

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.<sup>34</sup>

At the FAC, the petitioner called upon Dr. Gilbert Omenn<sup>35</sup> to present results from intervention studies with beta-carotene.<sup>36</sup> 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.<sup>37</sup>

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.<sup>38</sup>

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.<sup>39</sup>

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

<sup>34</sup> Transcript, vol. 2, pp. 197, 201, 210.

<sup>35</sup> 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.

<sup>36</sup> Transcript, vol. 2, pp. 154–160.

<sup>37</sup> Transcript, vol. 2, pp. 32–34, 42–44.

<sup>38</sup> Transcript, vol. 2, pp. 233–247.

<sup>39</sup> Transcript, vol. 3, pp. 102–174.