International Journal of Toxicology, 27(Suppl. 4):83–106, 2008

ISSN: 1091-5818 print / 1092-874X online
DOI: 10.1080/10915810802550611

Final Report of the Cosmetic Ingredient Review Expert Panel on the Safety Assessment of Polyisobutene and Hydrogenated Polyisobutene as Used in Cosmetics[1]

Polyisobutene and Hydrogenated Polyisobutene are homopolymers of isobutene. These ingredients are produced in a wide range of molecular weights. Polybutene is a chemically related cosmetic ingredient previously determined to be safe as used in cosmetic products. Polyisobutene is used in cosmetic products as a binder, film former, and nonaqueous viscosity-increasing agent. Hydrogenated Polyisobutene functions as a skin-conditioning agent—emollient and nonaqueous viscosity-increasing agent with a wide range of uses in cosmetic formulations. The estimated octanol water partition coefficient for Hydrogenated Polyisobutene and Polybutene is log K_{ow} of 13.27 and the estimated water solubility was 5.6×10^{-3} ng/L for Hydrogenated Polyisobutene and Polybutene. Acute oral toxicity testing demonstrated no effects other than lethargy in one rat study. The oral LD_{50} was >5.0 g/kg in rats. No short-term or subchronic animal toxicity data were available. A 2-year chronic oral toxicity study of Polybutene revealed no gross or microscopic pathological changes, and no changes in body weights or food consumption, hematological results, urology, or tumor formation that could be correlated with Polybutene ingestion, except that in the 20,000 ppm group, three out of six males that died between weeks 17 and 24 exhibited hematuria. In a 2-year chronic oral toxicity study of Polybutene in Beagle dogs, no abnormalities in body weight, food consumption, survival, behavioral patterns, hematology, blood chemistry, urinalysis, liver function, gross and histopathologic examinations, or organ weights and ratios were reported. In a three-generation reproductive study in Charles River albino rats that ingested Polybutene, none of the animals in successive generations differed from controls with regard to weight gain, litter size, the number of stillborn, and the number of viable pups during lactation. The survival, body weights, and reactions of test animals were comparable to those of controls. Neither Polyisobutene nor Hydrogenated Polyisobutene were ocular irritants, nor were they dermal irritants or sensitizers. Polyisobutene was not comedogenic in a rabbit ear study. Polyisobutene did not induce transformation in the Syrian hamster embryo (SHE) cell transformation assay, but did enhance 3-methylcholanthrene–induced transformation of C3H/10T1/2 cells. In a carcinogenicity study in mice, Polyisobutene was not carcinogenic, nor did it promote the carcinogenicity of 7,12-dimethylbenz(α)anthracene. Clinical patch tests uncovered no evidence of dermal irritation and repeat-insult patch tests with a product containing 4% Hydrogenated Polyisobutene or 1.44% Hydrogenated Polyisobutene found no reactions greater than slight erythema. These products also were not phototoxic or photoallergenic. The product containing 4% Hydrogenated Polyisobutene was not an ocular irritant in a clinical test. The Cosmetic Ingredient Review (CIR) Expert Panel recognized that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicate a pattern of use, which was considered by the Expert Panel in assessing safety. Although there is an absence of dermal absorption data for Polyisobutene and Hydrogenated Polyisobutene, the available octanol water partition coefficient data and the low solubility in water suggest very slow absorption, so additional data are not needed. Gastrointestinal absorption is also not a major concern due to the low solubility of these chemicals. Although one in vitro study did report that Polyisobutene did promote cellular transformation, a mouse study did not find evidence of tumor promotion. Because lifetime exposure studies using rats and dogs exposed to Polybutene failed to demonstrate any carcinogenic or tumor promotion effect, and a three-generation reproductive/developmental toxicity study produced no adverse effects, the CIR Expert Panel does not believe these large, mostly insoluble polymers present any risks in the practices of use and concentration as described in this safety assessment.

INTRODUCTION

This report presents available information pertinent to the assessment of the safety of Polyisobutene and Hydrogenated Polyisobutene as cosmetic ingredients.

An earlier safety assessment of the chemically related ingredient, Polybutene, was published in 1982 (Elder 1982) and was re-reviewed in 2002, at which time a "safe as used" conclusion for this ingredient was confirmed (Andersen 2005). Information on Polybutene has been added to this report in further support of the safety of Polyisobutene and Hydrogenated Polyisobutene, based on its similarities in definition and structure to the isobutene isomer.

CHEMISTRY

Definition and Structure

Polyisobutene

Iversen (1990) stated that Polyisobutene is a pentamer of isobutylene, a highly branched molecule. Parslew et al. (1996) characterized Polyisobutene as the polymer of isobutene,

[1]Reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel. This report was prepared by CIR staff person Valerie C. McLain. Address correspondence to her at Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA.

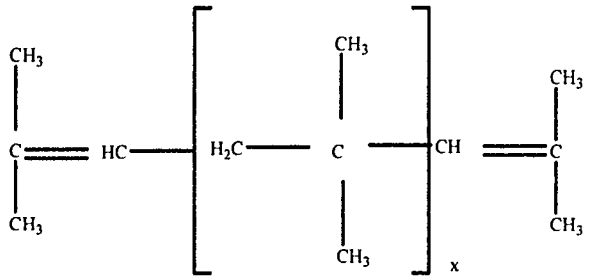

FIGURE 1
Polyisobutene.

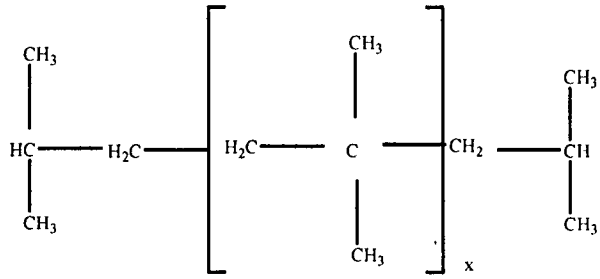

FIGURE 2
Hydrogenated Polyisobutene.

a long chain aliphatic hydrocarbon, with varying molecular weights.

Polyisobutene (CAS no. 9003-27-4) is defined in the *International Cosmetic Ingredient Dictionary and Handbook* (Gottschalck and McEwen 2006) as the homopolymer of isobutylene. Polyisobutene conforms generally to the structure shown in Figure 1. Technical/other names for Polyisobutene include

- Isobutene Homopolymer;
- Isobutylene Homopolymer;
- 2-Methyl-1-Propene, Homopolymer;
- Permethyl 108A;
- Polyisobutylene;
- 1-Propene, and
- -2-Methyl-, Homopolymer.

Trade names (manufacturer) include

- AEC Polyisobutene (A & E Connock);
- Creasil IC (C.I.T.);
- Creasil I.P. (C.I.T.);
- ESP PIB 0611 (Earth Supplied Products);
- ESP PIB 731 (Earth Supplied Products);
- ESP PIB 5011 (Earth Supplied Products);
- Permethyl 104A (Presperse);
- Permethyl 106A (Presperse);
- Permethyl 108A (Presperse); and
- Rewopal PIB 1000 (Degussa Care Specialties).

Trade name mixtures containing Polyisobutene include: Fancorsil P (Fanning) and Simulgel EPG (SEPPIC).

Hydrogenated Polyisobutene

In the *International Cosmetic Ingredient Dictionary and Handbook* (Gottschalck and McEwen 2006), Hydrogenated Polyisobutene (CAS no. 68937-10-0) is defined as a branched-chain aliphatic hydrocarbon. Hydrogenated Polyisobutene conforms generally to the structure shown in Figure 2. Trade names (manufacturer) for Hydrogenated Polyisobutene include

- AEC Hydrogenated Polyisobutene (A & E Connock);
- CREASIL ISO 20 (C.I.T.);
- CREASIL ISO 30 (C.I.T.);
- CREASIL ISO 40 (C.I.T.);
- CREASIL ISO 50 (C.I.T.);
- Fancol Polyiso 200 (Fanning);
- Fancol Polyiso 250 (Fanning);
- Fancol Polyiso 275 (Fanning);
- Fancol Polyiso 300 (Fanning);
- Fancol Polyiso 450 (Fanning);
- Fancol Polyiso 800 (Fanning);
- Keteol S (Prod'Hyg);
- MC 300 (Sophim);
- Panalane H-25E (Amoco Chemical);
- Panalane H-300E (Amoco Chemical);
- Panalane L-14E (Amoco Chemical);
- Panalane L-14E (Lipo);
- Panalane H-300 (Lipo);
- Polysynlane (NOF);
- PRISORINE 3758 (Uniqema Europe); and
- Squatol S (LCW).

Trade name mixtures containing Hydrogenated Polyisobutene include

- Cellini Blue (Engelhard Corp.);
- Cellini Coral (Engelhard Corp.);
- Cellini Green (Engelhard Corp.);
- Cellini Red (Engelhard Corp.);
- Cellini Yellow (Engelhard Corp.);
- Covascreen TI (LCW);
- Covascreen TIYO (LCW);
- Creagel RT PA/ISO (C.I.T.);
- CREASIL ISO 10 (C.I.T.);
- CREASIL ISO 170 (C.I.T.);
- CREASIL ISO 300 (C.I.T.);
- CREASIL ISO 325 (C.I.T.);
- CREASIL ISO 3400 (C.I.T.);
- CREASIL ISO 5000 (C.I.T.);
- DS-TAPS solution (5%) (Doosan);
- Emulzome (Exsymbol);
- Heliogel (Advanced Beauty);
- Jeechem HPIB (Jeen);
- Liant TW 406 (LCW);
- Liant TW 729 (LCW);
- Liant TW 876 (LCW);

- Oxyde de Zinc micropur Covasil S/Squatol S (LCW);
- PEC- 1414 (Sud-Chemie, United Catalysts);
- Polymoist Mask (Cognis Deutschland);
- Polysynlane Gel (Collaborative Labs);
- PW Covasil S1/Squatol S (LCW);
- Questamix H (Quest International);
- Versagel ME (Penreco); and
- Vitaphyle ACE (LCW).

Polybutene

According to the *International Cosmetic Ingredient Dictionary and Handbook* (Gottschalck and McEwen 2004), Polybutene (CAS no. 9003-28-5 or 9003-29-6) is defined as the polymer formed by the polymerization of a mixture of iso- and normal butenes. It conforms to the empirical formula: $(C_4H_8)_x$. Indopol® is a trade name for polybutene.

Physical and Chemical Properties

Polyisobutene

According to the *Kirk-Othmer Concise Encyclopedia of Chemical Technology* (Kresge1999), Polyisobutene is produced in a wide range of molecular weights. However, this author did not provide the specific molecular weight ranges.

In a review article, Tan et al. (1999) stated that polyisobutenes have a regular structure of a carbon-hydrogen backbone with only terminal unsaturation, which results in chemical inertness and good resistance to weathering, aging, heat, and chemicals. Polyisobutene is soluble in typical aliphatic and aromatic hydrocarbon solvents due to their highly paraffinic and nonpolar nature, but are insoluble in common alcohols, esters, ketones, and other oxygenated solvents. It was also stated by these authors that the higher the molecular weight of the polyisobutenes, the lower the permeability; however, no further details were mentioned. The low-molecular-weight polyisobutenes are very viscous, soft, and tacky semiliquids, and the high-molecular-weight grades are tough and elastic rubbery solids.

Infrared transmission values for Polyisobutene are shown in Table 1 (Nakano et al. 2001).

According to AzoM™ (2004), Polyisobutene, also known as butyl rubber, is a synthetic rubber or elastomer first commercialized in 1943. Key properties of Polyisobutene include air tight and gas impermeable; flexibility; good weathering resistance; resistance to ozone; good vibration damper; and biocompatible.

Additional reported physical and chemical properties of Polyisobutene are presented in Table 2.

Presperse Incorporated (2004) stated specifications for Permethyl 104A, a trade name for Polyisobutene, as shown in Table 3.

Unpublished data from the Cosmetic, Toiletry, and Fragrance Association (CTFA) (2006b) provided physical and chemical properties of Polybutene (Indopol® ; molecular weight varies from 910 for grade H-100 to 1300 for grade H-300E) and Hydrogenated Polyisobutene (Panalane® ; lowest molecular weight of 370 for Panalane L-14E), including their lack of water solubility and extreme hydrophobicity of the substances. The water solubility for these polybutenes was estimated at 5.6×10^{-9} mg/L. The log K_{ow} is estimated to be 13.27, which categorizes these substances as super hydrophobic and therefore biologically unavailable. Note, Indopol® and Panalane® conform to the requirements of the European Cosmetics Directive 76/768/EEC and its amendments.

TABLE 1
Infrared transmission values for Polyisobutene (Nakano et al. 2001).

Peak no.	Wave number	Transmittance (%)
1	924	49.08
2	951	46.85
3	1165.1	58.79
4	1230.7	15.4
5	1365.8	8.83
6	1388.9	13.07
7	1471.9	11.39
8	2681.4	75.41
9	2716.1	69.9
10	2733.5	68.37
11	2897.4	7.07
12	2953.4	5.07
13	4334.6	74.39

Hydrogenated Polyisobutene

Davis (1976) described a trade name polymer, Polysynlane (Hydrogenated Polyisobutene), as a novel synthetic substitute for squalene. Selectively polymerizing isobutene results in a saturated isoparaffin that contains virtually no ring structures. After hydrogenating and refining, the product is mainly the polymer ($C_{24}H_{50}$), which closely resembles natural squalene in both physical and chemical properties.

TABLE 2
Physical and chemical properties of Polyisobutene.

Property	Description	Reference
Appearance	White to yellowish or pale rubbery solid	Woods 1999
Odor	Slight rubber/ petroleum odor	Woods 1999
Specific gravity	0.92	Woods 1999
Solubility in water	Insoluble	Exxon Mobil Chemical Co. 2003
Viscosity	120	Amoco Chemical Company 2005

TABLE 3
Specifications for Permethyl 104A (Polyisobutene) (Presperse Incorporated 2004).

Appearance	Water-clear
Color Pt/Co	70 max.
Flash point	165°C or 329°F min.
Kinematic viscosity at 100°C	210–250 cSt
MW number average	900 min.
Water	50 mg/kg max.

Like natural squalene, the synthetic material is a colorless, odorless, tasteless liquid, miscible with vegetable and mineral oils, organic solvents, and lipophilic substances. It is also nonrancid, nondrying, nonoxidizing, and noncongealing. It is easily emulsified and combines good spreading and penetrating properties with an excellent feel. For the perfumer, according to this author, it has exceptionally good oxidation and chemical stability. Table 4 describes the compatibility of Polysynlane (Hydrogenated Polyisobutene) with other materials and Table 5 compares properties of Polysynlane and squalene (Davis 1976).

According to Buekens et al. (1998), Polyisobutene decomposes by both end-chain scission (broken up from the end groups successively yielding the corresponding monomers) and random-chain scission (broken up randomly into fragments of uneven length).

Uniquema (2004) provided a product specification sheet on Prisorine 3758 Squalene (Synthetic), which is a trade name for Hydrogenated Polyisobutene, data from which are given in Table 6.

Sophim (2004) reported that Hydrogenated Polyisobutene is available in two grades—Sophim MC 30 (liquid) and Sophim MC 300 (viscous). MC 300 is an effective waterproofing agent and MC 30 has excellent spreadability and fast penetration into the skin. Table 7 describes the suppliers specifications for these trade name Hydrogenated Polyisobutenes. In addition, this supplier indicated that these trade name Hydrogenated Polyisobutenes are soluble in many sunscreen filters, miscible with lipophilic substances, totally stable versus oxidation, stable across the pH range of use, and have a soft, nongreasy feel.

TABLE 4
Compatibility of Polysynlane (Hydrogenated Polyisobutene) with various materials (Davis 1976).

	Polysynlane		
Materials	10%	50%	90%
Castor oil	C[a]	IC[b]	IC
White oil	C	C	C
Soybean oil	C	C	C
Stearic acid	C	C	C
Soybean oil fatty acid	C	C	C
Beeswax	C	C	C
Coconut oil fatty acid	C	C	C
Polyethylene glycol	IC	—[c]	—

[a]C, compatible; [b]IC, incompatible; [c]—, not determined.

NOF Corporation (2005) reported that Parleum/Polysynlane (Hydrogenated Polyisobutene) has a molecular weight of 350, with the level of molecular weight less than 1000 daltons as 100%. This company provided no data on the level of monomers, because the monomer is in the form of a gas and it is believed there is no remaining monomer in the product. Also, no data were provided on the stability of the product at acidic pH.

Additional reported physical and chemical properties of Hydrogenated Polyisobutene are presented in Table 8.

The Fanning Corporation (2005), a manufacturer of various Hydrogenated Polyisobutene products, sold under the Fancol™ trade name, reported the average molecular weights as presented in Table 9.

CTFA (2006a) reported that Panalane L-14E has a number average (M_n) molecular weight of 370.

CTFA (2006b) also reported that Panalane® trade name products include Hydrogenated Polyisobutene products Panalane® L-14E and H-300E. Panalane® L-14E would be the grade with the lowest molecular weight. The typical number average (M_n) molecular weight for L-14E by a gel permeation chromatography method is 370. The M_n value for the higher molecular weight H-300E was 1300.

Panalane® is a hydrophobic compound whose accurate measurement of water solubility under experimental conditions is impractical. Therefore, determinations of water solubility and of log K_{ow} are more practically made by modeling with programs. For a discrete unit ($C_{28}H_{56}$) representing both the smallest and average molecular weight (392 dalton) of a polymerized chain of five subunits, the water solubility was estimated at 5.6×10^{-9} mg/L, or 5.6×10^{-6} μg/L, or 5.6×10^{-3} ng/L (0.0056 parts per trillion).

The octanol-water partition coefficient (log K_{ow}) also was modeled. The same assumption as in the modeling of water solubility applied in this case: model of the lowest molecular weight unit (392 daltons) to represent the lowest log K_{ow} calculated at 13.27 (CTFA 2006b).

Polybutene

CTFA (2006b) also reported that Indopol® includes products such as Indopol Polybutene H-100, H-300, and H-1900. The M_n values for the higher molecular weight grades were stated as: H-100, -910; H-300, -1300; and H-1900, -2500.

Hydrogenated Polyisobutene (Panalane®) also is a hydrophobic compound whose accurate measurement of water solubility under experimental conditions is impractical. The water solubility modeled for a discrete unit ($C_{28}H_{56}$) representing both the smallest and average molecular weight (392 dalton) of a

TABLE 5
Properties of Polysynlane (Hydrogenated Polyisobutene) and squalene (Davis 1976).

Properties	Polysynlane, specified	Polysynlane, typical	Natural squalene
Specific gravity (20°C)	0.810–0.830	0.8260	0.805–0.812
Refractive index (n20/D)	1.450–1.460	1.4580	1.4520–1.4525
Freezing point (°C)	Below–30	−50	Approx.−38
Acid value	Below 0.1	0.0	0.25
Saponification value	Below 0.5	0.0	5.0 max
Iodine value	Below 3.5	1.0	5.0 max.

polymerized chain of five subunits was estimated at 5.6×10^{-9} mg/L, or 5.6×10^{-6} μg/L, or 5.6×10^{-3} ng/L (0.0056 parts per trillion).

The octanol-water partition coefficient (log K_{ow}) was modeled using the same assumption as in the modeling of water solubility to yield a calculated log K_{ow} at 13.27 (CTFA 2006b).

Reactivity

One material safety data sheet (MSDS) states that Polyisobutene is stable, incompatible with strong oxidizers, produces CO, CO_2, and hydrocarbons on burning, and should be stored in a cool, dry area (Woods 1999). This MSDS goes on to state that the primary route of entry is dermal and that inhalation and ingestion are unlikely.

A MSDS from BASF Corporation (2003) stated that Polyisobutylene is noncorrosive and is not an oxidizer.

In an MSDS, Amoco Chemical Company (2005) stated that Hydrogenated Polyisobutene is stable, except to note that burning can produce carbon monoxide and/or carbon dioxide and other harmful products.

Method of Manufacture

According to Iversen (1990), commercial, low-viscosity Polyisobutenes are manufactured by polymerization of isobutylene in the presence of a catalyst. The type of catalyst used was not mentioned.

TABLE 6
Prisorine 3758 Squalene (Synthetic) specifications (Uniquema 2004).

	Units	Min/Max
Acid value	mg KOH/g	0.1
Saponification value	mg KOH/g	0.5
Iodine value	g/100 g	3.0
Color APHA	Hazen	20
Viscosity (25°C)	mPa·s	20–70
Odor	—	PASS
Density (20/20°C)	g/cm^3	0.810–0.875
Typical refractive index (N25/D)	—	1.455

According to AzoM™ (2004), Polyisobutene is derived from the monomer isobutylene via cationic vinyl polymerization.

CTFA (2006b) reported that Indopol® and Panalane® polybutenes are synthetic hydrocarbon liquid polymers made by the polymerization of C_4 olefins (primarily isobutene mixed with some n-butene) and are available in a wide range of viscosities for use in numerous applications.

Kresge (1999) described a highly complex mechanism of cationic polymerization of isobutylene (a.k.a. isobutene) and copolymerization of isobutylene with isoprene with Lewis acids. Friedel-Crafts Lewis acid and Bronstead acid coinitiators at low temperatures give an extremely high polymerization rate in hydrocarbon or halogenated hydrocarbon diluents. Isobutylene polymerizes in a regular head-to-tail sequence to produce a polymer having no asymmetric carbon atoms. The glass transition temperature is approximately −70°C.

AzoM™ (2004) reported that Polyisobutene polymers are formed by highly exothermic cationic vinyl polymerization. The use of an initiator or cation was involved, which attracted a pair of electrons from the carbon-carbon double bond, therefore forming a single bond with the initiator. One of the previously double-bonded carbons is then positively charged and will react with another monomer, similarly to the initiator. The process is repeated and the polymer is formed. The polymerization reaction

TABLE 7
Specifications of trade name Hydrogenated Polyisobutenes (Sophim 2004).

Property	MC 30	MC 300
Appearance	colorless, odorless, tasteless	clear, odorless, tasteless
Specific gravity	0.810–0.830	0.880–0.910
Refractive index	1.4500–1.4600	1.4950–1.4990
Viscosity at 40°C	15–25	—
Viscosity at 100°C	—	590–630
Acid value	0.1 max	0.1 max
Iodine value	1.0 max	4.0 max
Saponification	0.5 max	1.0 max

TABLE 8
Physical and chemical properties of Hydrogenated Polyisobutene (Amoco Chemical Company 2005).

Property	Description
Appearance	Clear liquid
Specific gravity	0.88 to 0.93
Solubility in water	Negligible, below 0.1%
Viscosity	636–690 cSt at 210°F (99°C)
Stability	Stable
Boiling point	95°F (35°C)

is usually carried out at temperatures in the range of −100°C to control the reaction rate.

Analytical Methods

According to Powles (1956), the proton magnetic resonance absorption in Polyisobutene has been measured over the temperature range −196°C to 90°C. Due to the close approach of the methyl groups on alternate carbon atoms, there is an unusually large width of the absorption line at the lowest temperatures. The usual reduction in line width associated with reorientation of methyl groups about their C_3 axis is notably absent and supports arguments that the methyl groups are severely interlocked. A reduction in the second moment of the absorption line, which sets in over a range of temperature near −10°C, is associated with chain motion.

Impurities

Parslew et al. (1996) mentioned a Polyisobutene with a molecular mass of 85,000 (Oppanol B 15) with ash content less than 100 ppm (a majority of the ash contains the oxides and silicates of iron, potassium, and sodium). The total heavy metal content was reported to be <1 ppm. A stabilizer (2,6-di-tert-butyl-4-methylphenol), at a concentration of 400 ppm, prevents oxidation.

TABLE 9
Average molecular weights for Fancol™ Polyiso products (Fanning Corporation 2005).

Product	Average molecular weight
Fancol Polyiso 200-CG	216
Fancol Polyiso 250-CG	261
Fancol Polyiso 275-CG	268
Fancol Polyiso 300-CG	326
Fancol Polyiso 450-CG	456
Fancol Polyiso 800-CG	806
Fancol Polyiso 1200-CG	1242

AzoM™ (2004) indicated on its Web site that the typical composition of butyl rubber is 98% Polyisobutene, with the balance being 2% isoprene.

The Fanning Corporation (2005) reported that there are no known impurities (monomers or residual catalysts) in any of the following Fancol™ Polyiso ingredients: Fancol Polyiso 200-CG, Fancol Polyiso 250-CG, Fancol Polyiso 275-CG, Fancol Polyiso 300-CG, Fancol Polyiso 450-CG, Fancol Polyiso 800-CG, and Fancol Polyiso 1200-CG.

NOF Corporation (2004) reported that Parleam, Parleam 4, Parleam LITE, Parleam V, Parleam HV, and Parleam SV (all product names for Hydrogenated Polyisobutene) do not contain the impurities, such as: pesticides, polycyclic aromatic hydrocarbons, dioxine, 1,4-dioxane, ethylene oxide, nitrosamine, free amines, diethanoleamine, triethanolamine, monomers, formaldehyde, sulphite, dimethyl sulphate, ethylene chlorohydrine, monochloro/dichloro acetic acid, octamethylcyclotetrasiloxane (D4), dibutylphthalate, and diethylhexylphthalate.

USE

Cosmetic

According to Davis (1976), Polysynlane (Hydrogenated Polyisobutene) has found wide use as a squalene substitute in both Europe and Japan and is now finding approval in the United States. It is also being considered as an additive to improve the feel of and generally upgrades the spreading and penetrating properties of lotions based on mineral oil and petrolatum and offered on the mass market. This author described uses of this trade name Hydrogenated Polyisobutene in moisturizing skin milk at 6.0%, night cream at 15.0%, and vanishing cream at 7.0%.

Sophim (2004) reported some possible uses of Hydrogenated Polyisobutene in hydrating creams, after shave balms, antiperspirants, color cosmetics, acne creams, hair grooms, sunscreen formulations, lipsticks, hair relaxers, baby care, cleansing creams, and shaving gels.

According to the *International Cosmetic Ingredient Dictionary and Handbook* (Gottschalck and McEwen 2006), Polyisobutene functions as a binder, film former, and nonaqueous viscosity-increasing agent with uses in product categories such as lipsticks and mascara, and Hydrogenated Polyisobutene functions as a skin-conditioning agent—emollient and nonaqueous viscosity-increasing agent with uses in a wide variety of cosmetic product categories.

The most recently available frequency of use data provided by industry to the Food and Drug Administration (FDA 2006) under the voluntary cosmetic registration program (VCRP) are given in Table 10. Concentration of use information in Table 10 was based on an industry survey (CTFA 2006a) of current practice.

Polyisobutene has 30 uses, and a high concentration of 76% in lipsticks as obtained from an industry-wide survey provided by CTFA (2005a). The lowest reported concentration for this ingredient is 0.3% in blushers and foundations.

TABLE 10
Uses and concentrations of Polyisobutene and Hydrogenated Polyisobutene in cosmetics.

Product category (FDA 2006a)	2005 ingredient uses (total number of products in each category [FDA 2006])	2005 concentrations (CTFA 2005a) (%)
	Polyisobutene	
Eye makeup preparations		
Eye shadow	1 (576)	5–25
Eye lotions	—[a] (25)	30
Mascara	8 (195)	5–13
Other eye makeup preparations	2 (152)	1[b]–25
Noncoloring hair preparations		
Hair sprays/aerosol fixatives	2 (275)	—[c]
Shampoos	1 (884)	—[c]
Makeup preparations		
Blushers	1 (245)	0.3
Foundations	—[a] (324)	0.3–3
Lipsticks	12 (962)	4–76
Makeup bases	—[a] (141)	1
Other makeup preparations	2 (201)	4–46
Shaving preparations		
Shaving cream	—[a] (134)	4
Skin care preparations		
Night skin care preparations	1 (200)	—[c]
Suntan preparations		
Suntan gels, creams, and liquids	—[a] (131)	0.5
Total uses/ranges for Polyisobutene	30	0.3–76
	Hydrogenated Polyisobutene	
Baby products		
Lotions, oils, powders, and creams	—[a] (60)	4
Bath preparations		
Oils, tablets, and salts	—[a] (143)	85
Bubble baths	—[a] (215)	3
Soaps and detergents	1 (421)	40
Eye makeup preparations		
Eyebrow pencils	3 (102)	4–38
Eyeliners	29 (548)	0.1–39
Eye shadow	18 (576)	3–40
Eye lotions	1 (25)	—[c]
Eye makeup remover	1 (100)	—[c]
Mascara	5 (195)	0.5–15
Other eye makeup preparations	21 (152)	4–24
Fragrance preparations		
Perfumes	—[a] (235)	10
Powders	—[a](273)	0.8
Other fragrance preparations	5 (173)	—[c]
Noncoloring hair preparations		
Hair tonics, dressings, etc.	—[a] (598)	15
Other noncoloring hair preparations	—[a](277)	17[d]
Hair-coloring preparations		
Other hair-coloring preparations	1 (55)	—[c]

(Continued on next page)

TABLE 10
Uses and concentrations of Polyisobutene and Hydrogenated Polyisobutene in cosmetics. *(Continued)*

Product category (FDA 2006a)	2005 ingredient uses (total number of products in each category [FDA 2006])	2005 concentrations (CTFA 2005a) (%)
Makeup preparations		
Blushers	14 (245)	2–30
Face powders	24 (305)	0.1–5
Foundations	16 (324)	2–47
Lipsticks	318 (962)	0.001–96
Makeup bases	1 (141)	4
Makeup fixatives	5 (20)	—[c]
Rouges	70 (28)	16–50
Other makeup preparations	36 (201)	17–77
Nail care products		
Creams and lotions	1 (15)	3
Polishes and enamels	4 (123)	0.2–0.4
Personal hygiene products		
Underarm deodorants	—[a] (247)	2
Other personal hygiene products	4 (308)	24
Shaving preparations		
Aftershave lotions	1 (231)	4
Shaving cream	2 (134)	4
Other shaving preparations	3 (63)	—[c]
Skin care preparations		
Skin cleansing creams, lotions, liquids, and pads	1 (775)	4–85
Depilatories	—[a] (34)	6
Face and neck skin care preparations	13 (310)	0.8–42
Body and hand skin care preparations	5 (840)	0.5–37
Foot powders and sprays	—[a] (35)	4
Moisturizers	26 (905)	3–4
Night skin care preparations	4 (200)	3–6
Paste masks/mud packs	2 (271)	2–7
Other skin care preparations	10 (725)	8
Suntan preparations		
Suntan gels, creams, and liquids	6 (131)	15
Indoor tanning preparations	1 (71)	—[c]
Other suntan preparations	2 (38)	—[c]
Total uses/ranges for Hydrogenated Polyisobutene	654	0.001–96

[a]No uses reported to FDA in the VCRP.
[b]1% in a concealer.
[c]No use concentrations reported in industry survey.
[d]A hair shine product.

Hydrogenated Polyisobutene has 654 reported uses (FDA 2006) with a wide concentration range of 0.001% to 96% in lipsticks; use concentrations in other product categories fall within that range (CTFA 2005a).

Also given in Table 10 are the current data from the VCRP on the total number of products in each product category, allowing the reader to determine how frequently these ingredients are used in a particular product category. For example in Table 10, 12 of the 962 lipstick products reported to be on the market contain Polyisobutene.

Although uses were voluntarily reported to the FDA VCRP (FDA 2006), in some cases no use concentrations were reported

in the industry survey (CTFA 2006a). For example in Table 10, uses of 4 Polyisobutene were voluntarily reported to the FDA but no use concentrations were reported in the industry survey.

In addition, the industry survey (CTFA 2006a) reported use concentrations in product categories for which no reports had been submitted to the FDA VCRP (FDA 2006). For example in Table 10, no uses were reported in shaving cream, yet a use concentration of 4% was identified. This information suggests that at least one currently marketed shaving cream contains polyisobutene.

CTFA (2006c) provided an indication of the molecular weight of Polyisobutene and Hydrogenated Polyisobutene used in certain product categories as shown in Table 11 (CTFA 2006c).

Polybutene

For comparison purposes, the functions of the related ingredient, Polybutene, include binder, epilating agent, and nonaqueous viscosity-increasing agent (Gottschalck and McEwen 2006). Its reported uses are in lipsticks primarily, but also in mascara, makeup preparations (not eye), eye shadow, eye makeup preparations, foundations, eyebrow pencils, eyeliners, and moisturizing preparations at concentrations ranging from 0.002% to 96%.

Noncosmetic

Iversen (1990) reported that the higher branched polyisobutenes are the most widely used polyolefins in electrical

TABLE 11

Polyisobutene and Hydrogenated Polyisobutene molecular weights as a function of product category (CTFA 2006c).

Ingredient	Product category	Average molecular weights
Polyisobutene	Lipstick	950
Polyisobutene	Shaving cream (aerosol, brushless, and lather)	950
Polyisobutene	Suntan gels, creams, and liquids	950
Hydrogenated Polyisobutene	Baby lotions, oils, powders, and creams	350
Hydrogenated Polyisobutene	Bath oils, tablets, and salts	350
Hydrogenated Polyisobutene	Eyebrow pencil	400; 2650
Hydrogenated Polyisobutene	Eyeliner	350; 2650
Hydrogenated Polyisobutene	Eye shadow	350; 2650
Hydrogenated Polyisobutene	Mascara	350; 920–1000; 1300; 2650
Hydrogenated Polyisobutene	Other eye makeup preparations	400
Hydrogenated Polyisobutene	Perfumes	350
Hydrogenated Polyisobutene	Powders (dusting and talcum)	400
Hydrogenated Polyisobutene	Tonics, dressings, and other hair-grooming aids	350
Hydrogenated Polyisobutene	Other hair preparations (noncoloring)	370
Hydrogenated Polyisobutene	Blushers (all types)	350–400; 2650
Hydrogenated Polyisobutene	Face powders	2650
Hydrogenated Polyisobutene	Foundations	350; 1000; 2650
Hydrogenated Polyisobutene	Lipstick	350–400; 1000; 1300–1345; 2650
Hydrogenated Polyisobutene	Makeup bases	1345
Hydrogenated Polyisobutene	Rouges	1000
Hydrogenated Polyisobutene	Other makeup preparations	1000; 2650; 1300
Hydrogenated Polyisobutene	Nail creams and lotions	350
Hydrogenated Polyisobutene	Nail polish and enamel	350
Hydrogenated Polyisobutene	Aftershave lotions	220; 350
Hydrogenated Polyisobutene	Shaving cream (aerosol, brushless, and lather)	350
Hydrogenated Polyisobutene	Skin cleansing (cold creams, cleansing lotions, liquids, and pads)	350–363
Hydrogenated Polyisobutene	Depilatories	363
Hydrogenated Polyisobutene	Face and neck creams, lotions, and powders	220; 350–370; 400 - 600; 1000
Hydrogenated Polyisobutene	Body and hand creams, lotions, and powders	220; 350–370
Hydrogenated Polyisobutene	Night creams, lotions, and powders	220; 363
Hydrogenated Polyisobutene	Paste masks (mud packs)	350–370
Hydrogenated Polyisobutene	Other skin care preparations	370
Hydrogenated Polyisobutene	Suntan gels, creams, and liquids	350

equipment. In addition, they may be used as raw material for detergents and as lubricants.

Tan et al. (1999) reported that low-molecular-weight Polyisobutene polymers are mainly used as tackifiers to provide tack to the high-molecular-weight Polyisobutene or other adhesive polymers. High-molecular-weight Polyisobutene is used to impart internal strength and flow resistance of pressure-sensitive adhesives.

According to the *Kirk-Othmer Concise Encyclopedia of Chemical Technology* (Kresge 1999), Polyisobutylene has a variety of uses. The low-molecular-weight polybutenes are used as adhesives, sealants, coatings, lubricants, plasticizers, and for the impregnation of electrical cables. Moderate weight Polyisobutylene was among the first viscosity-index modifiers for lubricants. The high-molecular-weight Polyisobutylene is used in the production of unpreserved rubbery compounds, and as an impact additive for thermoplastics.

According to the Household Products Database (2004), John Deere Universal 2 Cycle Oil is an auto product that in liquid form contains 15% to 25% Polyisobutene.

Pharmaceutical Capsules

Nixon et al. (1982) described the effects of Polyisobutene on the properties of ethyl cellulose-walled microcapsules of phenobarbitone sodium. It was concluded that the size and wall thickness changed as the proportion of Polyisobutene increased, which affected the first-order release kinetics of the drug.

Kawashima et al. (1984) reported on a study in which Adriamycin hydrochloride was microencapsulated with ethylcellulose by a phase separation method for developing a controlled release dosage form. The authors also studied the effect of Polyisobutene in the production of a liquid phase and in the drug release properties of the microcapsules. With increasing concentration of Polyisobutene (1% to 3%), the average diameter of the microcapsules decreased. At the low concentration, the resultant microcapsules were agglomerated, which resulted in increasing the size. The microcapsules prepared with 2% Polyisobutene prolonged the drug release from the capsule.

Das (1991) investigated the in vitro drug release profile of theophylline from microcapsules prepared with Polyisobutene as protective colloid, with a view to developing a controlled release dosage form of theophylline. It was found that an optimum concentration of 5% w/w of Polyisobutene gives satisfactory controlled theophylline release profile.

Kristl et al. (1991) described the preparation of ethylcellulose microcapsules containing bacampicillin in which a saturated solution of Polyisobutene in cyclohexane was used in the synthesis. Polyisobutene lowers the solubility of ethylcellulose in cyclohexane. The aggregation of microcapsules decreases by increasing molecular weight of Polyisobutene. When Polyisobutene of high molecular weight is used in the process of microencapsulation, smaller liquid phase droplets are formed and larger liquid phase volume is produced.

Sveinsson et al. (1991) prepared naproxen microcapsules from ethylcellulose and Polyisobutene.

The role of Polyisobutene used as a liquid phase inducing agent in the preparation and assessment of Eudragit RS (ERS) microcapsules (MCs) in trichloroethane (TCE) was studied with isoniazid (INH) as the core material (Barick et al. 1994). Polyisobutene improves the overall efficiency of microencapsulation and in vitro release patterns.

Guo (1994) investigated the surface properties and bioadhesion of buccal patches. Using a two-roll milling method, a new bioadhesive polymer patch formulation for drug controlled delivery, which consisted of Carbopol 934P (CP), Polyisobutene (PIB), and polyisoprene (PIP) was prepared.

Pressure-Sensitive Adhesives

Chiang et al. (1998) described a transdermal delivery system for ketotifen that utilized Polyisobutene as an adhesive with liquid parafin and fatty acids making up the rest of the patch. Adjusting the relative proportion of the paraffin can be used to control the rate of drug delivery.

A review article by Tan et al. (1999) discussed pressure-sensitive adhesives (PSAs) for transdermal drug delivery systems, noting that Polyisobutenes are excellent for use in such devices because of their stability, inertness, and broad acceptance in FDA-regulated applications. Table 12 lists products marketed in the U.S. that use Polyisobutenes as the pressure-sensitive adhesive.

GENERAL BIOLOGY

Absorption, Distribution, Metabolism, Excretion

No data were available on the absorption, distribution, metabolism, or excretion.

Bioaccumulation

According to CTFA (2006b), polybutenes are not bioconcentrated or bioaccumulated by organisms due to their poor water solubility and/ or poor solubility in various organic solvents/dissolved organic matter. Also, the log K_{ow}, estimated from a modeling program, of the lowest molecular weight was approximately 13.27 and the molecular size of 392 Da decreases

TABLE 12

Transdermal drug delivery products that use Polyisobutenes as the pressure-sensitive adhesive (Tan et al. 1999).

Drug	Product	Developer/marketer
Clonidine	Catapres-TTS®	Alza/Boehringer Ingelheim
Estradiol	Estraderm®	Alza/Novartis
Nicotine	Nicoderm®	Alza/SmithKline Beecham
Nitroglycerin	Deponit®	Lohmann/Schwarz Pharma
Scopolamine	Transdermal-Scop®	Alza

the likelihood that these compounds become bioavailable. It is widely accepted that the bioavailability of superhydrophobic chemicals (compounds with log K_{ow}'s greater than 6), such as in these polybutenes, is largely insignificant. Therefore, these authors concluded that polybutene compounds are nonhazardous to the environment.

Biocompatibility

Bergdahi et al. (1974) reported on the biological compatibility of Polyisobutene as a possible new root canal sealer.

Test material was filled into Teflon tubes. A total of 96 soft tissue implants of either Polyisobutene, gutta percha, or AH26 were inserted into the backs of guinea pigs for 3 and 8 weeks. Also, 62 implants of either Polyisobutene or AH26 were placed into the mandible of guinea pigs. After 2 or 12 weeks, the animals were killed.

All three materials exhibited mild tissue irritation after implantation in subcutaneous tissue. However, Polyisobutene was found to be less irritating than the other materials. Following bone tissue implantation, AH26 showed an acceptable tissue compatibility whereas Polyisobutene was rated excellent. The authors concluded that Polyisobutene had very low toxicity and negligible irritating effects of tissues in vivo after implantation (Bergdahi et al. 1974).

ANIMAL TOXICOLOGY

Acute Oral Toxicity

Davis (1976) stated that acute oral toxicity testing using mice resulted in no deaths with a maximum of 89.6 g/kg of Polysynlane (Hydrogenated Polyisobutene).

Product Safety Labs (1987a) evaluated the oral toxicity of a single dose of 5 g/kg Hydrogenated Polyisobutene (Permethyl 104A/105A Blend Aliphatic Hydrocarbon; 900 minimum number average molecular weight). Five male and five female albino Wistar rats, weighing 237 to 270 g, were used in this study. Each rat received the undiluted test material by gavage using a stainless steel intubation needle. The rats were observed at 1, 2, 4, and 6 h after administration and at least once daily thereafter for signs of toxicity and mortality. Body weights were recorded initially and at termination on day 14. No mortalities were observed during the study period; however, all of the animals appeared lethargic after dosing. Overall, all the rats appeared active and healthy from 2 h to termination on day 14. At 1 h, one rat developed irregular respiration and facial staining on days 1 and 2. By day 3, these signs disappeared. All of the animals gained weight during the course of the study.

The Fanning Corporation (1998a) studied the single dose oral toxicity in 10 male Wistar albino rats. The animals were orally dosed with Hydrogenated Polyisobutene (Poly Iso 6-50-DN, clear liquid) at 5.0 g/kg body weight. Mortality and systemic observations were recorded 3 to 4 h after dosing and once daily thereafter for 14 days. The body weights were recorded prior to testing (212 to 242 g). All of the animals survived the 5.0 g/kg oral dose. There were instances of wetness of the anogenital area observed on the day of dosing only. The animals were not examined for gross pathology. The authors concluded that the LD_{50} is greater than 5.0 g/kg body weight. Therefore, the Poly Iso 6-50-DN is nontoxic as defined in 16 CFR 1500.3 (c)(2)(I).

The Fanning Corporation (1998d) studied the single-dose oral toxicity in 10 male Wistar albino rats administered 5.0 g/kg body weight Hydrogenated Polyisobutene (Poly Iso 4-50-EN). The maximum amount of liquid given at one time did not exceed 2.0 ml/100 g of body weight. Mortality and systemic observations were recorded 3 to 4 h post dose and once daily thereafter for 14 days. The animals were not examined for gross pathology. Body weights were recorded pretest (213 to 286 g). All animals survived the 5.0 g/kg oral dose. Wetness of the anogenital area was noted on the day of dosing only. All animals appeared normal from day 1 through day 14. The LD_{50} is greater than 5.0 g/kg of body weight. Therefore, the authors noted that the test material is nontoxic as defined in 16 CFR 1500.3 (c)(2)(I).

Short-Term/Subchronic Toxicity

No short-term or subchronic animal toxicity data were available.

Chronic Toxicity

Polybutene

In the Cosmetic Ingredient Review (CIR) safety assessment of the chemically related ingredient, Polybutene (Elder 1982), a 2-year chronic oral toxicity study of Polybutene H-100 (75% concentrate) in Charles River albino rats was presented. The animals were separated into four groups of 60 (30 males and 30 females per group). The animals were given 0 (control), 800 (0.08%), 4000 (0.40%), or 20,000 (2.0%) ppm Polybutene blended into their regular diets. The rats were monitored for their body weights, mortality and reactions, tumor incidence, and hematologic, urologic, and pathologic changes. After 12 months of testing, five animals from each group were killed for evaluation. No gross or microscopic pathological changes could be correlated with Polybutene ingestion. No significant differences were found after 24 months of feeding in the body weights or weight of food consumption, hematological results, urology, or tumor formation between the animals fed Polybutene and those that were not.

In the 20,000 (2.0%) ppm group, three out of six males that died between weeks 17 and 24 exhibited hematuria. Another male in this group showed similar reactions, but recovered completely within 2 weeks. Necropsies of the three rats revealed that two had clotted blood in the urinary tract, bladder, stomach, and intestines. The third animal, however, revealed no significant gross pathologic changes. No abnormal reactions were noted in any other tested animal.

A 2-year chronic oral toxicity study of Polybutene H-100 (75% concentrate) in Beagle dogs was also summarized by this author. The substance was orally administered daily to three test

groups, each consisting of eight pure-bred Beagle hounds (four males, four females). Each group was given one of the following doses: 40, 200, and 1000 mg/kg body weight (bw), or 0.045, 0.227, and 1.14 ml of test material. An untreated control group consisted of 5 male and 2 female dogs. Complete hematologic studies, blood chemistry, urinalysis, and liver function tests were conducted on the control and the highest dosage group after 90, 180, and 540 days of testing, as well as on all four groups after 360 and 720 days of testing.

Following 1 year of testing, one male and one female from each group were killed. At 2 years, all surviving dogs from all groups were killed and the major tissues and organs were examined. The authors of this study found that daily oral administration of Polybutene H-100 to pure-bred Beagle dogs over a period of 2 years at the specified dosages caused no abnormalities in body weight, food consumption, survival, behavioral patterns, hematology, blood chemistry, urinalysis, liver function, gross and histopathologic examinations, or organ weights and ratios (Elder 1982).

Ocular Irritation

CTFA (1973b) submitted an eye irritation study in 9 rabbits using Polysynlane (Hydrogenated Polyisobutene). The rabbits were treated once and then observed for 7 days. One-tenth of a milliliter of the test material was instilled in one eye of each animal. The other eye remained untreated and served as the control. Two seconds after instillation of the test material, a washout was performed in three other rabbits using 30 ml of warm water. Four seconds after instillation of the test material, washout was performed in three additional rabbits using 20 ml of warm water. No eye irritation was observed in any of the washed or unwashed rabbit eyes. The material was therefore considered to be nonirritating.

Product Safety Labs (1987b) investigated the irritant and/or corrosive effects of a single installation of Permethyl 104A/105A Blend Aliphatic Hydrocarbon (Hydrogenated Polyisobutene) into the eyes of rabbits. Six healthy, New Zealand white rabbits were used for this experiment. The conjunctival sac of the right eye of each rabbit was treated with 0.1 ml of the test material. The opposite eye remained untreated and served as the control. The treated eyes were scored for irritation at 24, 48, and 72 h following administration using the Draize scale. No corneal or iridial damage was observed during the study. At 24 h, five of the six eyes had a slight to moderate hyperemia and all had a slight to moderate discharge. Three eyes were clear of irritation by 48 h and the remaining three had moderate hyperemia. Only one eye had irritation to the conjunctivae by 72 h present as slight hyperemia.

Data submitted by CTFA (1976) included rabbit eye irritation scores using the test material Prisorine 3758 (Hydrogenated Polyisobutene). Six rabbits were used in the study. The test material was administered into the right eye of each animal; the left eye served as the control. Mild redness was observed in 3 of the rabbits with a score of 1 on the Draize scale. No other effects were reported. No further details were provided on this study.

Fanning Corporation (1998c) examined the irritation potential of Poly Iso 6-50-DN (clear liquid) when instilled into the eye of the rabbit. Six New Zealand white rabbits were given 0.1 ml of the test substance into the conjunctival sac of one eye of each rabbit. The contralateral eye served as a control. On days 1, 2, and 3, the eyes were examined and scored using the Draize method. The primary eye irritation score for each rabbit and each day was calculated. Body weights were recorded pretest (2.0 to 2.5 kg).

Four of the six eyes appeared normal at each period of observation. Slight conjunctival irritation, observed in two out of six eyes, cleared up by day 2. There was one instance of soiling of the anogenital area, which was the only abnormal systemic sign noted during the observation period. The authors stated that Poly Iso 6-50-DN is not an eye irritant (Fanning Corporation 1998c).

Fanning Corporation (1998f) investigated the primary eye irritation of Poly Iso 4-50-EN in rabbits. The test material (0.1 ml) was used to dose six female New Zealand white rabbits. The Poly Iso 4-50-EN was placed into the conjunctival sac of one eye of each rabbit. The contralateral eye served as a control. The eyes were examined and scored according to the Draize method at 1 h post administration and on days 1, 2, and 3. Sodium fluorescein was used to determine the corneal effects on day 1. The eyes were washed with 20 ml of distilled water following the 24-h observations. Prior to testing, the body weights were recorded (2.3 to 2.6 kg). The primary eye irritation score for each rabbit was calculated everyday, as well as the mean total scores for each time period.

Four out of six eyes appeared normal on days 1, 2, and 3. Slight conjunctival irritation, observed in two out of six eyes, cleared by day 2. There were no abnormal systemic signs noted during the observation period. The authors concluded that Poly Iso 4-50-EN is not an eye irritant based on the results of this study (Fanning Corporation 1998f).

A Draize eye irritation study was performed with a facial lotion (12F) containing 3.0% Hydrogenated Polyisobutene (CTFA 1987). The right eyes of three rabbits were tested and according to the data sheet, no signs of irritation were observed. No further details were provided on this study.

According to CTFA (2006b), irritation tests with approved surrogate systems/animals have shown that Indopol® polybutenes are not likely to be more mild than eye irritants (the maximum primary eye irritation score [PEIS] of 3.0/110 with complete disappearance of effects in 72 h for the lighter grades; maximum PEIS score of 8.0/110 with complete disappearance of effects in 72 h for the heavier grades).

Dermal Irritation

CTFA (1973a) reported on a skin irritation study in rabbits using Polysynlane. Six rabbits were patched with four patches, each containing 0.5 g/patch of the test material. There were no

reactions in any of the animals on intact or abraded skin. The primary irritation index was 0.0.

Davis (1976) found that Polysynlane (Hydrogenated Polyisobutene) was not irritating to intact or abraded rabbit skin when using synthetic squalene on four patches on each of the six animals. Specific concentrations were not provided by this author.

Product Safety Labs (1987c) studied the irritant and/or corrosive effects of a single 24-h exposure of Permethyl 104A/105A Blend Aliphatic Hydrocarbon (Hydrogenated Polyisobutene) on the intact and abraded skin of rabbits. The undiluted test material was a clear, viscous liquid. Six healthy New Zealand albino rabbits were clipped free of hair over approximately 10% of their body surface (dorsal and ventral surfaces from scapular to pelvic area). Two 2.5-cm^2 test sites were delineated; one remained intact and the other was abraded with a needle.

Test material (0.5 ml) was placed on each site and occluded for 24 h. The patches were then removed and the test sites were wiped clean to prevent further exposure. The sites were evaluated 24 and 72 h after initial exposure. At 24 h, all abraded and intact sites had well-defined erythema. By 72 h, the degree of erythema was reduced to very slight on two abraded and one intact site. One intact site was clear of irritation. No edema was observed in any of the animals. All animals appeared active and healthy throughout the study. The primary skin irritation score was 1.8 (Product Safety Labs 1987c).

Fanning Corporation (1998b) investigated the primary dermal irritation and corrosion in rabbits. Six female New Zealand white rabbits were dosed dermally with 0.5 ml Poly Iso 6-50-DN (clear liquid). The left side of each animal was abraded with a bent tip needle. Three abrasions, about 2 to 3 cm apart, extending the length of the exposure site were made. The abrasions were deep enough to penetrate the stratum corneum, but not deep enough to cause bleeding. The right side of each animal remained intact. The test substance was applied to one intact and one abraded site on the clipped back of each rabbit for a total dose of 1.0 ml per rabbit. The sites were occluded for 24 h, followed by evaluations for skin reactions by the Draize method at 24 and 72 h after dosing. The body weights were recorded pretest (2.0 to 2.4 kg).

Erythema and edema was recorded as absent to very slight at 24 h post dose, and were absent at 72 h. There were no abnormal systemic signs noted during the observation period. The primary irritation index was 0.38, therefore, the authors concluded that the test substance is not a dermal irritant as defined in 16 CFR 1500.41 and 16 CFR 1500.3 (c)(4) (Fanning Corporation 1998b).

Fanning Corporation (1998e) determined the irritation potential of Poly Iso 4-50-EN (clear liquid) in 6 New Zealand white rabbits. The backs and sides of each animal were clipped free of hair. The left side of each animal was abraded. Three abrasions, about 2 to 3 cm apart, were made that extended the length of the site. The abrasions were deep enough to penetrate the stratum corneum, but not enough to cause bleeding. The material was applied to one intact and one abraded site on the clipped back of each rabbit at a dose of 0.5 ml. Therefore, the total per rabbit was 1.0 ml. For 24 h, the sites were occluded and skin reactions were evaluated using the Draize scale at 24 and 72 h following dosing. The primary irritation index was calculated to be 0.96. Animal body weights were recorded pretest (2.2 to 2.7 kg).

Erythema, absent to very slight at 24 h post dose, was absent by 72 h. Edema, absent to slight at 24 h post dose, was absent by 72 h. Diarrhea, noted in one animal, was the only abnormal systemic sign found during the observation period. Therefore, the authors concluded that the Poly Iso 4-50-EN is not a dermal irritant as defined in 16 CFR 1500.41 and 16 CFR 1500.3 (c)(4) (Fanning Corporation 1998e).

Dermal Sensitization

CTFA (1973c) submitted unpublished data on sensitivity testing in guinea pigs using Polysynlane. Ten male white guinea pigs, weighing 300 to 500 g, were used in the study. The test substance was injected intradermally in an area of skin on the back and flanks that were clipped free of hair. The first dose was 0.05 ml of a 0.1 dispersion in sesame oil. The following nine injections were 0.1 ml, given three times weekly, for a total of 10 doses. After a 14-day rest period, the animals were then given a challenge dose of 0.05 ml. Twenty-four hours after each injection, the reactions were observed. Erythema and edema were observed after most inoculations. The author(s) of this study concluded that under the test conditions described, Polysynlane is not a sensitizing material.

Davis (1976) stated that Polysynlane (Hydrogenated Polyisobutene) was nonsensitizing when injected intradermally in guinea pigs after 10 injections given over a week followed by a challenge injection after 14 days.

CTFA (1981) determined the allergic contact sensitization potential of Hydrogenated Polyisobutene on the skin of female guinea pigs. The Magnusson-Kligman maximization procedure consisted of four or five stages—induction phase, dose range phase, booster phase, challenge phase I, and challenge phase II (if necessary). The vehicle used for induction was mineral oil.

A week after the 5.0% induction injections, a topical booster with a slightly irritating concentration of test material in petrolatum was administered. The control animals received petrolatum only. Sodium lauryl sulfate (SLS) (10% in petrolatum), if necessary, was applied to the induction site of animals in groups with nonirritating test material 24 h prior to material booster. Two weeks later, the animals were challenged with a subirritating concentration of the test material, as well as a level 50% of the subirritating concentration at specific sites. Petrolatum was the challenge vehicle. The guinea pigs were all shaven 3 h before grading. The second challenge occurred 1 week after challenge phase I. Only those guinea pigs that were sensitized, as well as the appropriate controls, were challenged with 100% concentration of the test material. The authors concluded that

Hydrogenated Polyisobutene is a nonsensitizer. There were no reactions observed and the irritation index was 0.0 in both challenge phases I and II (CTFA 1981).

According to CTFA (2006b), laboratory tests with approved surrogate systems/animals revealed that skin contact testing showed only slight irritation (primary dermal irritation score [PDIS] of 1.5/8.0). There were no observed sensitivity reactions. Also, acute dermal irritation testing indicated that polybutenes are practically nontoxic because the LD_{50} is greater than 10,250 mg/kg. Lastly, polybutenes are relatively nontoxic when tested in an acute oral test (LD_{50} > 34,600 mg/kg, rat).

Comedogenicity

Product Safety Labs (1987d) studied the comedogenic potential of Permethyl 104A/105A Aliphatic Hydrocarbon (Hydrogenated Polyisobutene). Three adult New Zealand white rabbits were treated with the undiluted test material following an 8-day adaptation period. The test material was applied to the internal base of the right ear of each animal daily on 5 consecutive days per week for 3 weeks. The left ear was untreated and served as the negative control. The test material was applied at approximately the same time each day. The negative-control ears were scored for hyperkeratosis and comedone formation. There were no signs of hyperkeratosis or comedone formation during weeks 1 and 2. At week 3, two treated ears showed signs of hyperkeratosis. One ear remained clear. Histological examination revealed no signs of follicular hyperkeratosis on the treated, untreated, or control ears of any rabbits.

GENOTOXICITY

Aarsaether et al. (1987) studied the ability of different insulating fluids to induce transformation in the Syrian hamster embryo (SHE) cell transformation assay and to enhance 3-methylcholanthrene–induced transformation of C3H/10T1/2 cells. Cultures were grown in Dulbeccos's modified Eagle's medium (DMEM), supplemented with 10% fetal bovine serum at 37°C in a 10% CO_2 atmosphere.

A feeder layer of 6×10^4 lethally x-irradiated SHE cells (4500 rad) was seeded in 3 ml complete medium (DMEM supplemented with 15% fetal bovine serum [FBS], 2 μg/ml insulin, no antibiotics). The next day, 150 target cells in 1 ml medium were added. After 24 h, the chemical to be studied was added in 4 ml medium and the cells were incubated for 5 days. The medium was then removed, the dishes were rinsed with phosphate-buffered saline (PBS), and the same chemical was added in 6 ml complete medium. Two days later, the dishes were washed with PBS, and the colonies fixed with methanol and stained with Giemsa before counting and examination.

Morphological transformation is defined as altered colony morphology consisting of criss-crossing and piling up of cells. A test was considered positive when a transformation frequency higher than 1% was obtained.

In the C3H/10T1/2 transformation assay, the mouse embryo fibroblast cell line was obtained and cells between passages 7 and 12 were used. These cells are highly susceptible to postconfluent inhibition of cell division and do not form tumors in mice under normal test conditions. The cells were grown in basal Eagle's medium supplemented with 10% heat-inactivated FBS and incubated at 37°C in a humidified atmosphere of 5% CO_2 in air.

The cells harvested from logarithmically growing stock cultures were used to innoculate petri dishes. After 24 h of incubation, 0.37 μM 3-methylcholanthrene (MCA) was added to the dishes. The medium was removed and new medium added after 24 h. The cells were then exposed to an oil-containing Polyisobutene dissolved in acetone from day 5 throughout the remaining test period. The cell culture medium was changed twice weekly. The cells were fixed and stained after 6 weeks of incubation. The Polyisobutene used was primarily composed of branched isomers of dodecene, hexadecene, and eicosene. The T3700 fluid was a mixture of a polyisobutene-based oil and a mineral oil. The fluids were dissolved in acetone. The final acetone concentration was always less than 0.2% in the SHE cell transformation assay and 0.5% in the C3H/10T1/2 assay. These concentrations of acetone have been shown not to affect the transformation frequencies.

Table 13 gives the cytotoxic effects of Polyisobutene and T3700 fluid for both SHE cells and C3H/10T1/2 cells. The authors concluded that there was low cytotoxicity.

Table 14 gives the transformation data using SHE cells. The authors concluded that there was no transformation activity of Polyisobutene and T3700 fluid.

In the two-stage transformation assay of 3-methylcholanthrene–induced transformation of C3H/10T1/2 cells, promoter activity was obtained with a Polyisobutene-based oil as shown in Table 15 (Aarsaether et al. 1987).

TABLE 13
Cytotoxic effects of Polyisobutene and T3700 fluid in cell transformation study (Aarsaether et al. 1987).

Treatment		Relative plating efficiency (% ± SD)	
Agent	Concentration (μg/ml)	SHE cells	C3H/10T1/2 cells
Control	—	100 ± 10	100 ± 15
Polyisobutene A	67	105 ± 9	—
	200	105 ± 6	—
	50	—	100 ± 37
T3700[a]	67	100 ± 14	—
	200	90 ± 5	—
MCA	0.37 μM	—	72 ± 30
	3.70 μM	—	50 ± 22

[a]Mixture of a Polyisobutene-based oil and a mineral oil.

TABLE 14
Transformation of SHE cells by Polyisobutene and T3700 fluid (Aarsaether et al. 1987).

Treatment	Concentration (μg/ml)	Number of colonies	Plating efficiency	Transformed colonies	Transformation frequency (%)
Control	—	283	21	0	0.0
Polyisobutene A	67	297	22	0	0.0
	200	297	22	0	0.0
T3700	67	283	21	3	1.1
	200	256	19	0	0.0
Benzo [a]pyrene[a]	0.005	338	25	4	1.2
	0.05	216	16	6	2.8

[a]Positive control.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Polybutene

Elder (1982) reported on a three-generation reproductive study in Charles River albino rats that ingested Polybutene H-100. The animals were divided into three groups (8 males and 16 females per group) and fed Polybutene in the following three dosage levels in the diet: 0 ppm (control), 800 ppm, and 20,000 ppm. Except for the test (F_2) male parental animals that were fed 20,000 ppm Polybutene, none of the animals in successive generations differed from controls with regard to weight gains. The F_2 male parental animals showed slight weight depression, although their growth patterns were still within the normal range. Differences in mortality or reaction or in gross or microscopic histology could not be correlated with the ingestion of Polybutene. Organ weight and ratio data revealed a few intergroup differences, which were considered "random effects."

Reproductive performances (mating indices, fertility indices, incidence of pregnancy and parturition, and gestation times) of control and test animals were essentially comparable. Lactation indices ranged from 83% to 94% in the control group and from 89% to 99% in the 20,000 ppm. In all three generations, there were no significant differences between test and control animals with regard to litter size, the number of stillborn, and the number of viable pups during lactation. The survival, body weights, and reactions of test animals were comparable to those of controls (Elder 1982).

CARCINOGENICITY

Polyisobutene

Iversen (1990) conducted a study to determine the tumor promotion effects of certain oils used for the impregnation of paper-insulated power cables and their synthetic alternatives, including Polyisobutene.

Male and female *hr/hr* Oslo strain mice (32 mice in each treatment group) were used in one of two protocols. In a two-stage protocol, 7,12-dimethylbenz(α)anthracene (DMBA) in acetone (either 51.2 or 25.6 μg of DMBA) was applied to the skin of these hairless mice one time, followed by application twice per week for 18 months of 40% or 20% Polyisobutene in acetone. In a complete tumorigenesis protocol, 80%, 40%, or 20% Polyisobutene was applied to the mouse skin twice a week for 18 months. The

TABLE 15
Promoter activity of insulation oils in two-stage transformation of C3H/10T1/2 cells (Aarsaether et al. 1987).

Treatment			Transformation		
MCA[a] concentrations (μM)	Promoter	Component concentration	Total no. of dishes scored	Total no. of dishes with type III foci	Dishes with type III foci (%)
		Controls			
0	Acetone	0.5%	96	1	1
3.7	Acetone	0.5%	72	9	12.5
0.37	Acetone	0.5%	86	2	2.4
0.37	TPA	0.17 μM	85	43	50
		Polyisobutene			
0.37	Polyisobutene-based oil	50 μg/ml	41	11	26.8

[a]MCA = 3-methylcholanthrene.

TABLE 16
Final number of tumors and lesions in mice given DMBA followed by Polyisobutene (Iversen 1990).

Type of tumor/lesion	51.2 μg DMBA once (normalized to 32 mice)	51.2 μg DMBA then Polyisobutene 2×/ week for 18 months		25.6 μg DMBA once (normalized to 32 mice)	25.6 μg DMBA then Polyisobutene 2×/ week for 18 months	
		40%	20%		40%	20%
Papillomas	17/9	5/4	18/8	2/2	0	6/5
Carcinomas	1/1	2	1	1	0	2
Sarcomas	1/1	0	0	0	0	0
B cell lymphoma	0	2	0	0	1	1
Lymphoma NOS	0	1	0	0	1	1
Reticulosis	0	1	0	1	1	2
Lung adenomas	1/1	1/1	3/3	1/1	4/4	4/4
Lung adenocarcinoma	1	0	0	0	0	0
Hepatoma	0	0	1	0	0	0
Ovary adenocarcinoma	0	0	1	0	0	0
Teratoma of the ovary	0	0	0	0	0	0
Kidney adenocarcinoma	0	0	0	0	0	0
Spindle cell carcinoma	0	0	0	0	0	0
Amyloidosis	1	0	1	1	3	0
Skin toxicity	0	0	(++)	0	(+)	(+)
Mast cell hyperplasia	0	0	(+)	0	(+)	0
Pigment leakage	0	0	0	0	0	0
Pronounced hyperplasia	0	0	(+)	0	(+)	(+)

Polyisobutene (Polyisobutylene, as given by the author) used had an average molecular weight of 250 and a viscosity of 5 mm^2/S (at 50°C).

Controls received acetone alone twice a week for 50 weeks (32 animals—negative control), acetone alone one time (32 animals—second negative control), 51.2 μg DMBA alone (48 animals—positive control), or 25.6 μg DMBA alone (48 animals—positive control). In controls and treatment groups, the application volume was 100 μl. Data were also reported on 128 positive, historical control hairless mice that had received 51.2 μg DMBA alone.

After treatment, animals were returned to their cages, where they were observed to lick each other. Also a noticeable odor attributed to vapor from the fluid painted on the skin was present in the cages for 2 to 4 h.

Table 16 shows the final number of tumors and lesions in mice given DMBA once followed by chronic exposure to Polyisobutene in acetone. The author concluded that treatment with Polyisobutene oil alone had no tumerogenic or carcinogenic effect. In the studies with DMBA pretreatment followed by Polyisobutene exposure, the author stated that no evidence of tumor promotion was found, and that 40% Polyisobutene oil may have reduced the number of tumors in comparison with DMBA alone or DMBA and 20% Polyisobutene oil.

The author also stated that Polyisobutene increased the death rate at higher doses, but no data were provided. Although the original study design was to evaluate skin tumor formation only, observations of skin irritation at the site of application, amyloidosis, and swelling of the lymph nodes caused the author to begin recording these findings and conducting necropsies on all the animals. However, upon reviewing the amended experimental design, the CIR Expert Panel concluded that the protocol did not support any conclusions of systemic carcinogenicity.

CLINICAL ASSESSMENT OF SAFETY

Dermal Irritation

Hydrogenated Polyisobutene

CTFA (1974a) submitted results of a 72-h primary skin irritation study aimed to determine whether the following ingredients produced irritation in human skin: 100% Polysynlane (Hydrogenated Polyisobutene); 60% Polysynlane–40% petrolatum; 40% Polysynlane–60% petrolatum; 20% Polysynlane–80% petrolatum; 100% squalene (Robane); 40% squalene–60% petrolatum; 20% squalene–80% petrolatum; and 100% petrolatum (control sample). Twenty-five male and female subjects, ages 11 to 59, were used for the study. They were patched with

the eight test products under occlusive patch for 72 h. There were no reactions in any of the subjects for each of the eight samples. Therefore, the author(s) concluded that within the limits set forth in this study, none of the products produced primary skin irritation.

CTFA (1974b) submitted results of a 24-h primary skin irritation test using (a) Polysynlane (as is), (b) 50% concentration of Polysynlane in olive oil, and (c) olive oil (as is). Fifty-one male and female subjects, ages 18 to 59, participated in the study. The closed patch test was performed using the forearm's flexsure site of the subjects. The patches were removed after 24 h and the site was observed for irritation. Polysynlane, under these test conditions, produced no skin irritation in any of the subjects.

Davis (1976) reported that Polysynlane (Hydrogenated Polyisobutene), tested side by side with synthetic and natural squalene in 25 men and women, produced no dermal irritation in a 72-h primary skin irritation patch test.

A Clinical Evaluation Report submitted by CTFA (1999) summarized a 24-h single-insult patch testing procedure in humans with a lip gloss containing 66.11% Hydrogenated Polyisobutene. The control material was a lip shape and shimmer gloss and the test material was a lip polish—glaze (clear). The concentration used was considered full strength. No irritancy was observed as a result of test or control samples (Table 17).

Dermal Sensitization

CTFA (1974c) submitted a study that investigated whether the following ingredients caused any allergenic sensitization of the human skin: (a) 100% Polysynlane, (b) 20% Polysynlane–80% petrolatum, (c) 100% squalene, and (d) 20% squalene–80% petrolatum. Two-hundred seven subjects participated in the study; however seven subjects dropped from the study for unknown reasons. The subjects were patched with the 4 materials using the Draize repeat-insult patch test procedure. The materials were applied to the skin of the upper back and covered for occlusive patching. The occlusive insults were applied every Monday, Wednesday, and Friday for 3.5 weeks, for 10 insults. An 11th insult was applied following a 14-day rest period. The site was scored 48 h later. Note, a modification of the maximization test was performed on subjects 1 through 55. The outer layer of skin was stripped away before the application of each patch. Patch products were then applied to the stripped areas. Polysynlane (100%), Polysynlane (20% with 80% petrolatum), squalene (100%), and squalene (20% in 80% petrolatum) did not produce any allergic sensitizing potential.

Davis (1976) stated that Polysynlane (Hydrogenated Polyisobutene), tested side by side with natural squalene in a panel of 200 men and women, produced no dermal irritation in a modified Draize-Shelanski repeat-insult patch test.

CTFA (1996a) performed repeat-insult patch tests to evaluate the primary irritancy/sensitization of the following coded test materials: JMB-423 (containing 4% Hydrogenated Polyisobutene) and JMB-426 (containing 1.44% Hydrogenated Polyisobutene). The Hydrogenated Polyisobutene used in these coded products has an average molecular weight of 370 and contains six to seven isobutene units. Although there were initially 61 male and female volunteers, only 54 subjects, ages 18 to 69, completed this study. Seven dropped out of the study for various reasons, one being due to severe tape reactions.

All of the test samples were liquids, which, when applied to the patch with a dropper, contained approximately 0.2 to 0.3 ml of the material. Each of the participants was patched with a total of six patches on the lateral part of the upper arm (three sites per arm); the patch sites were randomized using the standard Latin square. The test period was five weeks. During weeks 1 and 2, eight induction applications were made, followed by a 2-week hiatus. A single challenge application of each formulation was made on sites adjacent to the induction sites in week 5.

Reactions were scored 24 h after each induction application (about 5 to 15 min after patch removal) and 24, 48, and 72 h following the challenge phase. Evaluation of the challenge patch was made at 96 h. Reactions were scored as 0 = no reaction; ± = questionable erythema; 1+ = slight erythema; 2+ = moderate erythema; 3+ = severe erythema; 4+ = edema and/or papules (with/without erythema); and 5+ = vesticulation (with/without edema and erythema). There were no reactions >1+ during the induction or challenge phases of this study (CTFA 1996a).

CTFA (2003a) submitted a study designed to determine the irritating and sensitizing potential of a makeup remover containing 51% Hydrogenated Polyisobutene on human skin. The study was a modified repeat-insult patch test conducted under double-blind conditions. One hundred ten subjects (35 male, 75 female), ages 18 to 76, participated in the study. The investigation consisted of nine sequential 24-h induction applications and two concurrently conducted 24-h challenge applications, one on the induction site and one on a naive site (left side of the back).

TABLE 17
Results of a single human patch test using lip gloss containing Hydrogenated Polyisobutene (CTFA 1999).

Test material concentration	Subjects	Irritation score*									
		0	±	1	1+	2	2+	3	3+	4	PII
66.11%	19	17	2	0	0	0	0	0	0	0	0.05
0% (control)	19	18	1	0	0	0	0	0	0	0	0.03

*Skin staining noted. Erythematous response were read "through" the stain.

During the initial phase, the skin sites were graded and recorded on Wednesdays, Fridays (24 h following patch removal), and Mondays (48 h following patch removal). During the challenge phase, the skin sites were graded after the patches had been removed and then again 24 and 48 h later.

No responses were seen in 109 of the 110 subjects; however, intense redness was observed in 1 of the subjects. Further exposure to this material was halted for this individual for the remainder of the induction period. During the challenge phase, there were no signs of irritation or sensitization in any of the subjects, including the one subject with intense redness in the induction phase. The author therefore concluded that the test material was found to be a nonirritant and nonsensitizer under the conditions of this study (CTFA 2003a).

Ivy Laboratories (2004a) evaluated the contact-sensitizing potential of a face powder containing 17.1% Hydrogenated Polyisobutene by means of the maximization test. Twenty-eight healthy volunteers (17 male, 11 female), ages 20 to 55, participated in this study; however, only 25 completed the study (2 dropped from study; 1 voluntarily withdrew). The study included an induction phase and a challenge phase. Patches were applied to the upper outer arm, volar forearm, or back of each subject.

During the induction phase, approximately 0.05 ml of aqueous SLS (0.25%) was applied to a specific site and the patch was left on for 24 h. After 24 h, the patch was removed and 0.05 ml of the test material (bronzer) was applied to the exact same site and covered (induction patch). The patch remained in place for 48 h (72 h when placed over a weekend). After removal, the site was examined for irritation. If there was no irritation present, a 0.25% aqueous SLS patch was reapplied to the same site for 24 h, followed by reapplication of a fresh induction patch with the test material to the same site. This procedure, 24-h SLS pretreatment followed by 48 h of test material, continued for five exposures. If at any point irritation developed during the induction phase, the 24-h SLS pretreatment patch was omitted and only the test material was reapplied to the same site after a 24-h rest period, during which no patch was applied.

After the 10-day rest period, the subjects were challenged with a single application of the test material to a new skin site on the opposite arm, forearm, or side of back in order to determine if sensitization had developed. Prior to the challenge, pretreatment with SLS was performed. Approximately 0.05 ml of a 5.0% aqueous solution was applied to a fresh skin site and covered. The SLS patch remained in place for 1 h. After removal, the test material was applied to the same site and the challenge patch remained in place for 48 h. After 48 h, the patch was removed and the site graded 1 h later and again at 24 h.

There were no adverse reactions observed in any of the subjects during the induction phase. During the challenge phase, there were no instances of contact allergy present at either 48 or 72 h. The authors concluded that under the conditions of this test, the test sample labeled bronzer did not have a contact-sensitization potential, and is therefore unlikely to cause sensitivity reactions under normal use (Ivy Laboratories 2004a).

Ivy Laboratories (2005) evaluated the contact sensitization potential of a topical coded product (eyeshadow containing 10.5% Polyisobutene) in human, by means of the maximization assay. Twenty-eight (4 male and 24 female) volunteers, ages 18 to 58 years, participated in the study. Patches were applied to the upper outer arm, volar forearm, or back of each subject. The overall test consisted of two phases—an induction phase and a challenge phase.

During the induction phase, approximately 0.05 ml of aqueous SLS (0.25%) was applied to a certain site and the patch remained in place for 24 h. After 24 h, the SLS patch was removed and 0.05 ml of the coded test material (1003213-001, Pencil) was applied to the exact same site. The induction patch remained in place for 48 h (or 72 h when placed over the weekend). Once the patch was removed, the site was examined for irritation. If there was no irritation present, a 0.25% aqueous SLS patch was reapplied to the same site for 24 h, followed by reapplication of a fresh induction patch with the test material to the same site. This sequence, 24-h SLS pretreatment followed by 48 h of test material, was continued for a total of five induction exposures.

No adverse reactions were found in any of the subjects during the induction phase.

During the challenge phase, the subjects were challenged with a single application of the test material to a new skin site on the opposite arm, forearm, or side of back in order to determine if sensitization had developed. This phase followed a 10-day rest period after the last induction patch application. Prior to the challenge, pretreatment with SLS was performed. Approximately 0.05 ml of a 5.0% aqueous solution was applied to a fresh skin site. The SLS patch remained in place for 1 h. Then, it was removed and the test material was applied to the same site. The challenge patch was covered and left in place for 48 h, followed by removal and grading 15 to 30 min later and again 24 h later for any reaction.

There were no instances of contact allergy observed at either 48 or 72 h following application of the challenge patches. According to the authors, the test sample labeled pencil does not possess a contact-sensitization potential and is therefore not likely to cause reactions under normal use conditions (Ivy Laboratories 2005).

Ivy Laboratories (2000) evaluated the contact-sensitization potential of lip gloss containing 66.11% Hydrogenated Polyisobutene in human skin by means of the maximization assay. Twenty-seven healthy male (8) and female (19) volunteers, ages 18 to 52, participated in the study. One male subject did not want to continue following the third induction exposure and voluntarily withdrew from the study. Patches were applied to the upper outer arm, volar forearm, or back of each subject. The test consisted of an induction phase and challenge phase.

During the induction phase, approximately 0.1 ml of aqueous SLS (0.25%) was applied to a designated site and the patch was

allowed to remain in place for 24 h. The patch was removed after 24 h and 0.1 ml of the test material (lip gloss) was applied to the same site and covered (induction patch). The induction patch remained in place for 48 h (or 72 h when placed over a weekend). It was then removed and examined for irritation. If there was no irritation present, a 0.25% aqueous SLS patch was reapplied to the same site for 24 h, followed by reapplication of a fresh induction patch with the test material to the same site. This procedure was continued for a total of five induction exposures. If irritation developed at any point and time during the induction phase, the 24-h SLS pretreatment patch was eliminated and only the test material was reapplied to the same site after a 24-h rest period, during which no patch was applied.

After the 10-day rest period, the subjects were challenged with a single application of the test material to a new skin site on the opposite arm, forearm, or side of back to determine if sensitization had developed. Prior to the challenge, pretreatment with SLS was performed. Approximately 0.1 ml of a 5.0% aqueous solution was applied to a fresh test site and covered with occlusive tape. The SLS patch remained in place for 1 h. When removed, the test material was applied to the same site. The challenge patch remained in place for 48 h. The patch was then removed, and the site graded 1 h and again 24 h later for any reaction.

There were no adverse or unexpected reactions observed in any of the subjects during the induction phase. Likewise, no instances of contact allergy were recorded at 48 or 72 h following application of the challenge patches. The authors concluded that under the test conditions, the test sample labeled lip gloss does not possess a detectable contact-sensitizing potential and hence is not likely to cause contact sensitivity reaction under normal use (Ivy Laboratories 2000).

Ivy Laboratories (2004b) used the same protocol as above using lip gloss containing 31.65% Hydrogenated Polyisobutene. Twenty-six healthy, adult volunteers of both sexes participated in the study; however, only 25 completed the study (1 female subject failed to return to the laboratory following the first exposure and dropped from the study). There were 23 females and 3 males, ages 18 to 59. There were no instances of contact allergy observed at either 48 or 72 h following application of the challenge patches.

The authors concluded that under the conditions of this study, the test sample labeled lip gloss does not possess a detectable contact-sensitizing potential, and is therefore unlikely to cause contact sensitivity reactions under normal use conditions (Ivy Laboratories 2004b).

Photoallergy

CTFA (1996c) reported that three products, JMB-442 (4% Hydrogenated Polyisobutene), JMB-441 (1.44% Hydrogenated Polyisobutene), and JTP-81, were evaluated to determine their ability to induce a photoallergic reaction in the skin of normal volunteer subjects under semiocclusive patch conditions. A distilled water patch served as a control. Thirty subjects, ages 18 to 69, completed the study. The experiment consisted of three phases—induction, rest, and challenge. All patch sites were located on the back in columns to the right and left of the spine (one side for irradiated sites and opposite for nonirradiated sites). For the sites designed for irradiation, ultraviolet light exposure was performed within 10 min of patch removal.

During the induction phase (weeks 1 to 3), a series of 12 applications of the test materials was made to a naive test site. The applications were made on Monday through Thursday of each of 3 consecutive weeks. The patches were removed approximately 24 h after application and site responses were evaluated and scored. After the removal of the induction patches on Tuesday and Thursday, the test sites were exposed to approximately twice the minimum erythemic dose and 6 to 8 joules of ultraviolet A (UVA).

During the rest period (weeks 4 and 5), no applications of test materials were made for 2 weeks. The challenge phase in week 6 involved a single application of duplicate contact patches of the test materials made to naive sites. One of each of the pair of patches was removed after approximately 24 h and was exposed to UVA (16 to 20 joules) within 10 min. The other duplicate patch was then removed. All sites were evaluated and scored approximately 1, 24, 48, and 72 h following the removal of patches.

Under the conditions employed in this study, no evidence of photoallergic reactions was found to JMB-441, JMB-442, and JTP-81 (CTFA 1996c).

Phototoxicity

CTFA (1996b) determined the phototoxic potential of the foundations/concealers JMB-442 (4% Hydrogenated Polyisobutene), JMB-441 (1.44% Hydrogenated Polyisobutene), and a blank patch under UVA light source (320 to 400 nm). The lamp output ranged from 3.5 to 3.9 mW/cm^2 during the study. Irradiation time was increased to 20 min on all subjects to ensure adequate UVA exposure. There were 26 fair-skinned volunteers between the ages of 18 and 69 who completed this study. One subject was dropped from the study due to an adverse reaction. This subject developed hives 5 h after the patches were applied on day 1.

Four sites on the right side of the back of each subject was selected for the phototoxic evaluation and each subject was patched with the three test materials, which were randomized by use of the Latin square. Duplicate patches (using the same randomization) were applied to the left side of the back and served as the nonirradiated controls. The test period was 4 days.

On day 1, patches were applied and subjects were instructed that the patches were to remain in place and dry for approximately 24 h (until they returned to the laboratory). On day 2, the patches on the sites designated to be irradiated were removed at the laboratory and examined for irritation. The sites were treated with approximately 0.1 g of the test sample, which were

allowed to dry for 5 to 10 min. The excess, if any, was gently removed by blotting and the sites were irradiated at a distance of 10 cm for 15 min. On the nonirradiated control sites, patches remained in place until after the light exposure. Additionally, these sites were covered with a towel to ensure complete exclusion of light. After irradiation, the exposed sites and the nonirradiated controls were evaluated for irritation. The subjects were instructed to avoid exposing the treated areas to sunlight or excessive amounts of indoor lighting for the remainder of the study.

The scoring system used was the same 0 to 5+ scale described earlier. On days 3 and 4, follow-up evaluations for irritancy were made. There were no reactions greater than ± to any of the samples tested and thus no indication of primary irritancy or phototoxicity (CTFA 1996b).

Ocular Toxicity

CTFA (1996d) evaluated the ocular irritation potential of three shades of concealer (JMB-428, JMB-429, and JMB-442) when used for 29 days. JMB-442 consisted of 4% Hydrogenated Polyisobutene. Fifty-nine subjects, ages 18 to 55 years, completed the study. Thirty-two wore contact lenses. On day 1, all of the prospective candidates underwent screening of the eyes and skin, as well as vision exams. Eye area skin and the eyes were graded on a scale of 0 to 3 (0 being no reaction and 3 the most extreme reaction).

After cleansing and prior to applying foundation, the subjects were instructed to apply the concealers sparingly under the eyes to cover dark circles at least once daily. Contact lens wearers were required to insert contact lenses prior to applying the concealer and no other concealers were to be worn throughout the study. After 1, 2, and 3 weeks (days 8, 15, and 22) of use, all of the subjects were evaluated for irritation. For the three formulations, there were no adverse reactions during this study. All subjects had 0's on all ophthalmologist gradings. Slight irritation was noted on day 8 for one of the subjects, and there were three reports of itching and eye irritation during the final examination. Overall, there was no observed ocular irritation and visions stayed the same or within normal limits throughout the course of the study (CTFA 1996d).

CTFA (2003b) assessed the eye irritancy of a product containing 10% Hydrogenated Polyisobutene (Permethyl 104). The subjects were five healthy, adult females who experienced strong stinging to 10% lactic acid and/or who had a history of self-assessed sensitive skin or sensitive eyes. The author noted that lactic acid stingers have more reactive skin and are more likely to respond to mild irritants. The product was applied to the exterior skin around both eyes on the morning and afternoons of 5 weekdays. As a result, no subject experienced signs of irritation during the 5 days of treatment. Therefore, this product was concluded by the authors to be nontoxic to the external eye area when applied twice a day for 5 days to lactic acid stingers and/or those with sensitive skin or eyes.

Case Report

Parslew et al. (1996) reported on the case of a 48-year-old woman who was diagnosed as having Crohn's disease. The patient underwent a total colectomy and ileostomy following numerous fistulae. Briefly after wearing her stoma bag, she developed an eroded eczematous area around the stoma. A skin biopsy indicated dermatitis and excluded Crohn's disease.

When the patient discontinued use of the stoma bag, symptoms would disappear within 10 to 14 days. However, when she began reusing the stoma bag, symptoms would consistently reappear within 2 days. The initial patch testing showed reactions (++ at day 4) to colophony, benzoyl peroxide, and the adhesive ring of the bag. Concerns involving the constituents of the ring revealed that colophony and benzoyl peroxide were absent. The ring itself consisted of a hydrocolloid laminated with a polyethylene film. The hydrocolloid component was made up of a citrus-derived pectin of edible food grade, sodium carboxymethylcellulose, gelatine BP, and Polyisobutene.

The patch test carried out with Polyisobutene brought forth a contact urticaria after 10 min and a ++ eczematous reaction at day 4. Polyisobutene (diluted to 0.1%, 0.5%, 1.0%, and 5% solutions in ether) was tested on the patient and five control subjects. There was a positive reaction to 5% Polyisobutene in ether with the patient, but negative reactions in the five control subjects. The authors note that irritant reactions to stoma appliances and drainage fluid are common, but allergic reactions are rare (Parslew et al. 1996).

SUMMARY

Polyisobutene and Hydrogenated Polyisobutene are both homopolymers of isobutene. Polyisobutene has a double bond in its end unit, whereas the final carbon is fully hydrogenated in Hydrogenated Polyisobutene. These ingredients are produced in a wide range of molecular weights. Polybutene is a chemically related cosmetic ingredient previously determined to be safe as used in cosmetic products.

Polyisobutene is used in cosmetic products as a binder, film former, and nonaqueous viscosity-increasing agent. In addition to its cosmetic uses, Polyisobutene is also used in a number of noncosmetic applications such as adhesives, sealants, coatings, lubricants, and plasticizers. Hydrogenated Polyisobutene has an additive function, which improves the feel of and generally upgrade the spreading and penetrating properties of lotions based on mineral oil and petrolatum. It functions as a skin-conditioning agent—emollient and nonaqueous viscosity-increasing agent, with a wide range of uses in cosmetic formulations. Furthermore, Polybutene functions as a binder, epilating agent, and nonaqueous viscosity-increasing agent in a variety of cosmetic products.

The water solubility was estimated at 5.6×10^{-3} ng/L (0.0056 parts per trillion) for the Indopol® (trade name Polybutene) and the Panalane® (trade name Hydrogenated Polyisobutene).

Acute oral toxicity testing with mice caused no deaths with a maximum of 89.608 g/kg of Polysynlane (trade name Hydrogenated Polyisobutene mixture).

Oral toxicity using a single dose of 5 g/kg Permethyl 104A/105A Blend Aliphatic Hydrocarbon (trade name Polyisobutene) caused no deaths in rats; however, all of the animals appeared lethargic after dosing.

Single-dose oral toxicity studies in rats dosed with two Hydrogenated Polyisobutenes (Poly Iso 6-50-DN and Poly Iso 4-50-EN) at 5.0 g/kg body weight caused wetness in the anogenital area on the day of dosing. All animals survived the 5.0 g/kg oral dose and both Hydrogenated Polyisobutenes were found to be nontoxic. The authors of these studies also concluded that the LD_{50} is greater than 5.0 g/kg body weight.

A 2-year chronic oral toxicity study of Polybutene H-100 (75% concentrate) in Charles River albino rats given up to 20,000 ppm Polybutene blended into their regular diets revealed no gross or microscopic pathological changes that could be correlated with Polybutene ingestion. No significant differences were found after 24 months of feeding in the body weights or weight of food consumption, hematological results, urology, or tumor formation between the animals fed Polybutene and those that were not. In the 20,000 ppm group, three out of six males that died between weeks 17 and 24 exhibited hematuria.

In a 2-year chronic oral toxicity study of Polybutene H-100 (75% concentrate) in Beagle dogs, it was found by the authors that daily oral administration of Polybutene H-100 to pure-bred Beagle dogs over a period of 2 years at doses up to 1000 mg/kg/day caused no abnormalities in body weight, food consumption, survival, behavioral patterns, hematology, blood chemistry, urinalysis, liver function, gross and histopathologic examinations, or organ weights and ratios.

A three-generation reproductive study in Charles River albino rats that ingested Polybutene H-100 up to 20,000 ppm demonstrated that, except for the test (F_2) male parental animals that were fed 20,000 ppm Polybutene, none of the animals in successive generations differed from controls with regard to weight gains. The F_2 male parental animals showed slight weight depression, although their growth patterns were still within the normal range. In all three generations, there were no significant differences between test and control animals with regard to litter size, the number of stillborn, and the number of viable pups during lactation. The survival, body weights, and reactions of test animals were comparable to those of controls.

A 7-day eye irritation study on rabbits using 0.1 ml Polysynlane (trade name Hydrogenated Polyisobutene) produced no eye irritation in any of the washed or unwashed rabbit eyes.

Irritant and corrosive effects were examined using a single instillation of Permethyl 104A/105A Blend Aliphatic Hydrocarbon (trade name Polyisobutene) into rabbit eyes. No corneal or iridial damage was recorded in the study. One eye had irritation to the conjunctivae by 72 h, which was present as slight hyperemia.

An unknown concentration of Prisorine 3758 (trade name Hydrogenated Polyisobutene) instilled into the right eyes of six rabbits produced a score of 1 on the Draize scale. No other effects were observed.

When 0.1 ml Poly Iso 6-50-DN (trade name Hydrogenated Polyisobutene) was instilled into the conjunctival sac of rabbit eyes, the test material caused slight conjunctival irritation in 33% of eyes which cleared up by day 2. The authors determined that Poly Iso 6-50-DN is not an eye irritant. Poly Iso 4-50-EN, (another trade name Hydrogenated Polyisobutene), under similar test conditions, produced the same results.

A Draize eye irritation study in the right eyes of three rabbits using a facial lotion containing 3% Hydrogenated Polyisobutene caused no signs of irritation.

A skin irritation study in six rabbits using four patches each containing 0.5 g/patch of Polysynlane (trade name Hydrogenated Polyisobutene mixture) caused no reactions in any of the animals on intact or abraded skin. The primary irritation index was 0.0. There was a primary irritation index score of 1.8 for rabbits treated with Permethyl 104A/105A Blend Aliphatic Hydrocarbon (trade name Polyisobutene) on the intact or abraded skin. Rabbits dosed dermally with 0.5 ml Poly Iso 6-50-DN (trade name Hydrogenated Polyisobutene) on intact and abraded skin exhibited a primary irritation index of 0.38; not a dermal irritant. In a similar study, Poly Iso 4-50-EN (another trade name Hydrogenated Polyisobutene) produced a primary irritation index of 0.96; also not a dermal irritant. Polysynlane (trade name Hydrogenated Polyisobutene) was intradermally injected in an area of the skin on the back and flanks of guinea pigs. Erythema and edema were observed after most inoculations, but no sensitization reactions.

Hydrogenated Polyisobutene injections (5%) in guinea pigs using a maximization procedure resulted in no observed reactions and an irritation index of 0.0 in both challenge phases I and II.

The comedogenic potential of Permethyl 104A/105A Aliphatic Hydrocarbon (trade name Polyisobutene) was studied using adult New Zealand white rabbits. The test material was applied to the right ear of each animal daily on 5 consecutive days per week for 3 weeks. There were no signs of hyperkeratosis or comedone formation during weeks 1 and 2. By the third week, two treated ears exhibited signs of hyperkeratosis. The ear of the third rabbit, however, remained clear. Histological examination showed no signs of follicular hyperkeratosis on the treated, untreated, or control ears of any rabbits.

In a study to determine the ability of various insulating fluids to induce transformation in the SHE cell transformation assay and to enhance MCA–induced transformation of C3H/10T1/2 cells, it was found by the authors to be not active and low cytotoxicity was found for a low-viscosity Polyisobutene-based oil. In the two-stage transformation assay of C3H/10T1/2 cells, the Polyisobutene oil had promoter activity.

In a carcinogenicity study conducted to determine the skin tumorigenicity effects of certain oils used for impregnation of paper-insulated power cables and their synthetic alternatives, including Polyisobutene oil, no evidence of a direct tumorigenic or carcinogenic effect was reported and Polyisobutene oil appeared to reduce the number of DMBA-induced tumors.

Repeat-insult patch tests performed to evaluate the primary irritancy/sensitization potential of coded cosmetic foundations/concealer products JMB-423 (containing 4% Hydrogenated Polyisobutene) and JMB-426 (containing 1.44% Hydrogenated Polyisobutene) in 54 male and female subjects found no reactions greater than slight erythema.

No primary skin irritation was produced in a 72-h primary skin irritation patch test study with 100% Polysynlane (Hydrogenated Polyisobutene) in 25 male and female participants.

There was no irritancy observed in humans during a 24-h single-insult patch test with a lip gloss containing 66.11% Hydrogenated Polyisobutene. In a modified repeat-insult patch test under double-blind conditions, no irritation or sensitization was found in human skin patched with a makeup remover containing 51% Hydrogenated Polyisobutene.

The phototoxic potential of coded cosmetic foundations/concealer products JMB-442 (containing 4% Hydrogenated Polyisobutene), JMB-441 (containing 1.44% Hydrogenated Polyisobutene), and a blank patch under UVA light source (320 to 400 nm) was studied in 26 fair-skinned volunteers. No significant reactions were reported.

JMB-442 (containing 4% Hydrogenated Polyisobutene) and JMB-441 (containing 1.44% Hydrogenated Polyisobutene) were evaluated to determine their potential to induce a photoallergic reaction in the skin of 30 subjects. No response was reported at induction, rest, or challenge.

Three shades of coded cosmetic foundations/concealer products, JMB-428 (containing an unspecified concentration of Hydrogenated Polyisobutene), JMB-429 (containing an unspecified concentration of Hydrogenated Polyisobutene), and JMB-442 (containing 4% Hydrogenated Polyisobutene), were examined for signs of ocular irritation when used at least once a day for 29 days by 59 subjects. There were no adverse reactions reported.

DISCUSSION

The available acute, short-term, and subchronic toxicity studies do not suggest that any toxicity would be associated with the use of these ingredients in cosmetic products of a type and at the concentrations reported.

The CIR Expert Panel recognizes that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicate a pattern of use, which was considered by the Expert Panel in assessing safety.

Although one study did suggest possible systemic carcinogenic potential of Polyisobutene and Hydrogenated Polyisobutene, the CIR Expert Panel noted that there was no evidence of tumorigenicity in the study. On review of the study experimental design, it was not possible to make any implications regarding systemic carcinogenicity. Other chronic toxicity studies on the related material Polybutene using rats and dogs, including a 2-year chronic oral toxicity study and a three-generation reproductive and developmental toxicity study, did not result in any carcinogenic effect or reproductive/developmental toxicity, respectively.

The Panel acknowledged the absence of UV absorption data for these ingredients. Clinical tests of phototoxicity and photoallergenicity in which formulations containing Hydrogenated Polyisobutene were used, however, empirically demonstrated the absence of effects.

The Panel also noted the absence of dermal absorption data for Polyisobutene and Hydrogenated Polyisobutene. The available log K_{ow} data and the low solubility in water suggest very slow absorption, so additional data are not needed. Gastrointestinal absorption is also not a major concern due to the low solubility of these chemicals.

CONCLUSION

The CIR Expert Panel concluded that Polyisobutene and Hydrogenated Polyisobutene are safe as cosmetic ingredients in the practices of use and concentration as described in this safety assessment.

REFERENCES

Aarsaether, N., J. R. Lillehaug, E. Rivedal, and T. Sanner. 1987. Cell transformation and promotor activity of insulation oils in the Syrian hamster embryo cell and in the C3H/10T1/2 mouse embryo fibroblast test systems. *J. Toxicol. Environmen. Health* 20:173–185.

Amoco Chemical Company. 2005. Material Safety Data Sheet—Hydrogenated Polyisobutene. Web site accessed 2/23/2005. http://www.hazard.com.

AzoM™. 2004. Butyl Rubber—Polyisobutene. Web site accessed 2/23/2005. http://www.azom.com.

Barik, B. B., B. K. Gupta, and M. Pal. 1993. The role of polyisobutylene and the effect of its concentration in the microencapsulation of isoniazid. *Indian Drugs* 31:104-108.

BASF Corporation. 2003. Material Safety Data Sheet—Polyisobutene Polymer. 5 pages.[2]

Bergdahl, M., A. Wennberg, and L. Spangberg. 1974. Biologic compatibility of a possible new root canal sealer polyisobutene. *J. Dent. Res.* 53:1103.

Buekens, A. G., and H. Huang. 1998. Catalytic plastics cracking for recovery of gasoline-range hydrocarbons from municiple plastic wastes. *Resources Conserv. Recycl.* 23:163–181.

Chiang, C.-H., J.-L. Chen, Y.-T. Liu, and D.-P. Wang. 1998. Therapeutic effect and pharmacokinetics of Ketotifen transdermal delivery system. *Drug Develop. Indust. Pharmacy* 24:213-217.

Cosmetic, Toiletry, and Fragrance Association (CTFA). 1973a. Report on skin irritation studies in rabbits using polysynlane. Unpublished data submitted by CTFA on January 17, 2006. 2 pages.[2]

CTFA. 1973b. Report on eye irritation testing in rabbits. Unpublished data submitted by CTFA on January 17, 2006. 2 pages.[2]

[2]Available from the Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA.

CTFA. 1973c. Report on sensitivity testing in guinea pigs using polysynlane lot #471203. Unpublished data submitted by CTFA on January 17, 2006. 3 pages.[2]

CTFA. 1974a. Seventy-two hour primary skin irritation. Unpublished data submitted by CTFA on January 17, 2006. 7 pages.[2]

CTFA. 1974b. Twenty-four hour primary skin irritation. Unpublished data submitted by CTFA on January 17, 2006. 3 pages.[2]

CTFA. 1974c. Human contact allergy testing. Unpublished data submitted by CTFA on January 17, 2006. 19 pages.[2]

CTFA. 1976. Draize eye irritation—Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on November 29, 2005. 1 page.[2]

CTFA. 1981. Contact allergy—guinea pig—Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on November 29, 2005. 9 pages.[2]

CTFA. 1987. Draize eye irritation—Face lotion (12F) containing 3.0% Hydrogenated Polyisobutene. Unpublished data submitted by CTFA. 1 page.[2]

CTFA. 1996a. Primary irritancy/sensitization tests of JMB-423 and JMB-426. Unpublished data submitted by CTFA on November 14, 2005. 36 pages.[2]

CTFA. 1996b. Phototoxicity of JMB-442 and JMB-441. Unpublished data submitted by CTFA on November 14, 2005. 14 pages.[2]

CTFA. 1996c. Evaluation of human photoallergy and contact allergy of JMB-441 and JMB-442. Unpublished data submitted by CTFA on November 14, 2005. 26 pages.[2]

CTFA. 1996d. Ocular irritation potential of JMB-442. Unpublished data submitted by CTFA on November 14, 2005. 25 pages.[2]

CTFA. 1999. Single insult patch test—Lip gloss (FDA 07E) containing 66.11% Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on November 29, 2005. 1 page.[2]

CTFA. 2003a. Determination of the irritating and sensitizing propensities of a product on human skin containing 51% Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on January 11, 2006. 13 pages.[2]

CTFA. 2003b. Exaggerated in use study—eye area (10% Hydrogenated Polyisobutene). Unpublished data submitted by CTFA on January 11, 2006. 5 pages.[2]

CTFA. 2005a. Concentration of Use for Polyisobutene and Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on September 6, 2005. 2 pages.[2]

CTFA. 2005b. Data from industry on products containing Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on September 19, 2005; revised on December 7, 2005. 1 page.[2]

CTFA. 2006a. Polybutene compared to Polyisobutene and Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on January 27, 2006. 1 page.[2]

CTFA. 2006b. Properties of Indopol® and Panalane® Polybutenes used in cosmetics: An information report to the Cosmetics, Toiletry, and Fragrance Association. Unpublished data submitted by CTFA on March 6, 2006. 6 pages.[2]

CTFA. 2006c. Industry data on polyisobutene and hydrogenated polyisobutene molecular weights. Unpublished data submitted by CTFA on March 10, 2006. 3 pages.[2]

Davis, T. 1976. Polysynlane: Novel synthetic substitute for squalene. *Cosmet. Toiletries* 91:33–34.

Exxon Mobile Chemical Company. 2003. Material Safety Data Sheet—Polyisobutene. 6 pages.[2]

Elder, R.L. 1982. Final report on the safety assessment of Polybutene. *J. Am. Coll. Toxicol.* 1:103–118.

Fanning Corporation. 1998a. Single dose oral toxicity in rats (Polyiso 6-50-N). Unpublished data submitted by CTFA. 6 pages.[2]

Fanning Corporation. 1998b. Primary dermal irritation/corrosion in rabbits. Unpublished data submitted by CTFA. 8 pages.[2]

Fanning Corporation.1998c. Primary eye irritation study in rabbits (Polyiso 6-50-DN). Unpublished data submitted by CTFA. 9 pages.[2]

Fanning Corporation. 1998d. Single dose oral toxicity in rats (Polyiso 4-50-EN) Unpublished data submitted by CTFA. 6 pages.[2]

Fanning Corporation.1998e. Primary dermal irritation/corrosion study in rabbits Unpublished data submitted by CTFA. 8 pages.[2]

Fanning Corporation.1998f. Primary eye irritation study in rabbits (Polyiso 4-50-EN). Unpublished data submitted by CTFA. 9 pages.[2]

Food and Drug Administration (FDA). 2002. Frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

FDA. 2005. Frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

Gottschalck, T.E., and G.N. McEwen, Jr., eds. 2006. *International Cosmetic Ingredient Dictionary and Handbook*, 11th ed., vol. 2. Washington, DC: CTFA.

Grollier, J.F., and J. Cotteret. 1987. Sunscreen method containing polyisobutene for the protection of human epidermis against UV radiations. *US Patent and Trademark Office* 1078:2310.

Guo, J.H. 1994. Investigating the surface properties and bioadhesion of buccal patches. *J. Pharm. Pharmacol.* 46:647–650.

Household Products Database. 2004. Polyisobutene Chemical Information. *National Institutes of Health–National Library of Medicine—Specialized Information Services*. Web site accessed 12/29/2004. http://www.hpd.nlm.nih.gov.

Iversen, O.H. 1990. Tumorigenesis and carcinogenesis studies of a number of insulation oils and fluids on hairless and SENCAR mice with special reference to skin tumors and malignant lymphomas. *Acta Microbiol. Immunol. Scand. Suppl.* 13:3–60.

Ivy Laboratories. 2000. Human sensitization study—lip gloss (FDA 07E) containing 66.11% Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on November 29, 2005. 11 pages.[2]

Ivy Laboratories. 2004a. Human sensitization study for face powder (FDA 07B) containing 17.1% Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on November 29, 2005. 12 pages.[2]

Ivy Laboratories. 2004b. Human sensitization study—lip gloss (FDA 07E) containing 31.65% Hydrogenated Polyisobutene. Unpublished data submitted by CTFA on November 29, 2005. 11 pages.[2]

Ivy Laboratories. 2005. An evaluation of the contact-sensitization potential of a topical coded product in human skin by means of the maximization assay. Unpublished data submitted by CTFA on November 29, 2005. 10 pages.[2]

Kawashima, Y., S.Y. Lin, A. Kasai, et al. 1984. Drug release properties of the microcapsules of adriamycin hydrochloride with ethylcellulose prepared by a phase separation technique. *Drug Dev. Ind. Pharm.* 10:467–479.

Kresge, E. 1999. Butyl rubber. In: *Kirk-Othmer concise encyclopedia of chemical technology*. 4th ed., J. I. Kroswitz, 680–682. Wiley, Hoboken, NJ.

Kristl, A., M. Bogataj, A. Mrhar, and F. Kozjek. 1991. Preparation and evaluation of ethylcellulose microcapsules with bacampicillin. *Drug Develop. Indust. Pharmacy* 17:1109–1130.

Nakano, A., T. Ezawa, and Y. Kunitoshi. 2001. NMR and infrared spectra of Polyisobutene. *University of East Asia*. Web site accessed 2/23/2005. http://202.240.96.156/stnmr/1/kresult-e.aspPolyisobuteneNno=265.

Napadensky, E., D. Crawford, J. Sloan, and N. B. Tan. 2001. Viscoelastic and transport properties of sulfonated PS-PIB-PS block copolymers, Army Research Lab, Aberdeen Proving Ground. http://www.stormingmedia.us/

Nixon, J.R. and G.A. Agyilirah. 1982. The effect of polyisobutene on the properties of ethyl cellulose-walled microcapsules of phenobarbitone sodium. *Acta Pharmaceut. Technol.* 28:137–140.

NOF Corporation. 2004. Declaration for by-products/impurities (Hydrogenated Polyisobutene). Unpublished data submitted by CTFA on January 17, 2006. 2 pages.[2]

NOF Corporation. 2005. Raw material declaration—Parleum/Polysynlane (Hydrogenated Polyisobutene) Unpublished data submitted by CTFA on January 17, 2006. 1 page.[2]

Ouden, H, J. Theunissen, and A.M. Shelton. 1987. Prevention of plant injury by cabbage gall midge Contarinia-Nasturtii Kieffer and onion Thrips-Tabaci Lindemann using emulsions of polyisobutene. *J. Appl. Entomol.* 104:313–318.

Parslew, R., S. Evans, and C.M. King. 1996. Allergic contact dermatitis from Polyisobutene in stoma bags. *Contact Dermatitis* 35:178–179.

Powles, J.G. 1956. Nuclear magnetic resonance absorption in polyisobutene. *Proc. Phys. Soc. B.* 69:281–292.

Presperse, Incorporated. 2004. Specification Sheet for Permethyl® 104A. Unpublished data submitted by CTFA on November 29, 2005. 1 page.[2]

Product Safety Labs. 1987a. FHSA acute oral toxicity limit test. Unpublished data submitted by CTFA on January 11, 2006. 7 pages.[2]

Product Safety Labs. 1987b. FHSA primary eye irritation test. Unpublished data submitted by CTFA on January 11, 2006. 10 pages.[2]

Product Safety Labs. 1987c. FHSA dermal irritation test. Unpublished data submitted by CTFA on January 11, 2006. 7 pages.[2]

Product Safety Labs. 1987d. Comedogenicity assay. Unpublished data submitted by CTFA on January 11, 2006. 11 pages.[2]

Sadik, O.A., and D.M. Witt. 1999. Monitoring endocrine-disrupting chemicals. *Environ. Sci. Technol.* 33:368–374.

Sophim. 2004. Hydrogenated Polyisobutene—Sophim MC 30–Sophim MC 300. Web site accessed 2/25/2005. http://www.sophim.com.

Tan, H.S., and W.R. Pfister. 1999. Pressure-sensitive adhesives for transdermal drug delivery systems. *Rese. Focus PSTT* 2:60–69.

United States Environmental Protection Agency (EPA). 2004. Polyisobutene. *Substance Registry System.* Web site accessed 2/23/2005. http://www.oaspub.epa.gov.

Uniquema. 2004. Product data sheet for Prisorine 3758 squalene (synthetic). Unpublished data submitted by CTFA. 1 page.[2]

Woods, M.A. 1999. Material Safety Data Sheet for Polyisobutene. *Goldsmith & Eggleton.* 5 pages.[2]