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# **Safety Assessment of Prunus Amygdalus Dulcis (Sweet Almond) Meal Seed as Used in Cosmetics**

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Status: Re-Review for Panel Consideration  
Release Date: February 10, 2023  
Panel Meeting Date: March 6-7, 2023

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Christina Burnett, Senior Scientific Analyst/ Writer, CIR.



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**Memorandum**

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons  
From: Christina Burnett, MSES, Senior Scientific Analyst/Writer, CIR  
Date: February 10, 2023  
Subject: Re-Review of the Safety Assessment of Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published a review of the safety of Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal in 1983 (identified as *originalreport\_SweetAlmond\_032023* in the pdf); at that time, this ingredient was named Almond Meal. The Panel stated on the basis of the available animal data and limited clinical experience presented in the report, the Panel concludes this ingredient is safe for topical application to humans in the present practices of use and concentration (as described in that assessment). The Panel previously considered a re-review of this report and reaffirmed the 1983 conclusion, as published in 2005 (*2005rereview\_SweetAlmond\_032023*).

A second ingredient, Prunus Amygdalus Dulcis (Sweet Almond) Oil, was included in the original report and the initial re-review. (At the time of the original report, this ingredient was named Sweet Almond Oil.) However, this ingredient is not being considered in this re-review because it is included in the safety assessment of plant-derived fatty acids, published in 2017.

Because it has been at least 15 years since the previous rereview was published, in accord with Cosmetic Ingredient Review (CIR) Procedures, the Panel should consider whether the safety assessment of Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal should be re-opened. An extensive search of the world's literature was performed for studies dated 2001 forward. No relevant published data were found. An historical overview, comparison of original and new use data, and the search strategy used are enclosed herein (*newdata\_SweetAlmond\_032023*).

Also included for your review is a table of current and historical use data (*usetable\_SweetAlmond\_032023*). (As per the Panel's request at the December 2022 meeting, an updated use table format has been implemented. The frequency and concentration of use is presented both cumulatively by likely duration and exposure and individually by product category.) Since the initial re-review was considered, the frequency of use has decreased slightly from 15 to 14 uses. In 2002, the maximum concentration of use for this ingredient was reported to be 27% in leave-on products and 2% in rinse-off products. No concentration of use was reported in the 2022 survey for this ingredient.

If, upon review of the new studies and updated use data, the Panel determines that a re-review is warranted, a Draft Amended Report will be presented at an upcoming meeting.

**Re-Review - Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal - History and New Data**

(Christina Burnett – March 2023 meeting)

Ingredients (1)	Citation	Conclusion	Use - New Data	Results	Use - Existing Data	Results	Notes
Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal (originally named Almond Meal)	JACT-2(5):85-99, 1983 – original report;	safe for topical applications to humans in the present practices of use and concentration	frequency of use (2022) conc of use (2022)	14 none reported	frequency of use (2002) conc of use (2002)	15 0.5-27%	Use decreased by 1 since the 2002 re-review; no concentrations of use were reported in 2022.
<i>Change to Original List Prunus Amygdalus Dulcis (Sweet Almond) Oil (originally named Sweet Almond Oil) is included in the Plant-Derived Fatty Acid Oils report [IJT 36(S3): 51-159 (2017)], and therefore not included herein.</i>	IJT-24(Suppl 1):98-101, 2005 – re-review summary	conclusion reaffirmed					

Search (from 2001 on)

PubMed

((prunus amygdalus seed meal) OR (sweet almond seed meal)) OR (almond seed meal) =6 hits; 0 relevant

ECHA

No entries.

European Union

No restrictions and no opinions on safety.

**2022 and historical frequency and concentration of use according to duration and exposure and by product category**

	# of Uses		Max Conc of Use (%)	
	2022 <sup>1</sup>	2002 <sup>2</sup>	2022 <sup>3</sup>	2002 <sup>2</sup>
<b>Totals</b>	<b>14<sup>‡</sup></b>	<b>15</b>	<b>NR</b>	<b>0.5-27</b>
<b>summarized by likely duration and exposure*</b>				
<b>Duration of Use</b>				
Leave-On	12	3	NR	0.5-27
Rinse-Off	2	12	NR	0.5-2
Diluted for (Bath) Use	NR	NR	NR	NR
<b>Exposure Type**</b>				
Eye Area	1	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	2 <sup>a</sup> ; 1 <sup>b</sup>	1 <sup>b</sup>	NR	0.5 <sup>b</sup>
Incidental Inhalation-Powder	2; 1 <sup>b</sup>	1 <sup>b</sup>	NR	27; 0.5 <sup>b</sup>
Dermal Contact	14	14	NR	0.5-27
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	1	NR	NR
Mucous Membrane	1	3	NR	0.5-2
Baby Products	NR	NR	NR	NR
<b>as reported by product category</b>				
<b>Eye Makeup Preparations</b>				
Other Eye Makeup Preparations	1		NR	
<b>Fragrance Preparations</b>				
Powders (dusting/talcum, excl aftershave talc)		NR		27
<b>Makeup Preparations</b>				
Face Powders	2		NR	
Makeup Bases	1		NR	
Makeup Fixatives	2		NR	
Other Makeup Preparations	1		NR	
<b>Manicuring Preparations (Nail)</b>				
Cuticle Softeners		1		NR
<b>Personal Cleanliness Products</b>				
Bath Soaps and Detergents		2		0.5-2
Other Personal Cleanliness Products	1	1	NR	NR
<b>Skin Care Preparations</b>				
Cleansing	1	2	NR	NR
Body and Hand (exc shave)	1	1	NR	0.5
Moisturizing	2		NR	
Paste Masks (mud packs)	1	7	NR	2
Other Skin Care Preparations	1	1	NR	NR

NR – not reported

‡ Reported as Prunus Dulcis (Sweet Almond) Seed Meal in the 2022 VCRP.

\*likely duration and exposure is derived based on product category (see Use Categorization <https://www.cir-safety.org/cir-findings>)

\*\*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

<sup>a</sup> It is possible these products are sprays, but it is not specified whether the reported uses are sprays.<sup>b</sup> Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories**REFERENCES**

1. US Food and Drug Administration (FDA) Center for Food Safety & Applied Nutrition (CFSAN). 2022. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. (Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2022; received January 11, 2022).
2. Andersen FA (ed). Annual Review of Cosmetic Ingredient Safety Assessments - 2002/2003. Sweet Almond Oil and Almond Meal. *Int J Toxicol.* 2005;24(Suppl 1):98-101.
3. Personal Care Products Council. 2022. Concentration of use by FDA product category: Prunus Amygdalus Dulcis Seed Meal. Unpublished data submitted by Personal Care Products Council on October 28, 2022.

## 4

# Final Report on the Safety Assessment of Sweet Almond Oil and Almond Meal

Sweet Almond Oil is used as an emollient and emulsifier in cosmetic products. Almond Meal is used as a skin cleanser and in medicated soaps.

Pharmacological studies reveal that Sweet Almond Oil is absorbed slowly through intact skin, whereas it is easily absorbed and digested following oral administration. It is nontoxic when ingested, and products containing up to 25% Sweet Almond Oil are practically nonirritating to rabbit skin and only minimally irritating to rabbit eyes. In subchronic studies, Sweet Almond Oil at 100% concentrations was only slightly irritating to rabbit skin.

In clinical studies, undiluted Sweet Almond Oil and products containing up to 25% Sweet Almond were practically nonirritating and nonsensitizing. Formulations containing up to 2% Sweet Almond Meal were practically nonirritating and nonsensitizing when tested in a repeated insult patch test.

On the basis of the available data and clinical experience, it is concluded that Sweet Almond Oil and Almond Meal are safe for topical application to humans in the present practices of use and concentration.

## CHEMISTRY

### Composition and Preparation

#### Sweet Almond Oil

Sweet Almond Oil is the fixed oil obtained from the ripe seed kernels of various species of *Prunus*. Almond kernels contain as much as 50% oil, which can either be physically expressed (35% yield) or chemically extracted (50% yield).<sup>(1)</sup>

Sweet Almond Oil consists mostly of triglycerides of oleic and linoleic acids. Other fatty acid glycerides are also present.<sup>(2)</sup> Table 1 summarizes the fatty acid composition of Sweet Almond Oil. Trace quantities of other fatty acids, vitamins (including vitamins A, B complex, and E), and amino acids (especially glutamic acid, aspartic acid, and arginine) have been identified as components of this ingredient.<sup>(3-5)</sup>

#### Almond Meal

Almond Meal is the solid residue remaining after the expression of oil from the ripe seed kernels of the species *Prunus amygdalus* or *P. communis*. The resi-

**TABLE 1.** Concentrations of Various Fatty Acids in Sweet Almond Oil.<sup>a</sup>

<i>Fatty acid</i>	<i>C chain length: Double bond(s)</i>	<i>Concentration range (%)</i>
Oleic	18:1	66.3–72.4
Linoleic	18:2	18.4–22.3
Palmitic	16:0	5.7–7.9
Stearic	18:0	0.5–1.2
Palmitoleic	16:1	0.4–0.7

<sup>a</sup>Data from Refs. 6–8.

due cake is then dried and ground to a controlled particle size. Almond Meal consists of proteins, carbohydrates, fat, fiber, sugar, ash, and up to 10% water.<sup>(2)</sup>

## Properties

### Sweet Almond Oil

Sweet Almond Oil is a pale, straw-colored or colorless liquid with a faint odor and mild taste. It is slightly soluble in alcohol, miscible with benzene, chloroform, and ether, and insoluble in water.<sup>(9)</sup> Table 2 lists other physical and chemical properties of Sweet Almond Oil.

### Almond Meal

Almond Meal is a yellow to light-tan loose powder with an odor of fresh, ground almonds.<sup>(10)</sup>

**TABLE 2.** Chemical and Physical Properties of Sweet Almond Oil.

<i>Property</i>	<i>Value</i>	<i>Ref.</i>
Specific gravity	0.910,	11
	0.9311	12
Refractive index (20°)	1.541–1.546,	12
	1.4639,	1
	1.4626	8
Congealing temperature	–20°C	9
Acetyl value <sup>a</sup>	4.67	1
Reicher–Meissl number <sup>b</sup>	0.08	1
Saponification number	188	8
Iodine number	95–105	11
Peroxide number	0.61,	1
	0.00	8
Free fatty acid	0.027	8
Unsaponifiable material	0.53%	8
Unsaturated/saturated ratio	11.3	6

<sup>a</sup>Measures free OH groups.<sup>b</sup>Measures volatile, soluble fatty acid content.

### Reactivity/Stability

Sweet Almond Oil will undergo oxidation and other reactions typical of fixed oils. Autoxidation of this ingredient results in a decreased peroxide value, an increased acid value, and rancidity. The rate of autoxidation of Sweet Almond Oil increases as temperature increases. Marked changes in peroxide and acid values occurred when Sweet Almond Oil was either autoclaved at 122°C for 30 minutes and stored at 37.5°C, or stored at room temperature (20°–28°C) for ten weeks. The addition of antioxidants, such as propyl gallate, greatly increases the stability and shelf-life of Sweet Almond Oil.<sup>(13)</sup> Kedvessy<sup>(14)</sup> reported that almond oil tends to become rancid more quickly than other fixed oils.

### Analytical Methods

Chromatography is frequently used to determine the presence or composition of Sweet Almond Oil. A common technique for determining the composition of Sweet Almond Oil involves saponification, esterification of the fatty acids to their methyl ester derivatives, and identification by gas chromatography.<sup>(6,7)</sup> The following is a list of other analytical methods used to identify this ingredient:

Gas chromatography<sup>(5,15)</sup>

Gas chromatography plus ultraviolet spectroscopy<sup>(16)</sup>

Thin-layer chromatography<sup>(3,5,15)</sup>

Vapor-phase chromatography plus infrared spectroscopy<sup>(17)</sup>

Spectrofluorimetry<sup>(3)</sup>

Iodochlorometric titration<sup>(18)</sup>

Almond Meal can be identified by infrared spectroscopy.<sup>(19)</sup>

## USE

### Cosmetic

The use of almond derivatives began with the ancient Hindus, who employed a paste made of crushed almonds as a body cleanser. In cosmetics today, almond products are widely used. Sweet Almond Oil, in shampoos, imparts a desirable sheen to the hair and acts as an oil/water emulsifier. As an emollient in skin care products, this ingredient is mildly occlusive and produces hydration, softening, and increased flexibility of the stratum corneum.<sup>(20)</sup> Almond Meal is used as a cleanser by people whose skin cannot tolerate soaps; it is also used in medicated soaps for the treatment of acne.<sup>(21,22)</sup>

According to the industry's voluntary submissions to the Food and Drug Administration (FDA) in 1976 (Table 3), Sweet Almond Oil is used in over 280 cosmetic formulations in concentrations up to 50%; lipsticks containing up to 25% Sweet Almond Oil comprise nearly two-thirds of these formulations. Almond Meal is reportedly used in 16 formulations at concentrations up to 25%.

The cosmetic product formulation computer printout which is made available by FDA is compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.<sup>(25)</sup> Ingredients are listed in

TABLE 3. Product Formulation Data.<sup>a</sup>

Product category <sup>b</sup>	Total no. containing ingredient	No. product formulations within each concentration range (%) <sup>b</sup>						
		Unreported Concentration	>25-50	>10-25	>5-10	>1-5	>0.1-1	≤0.1
<i>Sweet Almond Oil</i>								
Bath oils, tablets, and salts	1	-	-	-	-	-	1	-
Fragrance preparations	3	-	-	-	-	3	-	-
Hair shampoo (noncoloring)	1	-	-	-	-	-	-	1
Blushers (all types)	3	-	-	-	3	-	-	-
Face powders	1	-	-	-	-	-	-	1
Makeup foundations	2	-	-	-	1	-	1	-
Lipstick	184	-	-	65	96	7	14	2
Makeup bases	5	-	-	-	-	2	3	-
Nail polish and enamel removers	1	-	-	-	-	-	-	1
Shaving cream (aerosol, brushless, and lather)	1	-	-	-	-	1	-	-
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	12	-	1	1	2	5	2	1
Face, body, and hand skin care preparations (excluding shaving preparations)	9	-	-	-	-	9	-	-
Moisturizing skin care preparations	21	-	-	2	2	11	5	1
Night skin care preparations	17	-	1	2	3	11	-	-
Paste masks (mud packs)	3	-	-	-	-	3	-	-
Other skin care preparations	6	-	-	1	1	3	1	-
Suntan gels, creams, and liquids	10	-	-	1	1	6	2	-
1976 TOTALS	280	-	2	72	109	61	29	7
1979 TOTALS <sup>c</sup>	114	-	1	6	20	61	20	60
<i>Almond Meal</i>								
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	6	-	-	1	1	4	-	-
Paste masks (mud packs)	6	-	-	-	-	5	1	-
Other skin care preparations	4	-	-	-	-	2	2	-
1976 TOTALS	16	-	-	1	1	11	3	-
1979 TOTALS <sup>c</sup>	15	-	-	-	1	11	3	-

<sup>a</sup>Data from Ref. 23.<sup>b</sup>Preset product categories and concentration ranges in accordance with federal filing regulations (21 CFR 720.4).<sup>c</sup>Data from Ref. 24.



prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the true, effective concentration found in the finished product; the effective concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to tenfold error in the assumed ingredient concentration.

Products containing Sweet Almond Oil or Almond Meal contact the lips, face, nails, skin, and hair. Such products are used daily or occasionally; contact with these ingredients could be continuous.

### **Pharmaceutical**

As a pharmaceutical aid, Sweet Almond Oil is used as an emollient and perfume.<sup>(9)</sup> Sweet Almond Oil has also been used as a solvent for parenterally administered drugs.<sup>(13)</sup> In Britain, it is used as a solvent in injectable solutions for hemorrhoid treatment.<sup>(26,27)</sup>

## **BIOLOGICAL PROPERTIES**

### **Antibacterial Effects**

In an early antimicrobial study of natural oils, Sweet Almond Oil was added to cultures of bacteria; numbers of viable organisms were counted at various intervals following treatment. After five hours, Sweet Almond Oil reduced the number of viable bacteria by 98.9%.<sup>(28)</sup> In another test, the bacteriocidal activity of various natural oils on *Staphylococcus aureus* was studied. Oils were added to bacterial cultures, and the time required to reduce the number of viable organisms to zero was measured. Sweet Almond Oil required 3–4 days; this value was much higher than the other oils tested, indicating lower activity.<sup>(29)</sup>

### **Absorption, Metabolism, and Excretion**

The percutaneous absorption of Sweet Almond Oil was studied in adult albino rats. A solution containing this ingredient and physostigmine was applied to the skin of each animal; latency time to muscle contraction was then measured. When compared to other oil mixtures tested, Sweet Almond Oil-physostigmine had a relatively long latency time, indicating lower percutaneous absorption. The authors concluded that increased amounts of short chain and polyunsaturated fatty acids in oils favor their percutaneous absorption.<sup>(30)</sup>

When ingested, di- and triglycerides are hydrolyzed to monoglycerides by lipases. In the duodenum, the monoglycerides form mixed micelles with the free fatty acids, bile salts, cholesterol, and sodium ions. The micelle then penetrates the mucosal cell brush border where the free fatty acids and monoglycerides are

resynthesized to triglycerides in the endoplasmic reticulum. Proteins and phospholipids, synthesized in the mucosal cell, combine with cholesterol to produce a specific lipoprotein, which coats the triglyceride, forming a chylomicron. The chylomicra then leave the intestinal mucosal cell and enter the lymphatic system and the blood. Capillary endothelial cell-bound lipoprotein lipases degrade the chylomicra, freeing the fatty acids and glycerol for cellular uptake and subsequent lipid storage or catabolism.<sup>(31,32)</sup>

Deuel and Holmes<sup>(33)</sup> studied the digestability of natural oils in humans. Two men were placed on a three-day, fat-free, basal diet which included a cornstarch pudding containing a test oil. Sweet Almond Oil was well-digested (97%) when compared to other oils. In another study, Sweet Almond Oil or whole almonds were added to a lipid-free basal diet at concentrations of 10% and 18%, respectively, and fed to groups of three rats for three days. Absorption of the Almond Oil was 98%–99% complete.<sup>(34)</sup>

The digestion of several edible vegetable oils was studied enzymatically, *in vitro*. At room temperature, Sweet Almond Oil was degraded slowly by pancreatic lipase when compared to other oils tested.<sup>(35)</sup> A comparatively slow rate of digestion by pancreatic lipase was also observed in an experiment performed at 37°C.<sup>(36)</sup>

## Animal Toxicology

### Acute Studies

#### *Oral Toxicity*

Undiluted Sweet Almond Oil and products containing 2%–18% Sweet Almond Oil were tested for acute oral toxicity. Test materials were administered to groups of five to ten animals, at one or more dose levels. Animals were then observed for 5–14 days for signs of toxicity, as well as changes in appearance or behavior. In some studies, animals were sacrificed and necropsied at the end of the observation period. Results of these tests indicate that undiluted Sweet Almond Oil and products containing up to 18% Sweet Almond Oil are practically nontoxic (Table 4).

A soap containing 2% Almond Meal was tested for acute oral toxicity. The test material was administered to a group of five rats at a dose of 5 g/kg. Animals were observed for up to 14 days for signs of toxicity, as well as changes in appearance or behavior. Results of this test, summarized in Table 4, indicate that the soap containing 2% Almond Meal was practically nontoxic.<sup>(37)</sup>

#### *Dermal Toxicity*

Undiluted Sweet Almond Oil was tested for acute dermal toxicity in guinea pigs. The test material was applied under occlusion to the clipped abraded and intact skin of 12 animals (6 M/6 F) at a dose of 3 g/kg. At 24 hours, excess material was rinsed off. Observations were made daily for seven days; animals were then sacrificed and necropsied. The acute dermal LD<sub>50</sub> was > 3 g/kg, indicating that Sweet Almond Oil is practically nontoxic by percutaneous absorption.<sup>(38)</sup>

TABLE 4. Acute Oral Toxicity.

Ingredient (product)	Effective conc. (%)	Dose (g/kg)	No. and spec. of animal	LD50 (g/kg)	Comment <sup>a</sup>	Ref.
Sweet Almond Oil	Undiluted	5	5 rats	>5	Practically nontoxic	38
Sweet Almond Oil	Undiluted	up to 14.7	5-10 rats/group	>14.7	Practically nontoxic	39
Sweet Almond Oil (18% in a moisturizer)	9	up to 15.9	5-10 rats/group	- <sup>b</sup>	Moisturizer was relatively harmless	40
Sweet Almond Oil (2.5% in a foundation)	2.5	up to 15.9	5-10 rats/group	-	Foundation was relatively harmless	41
Sweet Almond Oil (2% in a moisturizer)	2	10	10 mice	-	Moisturizer was practically nontoxic	42
Almond Meal (2% in a soap)	2	5	5 rats	-	Soap was practically nontoxic	37

<sup>a</sup>According to Hodge and Sterner, Ref. 43.

<sup>b</sup>The LD50 value for this product was not reached at the highest dose tested.

#### Subcutaneous Toxicity

Guinea pigs were injected subcutaneously with single or multiple doses of a 10% Sweet Almond Oil emulsion in saline (1 ml/dose). After a single injection, minute oil emboli were found in the lungs of these animals. After six to ten hours, emboli caused local infiltration of eosinophils in the lung parenchyma. Six days after repeated oil injections, investigators observed a peripheral blood eosinophilia, which reached a maximum increase of 16.5% by the third week. The eosinophilia was suggested to be a nonallergic reaction.<sup>(44)</sup>

#### Primary Skin Irritation

Undiluted Sweet Almond Oil was tested for irritancy in groups of six male albino rabbits. The test material was applied under occlusion to the clipped intact and abraded dorsal skin of each animal. Twenty-three hours later, patches were removed; sites were scored at 24 and 48 hours. The Primary Irritation Indices (PIIs) for seven test samples of Sweet Almond Oil ranged from 0 to 0.18 (maximum score = 8), indicating that this ingredient is practically nonirritating to skin.<sup>(45)</sup> Table 5 summarizes primary skin irritation data.

Undiluted Sweet Almond Oil and two formulations each containing 25% Sweet Almond Oil were tested for skin irritancy by the following procedure. The test material was applied under occlusion to the shaved intact dorsal skin of groups of nine female albino rabbits. Patches were removed and sites were scored for erythema at 24 and 72 hours. Undiluted Sweet Almond Oil was nonirritating (PII = 0; maximum score = 4); whereas, the formulations containing 25% Sweet Almond Oil were minimally irritating (PIIs = 0.28 and 0.72, respectively). Results are presented in Table 5.

Almond Meal, undiluted and in aqueous slurry, was tested for skin irritation in rabbits (Table 5). The test material was applied under occlusion to the shaved

**TABLE 5.** Primary Skin Irritation.

Ingredient (product)	Effective conc. (%)	No. of rabbits	Skin: intact(i) abraded(a)	Results		Comment	Ref.
				PII <sup>a</sup>	PSI <sup>b</sup>		
Sweet Almond Oil	Undiluted	6	i,a	0.04		Practically nonirritating	45
	Undiluted	6	i,a	0.00		Nonirritating	45
	Undiluted	6	i,a	0.00		Nonirritating	45
	Undiluted	6	i,a	0.18		Practically nonirritating	45
	Undiluted	6	i,a	0.00		Nonirritating	45
	Undiluted	6	i,a	0.04		Practically nonirritating	45
	Undiluted	9	i		0.00	Nonirritating	38
Sweet Almond Oil (25% in a moisturizer)	25	9	i		0.28	Practically nonirritating	46
	25	9	i		0.72	Practically nonirritating	47
Almond Meal	Undiluted	9	i		0.27	Practically nonirritating	48
	Aqueous slurry	9	i		0.20	Practically nonirritating	10

<sup>a</sup>Primary Irritation Index—maximum value = 8.0.

<sup>b</sup>Primary Skin Irritation—maximum score = 4.0 (erythema only).

intact dorsal skin of groups of nine female albino rabbits. Patches were removed and sites were scored for erythema at 24 and 72 hours. Almond Meal, undiluted and in aqueous slurry, was minimally irritating (PIIs = 0.27 and 0.20, respectively; maximum score = 4).<sup>(10,48)</sup>

#### Primary Eye Irritation

The Draize method or a modification of it was used to test the eye irritancy of undiluted Sweet Almond Oil and cosmetic formulations containing up to 25% Sweet Almond Oil. The test material was instilled into one eye of each of three to six rabbits; the other eye served as an untreated control. Irritation was evaluated one hour, as well as one, two, three, four, and seven days later. Undiluted Sweet Almond Oil was practically nonirritating or minimally irritating. Formulations containing up to 25% Sweet Almond Oil were nonirritating to minimally irritating. In most instances, reactions that occurred were limited to conjunctival irritation, which cleared by the third day of observation (Table 6).

Undiluted Almond Meal and a soap containing 8% Almond Meal were tested for primary eye irritation in groups of six rabbits. The test material was instilled into one eye of each animal; the other eye served as an untreated control. Irritation was evaluated as above. Results of these tests, summarized in Table 6, indicate that undiluted Almond Meal was practically nonirritating; whereas, the soap containing 8% Almond Meal was minimally irritating.<sup>(10,37)</sup>

### Subchronic Studies

#### Dermal Toxicity

A medicated soap containing 2% Almond Meal was tested for dermal toxicity in a 12-week rabbit study. A solution of the soap containing 0.5% Almond Meal

TABLE 6. Primary Eye Irritation.

Ingredient (product)	Effective conc. (%)	No. of rabbits	Draize eye irritation score <sup>a</sup>					AOI <sup>b</sup>	Comment <sup>c</sup>	Ref.
			Day							
			1 Hr.	1	2	3	4			
Sweet Almond Oil	Undiluted	6						8.17	Minimally irritating	45
Sweet Almond Oil	Undiluted	6						5.00	Minimally irritating	45
Sweet Almond Oil	Undiluted	6						6.50	Minimally irritating	45
Sweet Almond Oil	Undiluted	6						3.83	Minimally irritating	45
Sweet Almond Oil	Undiluted	6						4.00	Minimally irritating	45
Sweet Almond Oil	Undiluted	6						7.00	Minimally irritating	45
Sweet Almond Oil	Undiluted	6						3.50	Minimally irritating	45
Sweet Almond Oil	Undiluted	6		1	0	0	0	0	Practically nonirritating	38
Sweet Almond Oil	Undiluted	3		2	0	0	0	0	Practically nonirritating	39
-----										
Sweet Almond Oil (25% in a moisturizer)	25	6		1	0	0	0	0	Practically nonirritating	46
Sweet Almond Oil (25% in a moisturizer)	25	6		1	0	0	0	0	Practically nonirritating	47
Sweet Almond Oil (18% in a moisturizer)	9	3		4	0	0	0	0	Minimally irritating	40
Sweet Almond Oil (25% in a makeup)	2.5	3		4	2	0	0	0	Minimally irritating	41
Sweet Almond Oil (20% in a moisturizer)	2.0	3		0	0	0	0	0	Nonirritating	50
-----										
Almond Meal	Undiluted	6		1	1	1	0	0	Practically nonirritating	10
-----										
Almond Meal (8% in a soap)	0.16	6		9	1	0	0	0	Minimally irritating	37

<sup>a</sup>Maximum score = 110.<sup>b</sup>Acute Ocular Irritation Index (maximum score = 110).<sup>c</sup>According to Draize.

was applied daily, five days per week, to the clipped intact skin of 14 animals at a dose of 199 mg/kg (4 mg/kg Almond Meal). The solution was washed off one hour after application. Animals were observed daily for changes in weight, general appearance, and behavior. Skin sites were graded daily for irritation. Blood and urine were analyzed before, during, and after treatment. Animals were sacrificed and necropsied after 12 weeks. During the course of the experiment, six of the animals died or had to be sacrificed owing to an outbreak of Pasteurellosis. The disease complicated identification of systemic treatment-related effects. Dermatopathological examination of treated skin revealed a moderate inflammatory dermal response. Slight to moderate erythema, cracking, and desquamation, which are clinical indications of irritancy, were observed. No other treatment-

related effects were observed. The investigators suggested that the reactions were typical of exaggerated exposure to such products and would not be expected to occur in humans under normal conditions of use.<sup>(49)</sup>

#### *Skin Irritation*

A 60-day cumulative irritation test was used to evaluate the subchronic irritancy of Sweet Almond Oil in rabbits. The test material, at concentrations of 10% or 100%, was applied daily to the clipped dorsal skin of groups of three albino rabbits. Sites were scored daily. When tested in seven separate trials, 100% Sweet Almond Oil produced mean maximum irritation indices (MMIIs) ranging from 0.34 to 1.34 (maximum score = 8). At a concentration of 10%, MMIIs for this ingredient ranged from 0 to 0.66. Results indicated that, when applied to the skin over a long period of time, undiluted Sweet Almond Oil is slightly irritating; whereas, at 10% it is practically nonirritating.<sup>(45)</sup>

#### *Sensitization*

The Magnusson-Kligman Maximization Assay was used to determine the sensitizing potential of Sweet Almond Oil. Hartley-strain female guinea pigs were divided into groups of ten animals. Each animal received intradermal injections of 50% aqueous Freund's Complete Adjuvant (FCA), 5% Sweet Almond Oil in propylene glycol, and 5% Sweet Almond Oil in 50% FCA into different sites on epilated dorsal skin. Vehicle control animals were also used. In the dose-range phase of the experiment, each of 50 animals received a single dermal application of 5%, 10%, or 100% Sweet Almond Oil to determine "subirritating" and "slightly irritating" concentrations to be used for the challenge and booster phases. One week after the induction injection, 100% Sweet Almond Oil was applied occlusively to the treated sites for 48 hours as a topical booster. Animals were challenged two weeks later with 5% Sweet Almond Oil in petrolatum applied topically under occlusion for 24 hours. Patches were then removed and sites were scored 24 and 48 hours later. Sweet Almond Oil was nonsensitizing under these test procedures.<sup>(51)</sup>

## **Clinical Assessment of Safety**

### **Irritation and Sensitization**

A single insult patch test (SIPT) was used to determine the irritancy of undiluted Sweet Almond Oil. The test material was applied under occlusion to the backs of 101 subjects; 48 hours later, the patches were removed and the sites scored. Sweet Almond Oil produced no reactions in the test subjects and was determined to be nonirritating.<sup>(39)</sup>

A repeated insult patch test (RIPT) was used to study the irritancy and sensitizing potential of undiluted Sweet Almond Oil in 52 subjects. The test material was applied under occlusion to the back of each subject for 48 hours; sites were then read and the compound reapplied. This procedure was repeated three days per week for three weeks (nine applications). Following a two-week rest, one or two challenge patches were applied to previously untreated skin of each subject. Sites were scored 48 and/or 96 hours later. Undiluted Sweet Almond Oil pro-

duced no reactions in any of the 52 subjects and was concluded to be nonirritating and nonsensitizing.<sup>(39)</sup>

A repeated insult patch test was used to study the effects of cosmetic formulations containing 0.1%–25% Sweet Almond Oil in a total of 6906 subjects. Results indicate that these products are practically nonirritating and nonsensitizing to human skin (Table 7). Additionally, the Lanman-Maibach 21-day Cumulative Irritancy Assay was used to test the subchronic irritancy of a moisturizer containing 25% Sweet Almond Oil. The test material was applied under occlusion to the backs of ten subjects for 23 hours. Patches were then removed, the site rinsed and scored one hour later, and the compound reapplied. This procedure was repeated for 21 consecutive days. Of the ten subjects tested, seven reacted to one or more patches. The total irritancy score was 14 out of a maximum possible 630.<sup>(52)</sup>

TABLE 7. Clinical Assessment.

Ingredient (product)	Effective conc. (%)	Test	No. of subjects	Result	Comment	Ref.
Sweet Almond Oil	100	SIPT <sup>a</sup>	101	0/101	Nonirritating	39
Sweet Almond Oil	100	RIPT <sup>b</sup>	52	0/52	Nonirritating and nonsensitizing	39
Sweet Almond Oil (25% in a moisturizer)	25	SIPT	20	PII = 0.10 <sup>c</sup>	Practically nonirritating	56
Sweet Almond Oil (18% in a moisturizer)	18	RIPT	98	0/98	Nonirritating and nonsensitizing	57
Sweet Almond Oil (2.5% in a foundation)	2.5	SIPT	100	0/100	Nonirritating	40
Sweet Almond Oil (2.5% in a foundation)	2.5	SIPT	100	0/100	Nonirritating	41
Sweet Almond Oil (2% in a moisturizer)	2.0	RIPT	104	1/104	Two subjects showed "doubtful reactions" during induction phase and one during the challenge phase	58
Sweet Almond Oil (0.1% in a face powder)	0.1	RIPT	148	0/148	Nonirritating and nonsensitizing	55
Sweet Almond Oil (0.2–2% in a suntan lotion)	0.2–2.0	RIPT	6336	0/6336	Nonirritating and nonsensitizing	55
Almond Meal (2% in a medicated soap)	0.01	SIPT	19	PII = 0.05 <sup>c</sup> 1/19	Practically nonirritating	53
Almond Meal (2% in a soap)	0.01	RIPT	86	0/86	Nonirritating and nonsensitizing	54

<sup>a</sup>Single insult patch test.

<sup>b</sup>Repeat insult patch test.

<sup>c</sup>Primary irritation index (maximum score = 4).

A single insult patch test and a repeated insult patch test were used to evaluate the irritancy and sensitizing potential of two soaps, each containing 2% Almond Meal, in 19 and 86 subjects, respectively (Table 7). The test compounds were applied and sites were evaluated as outlined above. In the SIPT, only 1 of the 19 subjects reacted to the soap; the PII was 0.05 (maximum score = 4), indicating that the soap containing 2% Almond Meal was practically nonirritating.<sup>(53)</sup> In the RIPT, there were no reactions in any subject to induction or challenge patches, indicating that this soap was nonirritating and nonsensitizing.<sup>(54)</sup>

A six-week acne study compared the irritancy and efficacy of two medicated soaps, one of which contained 2% Almond Meal. Preliminarily, each subject's skin was graded by a dermatologist with regard to numbers of open and closed comedones, pustules, and papules, as well as oiliness, scaling, and overall complexion. Parameters were scored on a scale of 0–6, except oiliness, which was evaluated as mild, moderate, or excessive. On the basis of these gradings, 100 subjects were divided into two equal groups; each group was instructed to use one of the two test soaps twice daily in lieu of their usual soaps. Subjects were reexamined after 2, 4, and 6 weeks of treatment. Statistically, both products produced significant skin improvement; the product containing Almond Meal was judged superior to the other soap in three test parameters (overall complexion, as well as the numbers of open and closed comedones). The investigator concluded that both products, when used as directed, are safe and effective in reducing manifestations of mild acne. Except for one subject in each test group, neither product induced significant irritation or sensitization.<sup>(22)</sup>

### Photosensitivity

Formulations containing 0.1%–2.0% Sweet Almond Oil were tested for photosensitization in a total of 764 subjects. The test material was applied under occlusion to each subject's back. Twenty-four hours later, the patch was removed and the site scored and irradiated with ultraviolet light from a 150W Xenon Arc Solar Simulator (290–400 nm) at a dose equal to three times the individual's minimal erythema dose (MED). The site was again graded at 72 hours and the procedure repeated once. The products containing 0.1%–2.0% Sweet Almond Oil did not manifest photosensitivity in any of the test subjects.<sup>(55)</sup>

## SUMMARY

Sweet Almond Oil and Almond Meal are natural products obtained from the ripe seed kernels of various species of *Prunus*. Approximately 50% of the kernel consists of Sweet Almond Oil; the residue left after oil expression is the source of Almond Meal. Sweet Almond Oil consists mostly of triglycerides of oleic and linoleic acids. Other fatty acids, diglycerides, vitamins, and amino acids are also found in this ingredient. Almond Meal consists of proteins, carbohydrates, fat, fiber, and water.

Sweet Almond Oil is used as an emollient in skin care products and as an emulsifier in hair products. Almond Meal is used as a skin cleanser by people



whose skin cannot tolerate soaps; it is also used in medicated soaps intended for people with acne. Sweet Almond Oil and Almond Meal are used in over 280 and 16 cosmetic formulations at concentrations up to 50% and 25%, respectively.

Pharmacological studies reveal that Sweet Almond Oil is absorbed slowly through intact skin, whereas it is easily and completely digested and absorbed upon oral administration. When ingested, the fatty acid glycerides of Sweet Almond Oil are hydrolyzed, micellized, converted to triglycerides, and packaged into chylomicra. These then enter the lymphatic system, ultimately ending up in the blood and transferred to cells, where the fatty acids are released enzymatically from the chylomicra for cellular catabolism or lipid storage.

Animal toxicity studies indicate that undiluted Sweet Almond Oil is practically nontoxic when ingested and when applied undiluted to the skin of guinea pigs. Undiluted Sweet Almond Oil and products containing up to 25% Sweet Almond Oil are practically nonirritating to rabbit skin and practically nonirritating or minimally irritating to rabbit eyes. In subchronic studies, Sweet Almond Oil at 10% and 100% concentrations was practically nonirritating and slightly irritating, respectively, to rabbit skin in a 60-day cumulative irritancy test. In addition, Sweet Almond Oil was nonsensitizing in a Magnusson-Kligman Maximization test.

A soap containing 2.0% Almond Meal was practically nontoxic when ingested by rats in an acute oral toxicity study. Undiluted Almond Meal was practically nonirritating to rabbit skin. Undiluted Almond Meal was practically nonirritating to rabbits' eyes, whereas a soap containing 0.5% Almond Meal was minimally irritating. In a 12-week subchronic dermal toxicity test in rabbits, a soap solution containing 0.5% Almond Meal was slightly to moderately irritating; no other treatment-related effects were observed.

In clinical studies, undiluted Sweet Almond Oil and products containing 0.1%–25% Sweet Almond Oil were practically nonirritating and nonsensitizing when tested in a total of 7059 subjects. Additionally, a moisturizer containing 25% Sweet Almond Oil was minimally irritating when applied for 21 consecutive days to the backs of ten subjects. Results of photo patch tests of formulations containing up to 2% Sweet Almond Oil in 764 subjects indicated that these products do not manifest photosensitization.

Soaps containing 2% Almond Meal were practically nonirritating and nonsensitizing when tested in a single insult patch test involving 19 subjects and a repeated insult patch test involving 86 subjects. Results of a six-week acne-genic study indicated that a medicated soap containing 2% Almond Meal was safe and effective, as well as practically nonirritating and nonsensitizing.

## CONCLUSION

On the basis of the available animal data and limited clinical experience presented in this report, the Panel concludes that Sweet Almond Oil and Almond Meal are safe for topical application to humans in the present practices of use and concentration.

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## SWEET ALMOND OIL AND ALMOND MEAL

The CIR Expert Panel published the Final Report on the Safety Assessment of Sweet Almond Oil and Almond Meal in 1983 (Elder 1983), with the conclusion that these ingredients are safe for topical application to humans in the present practices of use and concentration.

Since that time, the naming convention for plant-derived cosmetic ingredients has been changed, and Sweet Almond Oil and Almond Meal have been renamed *Prunus Amygdalus Dulcis* Oil and *Prunus Amygdalus Dulcis* Seed Meal (Pepe et al. 2002). New studies since the original safety assessment are listed at the end of this review. These new studies, along with the updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

The number of cosmetic formulations using *Prunus Amygdalus Dulcis* Oil reported to the FDA increased from 280 in 1976 to 375 in 2002. Concentration of use has not changed appreciably, although there was a reported use of sweet almond oil at 76% in a manicuring product. In addition, the Panel noted new uses in baby products, hair sprays, and eye preparations. The number of cosmetic formulations using *Prunus Amygdalus Dulcis* Seed Meal reported to the FDA decreased from 16 in 1976 to 15 in 2002, with not significant change in use concentration. Table 26 provides the historic and current product uses and concentrations for *Prunus Amygdalus Dulcis* Oil and *Prunus Amygdalus Dulcis* Seed Meal.

Regarding use in hair sprays, the Panel noted that inhalation toxicity data are not included in the original report. A new study in which almond oil, in a nasal spray, was administered to female subjects, without evident toxicity to the lungs, indicates that Sweet Almond Oil and Sweet Almond Seed Meal could be used safely in a hair spray.

The effects of inhaled aerosols depends on the specific chemical species, the concentration, the duration of exposure, and site of deposition within the respiratory system. Particle size is the most important factor affecting the location of deposition (Jensen and O'Brien 1993). The mean aerodynamic diameter of pump hair spray particles is  $\leq 80 \mu$  and the diameter of anhydrous spray particles is 60 to 80  $\mu$ . Typically, less than 1% are below 10  $\mu$  which is the upper limit for respirable particles (Bower 1999). Based on the particle size, Sweet Almond Oil and Sweet Almond Seed Meal in aerosol formulations would not be respirable in formulation.

As with the use of all plant-derived cosmetic ingredients, the Panel also reminded manufacturers that cosmetic products should be formulated to limit the presence of heavy metal/pesticide residues as follows: lead  $\leq 0.1$  ppm; arsenic  $\leq 3$  ppm; mercury  $\leq 1$  ppm; and total PCB/pesticide contamination  $\leq 40$  ppm, with  $\leq 10$  ppm for any specific residue.

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<sup>27</sup> Available from Director, Cosmetic Ingredient Review, 1101 17th Street NW, Suite 310, Washington, DC 20036, USA.

TABLE 26

Historical and current product formulation data for Prunus Amygdalus Dulcis Oil and Prunus Amygdalus Dulcis Seed Meal

Product type	1976 uses (Elder 1983)	2002 uses (FDA 2002)	1976 use concentrations (Elder 1983) (%)	2002 use concentrations (CTFA 2002) (%)
<i>Prunus Amygdalus Dulcis Oil (formerly Sweet Almond Oil)</i>				
Baby shampoos	—	1	—	—
Baby lotions, oils, powders, and creams	—	4	—	—
Baby products (other)	—	2	—	—
Bath oils, tablets, and salts	1	5	>0.1–1	0.1
Bubble bath	—	1	—	0.01
Bath preparations (other)	—	4	—	0.05–0.1
Eye lotion	—	1	—	—
Eye makeup remover	—	2	—	—
Eye makeup (other)	—	3	—	0.4
Powders	—	5	—	2
Fragrance preparations (other)	3	4	>1–5	1
Hair conditioners	—	19	—	2
Hair sprays (aerosol fixatives)	—	3	—	—
Shampoos (noncoloring)	1	5	≤0.1	0.3
Hair tonics, dressings, etc.	—	16	—	1–3
Hair preparations (other noncoloring)	—	2	—	—
Hair lighteners with color	—	—	—	0.1
Hair bleaches	—	2	—	—
Blushers	3	—	>5–10	—
Face powders	1	—	≤0.1	—
Foundations	2	1	>0.1–10	—
Lipstick	184	3	≤0.1–25	0.5
Makeup bases	5	1	>0.1–5	—
Makeup (other)	—	—	—	0.4
Cuticle softeners	—	2	—	—
Nail creams and lotions	—	1	—	—
Nail polish and enamel removers	1	1	≤0.1	—
Manicuring preparations (other)	—	—	—	1–76
Bath soaps and detergents	—	16	—	0.5
Deodorants (underarm)	—	—	—	0.004
Personal cleanliness products (other)	—	3	—	—
Aftershave lotions	—	—	—	0.1
Shaving cream	1	2	>1–5	—
Skin-cleansing creams, lotions, liquids, and pads	12	32	≤0.1–50	0.1
Depilatories	—	2	—	—
Face and neck skin care preparations	9*	19	>1–5*	—
Body and hand skin care preparations	—	60	—	0.08–8
Foot powders and sprays	—	—	—	3
Moisturizers	21	60	≤0.1–25	0.2–11
Night skin care preparations	17	16	>1–50	0.4–3
Paste masks/mud packs	3	12	>1–5	0.5
Skin fresheners	—	1	—	—
Skin care preparations (other)	6	43	>0.1–25	3–5
Suntan gels, creams, and liquids	10	17	>0.1–25	0.01–2

(Continued on next page)

**TABLE 26**  
Historical and current product formulation data for Prunus Amygdalus Dulcis Oil and Prunus Amygdalus Dulcis Seed Meal  
(Continued)

Product type	1976 uses (Elder 1983)	2002 uses (FDA 2002)	1976 use concentrations (Elder 1983) (%)	2002 use concentrations (CTFA 2002) (%)
Indoor tanning preparations	—	2	—	0.5
Suntan preparations (other)	—	2	—	—
<b>Total uses/ranges for Prunus Amygdalus Dulcis Oil</b>	<b>280</b>	<b>375</b>	<b>≤0.1–50</b>	<b>0.004–76</b>
<i>Prunus Amygdalus Dulcis Seed Meal (formerly Sweet Almond Meal)</i>				
Powders	—	—	—	27
Cuticle softeners	—	1	—	—
Bath soaps and detergents	—	2	—	0.5–2
Personal cleanliness products (other)	—	1	—	—
Skin-cleansing creams, lotions, liquids, and pads	6	2	>1–25	—
Body and hand skin care preparations	—	1	—	0.5
Paste masks	6	7	>0.1–5	2
Skin care preparations (other)	4	1	>0.1–5	—
<b>Total uses/ranges for Prunus Amygdalus Seed Meal</b>	<b>16</b>	<b>15</b>	<b>&gt;0.1–25</b>	<b>0.5–27</b>

\*These categories were combined when the original safety assessment was performed and are now two separate categories.

Van Hoogmoed, L. M., D. W. Agnew, M. Whitcomb, D. W. Hyde, M. H. MacDonald, and J. R. Snyder. 2002. Ultrasonographic and histologic evaluation of medial and middle patellar ligaments in exercised horses following injections with ethanolamine oleate and 2% iodine in almond oil. *Am. J. Vet. Res.* 63:738–743.

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#### VINYL ACETATE/CROTONIC ACID COPOLYMER

A safety assessment of the Vinyl Acetate/Crotonic Acid Copolymer was published in 1983 with the conclusion that this ingredient is “considered safe as a cosmetic ingredient under present practices of product and concentration use” (Elder 1983). New studies (listed at the end of this section), along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

The name of Vinyl Acetate/Crotonic Acid Copolymer as listed in the *International Cosmetic Ingredient Dictionary and Handbook*, 9th edition, has been changed to VA/Crotonates Copolymer (Pepe et al. 2002).

VA/Crotonates Copolymer was used in 55 cosmetic products in 1976, with the largest use occurring in hair sprays at concentrations of >0.01% to 25%. In 2002, VA/Crotonates Copolymer was used in 38 cosmetic products (FDA 2002), at a maximum use concentration of 11% in hair sprays (CTFA 2002b). Table 27 presents the available use information for VA/Crotonates Copolymer.

The CIR Expert Panel acknowledged the use of Vinyl Acetate/Crotonic Acid Copolymer in aerosol hair sprays. The effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of exposure, and site of deposition within the respiratory system. Particle size is the most important factor affecting the location of deposition (Jensen and O’Brien 1993). The mean aerodynamic diameter of pump hair spray particles is  $\geq 80 \mu$ , and the diameter of anhydrous hair spray particles is 60 to 80  $\mu$ . Typically less than 1% are below 10  $\mu$ , which is the upper limit for respirable particles (Bower 1999). Based on the particle size, Vinyl Acetate/Crotonic Acid Copolymer would not be respirable in formulation.

Although there were reports associating vinyl acetate with nasopharyngeal carcinoma in rat inhalation studies, studies show that the reported carcinogenicity of vinyl acetate in rats is through a nongenotoxic mechanism, and the amount of residual vinyl acetate monomer in VA/Crotonates Copolymer was below the no-observed-effect level. Confirming this, occupational studies in which workers were exposed to vinyl acetate ranging from 5 to 10 ppm, with intermittent exposures near 50 ppm and acute exposures to 300 ppm, showed no long-term chronic effects.

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