

benefits, the agency agrees that epidemiological studies show an association between diets rich in fruits and vegetables and decreased cancer risk (61 FR 3118 at 3149).⁵ As shown in this section, all of the evidence and opinions cited by CSPI to support this objection is consistent with an association between fruit and vegetable consumption and health benefits.

Second, FDA concluded that the variation in serum levels of carotenoids associated with olestra consumption is within the normal range, given diet variations and the bioavailability of carotenoids. CSPI's objection does not directly address this second issue.⁶

CSPI offers essentially two arguments to support its view that FDA erroneously concluded that there is no demonstrated health benefit of carotenoids except the provitamin A function of beta-carotene. First, CSPI asserts that FDA's position on carotenoids is a minority view.⁷ To support this challenge, CSPI relies on statements of Drs. Regina Ziegler (CSPI exh. 10), Walter Willet (CSPI exh. 13), and Jerianne Heimendinger (CSPI exh. 8) to demonstrate that FDA's position is not well-founded. Importantly, Drs. Ziegler and Willet both state that fruits and vegetables, not carotenoids per se, are associated with reduction of the risk of cancer. (CSPI exh. 13, p. 1; CSPI exh. 10, letter dated October 23, 1995, p. 1, and letter dated January 21, 1996, p. 2.) Similarly, Dr. Heimendinger asserts merely that evidence is "increasing that * * * carotenoids *may* play important roles" in reducing cancer risk (emphasis added). (CSPI exh. 8, Heimendinger letter, p. 2). Thus, none of these statements support CSPI's claim that carotenoids have been demonstrated to have a significant beneficial health role.⁸ Accordingly,

FDA is denying CSPI's request for a hearing on this issue because the information identified in the objection is insufficient to justify the factual determination urged by CSPI (§ 12.24(b)(3)).⁹

CSPI also relies on the dietary guidelines issued by the Department of Health and Human Services (DHHS), 4th edition, to support its assertion that FDA's position on carotenoids is a minority view. Careful reading of the guidelines establishes that, once again, the evidence identified in the objection does not support the position urged by CSPI because the guidelines do not identify carotenoids per se as beneficial to human health.

Consumption of these foods [fruits and vegetables] is associated with a substantially lower risk of many chronic diseases, including certain types of cancers. (CSPI exh. 11, p. 13.)¹⁰

Elsewhere the guidelines describe the role of carotenoids in health as yet-to-be established.

The antioxidant nutrients found in plant foods (e.g., vitamin C, carotenoids, vitamin E, and certain minerals) are presently of great interest to scientists and the public because of their *potentially beneficial* role in reducing the risk for cancer and certain other chronic diseases. Scientists are also trying to determine if other substances in plant foods protect against cancer. (CSPI exh. 11, p. 13, emphasis added.)

Because the information regarding the DHHS dietary guidelines is insufficient to establish CSPI's claim regarding the role of carotenoids in human health, FDA is denying a hearing on this issue (§ 12.24(b)(3)).

As a third basis to show that FDA's position regarding carotenoids is a minority view, CSPI cites correspondence between FDA and two different institutes of the National Institutes of Health (NIH).¹¹ CSPI

examined the relationship between carotenoids and disease and concluded that there was insufficient evidence to recommend specifically the consumption of carotenoids, except to encourage the consumption of fruits and vegetables (61 FR 3118 at 3148). CSPI does not challenge this fact.

⁸ CSPI's objection and hearing request on this point also refer to an article published by Dr. Edward Giovannucci addressing the association between high intake of tomato products and reduced incidence of prostate cancer and claims that Dr. Giovannucci opposes the approval of olestra because of the additive's potential to deplete carotenoids, citing CSPI exh. 8. Although CSPI exh. 8 contains numerous letters from individuals opposing olestra's approval, there is no identifiable communication from Dr. Giovannucci in that exhibit. In the absence of specifically identified evidence demonstrating Dr. Giovannucci's position, FDA is denying CSPI's objection and hearing on this point (§ 12.24 (b)(2)). In addition, CSPI's reliance on the Giovannucci article is misplaced because, even as described by CSPI, the paper does not support CSPI's claim that carotenoids themselves have been shown to have distinct health benefits. Accordingly, FDA is denying CSPI's claim on this point (§ 12.24(b)(2) and (b)(4)).

⁹ CSPI also relies on its White Paper (CSPI exh. 1) and exhibits 3 through 7 to the White Paper.

challenges FDA's reliance on the letter from the NEI because it only addresses the role of beta-carotene, not lutein or lycopene. Even if CSPI's claims on this issue are correct, FDA is denying its request for a hearing because the assertion that lutein and lycopene have a beneficial role in eye health is not supported by specifically identified factual evidence. Accordingly, CSPI's allegations are mere speculation, which is not an adequate basis for a hearing request (§ 12.24(b)(2)).

With respect to the NCI, CSPI claims that there are conflicting views in the record from NCI and that FDA should determine, on the record, the "official" NIH position. Specifically, CSPI believes that Dr. Ziegler's views are significantly different from the views expressed by the then Director of the Division of Cancer Prevention and Control, NCI, NIH, Dr. Peter Greenwald.¹² CSPI does not demonstrate why such a determination is necessary, the authority under which it would be done, or how it would alter the outcome of this proceeding. Accordingly, FDA is denying CSPI's request for a hearing on this issue (§ 12.24(b)(2) and (b)(4)).

Finally, CSPI asserts that FDA staff, the OWG, and the FAC failed to acknowledge and accept data from in vitro, animal, and epidemiologic studies that all point to a protective role for carotenoids. In support of this portion of its second objection, CSPI cites two articles (CSPI obj. at p. 20, footnote 19).¹³ This portion of CSPI's objection is without foundation because the information specifically cited is not adequate to establish the factual issue urged by CSPI¹⁴ (§ 12.24(b)(3)). In particular, the first article cited (Garewal, H., "Antioxidants in Oral Cancer Prevention," *American Journal of Clinical Nutrition*, 62:1410S-1416S, 1995, at 1413S.) concludes that the reported results do not themselves demonstrate a reduction in human

¹² In fact, CSPI's own documents demonstrate that there is no conflict as to the official statements of the NCI regarding carotenoids because Dr. Ziegler acknowledges that she does not speak on behalf of the NCI (even though her two letters are written on NCI letterhead). (CSPI exh. 10, letter dated January 21, 1996, p. 1).

¹³ These articles are the only specific data identified by CSPI to support its second objection.

¹⁴ CSPI claims that FDA, the OWG, and the FAC ignored certain data on carotenoids. Importantly, however, the two journal articles cited by CSPI were published in a supplement to the December 1, 1995, issue of the *American Journal of Clinical Nutrition*. The FAC/OWG meeting was held November 14 through 17, 1995, and CSPI presents no evidence that these articles were even available at the time of the meeting. In fact, these two articles were not submitted to FDA until December 22, 1995.

⁵ Indeed, CSPI itself concedes that there may be "substances in fruits and vegetables for which carotenoids are markers" that are beneficial to health (CSPI obj. at 19).

⁶ Although not strictly relevant to the objections lodged by CSPI, it is important to note that in its 1996 final rule, FDA acknowledged the growing body of data and information regarding carotenoids and committed to reviewing such information within 30 months of olestra's initial approval (61 FR 3118 at 3168 and footnote 94). In June 1998, FDA presented the accumulated data and information to the FAC.

⁷ Although CSPI asserts that FDA's view is a minority view, the final rule noted that five different conferences or reviewing groups have examined the relationship between carotenoids and disease and concluded that there was insufficient evidence to recommend specifically the consumption of carotenoids, except to encourage the consumption of fruits and vegetables (61 FR 3118 at 3148). CSPI does not challenge this fact.

⁸ CSPI's objection and hearing request on this point also refer to an article published by Dr. Edward Giovannucci addressing the association