thus, FDA concludes that the petitioner's preapproval studies should be considered, but they must be considered in light of the postapproval studies which more directly address whether olestra-related effects warrant special labeling.

During FDA's review of P&G's petition for the use of olestra in savory snacks, FDA assumed that olestra-containing foods may be consumed more frequently than they are presently. For example, when estimating daily intake of olestra from savory snacks, the agency assumed that all savory snacks consumed would be olestra-containing savory snacks (61 FR 3118 at 3125). Such conservative assumptions are likely to over-estimate consumption.

Olestra is currently approved for use as a fat substitute only in ready-to-eat savory snacks. Any additional use will require agency approval through the food additive petition process in accordance with § 171.1 (21 CFR 171.1). When considering the approval of olestra for additional uses, FDA will consider consumers' cumulative exposure to olestra through the currently approved uses (savory snacks) as well as through any additional uses requested.

The question raised by this petition is not simply whether olestra causes GI effects, but whether customary or usual olestra consumption causes GI effects that warrant special labeling. As mentioned previously, while no study can rule out the possibility that olestra may cause GI effects in a small percentage of consumers, the petitioner's postapproval studies do show that customary or usual consumption of olestra-containing savory snacks does not cause GI symptoms with a frequency, severity, or impact on daily activity that warrant special labeling.

(Comment 34) A comment from CSPI to the current petition cited a study (Ref. 42) showing that consumption of 40 g olestra/day resulted in levels of fecal fat commonly observed in patients with steatorrhea caused by malabsorption syndrome. CSPI quoted the researchers' concerns that physicians may suspect malabsorption syndrome in patients who consume olestra and subject them to unnecessary diagnostic tests. CSPI stated that while the results of the study alone may not warrant label statements they should be factored in with studies demonstrating olestra's effects on nutrient levels and GI symptoms.

Consideration of the study cited by CSPI does not change the agency's decision on this food additive petition. CSPI does not explain how the study should be considered in the context of labeling or why the results warrant special labeling of olestra-containing foods. CSPI provides no reason to believe that customary or usual olestra consumption has resulted in patients having to undergo unnecessary diagnostic tests for malabsorption syndrome or that malabsorption syndrome has been incorrectly diagnosed because of customary or usual olestra consumption.[70] FDA notes that the study cited in the comment serves to alert physicians to the potential effects of olestra consumption on the measurement of fecal fat so that such misdiagnoses may be avoided.

(Comment 35) A comment from CSPI to the current petition addressed a statement that P&G made in its petition that the First Amendment, which includes the right not to speak, may bar the requirement of anything other than material information or information deemed essential under the act to appear on the food label. In its comment, CSPI stated that consumers must be informed of the possible side effects of olestra-containing foods so that they can avoid needless medical treatment or avoid the possibility of suffering side effects altogether. CSPI also stated that the disclosure of potential side effects provides material information and is ''reasonably related'' to the agency's interest in preventing misleading food labels. Therefore, in CSPI's view, the label statement does not violate the First Amendment right not to speak, as asserted by the petitioner.

FDA did not rely on the petitioner's First Amendment argument in concluding that olestra-containing products should no longer be required to bear the label statement required by the 1996 final rule. The issue raised by the current petition and the comment is whether olestra-related side effects are consequences of customary or usual olestra consumption that require disclosure in labeling. As stated previously, the agency has concluded that olestra-related side effects do not warrant required labeling because these effects are not consequences of customary or usual olestra consumption, and the comment provides no such data or information to demonstrate the contrary.

(Comment 36) A comment from CSPI to the current petition pointed out that the petition states that FDA may decline to require disclosure of material information when to do so would crowd other important information or confuse consumers. CSPI argued that a label statement revised for increased clarity would not confuse consumers, and snack food packages are large enough to provide a label statement without crowding other important information.

As noted, this final rule requires that the label of olestra-containing foods list vitamins A, D, E, and K in the ingredient statement followed by an asterisk and the phrase ''Dietarily insignificant.'' FDA has determined that, for the remainder of the label statement required by the 1996 final rule, the underlying factual basis no longer exists and thus, is removing the relevant requirement from § 172.867. These changes in the requirements for labeling of olestra-containing foods render moot the issue of ''label crowding.''

F. Safety of Olestra

(Comment 37) Several comments from individual consumers to the current petition stated that olestra-containing foods should no longer be sold. One comment stated that olestra-containing foods should no longer be sold because even a more prominent label statement would not prevent illness in those who ingest such products in situations where the products are served in unlabeled containers. These comments relayed GI reactions that were attributed to olestra. A comment from CSPI stated that other countries have not approved petitions for the use of olestra and that such decisions not to approve olestra should provide some guidance as to how a substance like olestra should be regulated.

[70] Subjects in the study cited by CSPI were fed 40 g olestra per day for 6 days. Based on the agency's preapproval estimate of olestra consumption, this level of olestra consumption is unlikely to be achieved under customary or usual consumption conditions. FDA's preapproval estimate of chronic daily olestra intake was 7 g/p/d at the 90th percentile snack eater and 20 g/p/d for short-term ''high'' consumption consumers (61 FR 3118 at 3124–3125). The estimate of chronic daily olestra intake assumes that olestra will be consumed at this level every day. FDA estimated that a ''high'' short-term consumer would consume olestra at a level equivalent to eating a 2 oz bag of olestra chips each day for 12 weeks (61 FR 3118 at 3124–25).

A comment from CSPI to the 1996 final rule suggested that the label should include a statement indicating that the long-term effects of olestra consumption are not known. The comment expressed concern that the human studies were too brief compared to the length of time people will be eating olestra-containing foods and stated that the problems observed in the human and animal studies warrant a broader advisory about the possible long-term effects of olestra consumption. CSPI also stated that labeling should be complemented with point-of-purchase health-hazard information and mass media consumer information campaigns. Comments from manufacturers of baked snacks expressed concern that without clear labeling consumers will believe that olestra-containing foods are as safe as baked snacks.

In comments to the 1996 final rule, CSPI and an individual consumer requested that the label statement be placed on restaurant menus so that diners will not unknowingly consume olestra at a restaurant.

FDA disagrees with these comments. FDA concluded in the 1996 final rule that the use of olestra in savory snacks meets the safety standard for food additives, reasonable certainty of no harm (61 FR 3118 at 3167). The label statement required by the 1996 final rule was never intended to prevent illness or warn against conditions of use that may be harmful as the agency concluded in 1996 that olestra is safe for its intended use in savory snacks even without the label statement. FDA required that olestra-containing foods bear the label statement to provide information about the presence of the vitamins listed in the ingredient statement and about potential nutrient and GI effects of olestra. FDA determined that these statements were necessary at the time to ensure that olestra-containing foods are not misbranded within the meaning of the act (61 FR 3118 at 3168).

Because olestra-containing foods are safe even in the absence of the label statement, olestra-containing foods served in unlabeled containers or in a restaurant do not represent a health risk. FDA has no evidence to confirm that there is a group of individuals who are so sensitive or intolerant to olestra when it is consumed under customary or usual conditions that such consumption presents a health concern or warrants special labeling. In fact, the petitioner's Rechallenge Study shows that when consumers who reported effects that they attributed to olestra, were rechallenged with olestra chips, they were no more likely to report GI symptoms compared to when they were challenged with triglyceride chips.

G. Allergenicity of Olestra or Olestra-Containing Foods

(Comment 38) A comment from CSPI to the current petition stated that while there is no reason to think that olestra itself causes allergic reactions, the agency or the petitioner should conduct tests to determine whether a contaminant in olestra, or another ingredient in olestra-containing chips, causes allergic reactions because allergic responses were reported. The comment added that FDA cannot design an accurate label statement until such studies have been conducted.

FDA does not agree that allergenicity testing of olestra or olestra-containing foods must be conducted before ruling on this petition. The agency addressed the potential allergenicity of olestra in the 1996 final rule (61 FR 3118 at 3166). Food allergens are generally known to be protein or glycoprotein in nature. Olestra, composed of six, seven, or eight fatty acids esterified to sucrose, is neither a protein nor a glycoprotein and does not contain these substances even as minor constituents. The comment provides no basis to alter FDA's original conclusion that olestra is unlikely to cause allergic reactions.

FDA acknowledges that some reports allege that unspecified allergic reactions or symptoms of allergic reactions were caused by an olestra-containing food. The comment provides no evidence or reason to conclude that the effects reported were caused by olestra. FDA notes that a published article reports that when individuals who reported an allergic reaction to olestra were rechallenged, none of the individuals were found to have a positive response to olestra upon eating olestra-containing potato chips or when given a skin prick test with olestra (Ref. 43).

FDA notes that olestra-containing foods, like non-olestra-containing foods, contain other ingredients that may be allergens to some individuals. Consumers are informed of the presence of such potential food allergens through the product ingredient statement, as is the case for products containing potentially allergenic substances like milk and eggs.

H. Nutrition Labeling and Claims

(Comment 39) A comment from CSPI to the current petition asserted that the amount of olestra contained in snacks should be declared in the Nutrition Facts label. The comment stated that the amount of total fat per serving should be listed with an asterisk pointing to a note stating, ''This product contains x grams of olestra, which is not digested by the body. These figures have been adjusted to reflect that reduced availability.'' The comment states that the amount of available fat, saturated fat, and polyunsaturated fat would be listed. Alternatively, the comment stated that if the Nutrition Facts label states ''Fat 0 g'' an asterisk should reference the statement, ''Contains x grams of olestra, which is not absorbed by the body.''

In a related comment to the 1996 final rule, P&G stated that the amount of olestra per serving should not be included on the label because the presence of olestra is already declared in the ingredient statement and because the position of olestra within the ingredient statement will reflect its predominance based on weight in the food. P&G's comment also stated that there is no precedent for requiring the declaration of the amount of an ingredient on the food label, and that many manufacturers offer consumers access to phone numbers from which they could obtain quantitative information about ingredients.

These comments on the information that should appear on the Nutrition Facts panel of olestra-containing foods fall outside the scope of this document. As stated in the notice of filing, this petition proposed to amend the food additive regulations by removing the requirement for the label statement prescribed in § 172.867(e), the requirement for which is found only in paragraphs (e)(1) through (e)(3).

FDA notes, however, that the current regulation on ingredient labeling (§ 101.4) requires food ingredients to be declared by their common or usual names in the ingredient statement of the food. Accordingly, olestra-containing foods must declare olestra as an ingredient of the food. Olestra's placement in the declaration of ingredients is determined by its predominance based on weight in the food. In addition, § 101.4(e) provides manufacturers with a uniform method to voluntarily declare the percentage of each ingredient in their product (58 FR 2850 at 2865, January 6, 1993).

(Comment 40) A comment from CSPI to the current petition stated that olestra-containing food should not be allowed to use the phrase ''fat-free.'' The comment stated that olestra is a fat; therefore, the term ''fat-free'' on the label of olestra-containing foods is inaccurate. Instead of using the phrase ''fat-free,'' CSPI suggested that olestra-containing food could declare ''no calories from fat'' or ''contains x grams of olestra.'' This type of labeling statement would help to differentiate baked snacks from olestra-containing

snacks. The comment stated that an ounce of baked chips provides an ounce of carbohydrate and protein, whereas an ounce of olestra-containing chips provides only two-thirds to three-fourths an ounce of carbohydrate and protein.

A comment from a potato chip manufacturer to the 1996 final rule stated that olestra-containing foods should not be allowed to declare ''fat-free'' and ''low fat'' because the fat content of olestra-fried chips is equal in quantity to that of any standard chip; therefore, the comment concluded that the label statement is misleading.

These comments on the declaration of ''fat-free'' on olestra-containing foods fall outside the scope of this document. As stated in the notice of filing, this petition proposed to amend the food additive regulations by removing the requirement for the label statement prescribed in § 172.867(e). The requirement for the label statement is found only in § 172.867(e)(1) through (e)(3). These comments relate to a requirement found in § 172.867(e)(5).

FDA notes that the agency previously concluded that olestra shall not be considered to be a source of fat or calories for purposes of nutrition labeling or nutrient content claims because olestra is neither a triglyceride nor is it absorbed or metabolized like a fat (§ 172.867(e)(5)).

I. Appearance of the Label Statement

(Comment 41) Comments to both the current petition and the 1996 final rule addressed the appearance of the label statement. Comments from individual consumers and CSPI requested that the label statement be larger, printed in bold type, and placed on the principal display panel of the package to increase its prominence. CSPI stated that many of those who used CSPI's telephone line to report reactions did not see the label statement prior to consumption, and several comments from consumers stated this as well. In its comments to the 1996 final rule, CSPI requested that the label statement be placed far enough from the edges of the container to provide a flat unobscured surface for the wording, that there be sufficient white space around the box to set off the wording within the box, that the label statement be black on a white background, that the size of the text increase as the package size increases, that a prefatory word such as ''Notice'' precede the label statement, and that the box around the label statement be retained because boxed statements increase the likelihood that consumers will read the statement.

Comments from a trade association to the 1996 final rule stated that the olestra label statement should use general food labeling typography (as described in §§ 101.2, 101.3, and 101.105), like that used for labels on products containing mannitol, sorbitol, and polydextrose. Frito-Lay argued that the appearance requirements of the olestra label should be aligned with those of other substances with similar effects and levels of concern. The comment pointed out that label statements for food additives that are proven to cause serious health problems, such as sulfites (21 CFR 130.9), do not have the stringent requirements for labeling prominence that are required of olestra, which has been determined to be safe. Comments from P&G and a trade association stated that the box around the label statement should be eliminated because it increases concern about the safety of the product. P&G stated that boxed statements are appropriate only when death or very serious illness is a possible outcome of customary or usual use.

As explained previously, FDA has concluded that olestra-containing foods should no longer be required to bear the label statement required by the 1996 final rule. Therefore, the appearance of the label statement is no longer an issue. The label for olestra-containing foods will be required to provide information about the added vitamins A, D, E, and K through an asterisk, in the list of ingredients, referencing the statement ''Dietarily insignificant.'' The prominence and placement of the phrase ''Dietarily insignificant'' will follow customary practice for other food products (such as §§ 101.60, 101.61, and 101.62) and will appear prominently and conspicuously as specified in § 101.2(c).

J. Labeling for Single-Serving Packages

(Comment 42) Comments from Frito-Lay and a trade association to the 1996 final rule stated that single serving packages of olestra-containing foods should be exempt from the requirement to bear a label statement because the small package of such containers is not compatible with the label statement, and because the portion contained in such packages is so small that the label statement may not disclose a material fact. Frito-Lay recommended that instead of the label statement required on larger packaging, single-serving packages include the statement, ''For information on olestra call 1–800–XXX–XXXX.''

In contrast, CSPI stated that single-serving packages should be required to bear the label statement because studies by P&G show that the amount of olestra contained in such packages is sufficient to increase the incidence of GI disturbances.

As explained previously, FDA has concluded that olestra-containing foods should no longer be required to bear a label statement that informs consumers about the potential GI effects of these products. Therefore, whether single-serving containers should be required to bear the label statement is no longer an issue. FDA does not believe that single serving packages should be exempt from the required labeling of added vitamins A, D, E, and K with an asterisk and the phrase ''Dietarily insignificant'', nor do the comments provide a basis for such an exemption.

K. 1995 and 1998 FAC Meetings

(Comment 43) A comment from CSPI to the current petition criticized the 1995 and 1998 FAC meetings held by FDA. CSPI asserted that the 1995 FAC did not provide objective advice to FDA regarding the approval of olestra.[71] CSPI also stated that the committee did not contain a single expert on carotenoids and that 9 of the 17 committee members who concluded that olestra meets the safety standard of ''reasonable certainty of no harm'' were affiliated with industry.

CSPI also stated that the conclusions of the 1998 FAC must be considered in light of the fact that the committee did not consider studies conducted prior to January 30, 1996, including those studies that CSPI stated prove that olestra can cause gastrointestinal symptoms and reduce serum carotenoid levels. CSPI also pointed out that the 1998 FAC did not consider the Fecal Parameters Study even though it was provided to FDA after the 1995 FAC meeting. CSPI also stated that reports of GI symptoms such as diarrhea, cramps, and nausea were downplayed at the 1998 FAC because they were not ''unexpected'' problems and the committee was asked only to consider whether there were any ''unexpected'' problems associated with olestra.

FDA does not agree that the 1995 FAC provided biased advice. CSPI raised this issue previously and FDA responded in the 1996 final rule (61 FR 3118 at 3164). As stated in the 1996 final rule, FAC members are screened prior to each meeting to determine if they have a conflict of interest with the material to be discussed at the meeting. Committee members are also expected to provide an objective opinion on the information presented. FDA believes that the committee was fairly balanced as

[71] In its comment CSPI cites Ref. 36.

required by the Federal Advisory Committee Act (FACA). FDA also believes that there is no basis to conclude that the 10 nutrition experts at the FAC meeting were not able to understand the views and information presented on carotenoids (61 FR 3118 at 3164).

As part of the 1996 final rule, FDA announced its intention to review and evaluate all data and information bearing on the safety of olestra received by the agency within the first 30 months after the approval of olestra and to present an evaluation of the data to the agency's FAC (§ 172.867(f)). Consistent with its obligation, in 1998 FDA presented to the FAC an evaluation of the data and information obtained since the 1996 approval of olestra. The purpose of the presentation was to receive advice from the Committee on whether there continued to be reasonable certainty that use of olestra is not harmful. Specifically, the 1998 FAC was asked to evaluate whether data and information obtained since the approval of olestra raised safety concerns regarding any GI effects that were not anticipated at the time of olestra's approval and whether any newly available data showed that consumption of olestra-containing foods had a significant adverse health effect due to olestra's interference with absorption of fat-soluble vitamins or other lipophilic substances.[72] The committee was also asked whether the label statement should be changed in light of new data and information. Because the FAC was asked if there were any new issues raised since the approval of olestra, the committee was asked to consider only the data and information obtained since the approval of olestra. Much of the new data focused on the effects of ''real life'' consumption of olestra-containing foods (*i.e.*, the Rechallenge Study, the Acute Consumption Study, and the Home Consumption Study). The studies conducted prior to the approval of olestra, such as the Fecal Parameters Study, examined the effects of olestra when consumed under conditions designed to assess safety and were previously considered by FDA in its review of the petition for the use of olestra in savory snacks. Although the 1998 FAC did not consider the petitioner's Fecal Parameters Study, the committee did consider the Stool Composition Study. Like the Fecal Parameters Study, the Stool Composition Study was designed to examine olestra's effect on objective stool characteristics but tested a higher dose of olestra and collected stool samples on a greater number of days than was done in the Fecal Parameters Study. The committee also considered FDA's analysis of the reports collected through passive surveillance by P&G and CSPI, which include reports of GI symptoms such as diarrhea and abdominal pain.[73] Upon review of the data and information received since the 1996 final rule, a majority of the FAC concluded that there continues to be reasonable certainty of no harm concerning the use of olestra in savory snacks.[74] FDA believes that the data and information considered by the 1998 FAC were appropriate for the objective of the meeting, to determine whether the data and information obtained since the approval and marketing of olestra raise any issue not anticipated at the time of approval.

[72] Transcript, vol. 1, pp. 22–25.

[73] Transcript, vol. 1, pp. 258–270.

[74] Transcript, vol. 3, pp. 101–174.

VI. Summary

In its petition, P&G requested that FDA amend the food additive regulations in § 172.867 *Olestra* by removing the requirement for the label statement prescribed in § 172.867(e). Based on its analysis of data and information in the petition, as well as data and information in FAP 7A3997 (which resulted in the establishment of § 172.867(e)), FDA has concluded that olestra-containing foods should no longer be required to bear a label statement informing consumers of possible GI symptoms from consumption of olestra. FDA also has concluded that olestra-containing foods should no longer be required to bear a label statement informing consumers of possible effects of olestra on the absorption of some vitamins and other nutrients. Finally, FDA has concluded that olestra-containing foods should no longer be required to bear a label statement informing consumers that vitamins A, D, E and K have been added. Instead, the listing of the vitamins in the ingredient statement of olestra-containing foods will now be followed by an asterisk that is linked to the statement ''Dietarily insignificant.''

VII. Environmental Impact

The agency has determined under 21 CFR 25.30(k) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Inspection of Documents

In accordance with § 171.1(h), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition (*see* **ADDRESSES**) by appointment with the information contact person. As provided in § 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

Additionally, a copy of P&G's December 1999 petition and additional supporting material that P&G supplied are publically available at the Division of Dockets Management (Docket No. 00F–0792.

IX. Objections

Any person who will be adversely affected by this regulation may file with the Division of Dockets Management (*see* **ADDRESSES**) written or electronic objections by (*see* **DATES**). Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

X. References

The following references have been placed on display in the Division of Dockets Management (*see* **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m. Monday through Friday.

1. Transcript of the meeting of the Food Advisory Committee (vols. 1–3), Reston, VA, June 15 through 17, 1998.

2. Memorandum from K. C. Klontz, FDA to M. Ditto, FDA, February 13, 1998.

3. Memorandum from A. S. Levy, FDA to H. Thorsheim, FDA, August 20, 1996.

4. Memorandum from D. A. Street, FDA to M. Ditto, FDA, October 23, 2000.

5. Memorandum from K. C. Klontz, FDA to M. Ditto, FDA, February 23, 2000.

6. Memorandum K. C. Klontz and E. F. Barker, FDA to H. Thorsheim, FDA, March 26, 1997.

7. Memorandum K. C. Klontz, FDA to H. Thorsheim, FDA, August 8, 1996.

8. Zorich, N. L., D. Biedermann, K. A. Riccardi, *et al.*, ''Randomized, Double-Blind, Placebo-Controlled, Consumer Rechallenge Test of Olean Salted Snacks,'' Regulatory Toxicology and Pharmacology, 26:200–209, 1997.

9. Zorich, N. L., D. Biedermann, K. A. Riccardi, *et al.*, ''Follow-Up to the Study: A Randomized, Double-Blind, Placebo-Controlled Consumer Rechallenge Test of Olean Salted Snacks,'' *Regulatory Toxicology and Pharmacology,* 27:2, 1998.

10. Memorandum from K. C. Klontz, FDA to M. Ditto, FDA, May 25, 2000.

11. Memorandum from K. C. Klontz, FDA, to M. Ditto, FDA, April 13, 1998.

12. Cheskin, L. J., R. Miday, N. Zorich, *et al.*, ''Gastrointestinal Symptoms Following Consumption of Olestra or Regular Triglyceride Potato Chips: a Controlled Comparison,'' *Journal of the American Medical Association,* 279:150–152, 1998.

13. Memorandum from P. V. McCarthy, FDA, to M. Ditto, FDA, August 26, 1998.

14. Sandler, R. S., N. L. Zorich, T. G. Filloon, *et al.*, ''Gastrointestinal Symptoms in 3181 Volunteers Ingesting Snack Foods Containing Olestra or Triglycerides. A 6-Week Randomized, Placebo-Controlled Trial,'' *Annals of Internal Medicine,* 130:253–261, 1999.

15. Memorandum from S. J. Chirtel, FDA to B. Timbo, FDA, July 16, 1998.

16. Memorandum from C. Barton, FDA to B. Timbo, FDA, May 7, 1999.

17. Memorandum from C. Barton, FDA to M. Ditto, FDA, May 7, 1999.

18. Memorandum from H. E. Gallo-Torres, FDA, June 5, 1998.

19. Jacobson, M. F., M. A. Brown, and E. B. Whorton, ''Gastrointestinal Symptoms Following Olestra Consumption,'' *Journal of the American Medical Association,* 280:325–326, 1998.

20. Jacobson, M. F., ''Olestra Snacks Compared with Regular Snacks,'' *Annals of Internal Medicine,* 131:866, 1999.

21. Memorandum from C. Barton, and S. Chirtel, FDA to M. Ditto, FDA, March 27, 2003.

22. Memorandum K. C. Klontz, FDA to H. Thorsheim, FDA, December 26, 1995.

23. Kristal, A. R., R. E. Patterson, M. L. Neuhouser, *et al.*, ''Olestra Postmarketing Surveillance Study: Design and Baseline Results from the Sentinel Site,'' *Journal of the American Dietetic Association,* 98: 1290–1296, 1998.

24. Memorandum from T.G. Wilcox, FDA to M. Ditto, FDA, November 22, 2000.

25. Cooper, D. A., A. L. Eldridge, and J. C. Peters, ''Dietary Carotenoids and Lung Cancer: a Review of Recent Research,'' *Nutrition Reviews,* 57:133–145, 1999.

26. Cooper, D. A., A. L. Eldridge, and J. C. Peters, ''Dietary Carotenoids and Certain Cancers, Heart Disease, and Age-Related Macular Degeneration: a Review of Recent Research,'' *Nutrition Reviews,* 57:201–214, 1999.

27. Institute of Medicine (U.S.), Panel on Dietary Antioxidants and Related Compounds, ''Beta-Carotene and Other Carotenoids,'' *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids: A Report of the Panel on Dietary Antioxidants and Related Compounds, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine,* pp. 325–382, Washington, DC: National Academy Press, 2000.

28. Memorandum of Meeting, August 31, 2000.

29. Letter from A. Rulis, FDA, to J. McLaughlin, NEI, September 15, 2000.

30. Letter from J. McLaughlin, NEI, to A. Rulis, FDA, October 17, 2000.

31. Age-Related Eye Disease Study Research Group, ''A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation with Vitamins C and E, Beta Carotene, and Zinc for Age-Related Macular Degeneration and Vision Loss,'' *Archives of Ophthalmology,* 119:1417–1436, 2001.

32. Memorandum from A. S. Levy, FDA to H. Thorsheim, FDA, July 30, 1996.

33. Memorandum from A. S. Levy, FDA to M. Ditto, FDA, November 16, 2000.

34. Kelly, S. M., M. Shorthouse, J. C. Cotterell, *et al.*, ''A 3-Month, Double-Blind, Controlled Trial of Feeding with Sucrose Polyester in Human Volunteers,'' *British Journal of Nutrition,* 80:41–49, 1998.

35. Memorandum from R. Pertel, FDA to N. Beru, FDA, September 6, 1995.

36. Blackburn, H., ''Sounding Board: Olestra and the FDA,'' *New England Journal of Medicine,* 334:984–986, 1996.

37. Westrate, J. A. and K. H. van het Hof, ''Sucrose Polyester and Plasma Carotenoid Concentrations in Healthy Subjects,'' *American Journal of Clinical Nutrition,* 62:591–597, 1995.

38. Lawton, C. L., ''Regulation of Energy and Fat Intakes and Body Weight: the Role of Fat Substitutes,'' *British Journal of Nutrition,* 80:3–4, 1998.

39. Giovannucci, E., ''Tomatoes, Tomato-Based Products, Lycopene, and Cancer: Review of the Epidemiologic Literature,'' *Journal of the National Cancer Institute,* 91:317–331, 1999.

40. Chasan-Taber, L., W. C. Willet, J. M. Seddon, *et al.*, ''A Prospective Study of Carotenoid and Vitamin A Intakes and Risk of Cataract Extraction in U.S. Women,'' *American Journal of Clinical Nutrition,* 70:509–516, 1999.

41. Brown, L., E. B. Rimm, J. M. Seddon, *et al.*, ''A Prospective Study of Carotenoid Intake and Risk of Cataract Extraction in U.S. Men,'' *American Journal of Clinical Nutrition,* 70:517–524, 1999.

42. Balasekaran, R., J. L. Porter, C. A. Santa Ana, *et al.*, ''Positive Results on Tests for Steatorrhea in Persons Consuming Olestra Potato Chips,'' *Annals of Internal Medicine,* 132:279–282, 2000.

43. Burks, A. W., L. Christie, K. A. Althage, *et al.*, ''Randomized, Double-Blind, Placebo-Controlled, Food Allergy Challenge to Olestra Snacks,'' *Regulatory Toxicology and Pharmacology,* 34: 178–181, 2001.

List of Subjects in 21 CFR Part 172

Food additives, Reporting and recordkeeping requirements.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 172 is amended as follows:

PART 172—FOOD ADDITIVES PERMITTED FOR DIRECT ADDITION TO FOOD FOR HUMAN CONSUMPTION

■ 1. The authority citation for 21 CFR part 172 continues to read as follows:

Authority: 21 U.S.C. 321, 341, 342, 348, 371, 379e.

■ 2. Section 172.867 is amended by revising paragraph (e) to read as follows:

§ 172.867 Olestra.

* * * * *

(e)(1) Vitamins A, D, E, and K present in foods as a result of the requirement in paragraph (d) of this section shall be declared in the listing of ingredients. Such vitamins shall not be considered in determining nutrient content for the nutritional label or for any nutrient claims, express or implied.

(i) An asterisk shall follow vitamins A, D, E, and K in the listing of ingredients;

(ii) The asterisk shall appear as a superscript following each vitamin;

(iii) Immediately following the ingredient list an asterisk and statement, ''Dietarily insignificant'' shall appear prominently and conspicuously as specified in § 101.2(c) of this chapter;

(2) Olestra shall not be considered as a source of fat or calories for purposes of §§ 101.9 and 101.13 of this chapter.

* * * * *

Dated: July 17, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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