Final Report on the Safety Assessment of Peanut (Arachis Hypogaea) Oil, Hydrogenated Peanut Oil, Peanut Acid, Peanut Glycerides, and Peanut (Arachis Hypogaea) Flour[1]

Peanut (Arachis Hypogaea) Oil is the refined fixed oil obtained from the seed kernels of *Arachis hypogaea*. Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides are all derived from Peanut Oil. Peanut Flour is a powder obtained by the grinding of peanuts. The oils and glycerides function in cosmetic formulations as skin-conditioning agents. The acid functions as a surfactant—cleansing agent, and the flour functions as an abrasive, bulking agent and/or viscosity-increasing agent. In 1998, only Peanut Oil and Hydrogenated Peanut Oil were reported in use. When applied to the skin, Peanut Oil can enhance the absorption of other compounds. Hepatic changes were noted at microscopic examination of rats fed diets containing 15% edible Peanut Oil for 28 days, although no control group was maintained and the findings were also noted in rats fed fresh corn oil. United States Pharmacopeia (USP)-grade Peanut Oil was considered relatively nonirritating when injected into guinea pigs and monkeys. Technical-grade Peanut Oil was moderately irritating to rabbits and guinea pigs and mildly irritating to rats following dermal exposure. This same oil produced reactions in ≤ 10% of 50 human males. Peanut Oil was not an ocular irritant in rabbits. Peanut Oil, either "laboratory expressed" or extracted using a food-grade solvent, was not carcinogenic to mice. Peanut Oil exerted anticarcinogenic activity when tested against known carcinogens. Peanuts are the food most likely to produce allergic and anaphylactic reactions. The major allergen is a protein that does not partition into Peanut Oil, Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides. Aflatoxins can be produced in stored agricultural crops such as peanuts, but do not partition into the oils, acids, or glycerides. Manufacturers were cautioned to make certain that the oils, acids, and glycerides are free of aflatoxins and protein. Formulators were cautioned that the oils, acids, or glycerides may enhance penetration and can affect the use of other ingredients whose safety assessment was based on their lack of absorption. The available studies on Peanut Oil supported the conclusion that Peanut Oil, Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides are safe for use in cosmetic formulations. Peanut (Arachis Hypogaea) Flour, however, is sufficiently different from the above ingredients such that its safety can not be supported by studies using the oil. The additional data needed for Peanut (Arachis Hypogaea) Flour are (1) concentration of use; (2) chemical specifications (i.e., aflatoxin and protein levels); (3) method of preparation; and (4) contact urticaria and dermal sensitization at concentration of use. Although data on aflatoxin levels are sought, it is expected that concentrations of aflatoxin should comply with U.S. government stipulations. Absent the additional data, it was concluded that the available data are insufficient to support the safety of Peanut (Arachis Hypogaea) Flour for use in cosmetic products.

INTRODUCTION

The following review is a compilation of data concerning Peanut (Arachis Hypogaea) Oil (CAS No. 8002-03-7), Hydrogenated Peanut Oil (CAS No. 68425-36-5), Peanut Acid (CAS No. 91051-35-3), Peanut Glycerides, and Peanut (Arachis Hypogaea) Flour. Most of the cited studies evaluated edible grade Peanut Oil. Like the edible oil, cosmetic grade Peanut Oil is a refined or hot-pressed oil (Wenninger and McEwen 1997). This clarification is noted because many of the findings, especially those regarding allergenicity, are likely applicable only to cold-pressed (unrefined) Peanut Oil, which is used in many "health foods" (Loza and Brostoff 1995).

CHEMISTRY

Definition

Peanut kernels contain approximately 45% to 50% oil, 25% to 30% protein, 8% to 12% carbohydrate, 5% water, 3% fiber, and 2.5% ash. Peanut proteins are classified as albumins (water soluble) or globulins (saline soluble). The albumin fraction contains agglutinins, lectin-reactive glycoproteins (see Noncosmetic Use), protease inhibitors, alpha-amylase inhibitors, and phospholipases. The globulin fraction is subdivided into arachin and conarachin fractions. Peanut skin contains 49% carbohydrate and 19% fiber as well as tannins and pigments (Bush, Taylor, and Nordlee 1989; Loza and Brostoff 1995).

Peanut (Arachis Hypogaea) Oil is the refined fixed oil obtained from the seed kernels of one or more of the cultivated varieties of *Arachis hypogaea* (Wenninger and McEwen 1997). Synonyms include Arachis Oil; Oils, Peanut; Peanut Oil

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(Wenninger and McEwen 1997); earthnut oil, groundnut oil; and katchung oil (Budavari 1989; RTECS 1996).

Hydrogenated Peanut Oil is the end product of controlled hydrogenation of Peanut Oil (q.v.) (Wenninger and McEwen 1997).

Peanut Acid is a mixture of fatty acids derived from Peanut Oil (q.v.) (Wenninger and McEwen 1997).

Peanut Glycerides is a mixture of mono-, di-, and triglycerides derived from Peanut Oil (q.v.) (Wenninger and McEwen 1997).

Peanut (Arachis Hypogaea) Flour is the powder obtained by the grinding of peanuts, *A. hypogaea*. Synonyms include Arachis Hypogaea Flour; Flour, Arachis Hypogaea; and Flour, Peanut (Wenninger and McEwen 1997).

Chemical and Physical Properties

Edible Peanut Oil is described by a U.S. manufacturer as comprised of 100% fat with no detectable protein, carbohydrate, water, ash, or fiber and only trace amounts of minerals (Taylor et al. 1981). The fatty acid composition of cosmetic grade Peanut Oil is specified as: ~57% oleic and 26% linoleic (both unsaturated acids), 8% palmitic (saturated), and smaller amounts of the saturated stearic, arachidic, behenic, and lignoceric acids (Nikitakis and McEwen 1990). Properties of cosmetic grade Peanut Oil listed in Table 1 match those of the United States Pharmacopeia/National Formulary (Committee of Revision of the United States Pharmacopeial Convention 1995).

TABLE 1
CTFA specifications for Peanut Oil (Nikitakis and McEwen 1990)

Property	Specification
Appearance	Pale yellow
Solubility	Alcohol, and miscible with ether, chloroform, and carbon disulfide
Identification	Positive match to CTFA IR-spectrum with no indication of foreign materials and positive identification of arachidic acid
Cottonseed oil	Negative
Specific gravity at 25°/25°C	0.912 to 0.920
Acid value	2.0 maximum
Unsaponifiable matter*	1.0% maximum
Saponification value	185 to 195
Iodine value	84 to 100

*Defined as tocopherols (and other antioxidants), sterols, squalene and other hydrocarbons (Swern 1979; Budavari 1989).

Impurities

Aflatoxin

Aflatoxins are metabolic products of the molds *Aspergillus flavus* and *Aspergillus parasiticus*. They are most often produced in stored agricultural crops (such as peanuts) when growth conditions and genetic requirements are favorable (Pease 1986; Budavari 1989; Wood 1989). Aflatoxins are identified as B_1, B_2, G_1, G_2, M_1 and M_2 (milk toxins), B_{2a}, and G_{2a} based on fluorescent color (B = blue, G = green) when separated chromatographically. Aflatoxins B_3, R_0, P_1, Q_1, RB_1, RB_2 and D_1 have also been isolated (Budavari 1989).

The International Agency for Research on Cancer (IARC) categorized aflatoxins as group 1 agents, "carcinogenic to humans" (IARC 1976, 1987). Epidemiological studies noted "positive correlation between estimated aflatoxin intake or level of aflatoxin contamination of market food samples and cooked food and incidence of hepatocellular cancer." The observations were supported by positive results in laboratory carcinogenicity and mutagenicity studies. Aflatoxin B_1 specifically is recognized as "one of the most potent environmental mutagens and carcinogens known" (Budavari 1989). Aflatoxins B_1 and B_2 are the most common aflatoxins found in peanuts (Wilson 1989).

The United States government places the following limitations on peanuts to be considered "negative" for aflatoxin: $\leq$15 ppb for "peanuts which have been certified as meeting edible quality grade requirements" and $\leq$25 ppb for "non-edible quality categories" (7 CFR Sections 997.30 and 998.200).

Parker and Melnick (1966) reported that crude Peanut Oil (obtained by solvent extraction or hydraulic pressing) has reduced aflatoxin concentrations compared to peanut kernels and that subsequent processing (alkali refining and bleaching) reduces the concentration still further. In one example, processed Peanut Oil from moldy peanuts (contaminated with 5500 ppb aflatoxin) had an aflatoxin concentration of $<$1 ppb.

USE

Cosmetic

Peanut Oil is used in cosmetics as a skin-conditioning agent—occlusive (Wenninger and McEwen 1997). As of January 1998, Peanut Oil was reported to be used in 22 cosmetic formulations (FDA 1998) (Table 2).

Concentration of use data are no longer reported to the FDA (FDA 1992). Data from 1984 indicated that Peanut Oil was used predominantly at concentrations $\leq$25% (19 uses), with 1 use at $>$50% (FDA 1984).

Hydrogenated Peanut Oil is used in cosmetics as a skin-conditioning agent—occlusive, and/or a viscosity-increasing agent—nonaqueous (Wenninger and McEwen 1997). As of January 1998, it was reported to be used in 19 formulations (FDA 1998) (Table 2).

Peanut Acid can be used as a surfactant—cleansing agent, and Peanut Glycerides can be used as a skin-conditioning

TABLE 2
Frequency of use of Peanut Oil and Hydrogenated Peanut Oil (FDA 1998)

Product category	No. of formulations in category	No. containing ingredient
Peanut Oil		
Hair conditioners	636	3
Lipstick	790	3
Shaving cream	139	1
Cleansing skin care	653	4
Face and neck skin care (excluding shaving)	263	1
Body and hand skin care (excluding shaving)	796	6
Moisturizing skin care	769	1
Other skin care preparations	692	1
Suntan gels, creams, liquids	136	2
1998 Total for Peanut Oil		22
Hydrogenated Peanut Oil		
Face and neck skin care (excluding shaving)	263	7
Body and hand skin care (excluding shaving)	796	4
Night skin care	188	3
Other skin care preparations	692	5
1998 Total for Hydrogenated Peanut Oil		**19**

agent—occlusive. Peanut Flour can be used as an abrasive, bulking agent, and/or a viscosity-increasing agent—aqueous (Wenninger and McEwen 1997). No uses were reported for Peanut Flour, Peanut Acid, or Peanut Glycerides.

International—Cosmetic

Peanut Oil is listed in the *Comprehensive Licensing Standards of Cosmetics by Category (CLS)*. Peanut Oil which conforms to the specifications of the *Japanese Cosmetic Ingredients Codes* has precedent for use without restriction in all *CLS* categories except eyeliner preparations (for which there has been no precedent). Peanut Oil as monographed in the *Japanese Pharmacopoeia* has no limitations regarding its use in lip or oral preparations (Rempe and Santucci 1997).

Noncosmetic

Food

Peanut Oil is recognized as a GRAS substance when used in the following condition: "substances migrating to food from cotton and cotton fabrics used in dry food packaging" (21 CFR 182.70).

The Federation of American Societies for Experimental Biology (FASEB) report on Peanut Oil estimated a United States per capita daily intake of 1.1 g Peanut Oil in 1970 (FASEB 1977).

Breast Implants

In a series of studies, Young et al. (1991a, 1993) investigated Peanut Oil as a filler for breast implants. They reported that it was a radiolucent substance with no evidence of allergic, toxic, inflammatory, or neoplastic responses when injected into rats. It produced no significant abnormalities of the lungs, liver, and kidneys when implanted into rabbits (a fibrous capsule was noted surrounding the oil implant and was also found around implants filled with saline [Young et al. 1991b]). The investigators simulated conditions of implant rupture by injecting [^{14}C]-Peanut Oil into rabbits and noted that it would be absorbed, metabolized, and either excreted or redistributed to the body's normal fat storage sites (See Absorption, Metabolism, Distribution, Excretion—Parenteral). Results of in vitro studies indicated that Peanut Oil did not support growth of common infection-producing bacteria and can have bactericidal properties (Young et al. 1996). Peanut Oil, as a filler for breast implants, is currently being tested in limited clinical trials.

GENERAL BIOLOGY

Absorption, Metabolism, Distribution, Excretion

Oral

The FASEB report (1977) cited a study in which 60% of an intubated dose of Peanut Oil (~6 g/kg) was absorbed by rats within 6 hours of administration.

In clinical studies, volunteers ingested 50 to 140 g of Peanut Oil over a period of 3 days; "digestibility" was 98% (Langworthy 1923).

The FASEB report (1977) noted decreased growth rate and/or feed utilization in rats fed Peanut Oil heated at 275°C for 30 minutes, but not when heated for only 15 minutes. Some investigators had considered that these effects "may be due to the presence of monomeric or dimeric acyl radicals that are 'inimical to the well-being of the animals'."

The FASEB report (1977) concluded that Peanut Oil is "rapidly absorbed after oral administration, metabolized, and the metabolic products are utilized and excreted."

Parenteral

Young et al. (1996) simulated the rupture conditions of a Peanut Oil–filled breast implant in rabbits. The test material was medical-grade Peanut Oil mixed with [^{14}C]-oleic acid to achieve a concentration of 10 μCi of ^{14}C/125 ml Peanut Oil. This mixture (125 ml) was subcutaneously injected into a hairless site on the dorsum of 20 anesthetized female New Zealand rabbits. The control rabbit was not injected. Weekly urine and feces samples were collected for 5 months, at which time the rabbits were killed. Tissue samples from the injection site, and of subcutaneous (SC) fat on the left side of the dorsum, the omentum, lungs, kidneys, liver, gallbladder, spleen, aorta, and an axillary lymph node were taken and analyzed by liquid scintillation.

The injected oil was absorbed gradually in all rabbits and, within a month, was no longer grossly apparent on inspection or by palpation. However, a significant amount of ^{14}C radioactivity was detected at the injection site as long as 5 months post injection. No evidence of toxicity or allergic reaction was noted. A thin film of oil was observed at the injection site at necropsy; all organs appeared normal macroscopically and microscopically. ^{14}C radioactivity was above background counts in samples of SC fat from the contralateral dorsum, the omentum, and the aorta. The investigators considered that the radioactive material had equilibrated with the natural triglycerides of the body's fat stores. Radioactivity in all other organs was within or below the background count. A declining trend of ^{14}C radioactivity was noted in the urine and feces samples, with the exception of a peak of activity in the urine noted at 4 weeks. That this peak corresponded with the diminished Peanut Oil at the injection site suggested that most of the oil was absorbed and metabolized at that time (Young et al. 1996).

An accompanying analysis of the study criticized the use of [^{14}C]-oleic acid instead of radioactive Peanut Oil and the lack of rate of metabolism information. However, the conclusion that released triglycerides "would not be expected to cause complications and they would be absorbed or removed by normal metabolic mechanisms" was noted to "appear quite reasonable" (Emken 1996).

Absorption Enhancement

A Peanut Oil vehicle increased the lymph absorption of isotretinoin (Nankervis et al. 1995), p,p = dichlorodiphenyltrichloroethane (DDT) (Palin et al. 1981, 1982), and the hypocholesterolemic agent, probucol (Palin and Wilson 1984), following oral administration in rats.

Holmberg et al. (1990) reported that the long chain fatty acids in Peanut Oil facilitated the absorption of vitamin D_3 in man (as measured by serum concentration).

Atherosclerosis

Saso et al. (1994) reported that white rabbits that had been orally dosed with 6% Peanut Oil and 0.5% cholesterol for 14 weeks had more severe aortic atheromatous plaques than those rabbits that had received cholesterol and 3% soybean oil. Because of the vascular lesions, Peanut Oil was not selected for use in animal models of atherosclerosis.

Earlier publications reported on the development of aortic fibrocellular lesions with minimal intracellular lipid deposition in rabbits maintained for 10 months on 14% Peanut Oil (Kritchevsky et al. 1976), and in rhesus monkeys that received 25% Peanut Oil and 2% cholesterol for 12 months (Vesselinovitch et al. 1980). Reviews noted that in spite of having a high linoleic acid content, Peanut Oil in an atherogenic diet produced the same effect as a saturated fat. Triacylglycerols (arachidic and behenic acids) were considered responsible (Anonymous 1972, 1983).

Lectin-Binding

Peanuts are among various plant seeds that contain hemagglutinating proteins called lectins. Lectins bind specifically to the branching sugar molecules of glycoproteins and glycolipids on the surface of cells. Certain lectins selectively cause agglutination of erythrocytes of certain blood groups and of malignant cells, but not their normal counterparts; others stimulate the proliferation of lymphocytes (Taylor 1988).

Peanut lectin is specific to D-galactose. This property has been used to positively identify renal neoplasms (Ulrich, Horvat, and Krisch 1985), thyroidal lesions (Vijayakumar et al. 1992) and neoplasms (Thiele et al. 1986), leukemia cell lines (Schwenk, Schneider, and Herzog 1980; Piller et al. 1989), colorectal adenomas (Orntoft et al. 1991), and endometrial and prostatic adenocarcinomas (Soderstrom 1987a, 1987b). Sometimes binding occurred only after treatment of the cells with neuraminidase. Gonzalez-Campora et al. (1988) noted that lectins do not distinguish between follicular carcinoma and papillary carcinoma (in the thyroid gland).

ANIMAL TOXICOLOGY

Oral Toxicity

Short-Term

Alexander, Valli, and Chanin (1987) studied the toxicity of commercial fats that had been subjected to the heat and oxidation of normal usage in fast-food or deep-fry cooking. Groups of 10 male weanling rats received feed containing: 15% (by weight) fresh (edible), laboratory-heated, or commercial pressure deep-fry Peanut Oil (FPO, HPO, or PPO, respectively) for 28 days. Other groups of rats received either fresh or laboratory-heated corn oil (FCO or HCO). No concurrent untreated or negative-control group was maintained. Animals were necropsied at the end of the study.

After 6 days of dosing, diarrhea, dermatitis, and seborrhea were noted in rats of the HPO (and HCO) group. Average weight

gain, feed consumption, and feed efficiency were significantly greater for rats fed FPO or PPO than in those dosed with HPO. HPO-dosed rats had heavier livers and kidneys; relative heart weight was comparable among groups. Blood taken at the end of the study from HPO-dosed rats had decreased values for mean cellular volume (MCV) and mean cellular hemoglobin (MCH). Other blood parameters were normal (compared to standard values obtained from published studies). The 24-hour urine of FPO (and FCO) rats (obtained during week 4 of dosing) contained a small amount of protein, but no unusual materials in the sediment. At microscopic examination, lesions were found in the thymus and periportal and perinuclear clear areas, and included homogeneity of the pericentral cytoplasm in the liver of all rats. These findings were most severe in the HPO-dose group. Damage to the testes and epididymides was noted in HPO and PPO groups, with a complete cessation of spermatogenesis in the PPO-dose group. The investigators suggested that trace amounts of mycotoxin could have been a factor in the testicular degeneration.

Parenteral Toxicity

Chronic

Peck, Woodhour, and Hilleman (1968) investigated the toxicity of an adjuvant containing 43% Peanut Oil (USP XVI grade) in albino guinea pigs and grivet and rhesus monkeys. The adjuvant was diluted with an equal volume of sterile phosphate-buffered saline (PBS); in some instances, the PBS also contained 1:10,000 thimerosal. (The three experiments described were also done with a mixture of adjuvant and influenza virus vaccine. This aspect of the study is not detailed in this summary.) A group of 100 guinea pigs received an intramuscular (IM) injection of the adjuvant-saline solution (0.5 ml) at 0, 1, 6, and 12 months. Groups of at least four guinea pigs were killed for necropsy at intervals of 3, 6, 12, 18, and 24 months after the first injection. In a second experiment, 16 grivet monkeys received IM injections on the same schedule as guinea pigs and were killed at 3.5, 6, 12, 18, and 25 months after the first injection. In a third experiment, grivet monkeys received IM, SC, and intradermal (ID) injections of the solution at 0, 2, 4, and 6 weeks (two monkeys), biweekly for 12.5 months (five monkeys), or at 0, 1, and 6 months (five monkeys). These groups of monkeys were killed at 3, 16, and 16 months after the first injection, respectively. Only the kidneys were examined in those monkeys of the third experiment that were killed at 3 months. In all other groups, the following were microscopically examined: injection sites, uninjected skeletal muscle, stomach, intestine, testes, prostate (or ovary and uterus), adrenal glands, thymus, pancreas, thyroid gland, lymph node, spleen, liver, gall bladder, kidneys, urinary bladder, salivary gland, heart, lungs, brain and spinal cord, pituitary gland, bone and joint, and bone marrow smears (monkeys). Weights of heart, liver, kidneys, spleen, brain, and testes were measured. Saline control groups were maintained in all experiments.

At necropsy and microscopic examination, lesions were found only at the injection site. Visually, a mild inflammatory reaction and oil cysts (lipid granulomas) were observed. Responses consisted of leukocyte infiltration and minimal degeneration. At microscopic examination of the tissues of the 16 grivet monkeys, small foci of necrosis and/or foreign body giant cells were noted in those killed in the first three sacrifice periods, and collections of macrophages were noted in those killed in the last two sacrifice periods. None of these changes were considered the types that would progress to abscess or nodule formation in humans. Lipid granulomas were noted in monkeys that had received IM doses, but no abscesses were noted. Macrophages and "relatively few" mononuclear cells were noted at the sites where the oil cysts had diminished in size, a finding indicating that the metabolizable Peanut Oil was removed by phagocytosis. The investigators considered that the local reactions at the injection sites corresponded to "those that might be expected following the injection of a relatively nonirritating material" (Peck, Woodhour, and Hilleman 1968).

Dermal Irritation

Undiluted technical grade Peanut Oil (0.1 g) was applied to the dorsal surface of groups of six albino angora rabbits, male Hartley guinea pigs, and male Wistar rats. Peanut Oil was 1 of 20 oils or synthetic perfumes tested; 3 test compounds and 1 control (n-hexadecane) were applied randomly to the rabbits, but guinea pigs and rats were treated with only 1 material. The application site had been clipped free of hair, and the sequence of application was rotated so that a particular test material was not applied to the same site more than twice. After 24 hours of dermal exposure, sites were evaluated, clipped free of hair, and 30 minutes later, the test compounds were again applied. Additional evaluations were made at 48 and 72 hours. After the last evaluation, the animals were injected with Evans blue, killed, and a sample of the dorsal skin was removed for examination. Peanut Oil was moderately irritating to the rabbit and guinea pig (reactions in 40%–70%, score: 2, maximum possible score: 3), and mildly irritating to the rat (reactions in 10%–40%, score: 1). The specific number and grade of reactions were not reported (Motoyoshi et al. 1979).

Peanut Oil (technical grade, 0.05 g) was applied for 48 hours under an occlusive patch to the dorsal surface (clipped free of hair) of six miniature swine. Sites were evaluated at the time of patch removal and the animals were injected with dye, killed, and the dorsal skin removed for examination. Peanut Oil was not irritating. That is, positive reactions were noted in $\leq$10% of the swine. The specific number and grade of reactions were not reported (Motoyoshi et al. 1979).

Ocular Toxicity

Oji (1982) tested the ocular toxicity of ketoconazole (full spectrum antimycotic drug) in rabbits. One eye of each of six rabbits was treated with 1%, 3%, or 5% ketoconazole in a Peanut Oil vehicle and the other eye was treated with undiluted Peanut Oil alone. Drops were applied hourly for 6 consecutive hours daily for 3 weeks. Eyes were examined by slit-lamp biomicroscopy.

Hyperemia was occasionally noted in control eyes but was not considered significant. Control eyes received total scores of 3, 3, and 1 (three controls for the three concentrations of ketoconazole); maximum possible score was 156.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Oral

A study on the effects of etretinate on male rat fertility maintained a control group dosed with the vehicle, Peanut Oil. The vehicle and/or drug was administered by daily intubation for 28 days prior to mating, and for 6 days during the mating period, at a dose of 0.5 ml/100 g body weight. (Male rats weighed between 205 to 234 g.) Males were killed after the mating period; serum hormone concentrations were measured from blood samples taken from the abdominal aorta; reproductive organs were examined and sperm counts were made. On gestation day (GD) 21, the untreated dams were killed and the uterine contents were examined. No unusual findings were noted in the vehicle control group (Hayashi et al. 1995).

Parenteral

Generoso et al. (1984) studied the effects of oil vehicles on early embryonic lethality in mice. Female (SEC × C57BL)F_1 mice received a single intraperitoneal (IP) injection of cold-pressed Peanut Oil (0.4 ml). Females were mated to untreated males for 6 days following dosing. A group of 46 untreated females was maintained as the control. Females were killed 12 to 13 days after mating for necropsy. Twenty-eight of the 40 females treated with Peanut Oil were pregnant; 5 of the 28 had uteri containing only deciduomata remnants. Thirty-four of the 46 control females were pregnant with none having only deciduomata. Total implants per pregnant female (not including those with deciduomata) were 9.0 and 9.1 for the Peanut Oil and control females, respectively. Living embryos per pregnant female were 7.5 and 8.8 for the Peanut Oil and control females, respectively. The rates of dead implants and females with ≥1 dead implants were respectively 17% and 78% for the Peanut Oil females and respectively 4% and 26% for control females. The results in repeat studies were the rates of dead implants and females with ≥1 dead implants were 28% and 90% for Peanut Oil females, and 3% and 23% for control females. The repeat study noted that 8 of 35 pregnant Peanut Oil–dosed females had more implants than corpora lutea, compared to 2 of 26 control females. The data were not analyzed for statistical significance, but the investigators noted that corn oil did not produce the same effects when administered orally versus intraperitoneally. Because of the increase in deciduomata, it was concluded that "plants oils proved to be unsuitable carriers of test mutagens in female dominant-lethal studies where the route of administration is via the peritoneal cavity" (Generoso et al. 1984).

A study that investigated the teratogenic effects of excess retinoic acid (RA) had a Peanut Oil vehicle control group. On day 8.5 postcoitum, groups of 12 to 13 pregnant CFHB rats received a single injection of either a 1% RA suspension dissolved in Peanut Oil to give 20 mg RA/kg body weight, or an equivalent volume of Peanut Oil. After 26 hours, one uterine horn was removed and the embryos were cultured in serum from untreated rats. When the cultures were terminated (at 48 hours), the second uterine horn was removed from the rats. Growth and development, both of the vehicle control and of RA treated embryos, were retarded in culture. The following findings were noted in embryos of the vehicle control that were harvested on day 11.5: normal closed anterior and posterior neuropore in 97% and 93%, respectively, presence of limb buds in 95%, microcephaly in 2%, and no incidence of brain cysts/edema, open trunk neural tube, swollen hind neural folds, unfused heart primordia, divided trunk, or externalized hind end. The findings for the vehicle control were not remarkable (Steele, Trasler, and New 1983).

Five pregnant New Zealand rabbits received a single IM injection of an adjuvant containing Peanut Oil diluted with PBS (effective Peanut Oil concentration of 21%) into each hind leg on GD 8. A saline control group was maintained. Dams were killed on GD 28 or 29. Body weight had been measured on GD 1 and again at the termination of the study. One dam of the Peanut Oil group had only one implant. No abnormal fetuses were noted and parameters such as number of resorptions, average number of viable fetuses/doe, and average weight and weight change of does were comparable among treated and control rabbits. The average number of implants/doe was lower in treated rabbits but was described as not treatment related (Peck, Woodhour, and Hilleman 1968).

GENOTOXICITY

Qu et al. (1992) tested the mutagenic potential of various heated cooking oils. Oils were heated to 270°C; condensates were collected in a filter and extracted with acetone that was then evaporated under nitrogen. Peanut Oil (dose range 0.1–5 mg/plate) was negative in the *Salmonella* mutation assay using strains TA98 without S9 activation and TA100 both with and without activation. Details were not reported.

A micronucleus test of benzene maintained a Peanut Oil negative-control group. Male and female Charles River mice received oral doses of either benzene or 10 ml edible grade Peanut Oil/kg body weight on each of 2 days. The positive control was treated with methyl methanesulfonate. Groups of at least 10 mice were killed at 6, 18, 24, 48 hours and 5, 9, and 16 days after the second dose and bone marrow was analyzed for micronuclei in polychromatic erythrocytes (PCEs). Both the positive- and negative-control groups produced expected results (Hite et al. 1980).

A subsequent micronucleus test evaluated the effects of vegetable oil vehicles on bone marrow proliferation. Five male Swiss mice received a single IP injection of 4 ml Peanut Oil (domestic cooking grade)/kg body weight. Femoral bone marrow

was sampled at 30, 48, and 72 hours post dosing. An untreated control group was maintained. Slides of the bone-marrow smears were analyzed for genotoxic (counting the frequency of micronuclei in 1000 PCEs) and cytotoxic responses (measuring the PCE/red blood cell [RBC] ratio, with a decreased value indicating a cytotoxic effect). Peanut Oil was not genotoxic in the assay at any sampling time, but the 30-hour slide did have a significant reduction ($p < .05$) in the PCE/RBC ratio. The effect was reversible and not observed at either the 48- or 72-hour sample slides. Because of the cytotoxic effect (also noted with olive and sunflower oils), the investigators cautioned that the vehicle effect must always be considered when interpreting results (Simula and Priestly 1991).

Carcinogenicity

Responding to reports of Peanut Oil being mutagenic to plant tissue, Gothoskar and Ranadive (1965) studied its carcinogenic potential for mice. Groups of at least nine hybrid mice (noted for detecting weak carcinogens) were dosed orally (for either 3 months or throughout lifetime), SC injected (single exposure), IP injected (4–5 exposures in 10–12 months), or dermally exposed (throughout lifetime) to one of two samples of "laboratory-expressed" Peanut Oil. One group of dermally exposed mice was also treated with croton oil as a cocarcinogen. An untreated group of 13 mice served as the control group.

No malignant neoplasms of the digestive tract were noted in orally dosed mice; 2 of the 12 that had been lifetime dosed had "well developed papillomatous growth in the inner wall of the cardiac end of the stomach," but one lesion was also noted in the control group. In SC injected mice, deposition of oil or its metabolites was noted in the subcutis up to 22 months after exposure; a slight inflammatory reaction in these areas was noted at microscopic examination. An "abnormal liver" (no further details) was noted in one of twelve mice that received the IP injections. A slight thickening of the epidermis and black pigmentation was noted in mice dermally treated with Peanut Oil and croton oil. These changes were not observed in mice treated dermally with Peanut Oil alone. Other findings among the groups (also observed to varying extent in untreated control mice) were necrosis of the liver, atrophic spleen, and enlarged lymph nodes. Neither Peanut Oil sample was considered a carcinogen (Gothoskar and Ranadive 1965).

Noting that the above study tested expelled Peanut Oil samples, other studies investigated whether solvent-extraction procedures used in large-scale edible oil extraction changed the carcinogenic potential of Peanut Oil. Five of six samples from a 1966 batch were carcinogenic when administered to C17 or Swiss mice via the cutaneous, subcutaneous, or oral route. The investigators noted that the commercial-grade solvent residue was also carcinogenic; 1 of 20 Swiss mice developed neoplasms following SC dosing with the solvent. In comparison, three of five refined 1969 Peanut Oil samples extracted using n-hexane were not carcinogenic when administered via the cutaneous or subcutaneous route. When applied dermally with croton oil, carcinomas developed in 2/19 and 1/22 mice treated with the other two samples, respectively. These two samples were considered to have been contaminated with "carcinogenic solvent-extracted samples" at the mill from which they were obtained. The investigators stressed that food-grade solvent (such as n-hexane) must be used in extraction procedures and that proper procedure must be followed to avoid contamination with solvent residue (Ranadive, Gothoskar, and Tezabwala 1972; Gothoskar and Ranadive 1973).

Various oral and subcutaneous route carcinogenicity studies which maintained a Peanut Oil as vehicle control are cited in Table 3.

COCARCINOGENICITY

Yarkoni and Rapp (1979) investigated whether oil emulsions affected the tumor regression activity of mycobacterial components against methylcholanthrene-induced fibrosarcomas. Male C3h/HeN mice were injected intradermally with tumor cells; 5 days later they received a single intratumoral injection of either cell walls of *Bacillus Calmette-Guérin* (CW) or trehalose-6,6′-dimycolate (TDM) (mycobacterial components) in a 0.1-ml volume of 1% to 10% Peanut Oil in a saline emulsion. Tumor incidence was monitored weekly for 2 months. No tumor regression was noted in any of 36 mice treated with either 9% or 10% Peanut Oil emulsion alone, or in groups of 12 mice treated with CW in 1% or 3% Peanut Oil. Regression (not statistically significant) was noted in 4/12 mice treated with CW in 10% Peanut Oil, in 1/12 treated with TDM in 1% Peanut Oil, and in 6/12 treated with TDM in 3% Peanut Oil. Statistically significant regression was noted in 6/12 treated (50% regression, $p < 0.01$), 11/12 (92% regression, $p < 0.001$), and 11/12 (92% regression, $p < 0.001$) of mice treated with TDM in 3%, 9%, and 10% Peanut Oil, respectively. Thus, TDM, but not CW, in emulsified Peanut Oil remained immunotherapeutically active.

Dermal

Lasne et al. (1991) performed several studies to determine the effects of a Peanut Oil vehicle on the action of complete carcinogens such as benzo(a)pyrene (BaP) and 7,12-dimethylbenz (a)anthracene (DMBA) and on the promotor 12-*O*-tetradecanoylphorbol-13-acetate (TPA). Two Peanut Oil preparations were used in the study: Peanut Oil and an excipient composed of 74.9% Peanut Oil, 25% isopropyl-myristate, and two sunfilters. The actions of the excipient were the primary focus of the study.

In a short-term assay, groups of 30 mice (female Swiss and male and female C3H) received three dermal applications of either BaP in excipient (0.1 ml), TPA in excipient, or excipient alone. The compounds were applied to shaved areas of dorsal skin. In an independent second experiment, groups of mice received BaP or TPA in acetone, or acetone alone. Mice were killed 8 days following the first application. Skin specimens were analyzed for epidermal hyperplasia (suggestive of either

TABLE 3
Carcinogenicity studies with a Peanut Oil vehicle control

Assay	Vehicle conditions	Vehicle control findings	Reference
Oral			
Induction of mammary and other subcutaneous neoplasms in Chester Beatty Wistar rats by DABI	24 rats received 0.5 ml Peanut Oil by gastric intubation (6 doses each 2–3 days apart)	3 females developed mammary tumors; 2 were fibroadenomas and 1 was an adenoma. No neoplasms of internal organs observed	Roe, Carter, and Barron 1969b
Safety of toothpaste containing chloroform (toothpaste base not containing chloroform used as vehicle control, but one part of study tested chloroform in Peanut Oil and maintained a Peanut Oil vehicle control as well)	52 ICI mice received 1 ml/kg/day of Peanut Oil, 6 days/week for 80 weeks. A group of 100 untreated mice also maintained	In Peanut Oil group: malignant tumors of lungs noted in 1, of liver in 2. None in untreated group. Malignant lymphomas noted in 8 of Peanut Oil group and in 11 of untreated control group	Roe et al. 1979
Induction of Wistar rat bladder cancer by NA	20 rats received 300 mg/kg Peanut Oil weekly for 57 weeks	No neoplastic disease of the urinary tract noted	Hicks, Wright, and Wakefield 1982
Adult Syrian hamsters used to test the inhibition of DMBA-induced oral cancer by retinyl acetate	8 hamsters received Peanut Oil for 8 weeks (4 drops by pipette, 3 times/week)	No tumors observed	Burge-Bottenbley and Shklar 1983
Regression of methyl bromide–induced forestomach lesions in the rat	12 rats received 10 ml/kg Peanut Oil, 5 times/week for 13 or 25 weeks.	No lesions of the forestomach noted	Boorman et al. 1986
Subcutaneous			
Carcinogenic activity of lactones	Rats injected repeatedly with 0.5 ml Peanut Oil for 61 weeks	1 rat with carcinoma of the thyroid and an enlarged adrenal gland; considered spontaneous	Dickens and Jones 1963a
Carcinogenic activity of aflatoxin	6 rats treated with 0.5 ml Peanut Oil (unspecified time)	No local tumors	Dickens and Jones 1963b
Carcinogenic activity of DMBA, BA, NA, EMS, and NHA in newborn mice	63 mice (<24 hours old) injected with 0.02 ml Peanut Oil	3 with lung tumors, none malignant	Roe, Mitchley, and Walters 1963
Induction of pulmonary tumors in mice by nitrosonornicotine	30 mice injected weekly with (0.1 ml) Peanut Oil for 41 weeks	1 mouse killed at 11th month had a small pulmonary adenoma	Boyland, Roe, and Gorrod 1964
Induction of colon tumors by 3:2′-dimethyl-4-aminobipheny1 hydrochloride in rats	40 rats injected with Peanut Oil (2 mg) for 5 days	Small areas of lymphoid hyperplasia noted in the rectum at 32nd week. 3 had adenomas at same site at 44th week.	Higgins et al. 1968
Carcinogenic activity of calcium chromate in rats	16 rats injected once weekly with 0.2 ml Peanut Oil for 20 weeks	No local or distant tumors noted. Some test and control rats developed bronchiectasis and cystic nephritis	Roe and Carter 1969
Induction of lung and liver tumors in mice by 6-aminochyrsene in first 3 days of life	39 Swiss albino mice injected with 0.02 ml Peanut Oil on each of first 3 days of life	Hepatoma noted in 1 male mouse	Roe, Carter, and Adamthwaite 1969a

(Continued on next page)

TABLE 3
Carcinogenicity studies with a Peanut Oil vehicle control *(Continued)*

Assay	Vehicle conditions	Vehicle control findings	Reference
Induction of liver and lung tumors in mice by DAB and its derivatives in first 5 days of life	61 Swiss mice injected with 0.02 ml Peanut Oil on each of first 5 days of life	Liver cell adenomas noted in 3 males (2 with multiple tumors), lung tumors noted in 3 males and 1 female	Roe et al. 1971
Carcinogenic activity of some benz(a)anthracenes in newborn mice	Swiss mice injected with 0.02 ml Peanut Oil on each of first 3 days of life	No local tumors noted; 1 female developed a malignant lymphoma of the thymus, 1 female developed a single lung tumor, 1 male developed a single liver tumor	Roe, Dipple, and Mitchley 1972
Role of oral zinc intake on 20-MCA induced sarcomas	One group (10 mice) received a single IM injection of Peanut Oil and was placed on standard diet; second group also received Peanut Oil, but feed was supplemented with zinc sulphate (10 mg/kg/day)	No tumors noted	Verma et al. 1982
Promoter effect of Δ3 on MNU-induced colon tumors in rats	During dosing week, groups of female Fischer rats received two intrarectal injections of either 0.5 ml distilled water (12 rats) or water containing MNU (30 rats). Dosing followed by 0.5 ml Peanut Oil, thrice weekly for 48 weeks	No colonic tumors noted in water/Peanut Oil group. Tumors noted in 5 of MNU/Peanut Oil group	Sawada et al. 1987

BA: 1,2-benzanthracene; DAB: 4-dimethylaminoazobenzene; DABI: 1-(4-dimethylaminobenzal)-indene; DMBA: dimethylbenz(a) anthracene; EMS: ethyl methane sulphonate; Δ3: 5β-chol-3-en-24-oic acid; MNU: *N*-methyl-*N*-nitrosourea; NA: 2-napthylamine; NHA: 2-naphthylhydroxylamine.

complete carcinogenic or promoting activity) and the number of sebaceous glands (destruction of which suggests complete carcinogenic or initiating activity). When applied in the Peanut Oil excipient, neither BaP nor TPA induced contrast. A "strong" reduction in the number of sebaceous glands was noted in both mice strains treated with BaP in acetone, and a "significant" reduction was noted in C3H mice treated with TPA dissolved in acetone. Thus, the excipient had "almost completely inhibited the activity of" the complete carcinogen and the promoter. Neither acetone nor the excipient alone affected either parameter. In a complement experiment, BaP and TPA were administered in Peanut Oil and a similar inhibition was observed (Lasne et al. 1991).

In the long-term skin assay, groups of 30 female CD mice received three weekly applications of BaP or DMBA in 0.1 ml of excipient for 14 and 10 months, respectively. Two groups of mice also received the carcinogens in an acetone vehicle. No tumors were observed in mice that had received either complete carcinogen in the excipient. Tumors had developed in 100% and 60%, respectively, of mice treated with BaP and DMBA in acetone. The Peanut Oil excipient had "exerted an anticarcinogen activity on mouse skin" (Lasne et al. 1991).

For initiation-promotion studies, groups of mice received a single treatment of DMBA in acetone as an initiator. Beginning 1 week later, mice received thrice weekly applications of the promoter TPA in 0.1 ml of either excipient or acetone for 14 months. Groups of uninitiated mice were also treated with the promoter. Tumors were not observed in initiated mice treated with the promoter in excipient; 80% of initiated mice treated with promoter in acetone had tumors. No tumors were noted in the uninitiated group treated with only the promoter in excipient; one papilloma was noted in the group which received the promoter in acetone (Lasne et al. 1991).

To distinguish whether the excipient affected tumor initiation or promotion, the investigators examined the ornithine decarboxylase (ODC) activity induced by TPA and the binding of BaP to epidermal cell DNA and RNA. In the ODC activity assay, a single dose of TPA dissolved in either Peanut Oil, Peanut Oil excipient, or acetone (0.1 ml) was applied by micropipet to the shaved dorsal area of female Swiss mice. In some instances, the

Peanut Oil or excipient was applied 1 hour before or after TPA treatment. Mice were killed 5 hours later, and the epidermis from the application site was removed and analyzed for ODC activity. Compared to treatment with acetone alone, TPA dissolved in acetone increased epidermal ODC by 11-fold, whereas TPA in excipient induced only a 3-fold increase in activity. Similar results were noted when a larger dose of TPA was used. The protective effect of the excipient was not noted when it was applied prior to TPA exposure, but decreased ODC activity was noted when the excipient was applied after TPA exposure. Results were comparable when TPA was dissolved in Peanut Oil alone (Lasne et al. 1991).

In the BaP binding assay, [^{3}H]-BaP was applied in 100 μl of either acetone or excipient to the shaved dorsal skin of Swiss male mice. Two mice were killed at 4, 9, 12, 26, 50, 72, and 168 hours after treatment. The DNA and RNA of the epidermis were isolated via centrifugation, quantified by absorbance analysis, and BaP binding was measured by liquid scintillation. Maximum binding was detected 12 hours after exposure and decreased progressively thereafter. BaP dissolved in the excipient did bind to a lesser extent to DNA and RNA as compared to the acetone vehicle, but the difference was "not sufficient to explain the anticarcinogenic effect of the excipient." The investigators considered Peanut Oil to act as a promotor (Lasne et al. 1991).

CLINICAL ASSESSMENT OF SAFETY

Allergic Reaction

The published literature recognizes peanuts to be among many common foods that cause allergic (immuoglobin E [IgE]-mediated, mastcell–dependent immediate hypersensitivity) reactions in both children and adults. Peanuts are the food most likely to produce an anaphylactic reaction. Reviews note that cases of in utero peanut sensitization, although rare, have been documented. The major allergen is a protein. Reactions were more common when individuals also suffered from asthma, and the intake of alcohol, aspirin, or exercise have been reported to hasten clinical symptoms (Bush, Taylor, and Nordlee 1989; Sampson 1990; British Industrial Biological Research Association (BIBRA) 1995; Loza and Brostoff 1995).

Taylor et al. (1981) performed a double-blind crossover trial using 10 peanut-sensitive patients (verified by documented clinical signs and increased amounts of serum IgE antibodies to both crude peanut extract and purified peanut allergen). The study tested the allergic potential of Peanut Oil in these individuals. All patients had tested negative in the initial puncture skin test to both Peanut Oil and olive oil (control). Patients then ingested 1, 2, and 5 ml of either Peanut Oil or olive oil (in capsule form) at 30-minute intervals. Two weeks later, patients who had previously received 8 ml of Peanut Oil were challenged with olive oil and those who had received olive oil received Peanut Oil. No adverse reactions were noted.

Nordlee et al. (1981) performed a radioallergosorbent test (RAST) in which the allergic potential of various peanut products was tested against the combined sera from five individuals highly sensitive to peanuts. Allergenicity was demonstrated by the inhibition of binding of serum IgE to solid-phase peanut allergen by the peanut product. Defatted extractions of Peanut Flour (food grade, eight samples), samples containing peanut butter, and raw and roasted peanut products were all allergenic. Peanut Oil and hydrolyzed peanut protein had no allergenic potential.

The above studies were cited by reviewers as evidence that refined (hot-pressed) Peanut Oil that does not contain protein is not allergenic to peanut-sensitive patients (BIBRA 1995; Loza and Brostoff 1995). The reviews acknowledged reports of allergic reactions in infants that were traced to Peanut Oil contained in either formula or vitamin D preparations. The reviewers agreed with the assertions of Sampson (1990) that "to be 95% certain that 95% of peanut allergic individuals will not react to a particular sample of peanut oil, 58 individuals would have to be challenged with no reactions."

In more recent studies, Teuber, Brown, and Haapanen (1997) tested the IgE-binding capacity of various refined and unrefined nut oils and crude nut extracts. The samples were tested against pooled sera from patients with a nut or peanut allergy and a history of anaphylaxis and a specific IgE score greater than class 3. Sera from atopic patients without food allergy were pooled and used as negative controls. IgE binding was assayed by slot-blot and Western immunoblotting. Peanut extract (protein concentration of 9000 μg/ml) did bind with the IgE and was identified as the "most reactive protein extract tested." The two minimally processed peanut oils (each with protein concentration of 11 μg/ml) were positive in the assay. The results for two refined, bleached, and deodorized Peanut Oil samples with protein concentrations of 6 and 3 μg/ml were negative and a "very light band" of binding, respectively.

A randomized double blind crossover challenge study was conducted using 62 panelists with demonstrated positive skin pricks to peanuts. Refined or crude Peanut Oil was administered in increasing doses of 1, 5, and 10 ml (disguised with peppermint oil or cocoa flavoring). The oil was offered with bread, soya milk, or mixed with pudding. An interval of 10 to 15 minutes was allowed between doses to observe for onset of symptoms. None of the panelists had a reaction to the refined Peanut Oil (Hourihane et al. 1997).

A patch testing reference book by DeGroot (1994) noted that the published literature does not contain recommended test concentrations concerning Peanut Oil. To serve as a guide to the reader, DeGroot reported that an unpublished (and at the time, ongoing) study found no irritant reaction in 1 to 20 patients suffering from or suspected to suffer from cosmetic product contact allergy who had been patch tested with 30% Peanut Oil in petrolatum. (The exact number of panelists tested with Peanut Oil was not reported.)

Irritation

In addition to testing the irritancy potential of oils and perfumes using rabbits, guinea pigs, rats, and miniature swine (see

Animal Toxicology, Dermal Irritation), Motoyoshi et al. (1979) also tested the materials using humans. Undiluted Peanut Oil (technical grade) was applied in a 48-hour patch to the back of 50 male panelists. Sites were evaluated 30 minutes after patch removal and, when necessary, at 72, 96, and 120 hours. Peanut Oil was classified "negative." That is, positive reactions were noted in $\leq$10% of the panelists. The specific number and grade of reactions were not reported.

Five Caucasian panelists participated in a chamber-scarification test of USP-grade Peanut Oil. The test material (100 μl) was applied to scratched skin via an aluminum chamber. Scratches were made with a 30-gauge needle and were done in a grid pattern such that the epidermis was broken but no blood was drawn. Applications occurred daily for 3 days; the length of each exposure was not stated. The 72-hour reading, made 30 minutes after removal of the last patch, was used in scoring (scale 0–4). Peanut Oil was classified as nonirritating, producing mean scores of 0 to 0.4 (Frosch and Kligman 1977).

SUMMARY

Peanut (Arachis Hypogaea) Oil is the refined fixed oil obtained from the seed kernels of *Arachis hypogaea*. Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides are all derived from Peanut Oil. Peanut Flour is a powder obtained by the grinding of peanuts.

Peanut Oil, Hydrogenated Peanut Oil, and Peanut Glycerides function in cosmetic formulations as skin-conditioning agents. Peanut Acid functions as a surfactant—cleansing agent, and Peanut Flour functions as an abrasive, bulking agent and/or viscosity-increasing agent. In 1998, only Peanut Oil and Hydrogenated Peanut Oil were reported in use; combined, these two ingredients were used in 41 formulations.

Peanut Oil delivered by the oral route is absorbed, metabolized, and excreted. It can enhance the absorption of other compounds.

Hepatic changes were noted at microscopic examination of rats fed diets containing 15% edible Peanut Oil for 28 days. No control group was maintained and the findings were also noted in rats fed fresh corn oil. USP-grade Peanut Oil was considered relatively nonirritating when injected into guinea pigs and monkeys.

Technical-grade Peanut Oil was moderately irritating to rabbits and guinea pigs and mildly irritating to rats following dermal exposure. This same oil produced reactions in $\leq$10% of 50 human males. Peanut Oil was not an ocular irritant in rabbits.

Peanut Oil has been used as the vehicle control in reproductive/developmental toxicity, mutagenicity, and carcinogenicity studies. In most of the studies, the use of Peanut Oil as the vehicle was without incident. Some studies reported that Peanut Oil, as well as other plant oils, may affect test results when used as the vehicle.

Peanut Oil, either "laboratory expressed" or extracted using a food-grade solvent, was not carcinogenic to mice. Peanut Oil exerted anticarcinogenic activity when tested against known carcinogens.

Peanuts are the food most likely to produce an anaphylactic reactions. The major allergen is a protein that does not partition into Peanut Oil, Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides.

DISCUSSION

The CIR Expert Panel was satisfied that the results of toxicity, mutagenicity, carcinogenicity, reproductive/developmental, and sensitization studies cited in this report supported the safety of Peanut (Arachis Hypogaea) Oil, Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides in cosmetic formulations. The Panel acknowledged the irritation observed in animal studies that used technical grade Peanut Oil, but relied on clinical studies in which subjects had no irritation. Further, these four ingredients are oils or oil-based and therefore escape the two major concerns associated with peanuts—the peanut protein responsible for allergic reactions and aflatoxins. The protein and aflatoxins do not partition into the oil. The Panel cautioned manufacturers to make certain that these ingredients are free from aflatoxins and protein.

Because of a lack of current concentration of use data, the Expert Panel elected to issue a "safe for use" conclusion. However, the Panel noted the evidence that Peanut Oil can enhance penetration. Formulators are cautioned that this enhanced penetration can affect the use of other ingredients whose safety assessment was based on their lack of absorption.

Peanut (Arachis Hypogaea) Flour is sufficiently different from the above ingredients, such that its safety cannot be supported by data generated using the oil. The Expert Panel expected that concentrations of aflatoxin in the flour comply with U.S. government stipulations. However, additional data are needed to address concerns about the presence of peanut protein. Section 1, paragraph (p) of the Cosmetic Ingredient Review (CIR) Procedures states that "A lack of information about an ingredient shall not be sufficient to justify a determination of safety." In accordance with Section 30(j)(2)(A) of the Procedures, the Expert Panel informed the public of its decision that the data on Peanut (Arachis Hypogaea) Flour were not sufficient for determining whether the ingredient, under relevant conditions of use, was either safe or unsafe. The Panel released a Notice of Insufficient Data on June 6, 1997, outlining the data needed. No response was received. At its March 20, 1998, meeting, the CIR Expert Panel deleted the need for ultraviolet absorption data. The finalized list of data needed for Peanut (Arachis Hypogaea) Flour is

1. Concentration of use.
2. Chemical specifications (i.e., aflatoxin and protein levels).
3. Method of preparation.
4. Contact urticaria and dermal sensitization at concentration of use.

CONCLUSION

Based on the available data, the CIR Expert Panel concludes that Peanut (Arachis Hypogaea) Oil, Hydrogenated Peanut Oil, Peanut Acid, and Peanut Glycerides are safe for use in cosmetic formulations. The available data are insufficient to support the safety of Peanut (Arachis Hypogaea) Flour for use in cosmetic products.

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