DID THE FDA PROPERLY ASSESS THE SAFETY OF OLESTRA AS A FOOD ADDITIVE?

Leah Lebel

INTRODUCTION

Olestra, a fat-substitute comprised of sucrose that has been esterified with fatty acids (Blume 1995), has been the subject of much controversy ever since its creation. Olestra is not absorbed (Mattson and Nolen 1972) because it cannot be hydrolyzed by pancreatic lipases (Mattson and Volpenhein 1972) or taken up across the enterocyte microvillus membrane (Freston et al. 1997), and thus, cannot be utilized for energy. Olestra has physical and organoleptic properties similar to those of traditional triglycerides (Jandacek and Webb 1978) and is emulsified together with triglyceride (Freston et al. 1997), yet it passes through the colon and is excreted unchanged (Fallat et al. 1976). It therefore adds no fat, sugar, or calories to the diet (Thomson et al. 1998)

There is a noteworthy advantage of replacing fat with olestra: olestra is far less energy-dense than its triglyceride counterpart and can, at least in theory, be a valuable asset to a weight-loss regimen. Olestra can serve to satisfy one's cravings for fatty-foods without containing the dense energy that triglycerides provide (Eldridge et al. 2002). By causing a reduction in energy intake for consumers, olestra, when incorporated with other calorie-saving methods, has the potential to cause weight loss when replaced with more energy-dense products (Rolls and Bell 1999).

After Procter & Gamble, the makers of olestra, obtained their first patent on olestra in 1971 (Nestle 1998), olestra underwent a more than 20-year struggle until it was finally

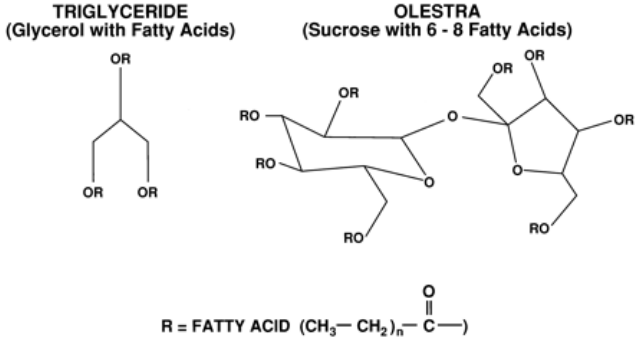

Figure 1: The chemical structure of olestra as compared with traditional triglyceride
Source: http://extoxnet.orst.edu/faqs/additive/olstru.htm

approved in January 1996 (Nightingale 1996). Much of the controversy surrounding this food additive stems from its versatility, as olestra can withstand high heating temperatures and can be used in virtually any food(Eldridge et al. 2002), and from its potential to be consumed in large quantities. Olestra presents a potential danger in that it is a macro-additive; a serving of olestra-containing food has several grams of the additive, rather than milligrams (as artificial sweeteners and many other additives have). This fact presented an unprecedented decision for the FDA—it was now choosing to approve something that would be consumed in potentially substantial quantities. Nevertheless, on January 25th 1996, the FDA released its ruling that olestra was to be approved for use in savory snacks. The FDA did, however, require that vitamin losses typically experienced from consuming olestra (particularly fat-soluble vitamins) be added to compensate for these losses. Thus, vitamins A,

Leah Lebel, B.S. '11, majored in Biology. She is currently attending the Brooklyn College M.S. degree program in Nutrition .

D, E, and K are added to olestra during manufacturing. Initially upon approving olestra, the FDA, still unsure about long-term safety at approval time, required a warning notice for all products (Nestle 1998) stating that "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" (Center for Science in the Public Interest).

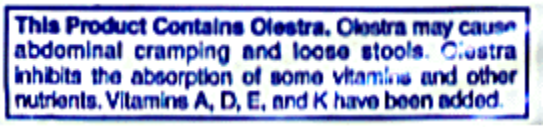

Figure 2: Sample of the warning label originally required on all olestra-containing products
Source: http://www.carboh.com/olestra.phtml

Much consumer controversy resulted from olestra's approval (Miller 2001). From olestra's entry into the market, there have been tens of thousands of adverse anecdotal reports from olestra consumers. People claimed they had suffered severe diarrhea, fecal incontinence, and/or abdominal cramps hours after eating olestra chips. Procter & Gamble, however, claimed that there is no proof that olestra is the cause of these effects (Center for Science in the Public Interest).

The Center for Science in Public Interest (CSPI) in particular was infuriated with olestra's passing into market and constantly collected data in an attempt to convince the FDA to withdraw their decision. Many other groups and independent challengers also believe that olestra should not have obtained FDA approval. They challenged the studies conducted by Procter & Gamble, pointing to the fact that some studies conducted by Unilever, Procter & Gamble's competition, show that olestra, when consumed at high levels, causes gastrointestinal problems in up to 30% of subjects, point to the large marketing campaigns used to promote the product, and claim that significant losses of fat-soluble vitamins, and particularly carotenoids, can increase the risk of chronic diseases. Yet because critics could not prove that carotenoid losses were harmful and because the product had a label warning of GI distress potential, no action was taken to remove the product from the market (Nestle 1998). According to Porterfield, "the PDA [sic] granted approval [of Olestra] acknowledging that some patients may experience abdominal cramps and diarrhea if they eat too much" (Porterfield 1997).

In 2003, the FDA chose to eliminate the requirement for a warning label, stating that it "was no longer warranted as post-market studies showed that olestra caused only infrequent, mild gastrointestinal effects" (FDA removes olestra warning 2003).

Michael F. Jacobson, the executive director of CSPI, notes, "P&G's own studies prove olestra causes diarrhea, cramps and other symptoms. If that weren't enough, the FDA has more than 20,000 complaints about olestra in its files--more than it has for all other food additives in history combined" (FDA removes olestra warning 2003). In a post marketing surveillance study, .4% of consumers were hospitalized, and suspected olestra to be the cause for their hospitalization (Allgood et al. 2000). Other consumers pointed to other side effects such as headaches and blame olestra as the cause (Blume 1995). Nonetheless, there is no direct proof that this is the case. As Procter and Gamble noted in their defense, it is quite possible that there was another unrelated cause to all these ailments and that experiencing ailments at some time after consuming olestra was a coincidental occurrence.

Despite this, many people began to question the FDA's approval of olestra. Many ask: how has the FDA been able to responsibly pass into market a product that may not be safe for such large segments of the population who may not realize the effects of olestra on their overall health? Olestra causes side effects of great magnitude; diarrhea, after all, can cause

complications including weight loss, dehydration and electrolyte imbalances (Tortora and Derrikson 2006). Moreover, Procter and Gamble contributed funds to the FDA, just weeks before the FDA actually approved olestra (Nestle 1998). Thus, many wonder if olestra is safe and if the decision was based solely on fact.

This study attempts to determine whether the FDA took the necessary scruples to avoid prematurely allowing olestra into market. An analysis of the standards utilized by the FDA, followed by a comparison of those standards with the research is warranted.

WHAT ARE THE CRITERIA UPON WHICH THE FDA MAKES ITS "SAFE" OR "UNSAFE" RULINGS?

ADDITIVE REGULATION GUIDELINES WHICH THE FDA ADHERES TO:

In an article aimed at explaining the requirements and procedures involved in the FDA's additive-approval process, Rulis and Levitt (2009) depict many of the factors that would explain what Procter and Gamble, the company that manufactures olestra, would have had to undergo to get olestra approved for consumer use. The article notes the fact that the FDA requires that additives undergo a strict approval regimen and employs an "unsafe until proven safe" mentality: "New food additives are presumed to be unsafe for their intended use unless and until they are proven 'safe'" (Section 3; 2008). The additive in question must meet with the FDA's standards of "reasonableness to cause no harm." Clearly, "reasonableness to cause no harm" is a subjective term and thus in the article's appendix, the author elaborates on just what "reasonableness" is defined as. Section 409(c)(3) of the FD&C act explains that the food additive in question requires a "fair evaluation of the data" and that the concept of safety involves the question of whether a substance is "hazardous to the health of man or animal." Primarily, calling a product "safe" requires proof of "a reasonable certainty that no harm will result from the proposed use of an additive" (House of Representatives, Report No. 2284, 85th Congress, 1958, as qtd. in appendix 10 of Rulis and Levitt 2009). Thus, in assessing the safety of olestra, the FDA would have been expected to determine (1) whether olestra could potentially be hazardous to the health of man or animal and if the substance in question has a reasonable certainty to cause harm based upon the data available prior to olestra's approval date on January 25th 1996.

The authors of the articles also reference the House of Representatives Report No 2284, 85th congress, 1958 statute 21CFR 170.3(i)) which elaborated upon the term "safe" to mean "a *reasonable certainty* in the minds of competent scientists that the substance is not harmful under the *intended conditions of use*" (italics added). It is important to note that, in this ruling, there must be a reasonable certainty only. In other words, the product in question is not guaranteed to be safe, but rather, it must present itself as reasonably harmless to health. Rulis and Levitt adeptly point out that this wording does "[result]in decisions inevitably being made without absolute certainty" (appendix 10).The burden to provide proof of safety lies with the petitioner (Rulis and Levitt 2009), and therefore Procter and Gamble would have had to demonstrate to the FDA that there is reasonable certainty that the item causes no harm in the minds of competent scientists. Hence, the questions that remain for this research paper to address is (2) were the competent scientists company based (and thus possibly biased) or were they independent researchers and (3) how credible are the studies upon which the scientists were basing their decision? A critical review of the literature available until olestra became approved is warranted in order to assess the meticulousness of the scruples taken before the FDA's decision was finalized. At least in theory, the research should have been able to persuade the FDA of olestra's reasonable safety.

Another inquiry to the above is what is olestra's "intended condition of use"? Rulis and Levitt's journal article then goes on to explain that "[there are] a range of technical functions in food…as outlined by Food Ingredients, as outlined in a brochure produced jointly by the FDA in collaboration with the international Food Information Council." The article then goes on to list some of these technical functions, and the one that best fits olestra would be the second one, or, "to improve or maintain nutritional value," which includes the point of "lowering the calorie or fat content of foods." Hence, reducing the energy consumed would be considered a sufficient benefit of the product's use. The purpose of reducing the energy content of a specific food would, in turn, be to lower the weight-gain by the consumer who chose to consume the food with the additive rather than the one without. In an age where obesity is reaching epidemic proportions (World Health Organization 1998), this is an important task to be accomplished. Over a long period, even modest caloric-reduction benefits can translate into significant weight loss. In light of this, olestra's use serves a very important function to lower the skyrocketing obesity rate. Thus, it is probably safe to infer that the "purpose" or benefit seen by the FDA for olestra's use would be to produce a weight-loss effect in the obese, thus opening a fourth underlying question that would provide the justification, or lack thereof, of ruling for olestra's approval:(*4*) whether olestra actually causes weight reduction in those who would benefit from weight loss. Section three of the article then goes on to state that "once approved, food additives must be safe for everyone—children and the very young; teenagers and adults; the elderly; pregnant and lactating women." This fact obviously raises a fifth question: how does olestra consumption affect those who may experience negative consequences resulting from a lower energy consumption (such as pregnant women who require a higher caloric intake to support a growing fetus or children reaching puberty who also require a higher energy intake to support growth spurts and maturation) and can these subgroups easily meet these increased energy needs while consuming lower-calorie versions of fat such as olestra. The FDA would have had to assess this (5) and would have had to provide special labeling so special-risk subpopulations can be properly informed, if necessary that they must avoid the product. At present, no food labels are featured on the package of olestra-containing products. Also, along with the question of whether olestra promotes weight loss, is a further question: does it lower the health risks associated with Obesity (6), such as the low-density lipoprotein (LDL)or serum triglyceride levels. (*7*) Does the added vitamin K promote coagulation and hinder the effects of warfarin therapy? (8) How does olestra interact with lipophilic drugs?

HOW MUCH DID THE FDA APPROVE AS SAFE?

CALCULATED ESTIMATED DAILY INTAKE (EDI):

In FDA's assessment of an additive's safety they consider the probable intake of the additive, the cumulative effect of all uses of the additive, and the relevant toxicological data needed to establish its safety (Rulis and Levitt2009). The FDA determined that the estimate for daily chronic intake was a mean of 3.1 grams per day, with the 90th percentile consumption at 6.9 grams per day. Even among the highest consumer levels (teens and men) the estimate for daily chronic intake was as low as 11.0 grams per day at the 90th percentile level. Primarily, *7* grams per day would be considered, according to the FDA, the average chronic consumption level. Because a 2-ounce bag of chips contains about 20g of olestra, the chronic consumption level would be in effect from one consuming merely about .*75* ounces daily (Prince and Welschenbach 1998), or about 8 chips daily.

Potential Problems and Benefits Associated with Olestra Consumption

What Procter and Gamble Submitted to the FDA for Olestra's Approval:

According to an article published in the Journal of the American Dietetic Association (Prince and Welschenbach 1998), Procter and Gamble provided data in five categories: the estimated daily intake (EDI), toxicological effects, olestra's effect on drug absorption, nutritional effect, and gastrointestinal effect. This study will provide both the studies submitted to the FDA before olestra's approval and the numerous studies from independent research pursuits that occurred subsequent to olestra's approval to provide an independent and comprehensive evaluation and answer not only if the FDA's decision was appropriate, but what effects of olestra that had not been found that may have been available had the FDA waited longer before approving olestra.

Toxicological Effects:

From studies performed on several animal species including rats, pigs, rabbits, mice, hamsters, and dogs, the FDA decided that the data supported the petitioner's conclusions for olestra's non-toxic and non-carcinogenic properties and that olestra is neither metabolized nor absorbed by the body(Prince and Welschenbach 1998). Many people pinpoint the fact that no human studies were conducted before FDA approval. While the reasoning behind this remains unanswered, the FDA had obviously believed that testing olestra on animals was sufficient for determining the safety for the general population's consumption.

Olestra's Potentially Negative Effects on Carotenoid Concentration, 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) and Drug Absorption

Hof and Weststrate (1995)concluded that, "Even at low doses, SPE[sucrose polyester] strongly reduces plasma carotenoid concentrations." "Sucrose Polyester and Plasma Carotenoid Concentrations in Healthy Subjects," concluded that, "Even at low doses, SPE strongly reduces plasma carotenoid concentrations. Studies suggest that carotenoids have provitamin A activity as well as antioxidant properties (Faulks and Southon 1997) and cause a reduced incidence of hypertension and cataracts (Thomson et al.1998). On the surface, therefore, this finding would appear to merit "careful consideration in its relevance to assessing the long-term health effects of SPE-containing consumer foods" (Hof and Weststrate 1995). A subsequent study, however, posits that although olestra would have an effect on potentially beneficial phytosterols, this effect would be miniscule and nutritionally insignificant (Cooper et al. 1997). Moreover, there is no scientific proof that carotenoids contribute to health and wellbeing. Therefore, the FDA determined that the assertion of olestra's negative impact on dietary carotenoid level did not warrant attention and did not deem it appropriate to force the company to add compensatory carotenoids to olestra-containing snacks (Thomson et al. 1998).

Another possible issue with olestra is that it increases fecal excretion of 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) by eight to ten fold. In turn, this reduces the elimination half-life of TCDD by about 5 years. The article's author states that these compounds may diffuse across the intestinal wall along the concentration gradient of the chemical between lumen fat and blood fat. This, according to the author, "would be expected

to increase the capacity of the lumen to take up lipophilic contaminants in the blood" (Geusau 1999). The results of this could be problematic but more needs to be assessed before conclusions can be drawn from this study.

Olestra is a lipophilic substance and therefore has the potential to affect the bioavailability of lipophilic drugs (Prince and Welschenbach 1998). In a 1990 study performed on rats, the researchers found little possibility for severe drug malabsorption due to olestra's presence. At first, the researchers hypothesized that "any effect that a nonabsorbable lipid, such as olestra, might have on the absorption of an oral drug will result primarily from interference with incorporation of that drug into the intestinal mixed-micelles by solubilization of the drug in the nonabsorbable lipid. The more lipophilic the drug is, the higher the potential for it to be solubilized by the lipid. The lipophilicity of a drug can be described by its oil-water partition coefficient…" (Miller et al. 1990) In other words, a highly lipophilic drug has far more potential to be affected by the presence of olestra simultaneously in the GI tract than a drug with modest lipophilicity. While Miller et al. (1990) found that "there is little potential for olestra to reduce absorption of oral drugs in general," it is up to competent doctors to recognize this and inform patients when olestra may affect the drugs the patient is taking. In theory, a patient's treatment can be hindered in the rare instance where olestra does inhibit a lipophilic drug's absorption and therefore a drug's efficacy is reduced. However, this is unlikely, particularly when adhering to the acceptable daily intakes established by the FDA. Another study performed on humans was also reviewed by the FDA, yet in this study, the experimental group's result data does not differ from the control group's (Prince and Welschenbach 1998), and therefore the FDA concluded, based on this study and the one conducted by Miller et al. (1990), that "olestra does not interfere with the absorption or bioavailability of lipophilic drugs…when administered at the 18g/day level" (Note that this is above the FDA approximated toxicity level). Still, it is important to underscore the fact that there is no direct proof that olestra does not hinder drug absorption and more research is warranted to assess the correlation (although minute) found by Miller et al.

GASTROINTESTINAL EFFECTS OF OLESTRA:

The FDA required two 56-day studies to determine the gastrointestinal effects plus a 4-week multicenter study on patients with inflammatory bowel disease, ulcerative colitis and Crohn's disease. Tests for those in the 4-week study were used to determine if olestra's presence in the GI tract aggravates already damaged epithelium. There was no statistically significant increase in bowel permeability, but the FDA decided that the study was too narrowly-ranged to rule out detrimental effects that olestra may have on gastrointestinal diseases (Food additive petition 7A3997 volumes 192-194 submitted Feb 1993 and volumes 183-184 submitted January 5th 1993 as cited in Prince and Welschenbach 1998).

Clinical trials following olestra's approval pointed to side effects experienced by some and sparked adverse publicity about olestra. This prompted Procter and Gamble to establish a panel of experts to independently analyze the studies relating to olestra and digestive system function. Procter and Gamble agreed to submit the panel of experts' findings regardless of their conclusions. The panel convened in September 1996 and "analyzed data from preclinical and clinical studies pertaining to the chemistry of olestra, its mechanism of action, and its potential for gastrointestinal effects" (Freston et al. 1997). An article published in *Regulatory toxicology and pharmacology* reviewed and analyzed olestra's effects on gastrointestinal functions and the symptoms experienced as a result of olestra consumption as determined by this board (Freston et al. 1997).

From the results of clinical trials, the board found that in a study in which subjects of the experimental group were consuming 18g of olestra daily rather than triglyceride, no statistically significant difference between the two groups with respect to bloating, belching, heartburn, nausea, cramping, or diarrhea was found. However, in two studies that involved consumption of 20 grams of olestra or more per day, "there was an increase in the number of symptom episodes and the total number of days on which symptoms were reported" (Freston et al. 1997). Another striking revelation about these two studies is that symptoms were reported several days after olestra ingestion. This allows for possibility that other studies of very short durations may not have had enough time elapse after olestra consumption for symptoms to appear, and therefore might have under-reported symptoms.

The group established by Procter and Gamble also reviewed studies of children. In the three studies that this board reviewed, no significantly worse incidence of symptoms has occurred in studies performed on children than on those performed in adults.

Obviously, consideration must be taken in realizing that the group of reviewers was funded by Procter and Gamble. Although this did not necessarily influence the findings of the group, it may have done so.

Post marketing surveillance for olestra via an established toll-free number reported 85 reports during the first 9 weeks. There were 65 incidences in diarrhea, 64 of cramping, and 16 of nausea among others. These are pertinent side effects that warrant attention (Freston et al. 1997). It is not known how much olestra the reporters of side-effects consumed. Not necessarily were these symptoms caused from olestra, and it is likely that at least some of the reports may have been misattributed to olestra. Nonetheless, the overwhelming number of people who suspected side-effects from olestra should necessitate more research in this area.

Other studies, including two sponsored by Procter and Gamble, including one which fed 20 to 32 grams of olestra, which, granted, is more than the FDA recommends, showed significant dose-related increases of diarrhea, loose stools, and an increase the severity and frequency of GI symptoms (Jacobson and Brown 1998). A rechallenge study confirmed this (at the 20g consumption per day level) and a similar study conducted over the course of 5 days found a significant increase in adverse GI effects at the 34g/day level.

In 1998, researchers conducted an experiment in a movie-setting (Cheskin et al. 1998) whereby subjects who were randomly selected to consume olestra chips were compared to those who were not. Of the more than 1,000 people studied, there was no statistically significant difference in gastrointestinal effects of the two groups. This serves to support the FDA decision. Note that in this study, the amount of olestra consumed by many subjects exceeded four servings. This supports the widened gap between the amount approved by the FDA (around 8 chips) and the amount consumers are actually ingesting. An important observation of this study is that consumers were given a 13-ounce bag of chips, but no measures were taken to check how much, or if any, olestra-containing (or regular) chips were actually consumed. This slightly invalidates the conclusion because the experimental group may not have consumed the chips.

In 2000, the Annals of Internal Medicine published a study that tested for steatorrhea, the presence of above-normal amounts of fat present in feces, in individuals who consumed olestra (Balasekaran et al. 2000). The purpose of the study was to determine the effect of olestra consumption on fecal fat excretion. "If olestra increases the amount of measurable fecal fat," the researchers hypothesized," physicians may suspect the malabsorption syndrome in patients who consume olestra and may subject them to unnecessary diagnostic tests" (Balasekaran et al. 2000). The researchers found that "by all three analytical methods [which

they used], apparent concentration of fecal fat was higher when the ten participants were consuming olestra chips than when they were consuming conventional chips" (Balasekaran et al. 2000). The mean number of bowel movements per day was significantly higher when subjects consumed olestra. "Olestra consumption increased stool frequency, wet stool weight, percentage of stool solids (measured by lyophilization), and fecal output of both water and solids. The output of fecal solids increased by an average of 36.2 g/d, which almost equals the quantity of Olestra ingested." (Balasekaran et al. 2000) In addition, fecal fat output increased as consumption of olestra did, a fact that seems to indicate the possibility that olestra causes loose or greasy stool. The article also mentions that "when stool from participants who were ingesting olestra was stained…more than 100 orange-red fat droplets were found per high-power field. Drop diameters ranged from 6 to 120 µm. The size and number of the fat droplets were not noticeably different after acidification and heating, which suggests that olestra was excreted intact rather than as a fatty acid" (Balasekaran et al. 2000). Nonetheless, steatorrhea, although uncomfortable, is not necessarily harmful and this would not have hindered the FDA's approval of the product.

Overall, there seems to be an increase in olestra-related side-effects in some studies where the amounts of olestra that the experimental group's subjects consumed exceeded the amount recommended by the FDA.

Does Olestra have Other Benefits Such as Lowering Low Density Lipoprotein (LDL) Cholesterol Levels or Serum Triglyceride Levels?

Studies have shown that olestra does lower LDL levels when olestra replaces 60g of saturated fat in the diet (far more than the FDA approved as safe) (Glueck et al. 1982). LDL levels were reduced without a significant reduction in High-Density Lipoprotein (HDL) levels. It is important to note that this change in cholesterol level may not necessarily be due to olestra's presence in the diet (and the possibility that it inhibits cholesterol absorption), but rather may be a mere result of lower saturated fat consumption (Miller et al. 1990).

Another study in which 50 grams of olestra was substituted for an equal weight of fat showed that olestra consumption has no effect on plasma triglyceride levels (Fallat et al. 1976). Serum triglycerides are also decreased after a meal containing olestra as compared with a meal containing triglyceride of equal amounts (as contrary to above where there was no significant relationship). Coronary blood flow was greater after olestra consumption above (Cook et al. 2000).

In general, there are health benefits of consuming olestra; however, these benefits appear when consuming olestra in exorbitant amounts. The FDA has not proved such large quantities as safe.

Does the Added Vitamin K in Olestra Affect Patients Receiving Warfarin Therapy?

Moderate intake of olestra does not seem to affect patients who are receiving long-term warfarin therapy despite the added Vitamin K in olestra (Beckey et al. 1999; Holbrook et al. 2005).

Are the Studies that were Reviewed Before FDA Approval Company-based or Otherwise Researched?

Petitioners must show the FDA proof of safety; the FDA does not have its own allocated funds for independent evaluation. Thus, the research is provided by the petitioner

seeking to get the additive approved (Nestle 1998). This addresses question three above: were the "competent scientists" company based?

Is Olestra's Intended Function of Use, Weight Loss, Likely?

There is mixed data regarding whether or not substitution of olestra for fat will result in weight loss or gain of weight. In theory, substitution of a higher caloric product with a lower caloric product would result in fewer calories consumed, and thus weight loss over the long term. Studies have demonstrated that when subjects consume lower-calorie, yet similar-appearing (portion-wise) meals, they do consume fewer calories from their meals (Bell and Rolls 2001). If one can consume the same serving size of a lower-calorie product and thereby save oneself over fifty calories per serving, thousands of calories per month, and possibly tens of thousands per year duration can theoretically be saved(Rolls and Bell 1999). In practice, however, this is may not be the case because consumers may compensate for their caloric deficits or consume more because they feel that it is a "diet" product.

The FDA approved olestra in 1996. Perhaps by examining the studies done prior to the approval date, a better analysis of the limited data available to the FDA can be obtained.

Studies Prior to or during Olestra's Approval

In a study conducted in 1994, researchers found that when lean males were fed 55 grams of sucrose polyester (far more than the FDA approved) during meals or throughout the day, they did not consume more during subsequent meals or throughout the following day. Hence, the males consuming sucrose polyester, as compared with those consuming triglyceride consumed a reduced total fat and energy intake over the 2-day study. There were no reported increases in hunger ratings (Burley et al.1994).In a subsequent study the same group fed their experimental groups of lean males the same 55 grams of sucrose polyester to replace triglyceride, but this time replacing it specifically at lunch or evening meals. The results were consistent with those from the previous study; energy intake and subjective hunger ratings (both following the meal and during the next day) of those consuming sucrose polyester were not significantly different from the control group consuming triglyceride. Again, this resulted in a decreased energy intake over the 2-day study (Cotton et al. 1996a). Other studies, such as the two studies done by Hulshof et al. (1995a and b), one by feeding normal weight adults buttered croissant preloads after a duration of food-deprivation which ranged from .25-4.75 hours and one by giving subjects high-carbohydrate preloads, seemed to agree that, when fat is replaced by a polyester substitute, a caloric deficit (and thus eventually potential weight loss) would result.

A study performed in weanling pigs, an animal with a GI tract similar to small children, suggested that olestra is not absorbed in children (like adults) (Dahler et al. 1996). Young children, however, do seem to compensate for the caloric deficit created by substituting full-fat foods for olestra-containing counterparts. In a 1993 study, 29 small children (ages 2-5) were studied to determine the compensatory effects of consuming olestra. The children were fed diets of either 10% fat or 10% non-fat triglyceride substitute. Children who consumed fat-substitute wound up consuming more on a subsequent day and the total energy intake difference was only approximately 100 kJ(kilojoules) over 2 days. Children adjusted their energy intake to replace the energy deficit from consuming the fat substitute rather than actual fat. Therefore, the use of fat-substitute did not produce a noticeable caloric deficiency in these children(Birch et al.1993).Eldridge et al. (2002)propose a rationale for this compensation: "Young children may regulate energy intake more precisely because of their high energy demands relative to body size. Food consumption in children may also be

influenced more by physiological factors than in adults in whom external factors may play a greater role." Nonetheless, the same principle is evident when olestra is fed to another group requiring high-energy needs per kg of body weight: lean young men. Apparently, it is not only children, but also other groups with higher caloric needs, that compensate calories lost by a higher consumption later on. Other authors reported that when olestra was substituted for fats in diets of lean men, the subjects completely counteracted the effect of the non-caloric replacer they were fed (namely, it created an energy deficit) and consumed more, balancing the energy intake to match the subjects who consumed the full-fat energy counterparts over course of the study (Rolls et al. 1992). This addresses question five (5) of this paper—the FDA would not have had to place targeted group warnings to those who would experience adverse effects from caloric reduction because the members of these subgroups compensate for the imposed caloric deficits.

Studies Following Olestra's Approval that May have Aided the FDA had they been Available Earlier

In a long-term study (9 months) performed by Bray et al. (2002) on overweight and obese men, subjects randomly received either a diet of 33% fat (diet A), a diet of 25% fat (diet B), or a diet of 25% fat plus 8% of their diet from a fat substitute (diet C). Diet C contained the palatability of enough fat equivalent to Diet A. Essentially, although it appeared to the subjects given Diet C that they were consuming the amount of fat present in Diet A, they were actually consuming a fat percentage resembling that of diet B, yet due to the presence of fat-substitute, made the fat content appear (or taste) larger than it actually was. Diet A serves as the control in the study; diet B mimics a traditional low-fat diet whereby fat content is reduced by 8% of total daily caloric intake, and diet C resembles the traditional diet but is actually reduced fat. While subjects of all groups were required to consume their diets, all groups were entitled to consume more of fixed-composition foods if desired. All groups lost weight over the first three months of the study, but over the next six months, members of the control (diet A) maintained the weight they reached after the three weeks, members of diet B (the low-fat diet without substituted olestra for the missing fat content) regained some weight and those consuming Diet C (the low-fat diet plus olestra to substitute for the fat) continued to lose weight (Bray et al. 2002). This study, although done after olestra was FDA approved, seems to indicate that over the long-term, when olestra replaces a portion of the diet's fat content, weight loss results. A similar study performed on women displayed that when subjects have access to products which are normally restricted on diets (such as olestra-containing potato chips) they feel less deprived and are more likely to comply with their diets (Bolton et al. 1996).

How would olestra's possible compensatory mechanism differ when olestra is found in liquids? Rolls et al. (1992) conducted a study whereby creamed soup (high-fat and non-fat (made with olestra)) was fed to subjects. This study was done on both normal-weight and obese-weight subjects and follow-up intake (the next meal) did not differ. Consequently, those consuming olestra-containing soup consumed a lower energy level over the course of the study, indicating that olestra consumption in liquid form does not promote compensatory overeating.

In another study, in groups of both normal weight and obese people of both genders, researchers substituted a tenth of some of the subjects' diets' fat at breakfast and dinner with olestra while some consumed traditional triglyceride. These results concur that total energy and fat intake was lower for subjects consuming olestra rather than triglyceride because,

although subjects did compensate for a percentage of the caloric deficit they assumed when consuming olestra, they nevertheless did not compensate for the total caloric reduction (Hill et al.1998).

Some presumed that the availability of a fat-free potato chip product would translate into a belief for consumers that they can eat as much as they desired without consequences. Because olestra provides no energy, foods made with olestra are considerably less energy dense than the full-fat options or other reduced-fat alternatives in which fat energy is substituted with carbohydrates. "There are concerns that consumption of reduced-fat foods, such as olestra, can lead to unrestrained eating if consumers believe these foods are calorie free. There is some research that consumers do not substitute equal amounts of high-fat with reduced fat foods; but rather, they may eat larger portions of reduced fat products." (Satia-Abouta et al. 2003)

Many worried that consumers would use the availability of fat-modified food products as a rationale to eat more of the reduced-fat food; they may falsely assume that it won't significantly affect weight-gain (Rolls and Miller 1997). In 1998, The American Journal of Clinical Nutrition published a study designed to test whether the knowledge that a product is fat free would result in more chips consumed by subjects. Ninety-five subjects were divided into groups of those informed about the fat-free product and those uninformed. The results demonstrated that indeed, along with knowledge that a product is "dietetic," comes a desire to consume more of that product. Unrestrained subjects consumed significantly larger amounts; however, because the product was lower in fat and calories, they consumed fewer calories as compared with the full-fat chip eaters (Miller 1998). This study seems to indicate that the FDA's approval would be worthwhile. Yet it's important to note the side effects encountered during the study among those consuming fat-free chips. The author states "There were no significant differences in the occurrence of illness or malaise related to the consumption of the two types of potato chips" (Miller 1998). This may have been the case when referring to headaches, cold, and flu symptoms, but there were five complaints of menstrual discomfort and eight reports of vertigo and dizziness from those consuming fat-free chips and no complaints for those consuming regular chips. Additional studies may be in order to determine if olestra is a potential cause for these symptoms. None of the effects or symptoms hindered subjects from continuing to participate in the study. Thus, although they may have been present, they were probably not very severe. Also, because the study was only ten days in length, it is not known if there are any long-term side effects. The study found: "No significant changes in body weight occurred in any group as a result of consuming either type of potato chip over the 10-d periods." This seems odd considering the fact that those consuming fat-free chips were ultimately consuming fewer calories from the chips. It is possible that the caloric savings were modest, and thus the product was not eaten over a long enough duration for the net calorie savings to appear as pounds lost (or not gained as compared to those eating regular chips)and that that changes in weight would have become apparent had the study continued over a longer period of time. It is also possible that the subjects were compensating the calories saved due to a stimulated appetite or subsequent hunger caused by the fat-free chips (in a similar mechanism to aspartame and other macronutrient substitutes). In either case, the study demonstrated that at least, over the short term, no significant weight loss results from the substitution of olestra in chips for fat and that indeed, consumers compensate the amount and eat more when aware that the product contains fewer calories (Miller et al. 1998).

In a study designed to measure the relationship between olestra consumption and changes in dietary intake, serum lipids, and body weight, participants were required to fill out

a thorough food questionnaire; researchers characterized subjects according to both weight and olestra intake. Subjects were "normal weight," "overweight," or "obese" and either had no olestra intake (0g/d), very low intake (0-.4g/d), low intake (.4-2g/d), or moderate/high intake (2 or more grams daily). In one ounce of a snack food containing olestra, there are eight grams of olestra, and thus those were classified as "moderate/high intake." This group was eating only one quarter or more of a serving per day, which essentially translates into only five chips per day. Only two percent of the sample fell into the high intake category. The sample included fewer than 1200 participants; thus, no more than twenty-four participants were considered to consume high intakes of olestra. As compared with a baseline clinic visit (before olestra had entered the market), carbohydrate intake increased by 37g/d and total energy increased by 209 kcal/day among high olestra consumers. Among non-olestra consumers, however, a decrease of 87 kcal/day and a carbohydrate intake decrease of 14 g/d were evident. The researchers concluded that there was no statistically significant relationship between the amount of olestra consumption and serum lipids or body weight. The article attributes the lack of significant findings to "the study sample [which] limited the ability of this study to detect significant effects" (Satia-Abouta 2003).

These findings, however, cannot be taken at face value; BMI, and, correspondingly, weight (since BMI is essentially a height-weight ratio),is not the most accurate measure of one's body fat (Burkhauser and Cawley 2008). Indeed, there are a number of factors, unrelated to body fat, which may affect a person's weight, and thereby affect his/her height-weight ratio, and therefore his/her BMI. For example, salt may cause a person to retain more water (Kumar and Berl 1998), making his/her body a heavier weight. Because the researchers only measured body weight, and not body fat, it cannot be assumed that excess body fat accompanied the excess weight gained from participants who consumed the chips. Yet this water-weight is short-lived and will disappear thereafter. Particularly because olestra is used for heavily-salty snacks, consumption of olestra would translate into increased sodium consumption as well. Thus, water retention may have caused the weight gain experienced by people in the study, and not the fat-substitute, olestra.

There is also concern that olestra may adversely affect those with binge-eating disorders: "Clinical experience has shown that persons with bulimia and other binge-eating disorders are increasingly using fat-free foods during binge episodes. Because persons with bulimia are frequently mortified by their abnormal eating behavior, the use of fat-free foods allows them to feel less guilt and provides some self justification [sic] for their behavior because they are bingeing on "healthful" foods" (Hampl and Sheeley 1998). In fact, to some bulimic people, the after-effects of consuming olestra may be considered a form of purging, as many Americans perceive olestra to have a laxative effect. (Hampl and Sheeley 1998). Apparently, this idea is believed, despite the fact that research results from a study have stated otherwise (Peters et al. 1997). Regardless of whether or not this concern is an accurate one, this prediction only became apparent after the FDA approved olestra, and hence, even if true, would not have been available to deter the FDA from allowing it to pass. More research is required in order to make definite claims for the possible danger of the binge-eating disordered population with olestra on the market.

Cotton et al. found that, in general, the lower the percentage of fat in the diet remaining after the replacement of triglyceride with olestra, the more likely caloric compensation will occur(Cotton et al. 1996b). Therefore, modest substitutions of fat in the diet would result in lower compensation and greater likelihood for weight loss.

In a post marketing surveillance study (Patterson et al. 2000), heavy consumers of olestra (consuming more than 2.0g/d) had experienced a minor weight loss effect (.55 kg/year) as compared with an even smaller weight-loss effect for those who were non-olestra consumers (.01 kg/year). In this study, olestra and weight loss seem to be insignificantly correlated. In fact, this serves to underscore the fact that, even with a large replacement of fat for olestra, large weight loss reduction does not necessarily result. Obviously, because this is merely a surveillance study, little is known about the people's eating habits excluding olestra. It is possible that consumers of olestra ate more calorie-dense foods, and thus olestra did not cause weight loss despite a significant caloric reduction. Also, it is possible that those who do not consume olestra do not eat regular chips either and are generally more health-conscience.

In sum, data on weight loss of olestra presents conflicting results from other studies. There is no reliable conclusion that can be drawn from the plethora of diverging statements and conclusions.

REITERATION OF ANSWERS TO THE EIGHT QUESTIONS ABOVE:

To recapitulate the answers to the eight questions posited: (1) Olestra can be potentially hazardous to the health of man or animal if consumed in amounts higher than those established as the toxicity level by the FDA. (2) The scientists whom the FDA used to evaluate olestra were company based. (3) A case-by-case analysis of individual studies was conducted throughout the research paper.(4) No conclusive statements can be made about olestra's cause of weight loss (or lack thereof). (5)Olestra's possible weight loss effect does not endanger subgroups that would be threatened by caloric deficiency because compensation occurs in groups who need the calories to maintain and/or gain weight. (6) Olestra seems to cause other benefits of weight loss such as lowering LDL cholesterol level and lowering serum triglyceride level when consumed in amounts greater than those stated as safe by the FDA. (7) Olestra's vitamin K addition, when olestra-containing products are consumed within FDA allowed amounts, does not interfere with warfarin therapy. (8) When consumed within FDA's proposed limits, olestra does not significantly interfere with lipophilic drugs.

CONCLUSION AND DISCUSSION

In light of the fact that FDA only approved olestra in the amount of approximately 18 grams or fewer per day, and in acknowledging that no statistically significant harmful data resulted from studies testing such small amounts of olestra, it is clear that the FDA did do a thorough assessment of the product when calculating the allowed amounts for consumption during data review. However, there seems to be a considerable mismatch between the amount of olestra the FDA approved for safe consumer use and what's actually being promoted as a safe limit and consumed. The stated serving size on a package of olestra-containing Lay's Light chips contains the amount of olestra that exceeds the amount approved by the FDA as safe. Moreover, in many of the studies reviewed (particularly those which resulted in side effects), it is clear that some people consume far more than one serving of chips. In order to avoid future side-effects experienced from olestra, there should be an emphasis placed on clearly informing the public of just how much olestra-containing product is at the safety level. Thus, better communication is vital in order to avoid potentially hazardous results.

Some may argue, due to much inconclusive or hazily concluded research (particularly papers stating that more research is necessary before making any claims), that olestra had been approved prematurely to obtaining assurance of the product's safety. While it is true that numerous studies have been conducted since olestra's approval which may have shed more light on this controversial product, the FDA may have had to weigh the possibilities of

damaging effects that might have emerged from a study conducted later against a glaring negative consequence of the delay—a possible increase in obesity that could have been lessened if olestra had been approved earlier. This is especially salient, as research bringing clear results may have taken a very long time to conduct; in fact, conclusive data from long-term studies and determination of effects are still underway.

While it is true that the FDA perhaps did approve olestra hastily and should have waited a bit longer until more published studies indicated the harmfulness (or lack thereof) of the product, it is important to remember that it is *not* the FDA's job to be assured of consumer safety; they merely have to possess a reasonable certainty that a product does not cause harm. From the data, indeed there was a reasonable certainty. At a later date, when conclusive data can be drawn from the multitudinous conflicting opinions and study outcomes, the FDA can reassess and once again determine whether olestra's market circulation is appropriate for the general population and the safety of the American consumer.

REFERENCES

[Anonymous]. 2003, August 11. FDA removes olestra warning. Chemical Market Reporter

Allgood GS, Kuter DJ, Roll KT, Taylor SL, Zorich NL. 2000. Postmarketing Surveillance of New Food Ingredients: results from the program with the Fat Replacer Olestra. Regulatory Toxicology and Pharmacology 33(2):224-233.

Balasekaran R, Porter JL, Santa Ana CA, Fordtran JS. 2000. Positive Results on Tests for Steatorrhea in Persons Consuming Olestra Potato Chips. Annals of Internal Medicine 132(4):279-282.

Beckey NP, Korman LB, Parra D. 1999. Effect of the Moderate Consumption of Olestra in Patients Receiving Long-term Warfarin Therapy. Pharmacotherapy 19:1075-1079.

Bell EA, Rolls BJ. 2001. Energy Density of Foods Affects Energy Intake Across Multiple Levels of Fat Content in Lean and Obese Women. Nutrition, American Journal of Clinical 73(6):1010-1018.

Birch L, Johnson S, Jones M, Peters J. 1993. Effects of a nonenergy fat substitute on children's energy and macronutrient intake. American Journal of Clinical Nutrition 58:326-333.

Blume E. 1995. The Trials of Olestra: Is a Fat-free Lunch Too Costly? Journal of the National Cancer Institute 87:1741-1743.

Bolton M, Cousins J, Pace P, West M, Cuccaro P, Reeves R, Foreyt J. 1996. Use of olestra in nutrition education program. Journal of nutrition recipe menu development 2:33-42.

Bray G, Lovejoy J, Most-Windhauser M, Smith S, Volaufova J. 2002. A nine-month randomized clinical trial comparing a fat-substituted and fat-reduced diet in healthy obese men: the Ole Study. American Journal of Clinical Nutrition 76(5):928-934

Burkhauser RV, Cawley J. 2008. Beyond BMI: The value of more accurate measures of fatness and obesity in social science research. Journal of Health Economics 27(2):519-529.

Burley V, Cotton J, Weststrate J, Blundell J. 1994. Effect on appetite of replacing natural fat with sucrose polyester in meals or snacks accross one whole day. Obesity in Europe 34:227-233.

Center for Science in the Public Interest. A Brief History of Olestra. Retrieved from: http://www.cspinet.org/olestra/history.html.

Cheskin L, Miday R, Zorich N, Filloon T. 1998. Gastrointestinal Symptoms Following Consumption of Olestra or Regular Triglyceride Potato Chips: A Controlled Comparison. Journal of the American Medical Association 279(2):150-152.

Cook B, Cooper D, Fitzpatrick D, Smith S, Tierney D, Mehy S. 2000. The influence of a high fat meal compared to an olestra meal in coronary artery endothelial dysfunction by rubidium (RB)-82 positron emission tomography (PET) and on Post Prandial Serum Triglycerides. Clinical Positron Imaging 3(4):150.

Cooper D, Webb D, Peters J. 1997. Evaluation of the potential for olestra to to affect the availability of dietary phytochemicals. Journal of Nutrition 1646-1665.

Cotton J, Burley V, Weststrate J, Blundell J. 1996a. Fat substitution and food intake: effect of replacing fat with sucrose polyester at lunch or evening meals. British Journal of Nutrition 75:545-556.

Cotton J, Weststrate J, Blundell J. 1996b. Replacement of dietary fat with sucrose polyester: effects on energy intake and appetite controls in nonobese males. American Journal of clinical nutrition 63(6):891-896.

Dahler G, Lawson K, Tallmadge D, Vanderploeg P. 1996. Disposition of ingested olestra in weanling mini-pigs. Food and Chemical Toxicology 34(8):693-699.
Eldridge AL, Cooper DA, Peters JC. 2002. A Role for Olestra in Body Weight Management. Obesity Reviews 3(1):17-25.
Fallat R, Glueck C, Lutmer R, Mattson F. 1976. Short-term study of sucrose polyester a nonabsorbable fat-like material as a dietary agent for lowering plasma cholesterol. American Journal of Clinical Nutrition 29:1204-1215.
Faulks R, Southon S. 1997. Dietary carotenoids. Nutrition and Food Science 97(6):246.
Freston JW, Dennis ASJ, Czinn DL, Earnest MJ, Gorbach SL. 1997. Review and Analysis of the Effects of Olestra, a Dietary fat substitute on Gastrointestinal Function and Symptoms. Regulatory Toxicology and Pharmacology 26(2):210-218.
Geusau A, Tschachler E, Meixner M, Sandermann S, Papke O, Wolf C, Valic E, Stingl G, McLachlan M. 1999. Olestra increases faecal excretion of 2,3,7,8-tetrachlorodibenzo-p-dioxin. The Lancet 1266.
Glueck C, Hastings M, Allen C, Hogg E, Baehler L, Gartside P, Phillips D, Jones MHE, Braun B, Anastasia J. 1982. Sucrose Polyester and covert caloric dilution. American Journal of Clinical Nutrition 35:1352-1359.
Hampl JS, Sheeley A. 1998. Sounding the Alarm for Misuse of Olestra-Containing Foods in Binge-Eating Disorders. Journal of the American Dietetic Association 98(9):971.
Hill J, Seagle H, Johnson S, Smith S, Reed G, Tran Z, Cooper D. 1998. Effects of 14 days of covert substitution on children's energy and macronutrient intakes. American Journal of Clinical Nutrition 67:1178-1185.
Hof K, Weststrate J. 1995. Sucrose polyester and plasma carotenoid concentrations in healthy subjects. American Journal of Clinical Nutrition 62(3):591-597.
Holbrook AM, Pereira JA, Labiris R, McDonald H. 2005. Systematic Overview of Warfarin and Its Drug and Food Interactions. Archives of internal medicine 165(10):1095-1106.
Hulshof T, DeGraaf C, Weststrate J. 1995a. Short Term satiating effect of the fat replacer sucrose polyester in man. British Journal of Nutrition 74(4):569-585.
Hulshof T, Degraaf C, Weststrate J. 1995b. Short-term effects of high-fat and low-fat high-SPE croissants and appetite and energy intake at three deprivation levels. Physical Behavior 57(2):377-383.
Jacobson MF, Brown MA. 1998. Gastrointestinal Symptoms Following Olestra Consumption. Journal of the American Medical Association 280(4):325-327.
Jandacek RJ, Webb MR. 1978. Physical properties of pure sucrose octaesters. Chemistry and physics of lipids 22:163-176.
Kumar S, Berl T. 1998. Sodium. The Lancet 352(9123):220-228.
Mattson FH, Nolen GA. 1972. Absorbability by Rats of Compounds from One to Eight Ester Groups. Journal of Nutrition 102(9):1171-1176.
Mattson FH, Volpenhein RA. 1972. Hydrolysis of Fully Esterified Alcohols Containing from One to Eight Hydroxyl Groups by the Lipolytic Enzymes in Rat Pancreatic Juice. Journal of Lipid Research 13(3):325-328.
Miller HI. 2001, Spring. Obstructing Olestra. Regulation 24(1):12-13.
Miller DL, Castellanos D, Shide JC, Peters JC, Rolls BJ. 1998. Effect of Fat-Free Potato Chips with and without Nutrition Labels on Fat and Energy intakes. American Journal of Clinical Nutrition 68(2):282-290.
Miller KW, Williams DS, Carter SB, Jones MB, Mishell Jr. DR. 1990. The Effect of Olestra on Systemic Levels of Oral Contraceptives. Clinical Pharmacology Therapy 48:34-40.
Nestle M. 1998. The Selling of Olestra. Public Health Reports 113(6):508-520.
Nightingale SL. 1996. From the Food and Drug Administration. The Journal of the American Medical Association 276(21):1710.
Patterson RE, Kristal A, Peters J, Neuhouser M, Rock C, Cheskin L, Neumark-Sztainer D, Thornquist M. 2000. Changes in diet, weight, and serum lipid levels associated with olestra consumption. Archives of Internal Medicine 160:2600-2604.
Peters JC, Lawson KD, Middleton SJ, Triebwasser KC. 1997. Assessment of the Nutritional Effects of Olestra, a nonabsorbed fat replacement: summary. Journal of Nutrition 127(8):1719S-1728S.
Porterfield LM. 1997. A mysterious case of loose stools and GI cramps. RN 60(1):67.
Prince D, Welschenbach M. 1998. Olestra: A new food additive. Journal of the American Dietetic Association 98(5):565-569.

Rolls B, Bell E. 1999. Intake of fat and carbohydrate: role of energy density. European Journal of Clinical Nutrition 53(Suppl 1):S166-S173.
Rolls BJ, Miller DL. 1997. Is the low-fat message giving people a license to eat more? Journal of the American College of Nutrition 16(6):535-543.
Rolls B, Pirraglia P, Jones M, Peters J. 1992. Effects of olestra, a noncaloric fat substitute, on daily energy and fat intakes in lean men. American Journal of Clinical Nutrition 56:84-92.
Rulis AM, Levitt JA. 2009. FDA's food ingredient approval process: Safety assurance based on scientific assessment. Regulatory Toxicology and Pharmacology 53(1):20-31.
Satia-Abouta J, Kristal A, Patterson R, Neuhouser ML, Peters JC, Rock CL, Neumark-Sztainer D, Cheskin LJ, Thornquist MD. 2003. Is olestra consumption associated with changes in dietary intake, serum lipids, and body weight? Nutrition 19(9):754-759.
Thomson A, Hunt R, Zorich N. 1998. Review Article: Olestra and its gastrointestinal safety. Aliment Pharmacological Therapy 12(12):1185-1200.
Tortora, Derrikson. 2006. Principles of Anatomy and Physiology.
World Health Organization. 1998. Obesity: Preventing and Managing the Global Epidemic. Geneva: World Health Organization.