

TABLE 1.

Category of Food	Maximum Levels in Food (As Served)
Breakfast cereals	350 IU/100 grams (g)
Grain products and pastas	90 IU/100 g
Milk	42 IU/100 g
Milk products	89 IU/100 g

Additionally, vitamin D is affirmed as GRAS for use in infant formula (§ 184.1950(c)(2)) and as an optional ingredient in margarine (§ 184.1950(c)(3)).

Vitamin D is essential for human health. Humans can synthesize significant amounts of vitamin D₃ in skin from its precursor, 7-dehydrocholesterol, under exposure to ultraviolet B radiation in sunlight. Other sources of naturally occurring vitamin D are foods such as butter, buttermilk, cheese, cream, eggs, fish, goat milk, meat fats and organ meats, mushrooms, and sour cream.

The major function of vitamin D is the maintenance of blood serum concentrations of calcium and phosphorus by enhancing the absorption of these minerals in the small intestine. Vitamin D deficiency can lead to abnormalities in calcium and bone metabolism such as rickets in children or osteomalacia in adults. The elderly, who have significantly decreased capacity for the production of vitamin D₃ in skin, and patients with intestinal malabsorption syndromes are especially prone to vitamin D deficiency. At high levels, vitamin D may be toxic. Because it is metabolized to inactive forms in the skin, vitamin D does not accumulate significantly in the body as a result of sun exposure. Excessive dietary intake of vitamin D elevates blood plasma calcium levels by increased intestinal absorption and/or mobilization from the bone.

Vitamin D₃, also known as cholecalciferol, is the chemical 9,10-seco(5Z,7E)-5,7,10(19)-cholestatrien-3-ol. Vitamin D₃ occurs in, and is isolated from fish liver oils. It also is manufactured by ultraviolet irradiation of 7-dehydrocholesterol that is derived synthetically from natural cholesterol. In both methods, vitamin D₃ is purified by crystallization.

To support the safety of the proposed use of vitamin D₃, The Minute Maid Co. submitted a summary of the metabolism of vitamin D, a number of publications pertaining to human clinical studies, bioavailability studies, and dietary intake estimates. Based on these data, the petitioner concludes that the proposed use of vitamin D₃ in calcium-

fortified fruit juices and juice drinks is safe.

II. Evaluation of Safety

In order to establish, with reasonable certainty, that a new food additive is not harmful under its intended conditions of use, FDA considers the projected human dietary exposure to the additive, the additive's toxicological data, and other relevant information (such as published literature) available to the agency.

In determining whether the proposed use of an additive is safe, FDA compares an individual's estimated daily intake (EDI) of the additive to an acceptable intake level established by toxicological data. The EDI is determined by projections based on the amount of the additive proposed for use in particular foods and on data regarding the consumption levels of these particular foods. The agency commonly uses the EDI for the 90th percentile consumer of a food additive as a measure of high chronic dietary exposure.

A. Acceptable Daily Intake for Vitamin D for Adults, Children, and Infants

In 1997, the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board at the National Academy of Sciences Institute of Medicine (IOM) conducted an extensive review of toxicology and metabolism studies on vitamin D published through 1996. The IOM published a detailed report that included a tolerable upper intake level (UL) for vitamin D (both D₂ and D₃) for infants, children and adults (Ref. 1). The IOM UL for vitamin D for children 1 to 18 years of age and adults is 2,000 IU/day and for infants is 1,000 IU/day.

The IOM considers the UL as the highest usual intake level of a nutrient that poses no risk of adverse effects when the nutrient is consumed over long periods of time. The UL is determined using a risk assessment model developed specifically for nutrients and considers intake from all sources: Food, water, nutrient supplements, and pharmacological agents. The dose-response assessment, which concludes with an estimate of the UL, is built upon three toxicological

concepts commonly used in assessing the risk of exposures to chemical substances: No observed adverse effect level, lowest observed effect level and an uncertainty factor.

B. Estimated Daily Intake for Vitamin D

The petitioner provided average and 90th percentile vitamin D intake estimates for consumers of fruit juices and juice drinks from: (1) The proposed use in calcium-fortified fruit juices and juice drinks, (2) current uses in conventional foods (including naturally occurring sources of vitamin D), (3) current and proposed uses in conventional foods, and (4) current and proposed uses in both conventional foods and dietary supplements. The petitioner presented intake estimates for the general population, 2 years of age and older, and for 15 population subgroups (including estimates for infants less than 1 year old; children 1 year to 3 years old; and adults). The agency has determined that the methodology used to calculate these estimates is appropriate (Ref. 2).

For the proposed food use, dietary intake of vitamin D₃ for 90th percentile consumers of fruit juices and juice drinks, 2 years of age and older, was estimated to be 211 IU per person per day (IU/p/d). The corresponding mean intake was estimated to be 110 IU/p/d.

For currently regulated uses in conventional foods (including naturally occurring sources), mean dietary exposure to vitamin D for consumers of fruit juices and juice drinks was estimated to be 197 IU/p/d for consumers 2 years of age and older. Intake at the 90th percentile was estimated to be 368 IU/p/day. For consumers of fruit juices and juice drinks 2 years of age and older, average and 90th percentile dietary intakes from current (including naturally occurring sources) and proposed food uses of vitamin D were estimated to be 306 IU/p/d and 519 IU/p/d, respectively.

The petitioner also considered the intake of vitamin D from dietary supplements. The National Health and Nutrition Examination Survey III (NHANES III) data indicate that approximately 40 percent of the U.S. population 2 months of age and older take dietary supplements. The NHANES