Final Report on the Safety Assessment of Elaeis Guineensis (Palm) Oil, Elaeis Guineensis (Palm) Kernel Oil, Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil[1]

Elaeis Guineensis (Palm) Oil is the natural oil obtained from mesocarp of *Elaeis guineensis*, the palm tree. Elaeis Guineensis (Palm) Kernel Oil is the natural oil obtained from the seeds of that tree. Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil are end products of the controlled hydrogenation of the natural oils. These ingredients are primarily used as skin conditioning agents in cosmetic formulations. Palm Oil is currently reported to be used at concentrations up to 2%. Undiluted Palm Oil has an oral LD_{50} in rats of >5g/kg. Short-term and subchronic feeding studies showed no evidence of toxicity. Chronic feeding studies produced results suggestive of metabolic hyperactivity. Serum cholesterol and liver size were greatly increased compared to a corn oil diet. Minimal ocular irritation and no skin irritation, sensitization, or photosensitization were reported in animals studies. Anomalies in 30% of the live fetuses delivered by female albino rats fed commercial grade Palm Oil were reported. Other studies including multigeneration tests of crude Palm Oil and heated Palm Oil (as would occur in cooking) reported no reproductive toxicity, developmental toxicity, or differences in endocrine function. Although some data show that Palm Oil can be mutagenic in certain Ames Test *Salmonella* strains, it was negative in other strains and negative in an assay of chromosomal aberrations in bone marrow samples taken from mice dosed orally. Several studies suggesting an inhibitory effect of Palm Oil on 7,12-dimethylbenz(α)anthracene (DMBA) tumorigenesis have attributed the effect to the high vitamin E content of the oil. There was no evidence of irritation or sensitization in clinical tests. Use testing of products containing Palm Oil produced no ocular or skin irritation. The Cosmetic Ingredient Review (CIR) Expert Panel noted that crude Palm Oil produced fetal anomalies in rats, but concluded that the findings likely related to contaminants and that daily use of cosmetic products would not be expected to result in the high levels of exposure in the animal study. Because of the potential for contamination of Palm Oil, however, the Panel recommends that levels of polycyclic aromatic hydrocarbons be kept at a minimum in cosmetic grades of these ingredients. On the basis of the animal and clinical data included in this report, the CIR Expert Panel concludes that Elaeis Guineensis (Palm) Oil, Elaeis Guineensis (Palm) Kernel Oil, Hydrogenated Palm Oil, and Hydrogenated Palm Kernel Oil are safe as used in cosmetic formulations.

INTRODUCTION

The safety of oils derived from *Elaeis guineensis* (palm tree)—Elaeis Guineensis (Palm) Oil, Elaeis Guineensis (Palm) Kernel Oil, Hydrogenated Palm Oil, and Hydrogenated Palm Kernel Oil—are reviewed in this report. The terminology with which the cosmetics industry describes these ingredients has changed over the past several years. Table 1 shows the progression of terminology. The terminology now highlights the plant genus and species and presents the common name (which may vary) in parentheses (Wenninger, Canterbery, and McEwen 2000). For convenience, the common terminology of Palm Oil and Palm Kernel Oil will be used in the text of this report.

Data on Palm Oil Sucrose Glyceride, the Isopropyl Ester of Hardened Palm Oil, the Methyl Ester of Unhardened Palm Oil, Ethoxylated Palm Kernel Oil, Hydrogenated Palm Glycerides, and Hydrogenated Palm Kernel Glycerides are also included in this safety assessment. These data, along with data on Palm Oil and Palm Kernel Oil, were received from the cosmetics industry in response to the Cosmetic Ingredient Review (CIR) Expert Panel's request for studies on the skin irritation, sensitization, phototoxicity, and photosensitization potential of Palm Oil. Of the six ingredients not included in this safety assessment, only Hydrogenated Palm Glycerides and Hydrogenated Palm Kernel Glycerides are listed in the *International Cosmetic Ingredient Dictionary*, and only Hydrogenated Palm Kernel Glycerides (see Table 6) is included in the Food and Drug Administration (FDA) frequency of use database for cosmetic ingredients.

CHEMISTRY

Chemical and Physical Properties

Palm Oil

Elaeis Guineensis (Palm) Oil (CAS No. 8002-75-3) is defined as a natural oil that is obtained from *Elaeis guineensis*. Other names for this oil include Oils, Palm and Palm Oil (Wenninger,

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TABLE 1
Evolution of terminology

1997 terminology[a]		2000 terminology[b]	
Name	Cosmetics function	Name	Cosmetics function
Palm (Elaeis Guineensis) Oil	Skin conditioning agent—occlusive	Elaeis guineensis (Palm) Oil	Skin conditioning agent—occlusive
Palm Kernel (Elaeis Guineensis) Oil	Skin conditioning agent—occlusive	Elaeis Guineensis (Palm) Kernel Oil	Skin conditioning agent—miscellaneous and skin conditioning agent—occlusive

[a]Wenninger and McEwen 1997.
[b]Wenninger et al. 2000.

Canterbery, and McEwen 2000); and Palm Oil (from fruit), Palm Butter, Palm Acidulated Soapstock, and Oils, Glyceridic, Palm (Chemline 1996). Heated Palm Oil has an average molecular weight of 886 (Husain, Sastry, and Raju 1991).

Palm Oil is obtained from the mesocarp of the *Elaeis guineensis* palm tree (Yaacob and Bek-Nielsen 1987). It is not a fully saturated oil, and contains equal amounts of saturated and unsaturated fatty acids, expressed as percent of total fatty acids as follows: Saturated (50%), Monounsaturated (39%), and Polyunsaturated (10%); cholesterol (13–19 ppm) is also present (Palm Oil Research Institute of Malaysia 1987). The fatty acid composition of and iodine values for Malaysian Palm Oils are included in Table 2. Additional properties of Palm Oil are summarized in Table 3. In its natural form, Palm Oil has an average melting point of 36°C (range = 34–39°C) (Kheiri 1987). Peroxide values for Palm Oil (oxidized by incubation in the dark) have been determined by coulometry (8.9 mEq/kg) and iodometry (8.9 mEq/kg). The peroxide value indicates the degree of oxidation of lipids (Oishi et al. 1992).

Unprocessed Palm Oil has been described as consisting of 99% triglycerides and 1% minor components. The main minor components are as follows: carotenes, vitamin E (tocopherols and tocotrienols), sterols, phospholipids, glycolipids, and the triterpenoid squalene (de Witt and Chong 1987).

Both processed and unprocessed forms of Palm Oil are rich in vitamin E, the tocopherols, and, particularly, the tocotrienols (unsaturated analogs of vitamin E) (Palm Oil Research Institute of Malaysia 1987). Crude Palm Oil contains 600 to 900 ppm tocopherols; during the refining process, half are retained (Berger and Kun 1987). Crude Palm Oil is one of the richest natural sources of the provitamin A pigment beta carotene (Palm Oil Research Institute of Malaysia 1987). The carotenoids in crude Palm Oil (≈500–800 ppm) are completely removed during the refining process (Berger and Kun 1987). The deep red color of crude Palm Oil is due to the presence of carotenoids (Clegg 1973).

Malaysia produces 60% of the world's Palm Oil and approximately 70% of the world's Palm Oil export (Yaacob and Bek-Nielsen 1987). A large proportion of the Palm Oil produced in Malaysia is fractionated, and three major Palm Oil products are marketed: Palm Oil, Palm Olein (the more liquid portion of Palm Oil), and Palm Stearin (the more solid fraction of Palm Oil) (Berger and Kun 1987). The fatty acid compositions and iodine values for Palm Olein and Palm Stearin are presented in Table 2.

TABLE 2
Fatty acid composition (%) of Malaysian palm oils (Yaacob and Bek-Neilsen 1987)

Fatty acids	Palm Oil (%)	Palm Olein (%)	Palm Stearin (%)	Palm Kernel Oil (%)
C6:0	—	—	—	0.3
C8:0	—	—	—	4.4
C10:0	—	—	—	3.7
C12:0	0.2	0.2	0.1% to 0.6	48.3
C14:0	1.1	1.0	1.1% to 1.9	15.6
C16:0	44.0	39.8	47.2% to 73.8	7.8
C16:1	0.1	0.2	0.05% to 0.2	—
C18:0	4.5	4.4	4.4% to 5.6	2.0
C18:1	39.2	42.5	15.6% to 37.0	15.1
C18:2	10.1	11.2	3.2% to 9.8	2.7
C18:3	0.4	0.4	0.1% to 0.6	—
C20:0	0.4	0.4	0.1% to 0.6	—
Others	—	—	—	0.2
Iodine values	53.3	58.0	21.6% to 49.4	17.8

TABLE 3
Properties of Palm Oil and Palm Kernel Oil

Property	Description	Reference
Palm Oil		
Color/form	Reddish-yellow to dark dirty red, fatty mass	Budavari et al. 1989
Odor	Faint odor of violet	Budavari et al. 1989
Melting point	27 to 42.5°C	Budavari et al. 1989
Flash point	323°F	Sax 1979
Autoignition temperature	600°F	Sax 1979
Density/specific gravity	0.920 to 0.927	Sax 1979
Solubility	Insoluble in water	Hazardous Substances Databank 1996
Index of refraction	1.453 to 1.459	Budavari et al. 1989
Saponification number	200 to 205	Budavari et al. 1989
Iodine number	53 to 57	Budavari et al. 1989
Palm Kernel Oil		
Color/form	White to yellowish	Budavari et al. 1989
Melting point	26 to 30°C	Budavari et al. 1989
Flash point	398°F	Sax 1979
Density/specific gravity	0.952	Budavari et al. 1989
Solubility	Insoluble in water	Hazardous Substances Databank 1996
Saponification number	≈247	Budavari et al. 1989
Iodine number	≈15	Budavari et al. 1989

Palm Olein is the major form of Palm Oil that is consumed and exported from Malaysia and contains more unsaturated than saturated fatty acids. The composition of Palm Olein (expressed as percent of total fatty acids) is as follows: Saturated Fatty Acids (myristic, palmitic and stearic), 46%; Monounsaturated Fatty Acids (oleic), 43%; Polyunsaturated Fatty Acids (linoleic), 11%.

According to the Palm Oil Research Institute of Malaysia (1987), Palm Oil does not contain trans fatty acid isomers. However, according to a more recent publication, the trans fatty acid content of refined Palm Oil ranges from 6.7% to 16.4% (average = 10.8%) (Kohiyama, Kanematsu, and Niiya 1991).

Palm Kernel Oil

Palm (Elaeis Guineensis) Kernel Oil (CAS No. 8023-79-8) is defined as the oil that is obtained from the seeds of *Elaeis guineensis*. Other names for this oil include Oils, Palm Kernel and Palm Kernel Oil (Wenninger, Canterbery, and McEwen 2000); Oils, Glyceridic, Palm Kernel (Chemline 1996); and Palm Oil (from seed) and Palm Nut Oil (Hazardous Substances Databank 1996). It is normally refined (by soap makers prior to use) by simple vacuum bleaching with an activated Fuller's earth/carbon mixture. Palm Kernel Oil has a neutralization value (fatty acids) of 258 (Allen, Padeley, and Whalley 1969). Additional properties of Palm Kernel Oil are summarized in Table 3.

The fatty acid composition (expressed as percent of total fatty acids) of Palm Kernel Oil is as follows: Saturated (88%), Monounsaturated (10%), and Polyunsaturated (15%). Cholesterol (9–40 ppm) is also present (Palm Oil Research Institute of Malaysia 1987). The fatty acid composition of and iodine value for Palm Kernel Oil is included in Table 2.

Hydrogenated Palm Oil

Hydrogenated Palm Oil (CAS Nos. 8033-29-2 and 68514-74-9) is defined as the end product of controlled hydrogenation of Palm Oil. Other names for this oil include Oils, Palm, Hydrogenated and Palm Oil, Hydrogenated (Wenninger, Canterbery, and McEwen 2000), and Palm Oil, partially hydrogenated (Chemline 1996). The carotenoid pigments is Palm Oil are destroyed during the process of hydrogenation (Cornelius 1977).

Hydrogenated Palm Kernel Oil

Hydrogenated Palm Kernel Oil (CAS No. 68990-82-9) is defined as the end product of controlled hydrogenation of Palm Kernel Oil. Other names for this oil include Oils, Palm Kernel, Hydrogenated and Palm Kernel Oil, Hydrogenated (Wenninger, Canterbery, and McEwen 2000); Partially Hydrogenated Palm Kernel Oleine; and Oils, Glyceridic, Palm Kernel, Oleins, Hydrogenated (Chemline 1996). Hydrogenated Palm Kernel Oil has a melting point of 46°C (Cornelius 1977).

The following two definitions are included because data on these ingredients were submitted by the cosmetics industry in response to the Expert Panel's request for data on Palm Oil.

Hydrogenated Palm Glycerides

Hydrogenated Palm Glycerides is the end product of controlled hydrogenation of palm oil glycerides (Wenninger et al. 2000).

Hydrogenated Palm Kernel Glycerides

Hydrogenated Palm Kernel Glycerides is defined as the end product of controlled hydrogenation of palm kernel glycerides (Wenninger, Canterbery, and McEwen 2000).

Analytical Methods

Palm Oil

Crude Palm Oil has been analyzed by high performance liquid chromatography (Pocklington and Dieffenbacher 1988), thin layer chromatography, followed by gas-liquid chromatography (Meijboom and Jongenotter 1979), ^{13}C nuclear magnetic resonance (NMR) spectroscopy (Ng and Ng 1983), centrifugation-spectrophotometric technique and wide-line NMR (Ong, Boey, and Ng 1982), Emmerie-Engel spectrophotometric method (Wong, Timms, and Goh 1988), and ultraviolet-visible (UV-VIS) spectrophotometry (Swoboda 1983). In the latter analysis, the absorption maximum occurred at approximately 450 nm and absorption minima were noted at approximately 270 and 340 nm.

Palm Oil has also been analyzed by thin-layer chromatography, (Changbumrung, Buavatana, and Migasena 1980), gas-liquid chromatography (Sylvester et al. 1986), gas and high-performance liquid chromatography (Sotirhos, Ho, and Chang 1986; Sundram et al. 1989), on-column capillary gas-liquid chromatography (Lin and Lam 1994), ^{13}C NMR spectroscopy (Ng and Koh 1988), and near infrared spectroscopy (Sato, Kawano, and Iwamoto 1991; Arof, Daud, and Radhakrishna 1991).

Palm Kernel Oil

Palm Kernel Oil has been analyzed by column chromatography (Allen, Padley, and Whalley 1969).

Methods of Production

Palm Oil

Palm Oil is produced during the process of separating fat from palm fruits (*Elaeis guineensis*) by expression or centrifugation. More specifically, the manufacturing process involves lipase deactivation by steam, followed by the separation of fruit from the bunches to prepare it for pressing. The pressed oil is freed from solids and moisture via centrifugation, and further drying occurs under vacuum (Hazardous Substances Databank 1996).

Palm Kernel Oil

Palm Kernel Oil is extracted from the center nuts of the same fruit cluster that yields Palm Oil (*Elaeis guineensis*) (Hazardous Substances Databank 1996).

Reactivity

The fire potential of Palm Oil is slight upon exposure to heat or flame. Additionally, Palm Oil can react with oxidizing materials (Sax 1979).

Impurities, Contaminants, and Additives

Palm Oil

Copper and iron impurities have been detected in crude Palm Oil. These impurities were extracted from Palm Oil into an aqueous solution using a 20-kHz ultrasonic probe. The average concentrations of iron and copper (five replicates) detected were 0.026 and 4.698 ppm, respectively. For comparative purposes, the average concentrations of iron and copper (five replicates) detected in crude Palm Oil using the standard dry ashing sample preparation method were 0.036 and 3.864 ppm, respectively (Saleh et al. 1991).

The following heavy metal impurities have been detected in refined Palm Oil: iron (0.02–0.07 ppm), copper (0.03 ppm), and nickel (0.01–0.03 ppm) (Kohiyama, Kanematsu, and Niiya 1991).

Using colorimetric analyses, inorganic phosphate was detected in crude Palm Oil (20% in hexane) samples in the range of 9 to 20 ppm (Goh, Tong, and Gee 1984).

As determined by gas-liquid chromatography, butylated hydroxyanisole (94.5 ppm) and butylated hydroxytoluene (99.5 ppm) were detected in a mixture consisting of 80% Palm Oil and 20% hardened Palm Oil. These two antioxidants are widely used in edible oils and fats (Senten,Waumans, and Clement 1977).

Benzo(a)pyrene has been detected in refined Palm Oil at concentrations ranging from 0 to 4 μg/kg using high-performance liquid chromatography (Stijve and Hischenhuber 1987).

Using gas chromatography, residues of PCBs (polychlorinated biphenyl) and organochlorine pesticides were detected in Palm Oil purchased from grocery stores in Bangkok, Thailand. The concentrations detected (ng/g wet weight basis) were as follows: PCBs (11 ng/g): total hexachlorocyclohexane (HCH) ($\alpha+\beta+\delta$) (3.1 ng/g); total DDT (1,1,1-trichloro-2,2-bis(chlorophenyl)ethane) (o,p'-DDT + p,p'-DDD + p,p'-DDE + p,p'-DDT) (0.88 ng/g); hexachlorobenzene (HCB) (0.08 ng/g); aldrin (0.55 ng/g); dieldrin (0.4 ng/g); hepatochlor (0.02 ng/g), and hepatochlor epoxide (0.97 ng/g) (Tanabe et al. 1991).

Palm Kernel Oil

Palm Kernel Oil has been described as being remarkably low in colored impurities and nonsaponifiable substances. It contains water (0.13%) and unsaponifiable matter (0.66%) (Allen, Padley, and Whalley 1969). Crude Palm Kernel Oil usually contains between 0.2% and 0.8% unsaponifiable matter (Cornelius 1977).

USE

Purpose in Cosmetics

Palm Oil and Palm Kernel Oil are used as skin-conditioning agents—occlusive in cosmetic products. Palm Oil is also used as a solvent in cosmetics (Wenninger, Canterbery, and McEwen 2000).

Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil are used as skin-conditioning agents—occlusive and viscosity-increasing agents—aqueous in cosmetic products (Wenninger et al. 2000).

Scope and Extent of Use in Cosmetics

The product formulation data submitted to the Food and Drug Administration (FDA) in 1997 indicated that, collectively, Palm Oil, Palm Kernel Oil, Hydrogenated Palm Oil, and Hydrogenated Palm Kernel Oil were used in a total of 89 cosmetic products (Tables 4 and 5) (FDA 1997). For completeness, uses of Hydrogenated Palm Kernel Glycerides are given in Table 6 (FDA 1977), even though this ingredient is not included in this safety assessment.

Concentration of use values are no longer reported to FDA by the cosmetics industry (FDA 1992). Thus, the CIR requests that these data be provided directly to CIR. In response to this request, the following use concentration data on Palm Oil for various product categories were received from the cosmetics Industry: Make-up (1.0%); Face and Neck Skin Care (2.0%); Body and Hand Skin Care (0.50%); Foot Powders and Sprays (1.3%); Moisturizing Skin Care (2.0%); Suntan Gels, Creams, and Liquids (0.5%); and Indoor Tanning Preparations (0.5%) (CTFA 1995).

Palm Kernel Oil has been used by soap manufacturers as a convenient source of shorter chain fatty acids. Normal toilet soaps have contained anywhere from 15% to 25% Palm Kernel Oil. However, certain "super-fatted" compositions have contained anywhere from 30% to 40% Palm Kernel Oil (Allen, Padely, and Whalley 1969). Palm Kernel Oil is used particularly in high quality soaps (Cornelius 1977).

Cosmetic products containing Palm Oil, Palm Kernel Oil, Hydrogenated Palm Oil, or Hydrogenated Palm Kernel Oil are applied to most parts of the body and can come in contact with the ocular, nasal, and oral mucosae. These products can be used on a daily basis, and have the potential for being applied frequently over a period of several years.

International Use

Palm Oil and Palm Kernel Oil are listed in the *Japanese Comprehensive Licensing Standards of Cosmetics by Category* (CLS) (Rempe and Santucci 1997). These ingredients, which conform to the specifications of the *Japanese Cosmetic Ingredients Codex*, have precedent for use without restriction in most of the CLS categories. Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil are not listed in the *Japanese Comprehensive Licensing Standards of Cosmetics by Category* (CLS) (Rempe and Santucci 1997).

Palm Oil, Palm Kernel Oil, Hydrogenated Palm Oil, and Hydrogenated Palm Kernel Oil are not included among the substances listed as prohibited from use in cosmetic products that are marketed in the European Union (EEC 1995).

Noncosmetic Use

The major end use for Palm Oil in the importing countries is for the manufacture of compound cooking fats and margarine. Palm Oil with a high free fatty acid content is used in the production of low quality soap, candles, and in tin plating (Cornelius 1977). Other uses of Palm Oil are listed as follows:

TABLE 4
Product formulation data on Palm Oil and Palm Kernel Oil (FDA 1997)

Product category	Total no. of formulations in category	Total no. containing ingredient
Palm Oil		
Other baby products	26	1
Other fragrance preparations	137	1
Foundations	283	1
Bath soaps and detergents	341	7
Face and neck (excluding shaving preparations)	251	3
Body and hand (excluding shaving preparations)	776	5
Foot powders and sprays	32	1
Moisturizing skin care preparations	743	4
Paste masks (mud packs)	247	1
Other skin care preparations	683	1
Suntan gels, creams, and liquids	134	7
Indoor tanning preparations	50	3
Other suntan preparations	43	1
1997 totals		36
Palm Kernel Oil		
Cleansing skin care preparations	630	2
Face and neck (excluding shaving preparations)	251	3
Suntan gels, creams, and liquids	134	5
Indoor tanning preparations	50	1
1997 totals		**11**

TABLE 5
Product formulation data on Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil (FDA 1997)

Product category	Total no. of formulations in category	Total no. containing ingredient
Hydrogenated Palm Oil		
Eyeliner	499	1
Foundations	283	1
Lipstick	758	3
Moisturizing skin care preparations	743	1
Night skin care preparations	185	3
Other skin care preparations	683	1
Suntan gels, creams, and liquids	134	3
1997 totals		13
Hydrogenated Palm Kernel Oil		
Eyeliner	499	1
Eye shadow	501	3
Other eye makeup preparations	116	1
Lipstick	758	2
Makeup bases	125	1
Other makeup preparations	122	1
Cleansing skin care preparations	630	2
Body and hand (excluding shaving preparations)	776	4
Moisturizing skin care preparations	743	5
Other skin care preparations	683	8
Suntan gels, creams, and liquids	134	1
1997 totals		**29**

soap manufacture, pharmacy, food shortening, cutting-tool lubricant, hot-dipped tin coating, teme plating, softener in rubber processing, cotton goods finishing, and substitute for tallow as mold-release agent (Lewis 1993).

The triglyceride 1-palmitoyl-2-oleoyl-3-stearin, commonly known as "cocoa butter substitute primarily from palm oil," is generally recognized as safe for use as a direct food substance in the following food categories: confections and frostings, coatings of soft candy, and sweet sauces and toppings. 1-Palmitoyl-2-oleoyl-3-stearin is manufactured according to the following two methods: (1) directed esterification of fully saturated 1,3-diglycerides (derived from Palm Oil) with the anhydride of food grade oleic acid in the presence of the catalyst trifluoromethane sulfonic acid; and (2) interesterification of partially saturated 1,2,3-triglycerides (derived from Palm Oil) with ethyl stearate in the presence of a suitable lipase enzyme preparation (FDA 1984, 1987).

TABLE 6
Product formulation data on Hydrogenated Palm Kernel Glycerides (FDA 1997)

Product category	Total no. of formulations in category	Total no. containing ingredient
Eyebrow pencil	8	5
Eyeliner	499	6
Eye shadow	501	1
Lipstick	758	6
Other makeup preparations	122	2
1997 totals		**20**

Palm Kernel Oil is used in formulations for margarine, shortenings, and cooking oils (Cornelius 1977). Other uses of Palm Kernel Oil are listed as follows: manufacture of soap; with coconut oil, in the manufacture of plant butter; and use in liniments and ointment (Budvari et al. 1989).

The food additive cocoa butter substitute, from Palm Kernel Oil, coconut oil, or both oils, is permitted for direct addition to the following foods: (1) coating material for sugar, table salt, vitamins, citric acid, succinic acid, and spices; and (2) in compound coatings, cocoa creams, cocoa-based sweets, toffees, caramel masses, and chewing sweets. Cocoa butter substitute is a mixture of triglycerides that is manufactured by esterification of glycerol with food grade fatty acids derived from edible Palm Kernel Oil, edible coconut oil, or both oils (FDA 1991).

Partially Hydrogenated Palm Oil is used mostly for the manufacture of shortening; this gives the product good plasticity and creaming properties for baking and cooking. Fully Hydrogenated

Palm Oil Stearin is used as a starting material for the preparation of monoglycerides and similar chemical derivatives (Cornelius 1977).

Adhesives containing Palm Oil, Palm Kernel Oil, or Hydrogenated Palm Kernel Oil can be used safely as components of articles intended for use in packaging, transporting or holding food (*Code of Federal Regulations*, 21 CFR 175.105, 1992). Materials containing Palm Oil derivatives can also be used safely as articles or components of articles intended for use in producing, packaging, transporting, or holding food (Code of Federal Regulations, 21 CFR 176.200; 21 CFR 176.210; and 21 CFR 177.2800, 1992).

BIOLOGICAL PROPERTIES

Hematological Effects

Palm Oil

In a review by the Palm Oil Research Institute of Malaysia (1987), the following assertions concerning the biological activity of Palm Oil were made: lowering of blood cholesterol in humans (oral feeding study); decreased atherosclerosis in rabbits (oral feeding study): improvement of coronary blood flow in isolated rat heart preparation, and antithrombic effect in rats (oral feeding study). These activities were associated with reduced platelet aggregation, reduced production of the prothrombic prostanoid thromboxane (TXA_2), and increased production of the antithrombotic prostanoid prostacyclin (PGI_2). Palm Oil in the diet has also resulted in elevated plasma cholesterol concentration and blood pressure in rabbits, compared to feeding of a low-fat diet (Kennedy, Burstyn, and Husbands 1978).

Cardiovascular and Respiratory Effects

Hydrogenated Palm Kernel Oil

The effect of fractionated Hydrogenated Palm Kernel Oil, in suppository form, on arterial pressure and respiration was evaluated using five cats (males and females; weights not stated). The animals were anesthetized with sodium nembutal (30 mg/kg), after which 1.5 mg of the test substance was introduced. Blood pressure was taken in the common carotid artery using a mercury pressure gauge, and respiration was measured with a Marey capsule before and after introduction of the suppository. It was concluded that Hydrogenated Palm Kernel Oil did not cause changes in arterial pressure or respiration. A slight lowering (<15%) of arterial pressure was observed in one cat at 2.5 hours post administration, and was considered due to the administration of anesthesia (Khadzhay, Nikolaeva, and Pavlova 1975).

The effect of fractionated Hydrogenated Palm Kernel Oil, 1.5-g suppository, on cardiac activity in two dogs (breed and weights not stated) was evaluated using electrocardiography. The researchers stated that either there were no changes in electrocardiographic (EKG) readings at 24 to 36 hours post administration or the readings varied within the ranges observed before administration and removal of the suppositories. Additionally, no significant changes were observed in EKG readings 1 month after daily administration of the suppositories (Khadzhay, Nikolaeva, and Pavlova 1975).

Nutritional Value

Information on the nutritional value of Palm Oil is available in the published literature (Lian et al. 1968; Cottrell 1991; Chandrasekharan 1992) and will not be discussed in this safety assessment.

Absorption and Distribution

Palm Kernel Oil

The absorption of Palm Kernel Oil, corn oil, and cocoa butter was evaluated using three groups of six adult male Wistar rats (weights ≈ 250–350 g). The rats were anesthetized and duodenal and thoracic duct catheters were inserted surgically. In the three groups, test emulsions containing Palm Kernel Oil, corn oil, and cocoa butter, respectively, were infused via the duodenal catheter; lymph was collected for 24 hours in graduated cylinders and immersed in ice. A lipid-free emulsion was infused into each of six control rats. Lipid concentrations in the lymph of control rats were considered the baseline, representative of the composition of endogenous fat present in the lymph. Digestion and absorption were estimated by recovering the total fatty acids in the thoracic duct lymph over the 24-hour collection period (after subtraction of the baseline "endogenous fatty acids" in the lymph). In order to determine fatty acid composition, 50-μl aliquots of the diet emulsion and 24-hour lymph collections (500 μl) were obtained for lipid extraction. Lymph aliquots were analyzed to determine the amount (μg) of each fatty acid that was present. The individual fatty acid content of each aliquot was multiplied by total (24 hours) lymph volume. In rats fed Palm Kernel Oil, the percentages of lauric acid (13.5%) and myristic acid (7.3%) increased and other fatty acids were reduced in the thoracic duct lymph. After corn oil feeding, the percentage of linoleic acid increased to 30.8%, whereas the relative percentages of the other fatty acids decreased. In rats fed cocoa butter, the percentages of lauric, stearic, and oleic acids increased in the thoracic duct lymph. Generally, the fatty acids of the lymph reflected the composition of the dietary fat (Chen et al. 1989).

ANIMAL TOXICOLOGY

Acute Oral Toxicity

Palm Oil

The acute oral toxicity of undiluted Palm Oil was evaluated using five rats (strain not stated; weights = 190–217 g). The two deaths that were reported occurred at 1 and 6 days post intubation, respectively. The LD_{50} was greater than 5.0 g/kg, and the test substance was classified as slightly toxic (CTFA 1978a).

Short-Term Oral Toxicity

Palm Oil

The short-term oral toxicity of crude Palm Oil was evaluated using four groups of 10 weanling Wistar albino rats (5 males, 5 females per group). Groups of rats received the following diets ad libitum for 28 days: group I (protein-free diet), group II (10% refined groundnut oil with 10% casein protein in diet), group III (10% crude Palm Oil with 10% casein protein in diet), and group IV (10% refined palm-olein oil [refined Palm Oil] with 10% casein protein in diet). The diets fed were adequate with respect to all nutrients. Groundnut oil and refined palm-olein oil were used as controls. No adverse effects were observed in the experimental groups with respect to the following parameters that were evaluated: growth rate, feed-efficiency ratio, protein-efficiency ratio, net protein utilization, digestibility, fat absorption, nitrogen balance, phosphorus and calcium retention, serum enzymes, and hematology. All values were comparable to control values (Manorama and Rukmini 1991).

Short-Term Parenteral Toxicity

Hydrogenated Palm Kernel Oil

Fractionated Hydrogenated Palm Kernel Oil (0.46-g suppository) was administered rectally to 13 rabbits (strain and weights not stated) daily for 5 weeks. Seven untreated rabbits served as controls. The functional state of the liver was determined at 10-day intervals using the bromsulfalein test. Renal function was also determined once every 10 days on the basis of daily diuresis and the presence of albumin in the urine. Bromsulfalein (5% solution; 5-mg/kg dose) was administered intravenously, and bromsulfalein content of the blood was determined at 1, 5, 10, and 15 minutes post injection using a photoelectrocolorimeter. After entering the bloodstream, bromsulfalein is rapidly removed by the liver and secreted into the bile. When liver function is disrupted, hepatic uptake of the bromsulfalein is reduced and its concentration in the blood decreases more slowly. The animals (test and controls) were necropsied at the end of the study and tissues were examined microscopically. No changes in appetite or activity were observed in any of the animals during the study. Weight gain was similar to that observed in the control group. Additional study results are given below (Khadzhay, Nikolaeva, and Pavlova 1975).

Hydrogenated Palm Kernel Oil had no effect on bromsulfalein uptake. Renal function tests indicated that daily diuresis (5-week period) for experimental animals was within the same range as that noted for controls. No changes were found in the color or transparency of the urine, and no albumin was detected. At necropsy, macroscopic changes were not observed in any of the internal organs examined. Also, no differences were found in the average weight coefficients of the organs or any changes in organ weight, expressed as a percentage of body weight, between test and control rabbits. No changes were noted in the following organs (test and control rabbits) at microscopic examination: liver, kidneys, adrenal glands, heart, and distal portion of the rectum. Fractionated Hydrogenated Palm Kernel Oil did not have any effect on the functional state of the liver or disrupt the diuretic function of the kidneys (Khadzhay, Nikolaeva, and Pavlova 1975).

Subchronic Oral Toxicity

Palm Oil

The subchronic oral toxicity of 15% untreated Palm Oil and 15% heated Palm Oil (220°C) was evaluated using two groups of 20 (10 males, 10 females per group; weights ≈150 g) 6-week-old SPF Sprague-Dawley rats. The procedure for heating of Palm Oil was defined as a series of 15 consecutive heating sessions with, at each daily session, two successive increases to 220°C. Untreated Palm Oil (15%) and 15% heated Palm Oil (in 20% protein diet) were fed to the two groups, respectively, for 3 months. The animals were killed and hematological, blood biochemical, urine, and microscopic examinations performed. The growth (%) of animals between 0 and 13 weeks was comparable between the two groups. The hematological data were considered normal for rats of the ages and strain tested. Anomalies were not observed when blood biochemical parameters were measured and urinalyses were negative with respect to the presence of abnormal substances. At necropsy, no significant macroscopic lesions were observed. No significant differences were found in the following organ weights between the two test groups: brain, thyroid gland, heart, liver, spleen, kidneys, gonads, and adrenal glands. Particularly, no hepatic hypertrophy was observed in any of the animals tested. The histopathological alterations observed were insignificant. Lesions of toxicity were not observed in either of the two groups. Untreated Palm Oil (15%) and 15% heated Palm Oil were not toxic when administered orally to rats (Coquet et al. 1977). The reproductive toxicity of Palm Oil and its effects on newboms fed the same diet were also evaluated in this study and reported later in this safety assessment.

The subchronic oral toxicity of crude Palm Oil was evaluated using three groups of 30 (15 males, 15 females per group) weanling Wistar albino rats. The three groups were fed diets containing 10% refined groundnut oil, 10% refined palm-olein oil, and 10% crude Palm Oil, respectively, for 90 days. Refined groundnut oil and refined palm-olein oil (refined Palm Oil) served as controls. Each diet (fed ad libitum) was adequate with respect to all nutrients. No adverse effects were observed in the experimental groups with respect to the following parameters: growth rate, feed-efficiency ratio, protein-efficiency ratio, net protein utilization, digestibility, fat absorption, nitrogen balance, phosphorus and calcium retention, serum enzymes, and blood hematology. All values were comparable to control values (Manorama and Rukmini 1991).

Chronic Oral Toxicity

Palm Oil

A heated Palm Oil liquid fraction, derived from Palm Oil by transesterification, was evaluated for toxicity using male and female rats (number and strain not stated; weights ≈60 g). The

liquid Palm Oil was heated in a stainless steel tank for 8 days, 6.5 hours per day, at 210°C, under continuous stirring at 100 rpm. The rats were fed a diet consisting of 15% heated Palm Oil liquid fraction and 16% soybean protein for 1 year. The two control groups were fed heated (15%) and unheated (15%) peanut oil samples, respectively, in the diet, which also contained 16% soybean protein. Compared to rats fed the unheated peanut oil control diet, growth rate inhibition was observed in the two groups (both sexes) fed heated oil in the diet. This finding, based on statistical analysis, was evident during the first 8 weeks of feeding (females) and throughout the 13-week growth period (males). Growth inhibition was more pronounced in the group fed heated peanut oil in the diet. No differences were described in the following physiological parameters among the three dietary groups: general appearance, behavior, survival, and reproduction performance. The serum cholesterol concentration was significantly greater in females fed the heated peanut oil diet when compared to the other dietary groups. Alkaline phosphatase activity was significantly greater ($p < 0.01$) in rats of both sexes fed heated oils than in those fed heated oil in the diet. This effect was accompanied by hepatic hypertrophy, which can be indicative of liver metabolic hyperactivity (Cohen, Yannai, and Mokady 1983).

Palm Kernel Oil

Four groups of male, New Zealand white rabbits (average weight = 2500 g; 8–12 rabbits/group) were fed the following cholesterol-free diets, respectively, for 9 months: 14% Palm Kernel Oil, 14% cocoa butter, 14% coconut oil, and 14% corn oil. The diets also contained sucrose, casein, fiber, salts, and vitamins. After 9 months of feeding, the rabbits were killed and livers excised. The aortas of each group were pooled and extracted with a chloroform-methanol mixture. Serum cholesterol concentrations at 9 months were as follows: Palm Kernel Oil (436 mg/dl), corn oil (64 mg/dl), cocoa butter (220 mg/dl), and coconut oil (474 mg/dl). Absolute liver cholesterol levels of 1.61 g/liver (Palm Kernel Oil, 8 rats), 0.63 g/liver (corn oil, 12 rats), 1.31 g/liver (cocoa butter, 8 rats), and 0.91 g/liver (coconut oil, 5 rats) were also reported. Rabbits fed Palm Kernel Oil in the diet had the largest livers. Average atherosclerosis values (aortic arch + thoracic aorta/2) for the same groups were reported as follows: Palm Kernel Oil (1.28), corn oil (0.15), cocoa butter (0.53), and coconut oil (1.60). Cocoa butter (iodine value = 33) was significantly less cholesterolemic and atherogenic than Palm Kernel Oil (iodine value = 17) or coconut oil (iodine value = 6). The investigators stated that these differences could be due to the fact that approximately half of the fatty acids in Palm Kernel Oil are C_{16} or shorter, compared to 76% of the fatty acids being C_{18} or longer in cocoa butter (Kritchevsky et al. 1982).

Ocular Irritation

Palm Oil

The ocular irritation potential of undiluted Palm Oil was evaluated using six rabbits (strain not stated). Eyes were not rinsed after instillation of the test material. Ocular irritation reactions were scored using the Draize scale (0–110). The total ocular irritation score (six rabbits) was 3 at day 1 post instillation and 1 at day 2 post instillation. All reactions had cleared by day 3. The investigators concluded that undiluted Palm Oil induced minimal ocular irritation (CTFA 1978a). Two different hand creams containing 2.0% Palm Oil also induced minimal ocular irritation when tested according to the same procedure. Six rabbits were evaluated in each test. The total ocular irritation scores for one of the products were identical to those determined for undiluted Palm Oil. For the remaining product, the total ocular irritation score was 1 at day 1 post instillation, and all reactions had cleared by day 2 (CTFA 1981). A facial lotion containing 1.5% Palm Oil induced moderate ocular irritation in another ocular irritation study using six rabbits (same procedure). A total ocular irritation score of 1 was reported on days 1, 2, 3, 4, and 7 post instillation (CTFA 1983).

The ocular irritation potential of a lotion containing 1.5% Palm Oil was evaluated in an in vitro membrane partition assay. The test substance received an ocular safety classification of minimal when tested in an unspecified protocol in quantities of 30, 50, and 100 μl (National Testing Corporation 1988).

Hydrogenated Palm Kernel Oil

The ocular irritation potential of fractionated Hydrogenated Palm Kernel Oil (in suppository form) was evaluated using eight rabbits (strain not stated). Sections of the suppositories were instilled into the conjunctival sac of each rabbit over a period of 10 days. Hyperemia, lacrimation, and narrowing of the palpebral fissure were observed during the first minute after instillation. Reactions cleared within 5 to 30 minutes, at which time treated eyes did not differ from untreated control eyes with respect to the color of mucous membranes, and size of the pupil and palpebral fissure. Additionally, no visible changes were observed after 10 days. The ocular irritation observed was described as mild (Khadzhay, Nikolaevas and Pavlova 1975).

Mucous Membrane Irritation

Hydrogenated Palm Kernel Oil

The irritation potential of fractionated Hydrogenated Palm Kernel Oil was evaluated using five cats, two dogs, and 21 rabbits. Neither the strains nor weights of the animals tested was stated. The test substance was administered in the form of suppositories to rats and dogs (dose = 1.5 g) and to rabbits (dose = 0.46 g). No signs of mucous membrane irritation (rectum) were found in any of the animals tested. Macroscopic examination of mucous membranes (rabbits) 5 weeks after daily administration of Hydrogenated Palm Kernel Oil–based suppositories to 13 rabbits indicated that the mucous membranes of the rectum were normal in color and folding. No evidence of irritation was found at microscopic examination (Khadzhay, Nikolaeva, and Pavlova 1975).

Skin Irritation

Palm Oil

The primary skin irritation potential of undiluted Palm Oil was evaluated in a single-insult occlusive patch test using nine rabbits (strain not stated). At 2 hours post application, five rabbits had an irritation score of 0 and the remaining four had a score of 0.5. At 24 hours post application, one rabbit had a score of 0.5 and the remaining rabbits had a score of 0. The primary irritation index (PII) was 0.22 (maximum possible score = 8), and the test substance was classified as practically nonirritating (CTFA 1978a). In a second study (same procedure), the skin irritation potential of undiluted Palm Oil was evaluated using nine rabbits. Six of the rabbits had irritation scores of 1 at 2 hours post application. Four of these rabbits had the same score at 24 hours. The PII was 0.67, and the test substance was classified as minimally irritating (CTFA 1978a).

Skin Sensitization

Palm Oil

The skin sensitization potential of Palm Oil was evaluated in the Magnusson-Kligman Maximization Test (Magnusson and Kligman 1969) using four groups of 10 female, albino guinea pigs of the Hartley strain (weights = 300–325 g). Two of the groups served as controls. During induction, three pairs of sites (right and left upper back per pair) per animal in the first test group were injected with the following materials, respectively: 5% Palm Oil in propylene glycol, 5% Palm Oil in 50% aqueous Freund's Complete Adjuvant, and 50% Freund's Complete Adjuvant. Each material (.05 ml) was injected intradermally. In the second test group, except for the replacement of 5% Palm Oil with 5% phenylacetaldehyde, the induction protocol was the same. The three pairs of sites on each control animal were injected intradermally with full strength propylene glycol, 1:1 propylene glycol: 50% aqueous Freund's Complete Adjuvant, and 50% aqueous Freund's Complete Adjuvant, respectively, during induction. In the booster phase, initiated 1 week after induction, an occlusive dressing pad containing full strength Palm Oil (0.5 ml) was applied over the induction injection sites on each animal in the first test group; pads were removed after 48 hours. Booster applications of phenylacetaldehyde (25%) in petrolatum were made to animals in the second test group, and full strength petrolatum (booster) was applied to control animals according to the same procedure. Two weeks after the booster phase, animals in the first and second test groups and the two control groups were challenged with 0.5 ml of 5% Palm Oil and 0.5 ml of 2% phenylacetaldehyde in petrolatum, respectively. Patches were applied to previously untreated sites on the left or right flank and remained in place for 24 hours. Reactions were scored at 24 and 48 hours after patch removal according to the following scale: 0 (no evidence of any effect) to 4 (severe, deep red erythema with vesiculation or weeping with or without edema). The only challenge reactions reported (mild—pink uniform erythema covering most of the contact area) were observed in the second test group challenged with 2% phenylacetaldehyde. The investigators concluded that Palm Oil was nonallergenic (CTFA 1978b).

Phototoxicity

Palm Oil

The phototoxicity of a facial lotion containing 1.5% Palm Oil was evaluated in the phototoxicity yeast assay. Test cultures treated with 1.5% Palm Oil were irradiated with UV light for 18 hours, and evaluated for zones of inhibition at 48, 72, and 96 hours. Untreated cultures served as negative controls and positive control cultures were treated with 0.0001% 8-methoxypsoralen. Additional details concerning the experimental protocol were not included. The facial lotion was not classified as phototoxic (CTFA 1986).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Palm Oil

The teratogenicity of Palm Oil (commercial grade) was evaluated using four groups of female albino rats (n = 8–11/group; weights ≈ 200 g). Three experimental groups and one control group were used; female rats were mated with male rats of the same stock. Palm Oil was administered, in addition to the standard diet, orally to pregnant females of the three experimental groups at doses of 1, 2, and 3 ml, respectively, on days 5 through 15 of gestation. Doses were administered using a polyethylene tube attached to a 5 ml glass syringe. The control group received standard diet only. In experimental groups, the incidence of resorptions approached that noted for malformations. Mortality was increased and the incidence of malformations was dose-related. For fetuses that survived to day 20 of gestation, stunting of growth (compared to controls) was the most common finding. In the group dosed with 3 ml of Palm Oil, exencephaly was the most frequent anomaly, followed by ocular defects and cleft palate. Ocular defects and cleft palate were observed only in the fetuses of dams dosed with 3 ml of Palm Oil. Of the 191 implants that were collected from experimental dams on day 20, 20% were resorbed or dead. Thirty percent of the 152 live fetuses had abnormalities, the distribution of which was as follows: growth retardation (23%), exencephaly (7%), ocular defects (2%), and cleft palate, along with growth retardation (1%). Developmental anomalies were not observed in the negative-control group. The investigators stated that the defects observed resembled those caused by hypervitaminosis A, and could be attributed to the high carotene content of Palm Oil (Singh 1981).

The effect of 20% Palm Oil in the diet (fed ad libitum) on sexual maturation and endocrine function was evaluated using 15 to 16 weanling, Sprague-Dawley [Crl:CD(SD)BR] rats; 21 days old. Corn Oil (20%; high fat) was fed to another group of 15 to

16 rats and 5% (normal fat) corn oil was fed to 15 to 16 control rats. At between 50 and 60 days old, rats with regular 4-day estrous cycles were implanted (on diestrus) with saline-filled intracardiac silastic venous cannulas. The rats were injected with penicillin immediately after surgery. Serial blood samples (0.2 ml/sample; 6 samples/rat) were drawn at proestrus for measurement of serum prolactin and leutinizing hormone (LH). Four days later (on the following proestrus), the rats were placed under light anesthesia and blood (2 ml) was collected via orbital sinus puncture for assay of proestrous surge concentrations of estradiol. Blood samples were collected again 3 days later (at diestrus) via the same method for assay of basal estradiol concentration. The rats were then killed and uterine weights at diestrus were recorded. Vaginal opening was observed significantly earlier in rats fed 20% Palm Oil or 20% corn oil when compared to 5% corn oil controls. No significant differences in average body weights (determined on first day of estrus) were observed among the various dietary groups; estrous cycle regularity was also similar. Similar proestrus morning (basal) concentrations and proestrous afternoon (surge) concentrations of serum prolactin were observed in all dietary groups. The same was true for basal or surge concentrations of LH or estradiol. Additionally, no significant differences in diestrus uterine weights (whole uteri or on a 100-g body weight basis) were noted among the groups fed 20% Palm Oil, 20% corn oil, 5% corn oil (controls) (Sylvester et al. 1986).

The following substances were administered (in the diet) in a feeding study using Wistar rats (weights = 100–120 g): Diet 1, Nigerian Palm Oil, normally refined; Diet 2, Palm Oil heated to 220°C for 1 hour, then refined; Diet 3, Palm Oil heated to 220°C for 5 hours, then refined; Diet 4, Palm Oil heated to 260°C for 15 minutes, then refined; and Diet 5, 1.5% by weight (converted to the amount of oil) nonvolatile carotene decomposition product in refined Nigerian Palm Oil. In Diet 5, natural carotene was destroyed by heating, but additional amounts had been added to the oil at a dose far exceeding 100 times the usual concentration (relative to Palm Oil). Diet 1 (control diet) was tested using 60 male and 60 female rats. Diets 2 through 5 were tested using 30 males and 30 females per test substance. Each diet was fed over a period of 6 months, after which males were paired with females.

The first generation that resulted from the matings was introduced into the oral feeding study. Again, Diet 1 was fed to 60 male and 60 female first generation rats, and Diets 2 through 5 were fed to 30 male and 30 female first-generation rats per test substance. For generations 2 and 3, Diet 1 was fed to 40 rats per sex; Diets 2 through 5 were each fed to 20 rats per sex. For generation 4 (only animals from the mating of generation 3), Diet 1 was fed to 14 males and 15 females, and Diets 2 through 5 were each fed to 8 to 16 rats per sex. Rats of generations 1 through 3 were fed the diets until spontaneous death. The duration of feeding for rats of generation 4 was not stated. Initial weights for rats of generations 1 through 4 were 60 to 90 g. The study results are summarized below (Lang et al. 1966).

All values for weight gain and feed consumption (generations 1–4 for all dietary groups; averages inclusive of weeks 1–4) were similar. No significant differences were observed in protein efficiency (weight gain per gram of protein consumed) when all values (generations 1–4) were compared with results for the control group. However, when values for protein efficiency (generations 1–4 for all dietary groups; averages inclusive of weeks 5–8) were compared with results for the control group, significantly lower values were reported for females fed Diet 3 (Palm Oil heated to 220°C for 5 hours, then refined) and for males fed Diet 4. Significantly lower values were also reported for males and females fed Diet 5 (1.5% by weight [converted to the amount of oil] nonvolatile carotene decomposition product in Nigerian Palm Oil, normally refined) (Palm Oil heated to 260°C for 15 minutes, then refined). The investigators stated that these differences in protein efficiency need not necessarily be attributed to a poorer disposition of the animals; greater activity was observed in rats on Diet 5.

Information relating to mortality was reported for generations 1 and 3. For generation 3, mortality was expressed in terms of percent of rats from each dietary group that was alive after 870 days as follows: 37.5% (Diet 1, control), 35% (Diet 2), 35% (Diet 3), 20% (Diet 4), and 35% (Diet 5). In generation 1, the ages of the oldest rats (all dietary groups) were all greater than 1000 days old).

The number of females fed Diet 2 (Palm Oil heated to 220°C for 1 hours, then refined) that bore 10 or more young was significantly less (55 controls vs. 9 on Diet 2). The χ^2 boundary that may not be exceeded to four classes and three degrees of freedom is 4.719, and this value was exceeded only for females on Diet 4. This was the only significant finding with respect to litter size in all dietary groups. No evidence was detected that indicated that this difference was due to the toxicity of Diet 2. It was also determined that the percentage(s) of young delivered by females fed Diet 5 (1.5% by weight [converted to the amount of oil] nonvolatile carotene decomposition product in Nigerian Palm Oil, normally refined) that was actually raised was significantly less when compared to controls. The χ^2 method was also used in this statistical comparison. This was the only significant finding regarding the raising of young by females of all dietary groups.

The percentages (range) of rats with organ damage, all dietary groups considered, were as follows: fatty change in the liver (9.9%–11.9%), benign neoplasms (2.2%–4.8%), and malignant neoplasms (2.4%–4.3%). When all groups were compared, the values for organ damage were considered essentially the same. Particularly, the incidence of malignant neoplasms did not exceed the known random rate of spontaneous malignant neoplasms in rats (4%–5%).

The investigators stated that the results of this oral feeding study indicated that Palm Oil treated thermally in order to destroy carotene was not injurious to the health of any of the rats tested (Lang et al. 1966).

The reproductive toxicity of 15% untreated Palm Oil and 15% heated Palm Oil (220°C) was evaluated using two groups of 30 (10 males, 20 females per group; weights ≈150 g) 6-week-old, SPF Sprague-Dawley rats. Untreated Palm Oil (15%) and 15% heated Palm Oil (in 20% protein diet) were fed to the two groups, respectively, for 10 weeks. After feeding, 10 males were mated with 20 females from their respective groups over a period of 18 days. After weaning, dams and their offspring received the same diet that was fed prior to parturition. At 5 weeks of age, the young were killed and one male and two females per litter were necropsied; liver and kidneys were weighed. Necropsy was performed on 18 to 20 male offspring and 36 to 40 female offspring per group. Microscopic examination was performed on the tissues of five male and five female offspring per group (selected at random). The matings resulted in 234 live young (untreated Palm Oil) and 205 live young (heated Palm Oil). Both the number of implantations per dam and the average number of live young per litter were considered acceptable for both groups. The number of embryo losses during gestation was comparable between groups fed untreated Palm Oil and heated Palm Oil. The same was true for stillbirths, and perinatal and postnatal mortality. At necropsy, relative organ weights (liver and kidney weights for females; liver weights only for males) were significantly greater in the offspring of rats dosed with heated Palm Oil when compared to rats dosed with untreated Palm Oil. At microscopic examination, no lesions related to possible toxicity were observed in these organs. The researchers suggested that substances are present in heated Palm Oil that trigger a metabolic process of adaptation in liver cells, and did not consider the increase in organ weight as indicative of a toxic effect. Neither untreated Palm Oil (15%) nor 15% heated Palm Oil (in 20% protein diet) induced any anomalies with respect to fertility and in utero growth (Coquet et al. 1977).

In another study, the reproductive toxicity of red Palm Oil (also known as crude Palm Oil) was evaluated in a mutigeneration breeding study using two groups of Wistar/NIN inbred weanling albino rats (12 males, 12 females per group). Refined, bleached deodorized Palmolein Oil (refined Palm Oil) served as one of the controls. The two groups were fed a 20% protein diet, considered adequate with respect to its nutrient content, containing 10% red Palm Oil (group 1) and 10% Palmolein Oil (group 2, control), respectively, prior to mating. A second control group (12 males, 12 females) was fed groundnut oil in the diet. Weekly body weights and feed intake were recorded for 15 weeks (100–120 days). Twelve males and 12 females from each group were mated after 100 to 120 days. The F_0 rats were mated twice to produce the F_{1a} and F_{1b} litters. F_{1b} rats were mated twice to produce the F_{2a} and F_{2b} litters, and two matings of the F_{2b} rats produced the F_{3a} and F_{3b} litters. Feed consumption and weight gain of rats fed crude Palm Oil were similar to the two control groups. Also, in rats fed crude Palm Oil, the percentage of matings that resulted in pregnancies was similar to that of control groups. Mean litter size and birth and weaning weights were also comparable between experimental and control groups, and were not significantly different in all three generations. Preweaning mortality was increased in all three generations, but was not significantly different from controls. Neither behavioral abnormalities nor reflexological changes were observed in rats of any of the groups. Crude Palm Oil also did not cause significant changes in relative weights of the liver, heart, spleen, lungs, kidneys, testes/ovaries, or total body weight in the F_0, F_{1b}, and F_{2b} generations. Relative organ weights were considered normal in pups of both matings of the three generations. Lesions were not observed at necropsy. It was concluded that crude Palm Oil had no adverse effect on several reproductive parameters (Manorama, Chinnasamy, and Rukmini 1993).

Palm Kernel Oil

Adult Mongolian gerbils (highly resistant to atherosclerosis) and their sucklings (first generation) were randomly assigned to the following six dietary groups (5 couples/group): group 1, basal diet; group 2, 8.75% *w/w* Palm Kernel Oil in diet; group 3, 8.75% *w/w* sunflower seed oil; group 4, basal diet with 0.2% cholesterol; group 5, Palm Kernel Oil diet with 0.2% cholesterol; and group 6, sunflower seed oil diet with 0.2% cholesterol. After the first generation, cholesterol in the diet (latter three groups) was reduced to 0.05% because of increased mortality; one third of the adults died within the first 3 months of feeding. In the first generation sucklings (up to 4 weeks old), mortality was greatest in the Palm Kernel Oil + cholesterol (24% mortality) and basal diet + cholesterol (38% mortality) groups. The livers of animals fed diets containing cholesterol (Palm Kernel Oil diet included) were increased in weight four- to fivefold, and were pale yellow in color. The livers of animals fed diets without a cholesterol supplement (Palm Kernel Oil diet included) were without lesions. In the second generation, no statistically significant differences were found between the basal dietary group and Palm Kernel Oil or Palm Kernel Oil + cholesterol groups with respect to the following: frequency of litters, mean litter size, total of newborns, and suckling death. The same was true regarding similar comparisons involving the remaining three dietary groups (Temmerman et al. 1988).

MUTAGENICITY

Palm Oil

The mutagenicity of refined and unrefined Palm Oil was evaluated using *Salmonella typhimurium* strains TA1537, TA1538, TA97, TA98, TA100, and TA102 in the following bioassays: standard plate incorporation bioassay, a 20-minute preincubation protocol (Ames, McCann, and Yamasaki 1975; Maron and Ames 1983), and a modification of the liquid incubation method (Mitchell 1978). In the liquid incubation assay, both refined and unrefined Palm Oil induced reproducible weak mutagenicity only in strain TA1537. In the other two assays, no consistent evidence of mutagenicity was found in any of the strains tested.

Mutagenicity was not detected in the individual triacylglycerol sterol or fatty acid fractions (resulting from chromatographic fractionation), but the lipid peroxide fractions from both oils were weakly mutagenic. Mutagenicity was abolished by exogenous catalase, suggesting that the observed activity was moderated by hydrogen peroxide (Kensese, Teng, and Smith 1989).

In another study, the mutagenicity of Palm Oil was evaluated using *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538. Weak mutagenicity was noted in strains TA98, TA100, TA1535, TA1537, and TA1538 at a dose of 2 μl/plate. Mutagenicity was not noted at a dose of 1 μl/plate in any of the bacterial strains (Sivaswamy et al. 1991).

A heated Palm Oil liquid fraction, derived from Palm Oil by transesterification, as well as heated and unheated peanut oil were not mutagenic in the Ames test. Additional details concerning the conduct of this assay were not provided (Cohen, Yannai, and Mokady 1983).

The genotoxicity of Palm Oil was evaluated using bone marrow cells from Balb/C female mice (groups of 10 mice; weights = 25–30 g). Three groups were dosed with Palm Oil supernatant, Palm Oil sediment, and a mixture of the two, respectively, by gavage for 5 consecutive days. Mice in each group received daily doses of 4.5 g/kg. The negative-control group was dosed (by gavage) with corn oil, and the positive-control group was injected intraperitoneally with cyclophosphamide (20 mg/kg). The animals were killed by cervical dislocation 24 hours after administration of the last dose, and bone marrow samples obtained. One hundred bone marrow metaphase cells per mouse were analyzed for chromosomal aberrations (chromatid and chromosome gaps, breaks, fragments, and exchanges), and 1000 metaphase cells per mouse were used to determine the mitotic index. Compared to the negative-control group, no statistically significant differences were observed in the frequency of chromosomal aberrations and the mitotic index in bone marrow samples from all three test groups. More than one aberration per cell was identified in bone marrow samples from the positive control. Compared to the negative control, results for the positive-control group were significant at the 1% level (Oliveira et al. 1994).

CARCINOGENICITY

Palm Oil

The effects of such factors as treadmill exercise and dietary fat on mammary tumorigenesis were investigated using 184 Sprague-Dawley female rats (21 days old). Initially, the rats were fed a purified 5% fat diet up to 64 days of age. During the initial feeding period, 50-day-old rats were dosed orally (intubation) with 5 mg 7,12-dimethylbenz(a)anthracene (DMBA). At age 64, 14 days after DMBA administration, the rats were randomized into the following three dietary groups: group 1, 5% fat as corn oil; group 2, 24.6% fat as corn oil; or group 3, mixture of Palm Oil (21.8%) and corn oil (2.8%). Half of the rats in each dietary group were subjected to moderate exercise on a treadmill (belt speed = 20 m/min for 15 min/day) 5 days per week. The remaining rats were subjected to low-intensity exercise on a treadmill (belt speed = 2 m/min) at the same frequency and duration. The experiment ended 154 days after DMBA administration. DMBA-induced mammary neoplasms were classified as either benign or malignant. A reduction in animal days at risk (beginning 1 week after midpoint of experiment) was noted in high- and low-fat dietary groups subjected to moderate exercise. This problem was due to unscheduled termination due to necrotic neoplasms, and was 40% greater than that occurring in groups subjected to light exercise. Compared to rats subjected to light exercise, moderate exercise accelerated the appearance of neoplasms in high-fat (24.6% corn oil) and low-fat (5% corn oil) dietary groups. For rats that received the high-fat (24.6% corn oil) diet, the median neoplasm-free time was significantly shortened ($p = 0.028$) in rats subjected to moderate exercise (43 days) versus those subjected to light exercise (62 days). Similarly, for rats that received the low-fat (5% corn oil) diet, neoplasms were noted earlier ($p = 0.046$) in rats subjected to moderate exercise (day 57) versus those subjected to light exercise (day 67). In rats fed the diet containing 21.8% Palm Oil and 2.8% corn oil, exercise (moderate or light) had no effect on the time of neoplasm appearance (moderate exercise, day 58, and light exercise, day 62; $p = 0.502$). Therefore, the effect of exercise on mammary neoplasm induction was attenuated by feeding a high-fat diet formulated with a combination of Palm Oil and corn oil (Thompson et al. 1989).

Groups of young, female Sprague-Dawley rats (number and weights not stated) were fed either a chow diet or semipurified diet containing 5% corn oil or 20% corn oil, Palm Oil, lard or canola oil for approximately 6 weeks. At necropsy, the fat content of mammary glands obtained from rats fed chow, 5% corn oil, 20% Palm Oil, or 20% lard was less than that of rats fed 20% corn oil or 20% canola oil. The fatty acids of the lymph reflected the composition of the dietary fat. Rates of cellular proliferation were based on the incorporation of tritiated thymidine or the number of cells arrested in mitosis after dosing with vincristin. Rates of cellular proliferation were lower in the mammary glands of rats fed chow, 5% corn oil, or 20% Palm Oil than in those fed the other diets. These results were in accordance with the concept that the fat content of the mammary gland is positively correlated with susceptibility to mammary cancer (Kurowska, Guthrie, and Carroll 1993).

The effect of 20% Palm Oil in the diet (fed ad libitum) on mammary tumorigenesis was evaluated using 32 weanling, Sprague-Dawley Crl:CD(SD)BR rats (21 days old). Corn Oil (20%; high fat) was fed ad libitum to another group of 32 rats and 5% (normal fat) corn oil was fed to 32 control rats. The diets were fed prior to and during the initiation phase of carcinogenesis up to one week after oral administration of DMBA (7.5 mg) to each group. The rats were 52 days old at the time of DMBA administration, after which each group was fed the 5% corn oil (normal fat) control diet for the remainder of the experiment. Approximately 15% to 30% of rats from each group were killed prior to termination of the experiment, because they

became moribund from the increased tumor burden. Neoplasms from these rats, as well as those that had been palpable for at least 5 successive weeks and then regressed, were included in the tumor data. All remaining rats were killed at the end of the experiment, 19 weeks after DMBA administration. The effects on mammary tumor development 19 weeks after DMBA administration and 18 weeks after rats were returned to the 5% corn oil control diet are summarized as follows. Only adenocarcinomas were reported in the results. Neoplasms of mixed tissue types (adenocarcinoma + fibroadenoma) were considered adenocarcinomas in this analysis. The incidence of mammary neoplasms in rats fed the 20% Palm Oil or 20% corn oil diet did not differ from that observed in rats fed the 5% corn oil diet. Neoplasm incidence curves for the two diets did not differ statistically from that of the 5% corn oil controls. However, a trend toward a higher incidence was observed at 10 to 19 weeks after DMBA administration for rats fed the 20% corn oil diet. The fibroadenoma incidence was low (one in group fed 20% Palm Oil and one in 20% corn oil group). In this study, using diets high in vegetable oil, neither polyunsaturated (corn oil) nor saturated (Palm Oil) fatty acids had an effect on mammary tumorigenesis when fed to rats (Sylvester et al. 1986).

The effect of dietary Palm Oils on mammary carcinogenesis was also evaluated using three groups of 20 female Sprague-Dawley rats (45 days old). Initially, the rats were fed a laboratory chow diet and, at 50 days of age, were dosed intragastrically with DMBA (5 mg in 0.25 ml crude Palm Oil). Dosing was followed by feeding (laboratory chow) for an additional 3 days. The three groups were fed semisynthetic diets containing 20%, by weight, crude Palm Oil (CPO), 20% refined, bleached, deodorized palm oil (RBD PO), and 20% metabisulfite-treated Palm Oil (MCPO), respectively, for 5 months. RBD PO is a product of the refining process of CPO; 67% of the tocopherols are retained and all of the carotenes are lost during this process. The metabisulfite treatment of CPO results in the retention of 56% of the carotenes and the loss of approximately 32% of the tocopherols and 67% of the tocotrienols present in CPO. Two other groups of 20 rats were fed 20% corn oil (CO) and 20% soybean oil (SBO), respectively, according to the same procedure. The results for these two groups were compared with those for Palm Oil–fed rats. The two groups of rats fed 20% CO and 20% SBO, respectively, appeared to develop mammary tumors earlier than the three Palm Oil–fed groups. However, differences in mean latency periods were not statistically significant. The final incidences of palpable mammary tumors were 85%, 90%, 65%, 70%, and 70% for CO, SBO, CPO, RBD PO and MCPO groups, respectively. Mammary tumor incidences (palpable and nonpalpable) for Palm Oil–fed rats were as follows: 20% RBD PO diet (27 palpable, 3 nonpalpable); 20% CPO (23 palpable, 2 nonpalpable); and 20% MCPO (23 palpable, 5 nonpalpable). The two groups fed 20% CO and 20% SBO in the diet, respectively, had significantly more mammary tumors than the three groups that were fed Palm Oil diets. Additionally, the number of mammary tumors per rat in CO (4.18 tumors) and SBO (3.17 tumors)-fed rats was significantly greater than that for the RBD PO (2.14 tumors), CPO (1.92 tumors), and the MCPO (2.0 tumors) groups. In all dietary groups, the mammary neoplasms were mostly adenocarcinomas. The results of this study indicate that dietary CO and SBO enhanced mammary carcinogenesis, induced by DMBA, in female rats much more than semisynthetic diets containing 20%, by weight, CPO, 20% RBD PO, and 20% MCPO (Sundram et al. 1989).

In more recent publications in which mammary neoplasms were induced in female Sprague-Dawley rats by intragastric administration of DMBA, refined Palm Oil stripped of its vitamin E tocopherols and tocotrienols enhanced tumorigenesis, compared to Palm Oil that contained vitamin E (Nesaretnam et al. 1992a, 1992b). These results suggest that the inhibitory effect on tumorigenesis induced by Palm Oil in the above studies can be attributed to the vitamin E content.

Palm Kernel Oil

The effect of Palm Kernel Oil on DMBA-induced mammary tumorigenesis was evaluated using groups of female Sprague-Dawley rats (weights and number per group not stated). The rats were given a single oral dose of DMBA (5 mg/0.5 ml corn oil) at 50 days of age and, after 2 days, were fed high-fat diets for 15 weeks. The fats administered to the high fat (20%) dietary groups were as follows: group 1, corn oil; group 2, cocoa butter; group 3, peanut oil; group 4, Palm Kernel Oil; and group 5, butterfat. An additional group received a corn oil–cocoa butter combination (also a high-fat [20%] diet). At study termination, the total number of tumors (palpable and nonpalpable) in Palm Kernel Oil–fed rats was 57, and was greatest in corn oil–fed rats (78 tumors) and lowest in cocoa butter–fed rats (45 tumors). Tumor latency (time to development of the first palpable tumor) was similar in all dietary groups. No differences were observed in palpable tumors per tumor-bearing rat, total tumors per tumor-bearing rat, tumor weight, and tumor burden among the dietary groups. Palpable tumors and total tumors per treatment group were positively correlated with percent dietary polyunsaturated fat and polyunsaturated-to-saturated fatty acid (P/S) ratio. The researchers stated that the results suggest that the tumor-promoting effect of a high-fat diet can be minimized with a saturated fat source such as cocoa butter (Apgar and Shively 1990).

CLINICAL ASSESSMENT OF SAFETY

Hematological Effects

Palm Oil

The effects of dietary Palm Oil on certain aspects of the cardiovascular risk profile were investigated using 40 male volunteers (ages not stated). The subjects were given all major fat-containing food items either from commercial sources (control, containing hardly any Palm Oil) or as modified products, containing as much Palm Oil as possible (approximately 70% of total dietary fat). The study protocol was described as a double

blind cross-over design (two periods of 6 weeks, a run-in period of 3 weeks, and an intermission of 3 weeks). Blood was collected regularly for the measurement of lipid content. Palm Oil induced a significant increase in high-density lipoproteins (HDL_2) cholesterol, while significantly reducing low-density lipoprotein (LDL) and intermediate-density lipoprotein (IDL) triglycerides. Trends for reduced cholesterol content in LDL and IDL, for increased cholesterol content in HDL_1 and HDL_3, and for lower triglyceride amounts in very-low-density lipoprotein (VLDL) and HDL_5 were classified as nonsignificant (Hornstra 1989).

Ocular Irritation and Sensitization

Hydrogenated Palm Glycerides and Hydrogenated Palm Kernel Glycerides

The ocular irritation potential of eyeliner products containing 18.6% Hydrogenated Palm Glycerides and 18.6% Hydrogenated Palm Kernel Glycerides was evaluated using 60 female subjects (16–65 years old) who were daily users of eyeliner. In a pretest, a semiocclusive patch containing the eyeliner (blue or brown shade) was applied to the arm of each subject for 24 hours. None of the subjects had a reaction at the test site. This evaluation was conducted to rule out empaneling any subject who had an individual idiosyncratic reaction to the test eyeliner. Subjects were instructed to apply the eyeliner (choice of black or brown shade made by each subject) at least twice per day for 28 days. The week of study initiation was characterized as a severe seasonal allergy week, as evidenced by seven subjects with moderate ocular irritation on day 1. Thus, seven new subjects were empaneled on this day and applied the product for 27 days, rather than 28 days. In addition to the seven subjects who were replaced, one subject also withdrew from the study for personal reasons that were unrelated to product administration. Ophthalmological examinations were conducted at baseline and on days 7, 14, and 21 of the study. Reactions were scored according to the following scales: lid swelling, 0 (within normal limits) to 3 (severe); palpebral conjunctival irritation, 0 (within normal limits) to 3 (cherry to deep red); and bulbar conjunctival irritation, 0 (no reaction) to 3 (intense red vessels, dilated). Seventeen of the 59 subjects who completed the study had mild swelling (transient or persistent irritation) of the eyelids. Forty-six and 40 subjects had mild irritation (transient or persistent) of the palpebral and bulbar conjunctiva, respectively. It was concluded that the mild ocular irritation observed is commensurate with normal individual and/or seasonal phenomena, and that the eyeliners did not produce significant ocular irritation or sensitization under normal use conditions (Harrison Research Laboratories, Inc. 1994).

The irritation potential of an eyeliner pencil containing 17.3% Hydrogenated Palm Glycerides and 17.3% Hydrogenated Palm Kernel Glycerides was evaluated in a 28-day controlled use test using 50 healthy female subjects (14–60 years old; majority under 40 years). Forty-eight subjects completed the study. The subjects were instructed to apply the eyeliner pencil twice daily for 28 consecutive days. Initially, a baseline examination (day 0) of each subject was conducted by a certified dermatologist and ophthalmologist. Weekly examinations were conducted by a trained technician, and final examinations were made by the dermatologist and ophthalmologist. Reactions were scored according to the following scale: 0 (negative reaction) to 3+ (extreme positive reaction; bullous reaction). One subject had transient redness of the lid margins, which was considered unrelated to product application. It was concluded that under the conditions of this test, the eyeliner pencil did not induce irritation in any of the subjects tested (Biosearch Inc. 1988, 1989).

Skin Irritation and Sensitization

Palm Oil

The skin sensitization potential of 15% Palm Oil in petrolatum was evaluated in a modified Draize assay using 120 subjects. One hundred ten subjects (88 females, 22 males; 20–76 years old) completed the study; there were no adverse reactions in any of the 10 subjects who withdrew. During induction, the test substance was applied occlusively to skin sites on the scapular region of the back using a Finn Chamber. Each chamber contained 0.025 g of the test substance per application. Applications were made on Mondays, Wednesdays, and Fridays for 3 consecutive weeks, and on Monday of the fourth week. Thus, 10 induction applications were made to each subject. Induction reactions were scored at 48 hours post application (Monday and Wednesday applications) and at 72 hours post application (Friday applications) according to the following scale: 0 (no reaction) to 4 (erythema, edema, and bullae). At the end of the 12-day nontreatment period, initiated after scoring of 10th induction site, an occlusive challenge patch was applied to a new site in the scapular region. Challenge patches remained in place for 48 hours; reactions were scored at 48 and 96 hours post application. Reactions (1+) were observed in three subjects during induction, and no reactions were observed during the challenge phase. It was concluded that Palm Oil (15% in petrolatum) did not induce sensitization in either of the 110 subjects tested (International Research Services, Inc. 1997).

The skin sensitization potential of a body lotion containing 2.0% Palm Oil was evaluated in an repeat-insult patch test (RIPT) using 99 subjects (both sexes; age range: 18–60+ years). Of the original 109 participants, 9 withdrew from the study for reasons unrelated to testing and 1 withdrew due to lost challenge patches. The test substance (0.3 ml) was applied to an occlusive patch, and nine induction applications (one per day) were made to the back of each subject on Mondays, Wednesdays, and Fridays during the 22-day induction period. The patches were removed by the subjects at 24 hours post application. Induction reactions were scored at 48 or 72 hours post application according to the following scale: 0 (no evidence of any reaction) to 5 (vesicular/bullous reaction). Induction was followed by a 2-week nontreatment period. At the conclusion of the nontreatment period, two challenge patches were applied simultaneously to each subject for 48 hours. The two patches were applied to a new site and the induction site, respectively. Reactions were

scored after patch removal. None of the subjects had contact sensitization reactions to the body lotion containing 2.0% Palm Oil (Hill Top Research, Inc. 1982).

The skin sensitization potential of a tanning butter containing 1.0% Palm Oil was evaluated according to a modification of the procedure in the preceding paragraph using 94 subjects (both sexes; age range: 21–70 years). Of the original 103 participants, 9 withdrew for reasons unrelated to testing. Each patch applied contained 0.10 ml of the test substance. Induction and challenge reactions were scored according to the following scale: 0 (no evidence of any effect) to 4 (severe—deep red erythema with vesiculation or weeping with or without edema). A single challenge patch was applied to a new site on each subject. No erythematous reactions were noted during induction or challenge phases. The investigators concluded that the tanning butter containing 1.0% Palm Oil did not have any potential for inducing allergic sensitization (CTFA 1979).

In another study, the skin irritation and sensitization potential of a moisturizer containing 1.5% Palm Oil was evaluated in a RIPT using 103 subjects (21 males, 92 females; age range: 16–72 years). Ten of the original 113 subjects withdrew from the study for personal reasons that were unrelated to testing. An occlusive patch containing the test material was applied to an area of the back between the scapulae and waist (adjacent to spinal midline) of each subject. Patches were removed by the subjects at 24 hours post application. Tuesday and Thursday patch removals were followed by 24 hours nontreatment periods, and patch removals on Saturday were followed by 48 hours nontreatment periods. This test procedure was repeated for a total of nine patch applications. Reactions were scored by a trained examiner prior to application of the next patch throughout the RIPT. The following grading scale was used: 0 (no evidence of any effect) to 4 (deep red erythema with vesiculation or weeping). At 13 to 21 days after application of the final induction patch, a challenge patch was applied to a new test site on each subject. Reactions were scored at 24 and 48 hours post application. The subjects were instructed to report any delayed reactions that were observed after the 48-hour reading. Reactions classified as minimal, faint, uniform or spotty erythema (±reactions) were observed in seven subjects during induction. An eighth subject had ± reactions and reactions with a score of 1 (pink uniform erythema covering most of the contact site) during induction. The only challenge reaction (±reaction at 48 hours) was observed in one of the eight subjects with induction reactions. Neither of the reactions was considered irritant or allergic in nature, and it was concluded that the moisturizer containing 1.5% Palm Oil did not induce significant irritation or allergic contact dermatitis (Food and Drug Human Clinical Labs, Inc. 1983).

Palm Oil Fatty Acid and Palm Oil Esters

The skin sensitization potential of the Isopropyl Ester of Hardened Palm Oil Fatty Acid (undiluted) was evaluated in an RIPT using 47 subjects (males and females; ages not stated). Eight of the original 55 subjects withdrew from the study for various reasons. None of the eight subjects had sensitization reactions; however, mild erythema was observed in one subject (induction). During induction, an occlusive patch containing the test substance (0.5 ml) was applied to the dorsal surface of the upper arm of each subject for a total of nine 24-hour induction applications (Mondays, Wednesdays, and Fridays). The first induction patch was applied on January 23, 1978. Reactions were scored 48 or 72 hours (after a weekend only) post application according to the following scale: 0 (no visible reaction) to 5 (bullous reaction). During the final week of the study (first week of March) two challenge patches were applied for 24 hours to original and alternate sites, respectively, on the arm of each subject. Reactions were scored 48 and 96 hours post application. Of the 47 subjects who completed the study, reactions were observed in 20 subjects during induction; reactions classified as mild erythema (score = 1) predominated. Mild erythema was also observed in 2 of the 20 subjects during the challenge phase. Another subject (no reactions during induction) also had mild erythema during the challenge phase. The Isopropyl Ester of Hardened Palm Oil Fatty Acid (undiluted) did not induce sensitization, but was a mild primary irritant (CTFA 1978c).

In another test, the skin sensitization potential of the Methyl Ester of Unhardened Palm Oil (undiluted) was evaluated in an RIPT using 68 subjects (males and females; ages not stated). Seventeen of the original 85 subjects withdrew from the study for various reasons. None of the 17 subjects had sensitization reactions; however, 7 had mild erythema during induction. The test was conducted according to the protocol stated in the preceding paragraph. The date of application of the first induction patch (January 19, 1978) was different from the one indicated in the preceding experiment; challenge patches were applied during the final week of the study (first week of March). Of the 68 subjects who completed the study, 38 had reactions during induction; reactions classified as mild erythema (score = 1) predominated. Mild erythema was also observed in 11 of the 38 during the challenge phase; 1 of the 11 also had moderate erythema (score = 2) during induction and challenge. Four other subjects (no reactions during induction) also had mild erythema during the challenge phase. The Methyl Ester of Unhardened Palm Oil (undiluted) induced weak sensitization reactions in one subject and, overall, was a very mild primary irritant (CTFA 1978c).

Palm Oil Sucrose Glyceride

The skin sensitization potential of a foundation formulation containing Palm Oil in the form of Palm Oil Sucrose Glyceride (total amount of Palm Oil = 4%) was evaluated in an RIPT using 102 subjects (males and females; age range: 18–65+ years). Five of the original 107 subjects (21 males, 86 females) withdrew from the study for various reasons, none of which were related to test substance application. During induction, an occlusive patch containing the undiluted formulation (0.3 ml) was applied to the left upper arm of each subject for 24 hours. patch applications were made on Mondays, Wednesdays, and Fridays

for 3 consecutive weeks. The first induction patch was applied on May 24, 1993. Reactions were scored following the removal of each induction patch according to the following scale: 0 (no visible erythema) to 3 (severe erythema, very intense redness). The challenge phase was initiated on May 24, 1993. Two challenge patches were applied to the right and left upper arm, respectively, of each subject for 24 hours. Reactions were scored at 48 and 96 hours post application. Of the 102 subjects who completed the study, 33 had mild erythema during induction, and no reactions during the challenge phase. One subject (no induction reactions) had mild erythema during the challenge phase. The undiluted foundation formulation containing 4% Palm Oil induced a low level of irritation throughout the study; however, there was no evidence of skin sensitization (I S Consultancy Limited 1993).

Palm Kernel Oil

The skin irritation potential of bar soap flakes containing 21.35% Palm Kernel Oil and 44.2% palm oil/stearin fatty acid was evaluated using 12 subjects (10 females, 2 males; age range: 18–65 years). The following concentrations of the bar soap were tested simultaneously on each subject during each of the three tests in the series: 0.10%, 0.5%, 1.0%, 2.5%, 5.0%, and 10.0% in distilled water (effective concentrations of 0.002%, 0.106%, 0.213%, 0.531%, 1.06%, and 2.13%, Palm Kernel Oil, respectively). Distilled water served as the negative control. Three semiocclusive patches, each containing 0.3 ml of the test material, were applied to the lateral aspect of the upper arms of each subject and remained for 24 hours (total of six patch applications with respective concentrations). Within 24 or 48 hours (following a weekend only) after patch removal, sites were rinsed with warm water, and reactions were scored according to the following scale: 0–0.49 (very mild) to 3.0–4.0 (severely irritating). The scores reported represented average skin irritation scores for the group tested. Second and third patch applications (same procedure as first) in the test series were made immediately after reactions from the preceding series had been scored. None of the subjects had cutaneous reactions to either of the six test concentrations or to distilled water (Hill Top Research, Inc. 1995a).

The skin sensitization potential of bar soap flakes containing 21.25% Palm Kernel Oil and 44.2% palm oil/stearin fatty acid was evaluated in another RIPT using 119 subjects (87 females, 32 males). The age range of the subjects tested was not stated. However, it was stated that no more than 20% of the subjects was over age 65. Six of the original 125 subjects withdrew from the study for various reasons. During induction, three semiocclusive patches, each containing 0.3 ml of the test material, were applied to the lateral aspect of the upper arms of each subject and remained for 24 hours (total of six patch applications with respective concentrations). The following concentrations of the bar soap were tested simultaneously on each subject 0.10%, 0.5%, 1.0%, 2.5%, 5.0%, and 10.0% in distilled water (effective concentrations of 0.002%, 0.106%, 0.213%, 0.531%, 1.06%, and 2.13%, Palm Kernel Oil, respectively). Distilled water served as the control. Applications were made on Mondays, Wednesdays, and Fridays during the 3-week induction period (9 days of induction). Reactions were scored 48 or 72 hours (after a weekend only) after patch application according to the following scale: 0 (no visible erythema) to 3 (severe erythema, very intense redness). Twelve to 20 days after application of the last induction patch, 24-hour challenge patches were applied to the original sites and similar (alternate) sites on the opposite side of the body. Reactions were scored at 48, 72, and/or 96 hours after application. Of the 119 subjects who completed the test, 2 subjects had reactions (mild erythema) during induction only and 1 subject had reactions (mild erythema) during induction and challenge. No evidence was observed that the bar soap flakes induced delayed contact hypersensitivity at any of the concentrations tested (Hill Top Research, Inc. 1995b).

Ethoxylated Palm Kernel Oil

The skin sensitization potential of a bath gel containing 1% ethoxylated Palm Kernel Oil was evaluated in an RIPT using 106 subjects (68 females, 38 males; ages not stated). Of the 141 subjects who began the study, 35 withdrew for various reasons. An occlusive patch containing the test substance (0.2 ml) was applied to the upper arm of each subject during the 3-week induction period (total of nine induction applications). Reactions were scored according to the following scale at 48 hours post application (Mondays and Wednesdays) and at 72 hours post application (Fridays): 0 (no visible erythema) to 3 (severe erythema). At 14 to 20 days after the last induction application, two 24-hour challenge patches were applied to the original site and a similar (alternate) site on the opposite side of the body, respectively. Reactions were scored at 48 and 96 hours or 48 and 72 hours post application. Only one of the 106 subjects who completed the study had reactions during the challenge phase (mild erythema); mild erythema and moderate erythema were observed during induction. Mild erythema was also observed in one other subject who completed the study. Of the 35 subjects who withdrew from the study, only 2 had induction reactions (mild erythema); challenge reactions were not observed in this group. The investigators concluded that the bath gel containing 1% ethoxylated Palm Kernel Oil was essentially nonirritating, and no clinical evidence of delayed contact hypersensitization was identifiable (Hill Top Research, Inc. 1993).

Photoallergenicity

Palm Oil Sucrose Glyceride

The photoallergenicity of a foundation formulation containing Palm Oil in the form of Palm Oil Sucrose Glyceride (total amount of Palm Oil = 4%) was evaluated using 25 subjects (age range 32–64 years). Three of the original subjects in the study withdrew for reasons unrelated to test substance application. During the 3-week induction period, occlusive patches containing 0.2 ml of the undiluted formulation were applied to duplicate tests sites (irradiated and nonirradiated sites, respectively) on the back of each subject. The patches were air dried

prior to application and remained in place for 24 hours. Patch applications were made twice per week to duplicate test sites for a total of six induction applications. After each 24-hour application period, one of the two sites per subject was irradiated with twice the minimum effect dose (MED) using the full xenon lamp spectrum. A xenon arc solar simulator (150 W) with a continuous emission spectrum in the UVA-UVB range (290–400 nm) was used for UV exposure. A UVB absorbing filter that eliminated erythemogenic wavelengths (below 320 nm) was used for UVA dosing and removed for UVA/UVB dosing. Reactions (all test sites) were scored at 24 hours after test substance application and 48 or 72 hours after UV irradiation according to the following scales: − (no reaction) to +++ (marked/severe erythema) and * (minimal, doubtful edema) to *** (definite edema with erosion/vesiculation). After an 18-day nontreatment period, challenge patches were applied to new test sites. At 24 hours post application, one site was irradiated with 6 J/cm^2 of UVA light (320–400 nm) using a filtered light source and 1/2 MED of UVB light (290–320 nm). Additionally, an irradiated control site was exposed to 6 J/cm^2 of UVA light (320–400 nm) using a filtered light source and 1/2 MED of UVB light (290–320 nm). Challenge reactions were scored at the time of patch removal and at 24, 48, and 72 hours post irradiation. The incidence of challenge reactions was as follows: three subjects (irradiated sites), six subjects (nonirradiated sites), and zero subjects (irradiated control sites). With the exception of one subject with barely perceptible erythema and mild, but definite, erythema at nonirradiated sites, all of the challenge reactions were classified as barely perceptible erythema. Additionally, the three subjects with reactions at irradiated sites were among the six with reactions at nonirradiated sites. No evidence was found of photosensitivity to the foundation formulation containing 4.0% Palm Oil (TKL Research, Inc. 1993).

SUMMARY

Palm (Elaeis Guineenis) Oil is the natural oil that is obtained from the mesocarp of the *Elaeis guineenis* palm tree, and Palm (Elaeis Guineenis) Kernel Oil is defined as the oil that is obtained from the seeds of *Elaeis guineensis*. Both ingredients are used as skin-conditioning agents—occlusive in cosmetics. Palm Oil is also used as a solvent in cosmetic products.

Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil are defined as end products of the controlled hydrogenation of Palm Oil and Palm Kernel Oil, respectively. These ingredients are used as skin-conditioning agents—occlusive and viscosity-increasing agents—aqueous in cosmetic products.

According to 1997 FDA frequency of use data, collectively, the four Palm Oils have been used in as many as 89 cosmetic products. Data received from the cosmetics industry in 1995 indicated that Palm Oil has been used in cosmetics at concentrations up to 2.0%.

In a feeding study evaluating the absorption of Palm Kernel Oil in rats, the percentages of lauric acid and myristic acid in the thoracic duct lymph increased after feeding with Palm Kernel Oil; other fatty acids were reduced. Generally, the fatty acids of the lymph reflected the composition of the dietary fat.

Undiluted Palm Oil was classified as slightly toxic in rats, following oral administration. The acute oral LD_{50} was not achieved at a dose of 5.0 g/kg.

In short-term toxicity studies, crude Palm Oil did not induce any adverse hematological effects when administered (in diet) to groups of albino rats for 28 days, and Hydrogenated Palm Kernel Oil had no effect on hepatic or renal function when administred parenterally to rabbits daily for 5 weeks. The subchronic oral administration of 15% untreated Palm Oil and 15% heated Palm Oil (in diet) to groups of SPF Sprague-Dawley rats, and crude Palm Oil (in diet) to groups of weanling albino rats, was also without adverse effect. Hematological as well as hepatic and renal evaluations were included. Chronic oral toxicity data were not available on Palm Oil. However, a 15% heated Palm Oil liquid fraction, derived from Palm Oil by transesterification, induced hepatic hypertrophy when fed to rats for 1 year. It was suggested that the hepatic hypertrophy could have been due to metabolic hyperactivity. After New Zealand white rabbits were fed 14% Palm Kernel Oil in the diet for 9 months, serum cholesterol was elevated and absolute hepatic cholesterol and liver size were greatly increased when compared to rabbits fed corn oil.

Undiluted Palm Oil and hand creams containing 2.0% Palm Oil induced minimal ocular irritation in rabbits. Fractionated Hydrogenated Palm Kernel Oil also induced mild ocular irritation in rabbits. Moderate ocular irritation was observed in rabbits tested with a facial lotion containing 1.5% Palm Oil.

In a single-insult occlusive patch test, undiluted Palm Oil was practically nonirritating to the skin of rabbits. Palm Oil (5%) was nonallergenic in the guinea pig maximization test.

A facial lotion containing 1.5% Palm Oil was not phototoxic in an in vitro phototoxicity yeast assay.

Commercial grade Palm Oil induced anomalies in 30% of the 152 live fetuses delivered by female albino rats. It was noted that the defects observed resembled those caused by hypervitaminosis A, and could be attributed to the high carotene content of Palm Oil.

When diets containing heated, refined Palm Oil were fed to groups of male and female Wistar rats (total of four dietary groups) prior to mating, the number of females that bore 10 or more young was significantly less in only one of the groups. This was the only significant finding with respect to litter size, and was not believed to be due to toxicity of the diet administered. No significant differences were found with respect to the incidence of organ damage. Comparisons were made between each of the four dietary groups and the control group (refined Palm Oil, not heated).

Crude Palm Oil was not a reproductive toxicant in a study in which male and female Wistar/NIN inbred weanling rats were fed a diet containing this ingredient (10%) prior to mating. Mean litter sizes were comparable between test and control groups. No significant changes were found in liver or kidney weight in adult animals.

Neither untreated Palm Oil (15%) nor 15% heated Palm Oil in the diet induced anomalies with respect to fertility and in utero growth when fed to male and female Sprague-Dawley SPF rats prior to mating.

In a study investigating the effects of Palm Oil on sexual maturation and endocrine function, vaginal opening was observed significantly earlier (compared to 5% corn oil control) in weanling rats fed 20% Palm Oil in the diet. No significant differences were observed in endocrine function.

In the second generation resulting from the mating of adult Mongolian gerbils fed a diet containing 8.75% *w/w* Palm Kernel Oil, no statistically significant differences were found with respect to the following: frequency of litters, mean litter size, total of newborns, and suckling death. Animals receiving a basal diet served as the control.

In Ames tests (plate incorporation and preincubation assays), neither refined nor unrefined Palm Oil was mutagenic to the following *S. typhimurium* strains: TA1537, TA1538, TA97, TA98, TA100, and TA102. In the liquid incubation assay, both test substances induced reproducible weak mutagenicity only in strain TA1537.

Additional test results indicated that Palm Oil (2 μl/plate) was mutagenic to the following *S. typhimurium* strains: TA98, TA100, TA1535, TA1537, and TA1538. Mutagenicity was not observed at a dose of 1 μl/plate.

Neither Palm Oil supernatant, Palm Oil sediment, nor a mixture of the two induced a statistically significant difference in the frequency of chromosomal aberrations of the mitotic index in bone marrow samples from the three test groups of Balb/C female mice dosed orally (4.5 g/kg) for 5 consecutive days. Corn Oil served as the negative control.

The effect of exercise on mammary tumor induction (exercise accelerated the appearance of tumors) in Sprague-Dawley rats was attenuated by feeding a high-fat diet formulated with a combination of Palm Oil and corn oil. Additionally, other study results indicated that rates of cellular proliferation were lower in the mammary glands of Sprague-Dawley rats fed chow, 5% corn oil, or 20% Palm Oil than in those fed the other diets.

Following the oral administration of DMBA, no effects on mammary tumorigenesis were observed in Sprague-Dawley (Crl:CD(SD)BR) rats fed diets containing 20% corn oil or 20% Palm Oil. However, in another study, 20% dietary corn oil and 20% dietary soybean oil enhanced mammary carcinogenesis (induced by DMBA) in female Sprague-Dawley rats much more than diets containing 20% crude Palm Oil or 20% refined Palm Oil.

The results of other studies have suggested that the inhibitory effect of Palm Oil on tumorigenesis noted in some of the preceding studies can be attributed to its vitamin E content.

In a study evaluating the effect of 20% Palm Kernel Oil in the diet on DMBA-induced tumorigenesis in female Sprague-Dawley rats, the total number of neoplasms was 57, compared to 78 for corn oil–fed rats and 45 for cocoa butter–fed rats.

A moisturizer containing 1.5% Palm Oil did not induce significant irritation or allergic contact dermatitis in 103 subjects tested in a RIPT. Contact sensitization also was not observed in two RIPTs in which 99 subjects were tested with a body lotion containing 2.0% Palm Oil and 94 subjects were tested with a tanning butter containing 1.0% Palm Oil. At the highest test concentration of 15% in petrolatum, Palm Oil did not induce sensitization in any of the 110 subjects tested in an RIPT.

The Isopropyl Ester of Hardened Palm Oil, the Methyl Ester of Unhardened Palm Oil Fatty Acid, and Palm Oil Sucrose Glyceride were also tested in clinical studies. The Isopropyl Ester of Hardened Palm Oil Fatty Acid (undiluted) did not induce sensitization (3 subjects with mild erythema at challenge), but was classified as a mild irritant in an RIPT involving 47 subjects. Twenty of the 47 had induction reactions, most of which were classified as mild erythema. In a similar test involving 68 subjects, the Methyl Ester of Unhardened Palm Oil (undiluted) was classified as a very mild irritant, and induced weak sensitization in one of the subjects (moderate erythema at challenge). Induction reactions were observed in 38 subjects.

A foundation formulation containing Palm Oil Sucrose Glyceride (total amount of Palm Oil = 4.0%) induced a low level of irritation, but no skin sensitization, when tested on 102 subjects in an RIPT. No evidence of photoallergenicity to this formulation was observed in any of the 25 subjects tested in another study.

None of the twelve subjects patch-tested with bar soap flakes containing 21.35% Palm Kernel Oil (diluted with distilled water to concentrations up to 2.13%) had irritation reactions. In another study involving the same test concentrations of the diluted product, no evidence of delayed contact hypersensitivity was observed in either of the 119 subjects evaluated in an RIPT.

Hydrogenated Palm Glycerides, Hydrogenated Palm Kernel Glycerides, and Ethoxylated Palm Kernel Oil were also evaluated in clinical studies. Two eyeliner products, each containing 18.6% Hydrogenated Palm Glycerides and 18.6% Hydrogenated Palm Kernel Glycerides, did not elicit significant ocular irritation or sensitization in 59 female subjects who participated in a 28-day use test.

In a similar 28-day use test, an eyeliner pencil containing 17.3% Hydrogenated Palm Glycerides and 17.3% Hydrogenated Palm Kernel Glycerides did not induce irritation in the 48 subjects tested.

In an RIPT involving 106 subjects, a bath gel containing 1.0% Ethoxylated Palm Kernel Oil was classified as essentially nonirritating. No clinically identifiable evidence of delayed contact hypersensitization was found.

DISCUSSION

Data on Palm Oil and Palm Kernel Oil, received from the cosmetics industry in response to the Expert Panel's request for skin irritation, sensitization, photosensitization, and phototoxicity data on Palm Oil, demonstrate that these end points should

not be of concern. Data on Hydrogenated Palm Glycerides and Hydrogenated Palm Kernel Glycerides, showing little, if any, toxicity, provide a sufficient basis to establish the safety of Hydrogenated Palm Oil and Hydrogenated Palm Kernel Oil.

The Expert Panel did note that Palm Oil was teratogenic in albino rats dosed (up to 3 ml daily) on days 5 through 15 of gestation. Although the investigators in this study proposed that this finding could have been due to the beta-carotene content (which is generally lost during the refining process) of Palm Oil, the Expert Panel suggested that the results for this study also could have been related to the presence of one or more contaminants. The Expert Panel noted that benzo(a)pyrene, PCB, and organochlorine pesticide residues have been detected in some grades of Palm Oil. Regardless of the cause, the Panel determined that the teratogenicity of Palm Oil should not be a concern relative to cosmetic use, because the daily use of cosmetic products would not be expected to result in the high levels of exposure noted in the rat teratogenicity study. Because of the potential for contamination, the Expert Panel strongly recommends that concentrations of polycyclic aromatic hydrocarbon contaminants be kept at a level that does not produce adverse effects.

CONCLUSION

On the basis of the animal and clinical data included in this report, the CIR Expert Panel concludes that Palm (Elaeis Guineensis) Oil, Palm (Elaeis Guineensis) Kernel Oil, Hydrogenated Palm Oil, and Hydrogenated Palm Kernel Oil are safe as used in cosmetic formulations.

REFERENCES

Allen, A., G. H. Padley, and G. R. Whalley. 1969. The fatty acid composition of some soapmaking fats and oils. Part 2. Coconut and palm kernel oils. *Soap Perfum. Cosmet.* 42:372–378.

Ames, B. N., J. McCann, and E. Yamasaki. 1975. Methods for detecting carcinogens and mutagens with the *Salmonella*/mammalian-microsome mutagenicity test. *Mutat. Res.* 31:347–364.

Apgar, J. L., and C. A. Shively. 1990. Comparative effects of cocoa butter and other dietary fats on mammary tumorigenesis in rats. 74th Annual Meeting of the Federation of American Societies for Experimental Biology, Part I, Washington, DC, USA. *FASEB J.* 4:A666.

Arof, A. K., A. Daud, and S. Radhakrishna. 1991. Spectroscopic studies of thin films of palm oil. *Thin Solid Films* 202:373–377.

Berger, K. G., and T. Y. Kun. 1987. General characteristics of palm oil and its use in frying. Malaysian Symposium on Palm Oil in the U.S.A. Symposium's Papers, 259–279. Ministry of Primary Industries, Malaysia: Palm Oil Research Institute of Malaysia.

Biosearch, Inc. 1988. Cosmetic product usage study. Eye liner pencil (2738-12) containing 17.3% hydrogenated palm glycerides and 17.3% hydrogenated palm kernel glycerides, and nail polish materials (2626-35 and 2626-36). Unpublished data submitted by CTFA. (15 pages).[2]

Biosearch, Inc. 1989. Summary. Controlled use test—eyeliner pencil 2738-12. Eye liner pencil containing 17.3% hydrogenated palm glycerides and 17.3% hydrogenated palm kernel glycerides. Unpublished data submitted by CTFA. (1 page.)[2]

Budavari, S., M. J. O'Neil, A. Smith, and P. E. Heckelman, eds. 1989. *The Merck Index*, 11th ed, 1107. Rahway, NJ: Merck & Co.

Chandrasekharan, N. 1992. An appraisal of the nutritional and health aspects of palm oil. *Med. J. Malaysia* 47:93–97.

Changbumrung, S., T. Buavatana, and P. Migasena. 1980. α-Tocopherol in vegetable oils. *Int. J. Vitam. Nutr. Res.* 50:242–246.

Chemline. 1996. Chemical synonyms. *Chemline database*. Bethesda, MD National Library of Medicine.

Chen, I. S., S. Subramaniam, G. V. Vahouny, M. M. Cassidy, I. Ikeda, and D. Kritchevsky. 1989. A comparison of the digestion and absorption of cocoa butter and palm kernel oil and their effects on cholesterol absorption in rats. *J. Nutr.* 119:1569–1573.

Clegg, A. J. 1973. Composition and related nutritional and organoleptic aspects of palm oil. *J. Am. Oil Chem. Soc.* 50:321–324.

Cohen, D., S. Yannai, and S. Mokady. 1983. Toxicological evaluation of a liquid fraction derived from palm oil. *Arch. Toxicol. Suppl.* 6:182–185.

Coquet, B., D. Guyot, X. Fouillet, and J. L. Rounaud. 1977. Study of cooking oils. II. Toxicological and nutritional study in rats of peanut, palm, soybean, and sunflower oils [English translation]. *Fr. Rev. Fats* 24:483–488.

Cornelius, J. A. 1977. Palm oil and palm kernel oil. *Prog. Chem. Fats Other Lipids* 15:5–27.

Cosmetic, Toiletry and Fragrance Association (CTFA). 1978a. Acute oral toxicity, ocular irritation, and primary skin irritation studies on undiluted palm oil. Unpublished data submitted by CTFA. (4 pages.)[2]

CTFA. 1978b. Guinea pig allergy study. The Magnusson-Kligman maximization procedure. Palm oil. Unpublished data submitted by CTFA. (17 pages.)[2]

CTFA. 1978c. Human sensitization tests of two palm oil fatty acids. Isopropyl ester of hardened palm oil fatty acid (7801-4) and methyl ester of unhardened palm oil. Unpublished data submitted by CTFA (22 pages.)[2]

CTFA. 1979. Allergic contact sensitization test. (14A) Tanning butter 14077-02 containing 1.0% palm oil. Unpublished data submitted by CTFA. (8 pages.)[2]

CTFA. 1981. Eye irritation studies on two hand creams containing 2.0% palm oil. Unpublished data submitted by CTFA. (2 pages.)[2]

CTFA. 1983. Eye irritation study on a facial lotion containing 1.5% Palm Oil. Unpublished data submitted by CTFA. (1 pages.)[2]

CTFA. 1986. Phototoxicity yeast assay. Facial lotion containing 1.5% palm oil. Unpublished data submitted by CTFA. (4 pages.)[2]

CTFA. 1995. Use levels for various ingredients. Data on Palm Oil. Unpublished data submitted by CTFA.[2]

Cottrell, R. C. 1991. Introduction: Nutritional aspects of palm oil. *Am. J. Clin. Nutr.* 53:989S–1009S.

de Witt, G. F., and Y. H. Chong. 1987. The nutritional value of palm oil minor components. Malaysian Symposium on Palm Oil in the U.S.A. Symposium's Papers, 338–355. Ministry of Primary Industries, Malaysia: Palm Oil Research Institute of Malaysia.

European Economic Community (EEC). 1995. EEC Cosmetics Directive 76/768/EEC, as amended, Annexes I through VII. Brussels: EEC.

Food and Drug Administration (FDA). 1984. Direct food substances affirmed as generally recognized as safe; cocoa butter substitute primarily from palm oil. *Fed. Register* 49:22796–22799.

FDA. 1987. Cocoa butter substitute primarily from palm oil. *Fed. Register* 52:47918–47921.

FDA. 1991. Food additives permitted for direct addition to food for human consumption. *Fed. Register* 56:66969–66970.

FDA. 1992. Modification in voluntary filing of cosmetic product ingredient and cosmetic raw material composition statements. *Fed. Register* 57:3128–3130.

FDA. 1997. Frequency of use of cosmetic ingredients. *FDA database*. Washington: FDA.

Food and Drug Human Clinical Labs, Inc. 1983. Final Report. Clinical safety evaluation of moisturizer 27877-12 containing 1.5% palm oil. Unpublished data submitted by CTFA. (8 pages.)[2]

Goh, S. H., S. L. Tong, and P. T. Gee. 1984. Inorganic phosphate in crude palm oil: Quantitiative analysis and correlations with quality parameters. *J. Am. Oil Chem. Soc.* 61:1601–1604.

[2]Available from the Director, Cosmetic Ingredient Review, 1101 17th Street NW, Suite 310, Washington, DC 20036 USA.

Harrison Research Laboratories, Inc. 1994. Final report. HRL Panel 94-4007. Eyeliner use test. Black and brown eye marker pencils containing 18.6% hydrogenated palm glycerides and 18.6% hydrogenated palm kernel glycerides—Test materials 3815-11 (3817-61) and 3815-13 (3817-61). Unpublished data submitted by CTFA. (20 pages.)[2]

Hazardous Substances Databank (HSDB). 1996. *HSDB database*. Bethesda: National Library of Medicine.

Hill Top Research, Inc. 1982. Repeated insult patch test. Body lotion (12D) 23396-08 containing 2.0% palm oil. Report No. 92-6228-76 D. Unpublished data submitted by CTFA. (15 pages.)[2]

Hill Top Research, Inc. 1993. Repeated insult patch test. Bath gel RE-036501 containing 1.0% ethoxylated palm kernel oil. Unpublished data submitted by CTFA. (61 pages.)[2]

Hill Top Research, Inc. 1995a. Primary skin irritation study. Bar soap flakes containing 44.2% palm oil stearin fatty acid and 21.25% of palm kernel oil. Report No. 94-2422-72. Unpublished data submitted by CTFA. (36 pages.)[2]

Hill Top Research, Inc. 1995b. Human repeat insult patch test. Bar soap flakes containing 44.2% palm oil stearin fatty acid and 21.25% of palm kernel oil. Report No. 94-2423-72C. Unpublished data submitted by CTFA. (70 pages.)[2]

Hornstra, G. 1989. The influence of dietary lipids on thrombosis. Lessons from animal studies from human nutrition. *Acta Cardiol.* 44:454–456.

Husain, S., G. S. R. Sastry, and N. F. Raju. 1991. Molecular weight averages as criteria for quality assessment of heated oils and fats. *J. Am. Oil Chem. Soc.* 68:822–826.

International Research Services, Inc. 1997. A study to assess the skin sensitization potential of palm oil test product when applied to the skin of 100 healthy human subjects in a shared panel assay. (Protocol No. 13791096LAN.) Unpublished data submitted by CTFA. (33 pages.)[2]

I S Consultancy Limited. 1993. Human repeated insult patch test. Foundation formulation containing palm oil in the form of palm oil sucrose glyceride (total amount of palm oil = 4%). Report No. 03154. Unpublished data submitted by CTFA. (20 pages.)[2]

Kennedy, M., P. G. Burstyn, and D. R. Husbands. 1978. Fat induced hypertension in rabbits. 2. The effect of feeding diets containing high concentrations of safflower oil and palm oil. *Proc. Nutr. Soc.* 37:98A.

Kensese, S. M., J. I. Teng, and L. L. Smith. 1989. Mutagenic lipid peroxides from edible oils. *Teratog. Carcinog. Mutagen.* 9:133–145.

Khadzhay, Y. I., A. V. Nikolaeva, and V. V. Pavlova. 1975. Hydrogenated palm kernel oil studied as an innocuous suppository base [English translation]. *Farmatsiya (Moscow)* 24:13–15.

Kheirl, M. S. A. 1987. Utilisation of palm oil in food products. Malaysian Symposium on Palm Oil in the U.S.A. Symposium's Papers, Ministry of Primary Industries, Malaysia: Palm Oil Research Institute of Malaysia. 281–322.

Kohiyama, M., H. Kanematsu, and I. Niiya. 1991. Heavy metals, especially nickel, contained in refined and processed edible oils and fats. *Seikatsu Eisei* 35:141–145.

Kritchevsky, D., S. A. Tepper, G. Bises, and D. M. Klurfeld. 1982. Experimental atherosclerosis in rabbits fed cholesterol-free diets. Part 10. Cocoa butter and palm oil. *Atherosclerosis* 41:279–284.

Kurowska, E. M., N. Guthrie, and K. K. Carroll. 1993. Dietary palm oil, mammary fat and mammary cell proliferation (meeting abstract). *Proc. Annu. Meet. Am. Cancer Res.* 34:A3298.

Lang, V. K., J. Henschel, W. Kieckebusch, and V. V. Griem. 1966. Study of toleration of thermally treated palm oils in rats [*English translation*]. *Z. Ernahrungswiss* 7:109–127.

Lewis, R. J., ed. 1993. *Hawley's condensed chemical dictionary*, 7th ed., 868. New York: Van Nostrand Reinhold.

Lian, O. K., L. T. Tie, C. S. Rose, D. D. Prawiranegara, and P. György. 1968. Red palm oil in the prevention of vitamin A deficiency. A trial on preschool children in Indonesia. *Paediatr. Indones.* 8:192–202.

Lin, S. W., and N. W. Lam. 1994. Analysis of lipids in palm oil by on-column capillary gas-liquid chromatography. *J. Chromatogr. Sci.* 32:185–189.

Magnusson, B., and A. M. Kligman. 1969. The identification of contact allergens by animal assay. The guinea pig maximization test. *J. Invest. Dermatol.* 52:268–276.

Manorama, R., N. Chinnasamy, and C. Rukmini. 1993. Multigeneration studies on red palm oil, and on hydrogenated vegetable oil containing mahua oil. *Food Chem. Toxicol.* 31:369–375.

Manorama, R., and C. Rukmini. 1991. Nutritional evaluation of crude palm oil in rats. *Am. J. Clin. Nutr.* 53:1031S–1033S.

Maron, D. M., and B. N. Ames. 1983. Revised methods for the *Salmonella* mutagenicity test. *Mutat. Res.* 113:173–215.

Meijboom, P. W., and G. A. Jongenotter. 1979. A quantitiative determination of tocotrienols and tocopherols in palm oil by TLC-GLC. *J. Am. Oil Chem. Soc.* 56:33–35.

Mitchell, I. G. 1978. Microbial assays for mutagenicity: A modified liquid culture method compared with the agar plate system for precision and sensitivity. *Mutat. Res.* 54:1–16.

National Testing Corporation 1988. Eytex™ Screen Membrane Partition Assay. Lotion containing 1.5% palm oil. Unpublished data submitted by CTFA. (5 pages.)[2]

Nesaretnam, K., H. T. Khor, J. Ganeson, Y. H. Chong, K. Sundram, and A. Gapor. 1992a. The effect of vitamin E tocotrienols from palm oil on chemically induced mammary carcinogenesis in female rats. *Nutr. Res.* 12:63–75.

Nesaretnam, K., H. T. Khor, J. Ganeson, Y. H. Chong, K. Sundram, and A. Gapor. 1992b. The effect of vitamin E tocotrienols from palm oil on chemically induced mammary carcinogenesis in female rats. *Nutr. Res.* 12:879–892.

Ng, S., and H. F. Koh. 1988. Detection of *cis*-vaccenic acid in palmoil by ^{13}C NMR spectroscopy. *Lipids* 23:140–143.

Ng, S., and W. L. Ng. 1983. ^{13}C NMR spectroscopic analysis of the fatty acid composition of palm oil. *J. Am. Oil Chem. Soc.* 60:1266–1268.

Oishi, M., K. Onishi, M. Nishijima, K. Nakagomi, and H. Nakazawa. 1992. Rapid and simple coulometric measurements of peroxide value in edible oils and fats. *J. AOAC Int.* 75:507–510.

Oliveira, S. V., D. M. F. Salvadori, A. C. C. Rios, M. C. Sales, H. T. Godoy, and L. R. Ribeiro. 1994. Absence of genotoxic effects of crude and refined red palm oil on mouse bone marrow cells. *Rev. Bras. Genet.* 17:409–412.

Ong, A. S. H., P. L. Boey, and C. M. Ng. 1982. A spectrophotometric method for determination of solid fat content of palm oil. *J. Am. Oil Chem. Soc.* 59:223–226.

Palm Oil Research Institute of Malaysia. 1987. *Facts about palm oil*, 1–14. Ministry of Primary Industries, Malaysia: Palm Oil Research Institute of Malaysia.

Pocklington, W. D., and A. Dieffenbacher. 1988. Determination of tocopherols and tocotrienols in vegetable oils and fats by high performance liquid chromatography. Results of a collaborative study and the standardized method. *Pure Appl. Chem.* 60:877–892.

Rempe, J. M., and L. G. Santucci, eds. 1997. *CTFA list of Japanese Cosmetic ingredients*, 3rd ed., 74. Washington, DC: CTFA.

Saleh, M. I., M. S. Jab, B. Rahman, and S. Noraslah. 1991. Aqueous extraction of copper and iron from palm oil by ultrasonic cavitation. *Analyst (London)* 116:743–745.

Sato, T., S. Kawano, and M. Iwamoto. 1991. Near-infrared spectral patterns of fatty acid analysis from fats and oils. *J. Am. Oil Chem. Soc.* 68:827–833.

Sax, N. I., ed. 1979. *Dangerous properties of industrial materials*, 5th ed., 884. New York: Van Nostrand Reinhold.

Senten, J. R., J. M. Waumans, and J. M. Clement. 1977. Gas-liquid chromatographic determination of butylated hydroxyanisole and butylated hydroxytoluene in edible oils. *J. Assoc. Off. Anal. Chem.* 60:505–508.

Singh, J. D. 1981. Palm Oil induced congenital anomalies in rats. *Congenital Anom.* 20:139–142.

Sivaswamy, S. N., B. Balachandran, S. Balanehru, and V. M. Sivaramakrishnan. 1991. Mutagenic activity of south Indian food items. *Indian J. Exp. Biol.* 29:730–737.

Sotirhos, N., C. T. Ho, and S. S. Chang. 1986. HPLC analysis of oxidative and polymerized decomposition products in commercial vegetable oils and heated fats. *Fette Seifen Anstrichm.* 88:45–48.

Stijve, T., and C. Hischenhuber. 1987. Simplified determination of benzo(a)pyrene and other polycyclic aromatic hydrocarbons in various food materials by HPLC and TLC. *Dtsch. Lebensm. Rundsch.* 83:276–282.

Sundram, K., H. T. Khor, A. S. H. Ong, and R. Pathmanathan. 1989. Effect of dietary palm oils on mammary carcinogenesis in female rats induced by 7,12-dimethylbenz(α)anthra-cene. *Cancer Res.* 49:1447–1451.

Swoboda, P. A. T. 1983. UV-VIS spectrophotometric assays for palm oil quality. In *Palm Oil Production Technology Eighties. in the Report Proceedings of the International Conference*, 433–445.

Sylvester, P. W., M. Russel, M. M. Ip, and C. Ip. 1986. Comparative effects of different animal and vegetable fats fed before and during carcinogen administration on mammary tumorigenesis, sexual maturation, and endocrine function in rats. *Cancer Res.* 46:757–762.

Tanabe, S., K. Kannan, M. S. Tabucanon, C. Siriwong, Y. Ambe, and R. Tatsukawa. 1991. Organochlorine pesticide and polychlorinated biphenyl residues in foodstuffs from Bangkok, Thailand. *Environ. Pollut.* 72:191–203.

Temmerman, A. M., R. J. Vonk, K. Niezen-Koning, R. Berger, and J. Fernandes. 1988. Long-term and short-term effects of dietary cholesterol and fats in the Mongolian gerbil. *Ann. Nutr. Metab.* 32:177–185.

Thompson, H. J., A. M. Ronan, K. A. Ritacco, and A. R. Tagliaferro. 1989. Effect of type and amount of dietary fat on the enhancement of rat mammary tumorigenesis by exercise. *Cancer Res.* 49:1904–1908.

TKL Research, Inc. 1993. Photoallergy study. Foundation formulation containing palm oil in the form of palm oil sucrose glyceride (total amount of palm oil = 4%). TKL Study No. 937007-2. Unpublished data submitted by CTFA. (48 pages.)[2]

Wenninger, J. A., R. C. Canterbery, and G. N. McEwen, Jr., eds. 2000. International cosmetic ingredient dictionary and handbook, Vol. 1, 8th ed., 508, 654. Washington, DC: CTFA.

Wong, N. L., R. E. Timms, and E. M. Goh. 1988. Colorimetric determination of total tocopherols in palm oil, olein and stearin. *J. Am. Oil Chem. Soc.* 65:258–261.

Yaacob, T. M., and B. Bek-Nielsen. 1987. The future of the Malaysian palm oil industry. Malaysian Symposium on Palm Oil in the U.S.A. Symposium's Papers, 243–279. Ministry of Primary Industries, Malaysia: Palm Oil Research Institute of Malaysia.