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Final Report on the Safety Assessment of Polyethylene[1]

Polyethylene is an ethylene polymer used for a variety of purposes in cosmetics as an abrasive, adhesive, binder or bulking agent, an emulsion stabilizer, a film former, an oral care agent, and as a nonaqueous viscosity-increasing agent. Polyethylene is also used in food packaging materials and medical products, including prosthetics. The molecular weight of Polyethylene as used in cosmetics varies over a wide range. The lowest reported molecular weight is 198 Daltons and the highest is 150,000. In any given polymer preparation, there can be a broad range of molecular weights. Cellular and tissue responses to Polyethylene, determined as part of implant biocompatibility testing, include fibrous connective tissue build-up around the implant material that varies as a function of the physical form of the implant material. Specific assays for osteoblast proliferation and collagen synthesis demonstrated a reduction as a function of exposure to Polyethylene particles that is inversely related to particle size. The effect of Polyurethane particles on monocyte-derived macrophages, however, had a stimulatory effect, prolonging the survival of these cells in culture. The LD_{50} for Polyethylene, with an average molecular weight of 450, in rats was >2000 mg/kg. For Polyethylene with an average molecular weight of 655, the LD_{50} was >5.0 g/kg. Toxicity testing in rats shows no adverse effects at Polyethylene (molecular weight not given) doses of 7.95 g/kg or at 1.25%, 2.50%, or 5.00% in feed for 90 days. Dermal irritation studies on rabbits in which 0.5 g of Polyethylene (average molecular weight of 450) was administered in 0.5 ml of water caused no irritation or corrosive effects; Polyethylene with an average molecular weight of 655 was a mild irritant. Polyethylene (average molecular weight of 450) did not cause dermal sensitization in guinea pigs tested with 50% Polyethylene (*w*/*w*) in arachis oil BP. Polyethylene, with a molecular weight of 450 and a molecular weight of 655, was a mild irritant when tested as a solid material in the eyes of rabbits. Rabbit eyes treated with a solution containing 13% Polyethylene beads produced minimal irritation and no corneal abrasions. No genotoxicity was found in bacterial assays. No chemical carcinogenicity has been seen in implantation studies, although particles from Polyethylene implants can induce so-called solid-state carcinogenicity, which is a physical reaction to an implanted material. Occupational case reports of ocular irritation and systemic sclerosis in workers exposed to Polyethylene have been difficult to interpret because such workers are also exposed to other irritants. Clinical testing of intrauterine devices made of Polyethylene failed to conclusively identify statistically significant adverse effects, although squamous metaplasia was observed. The Cosmetic Ingredient Review (CIR) Expert Panel did not expect significant dermal absorption and systemic exposure to large Polyethylene polymers used in cosmetics. The Panel was concerned that information on impurities, including residual catalyst and reactants from the polymerization process, was not available. The Panel considered that the monomer unit in Polyethylene polymerization is ethylene. In the United States, ethylene is 99.9% pure. The other 0.1% includes ethane, propylene, carbon dioxide, carbon monoxide, sulfur, hydrogen, acetylene, water, and oxygen. The Panel believed that the concentration of these impurities in any final polymer would be so low as to not raise toxicity issues. Safety tests of cosmetic-grade Polyethylene have consistently failed to identify any toxicity associated with residual catalyst. Although it was reported that one process used to cross-link Polyethylene with an organic peroxide, this process is not currently used. In addition, cosmetic-grade Polyethylene is not expected to contain toxic hexanes. The Panel was concerned that the only genotoxicity data available was nonmammalian, but taking this information in concert with the absence of any chemical carcinogenicity in implant studies suggests no genotoxic mechanism for carcinogenicity. The solid-state carcinogenicity effect was not seen as relevant for Polyethylene as used in cosmetics. The available data support the conclusion that Polyethylene is safe for use in cosmetic formulations in the practices of use and concentrations described.

INTRODUCTION

Polyethylene is a polymer of ethylene monomers used in cosmetics as an abrasive, adhesive, binder, bulking agent, emulsion stabilizer, film former, oral care agent, and nonaqueous viscosity-increasing agent. It is also a commonly used plastic in food packaging and prosthetics. This review presents information relevant to the safety of Polyethylene as a cosmetic ingredient.

CHEMISTRY

Definition and Structure

The *International Cosmetic Ingredient Dictionary and Handbook* (Gottschalck and McEwen 2004) lists Polyethylene (CAS no. 9002-88-4) as a polymer of ethylene monomers that conforms generally to the empirical formula $(C_2H_4)_x$.

Polyethylene has the following technical/other names:

- ethene homopolymer,
- high melting point polyethylene powder,
- polyethylene powder,
- polyethylene wax, and
- synthetic wax.

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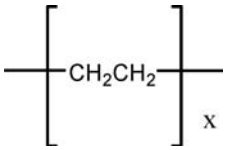
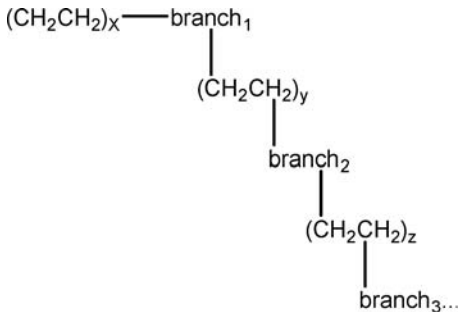
The structural formula from Gottschalck and McEwen (2004) is



where x determines the polymer size.

At least 19 manufacturers supply trade name products that are their own versions of Polyethylene for use in cosmetics and an equal number supply Polyethylene as part of a trade name mixture (Gottschalck and McEwen 2004).

According to Kissin (1999), Polyethylene is a generic name for a large family of semicrystalline polymers used mainly as commodity plastics. A majority of polyethylene molecules contain branches in their chains, which can be represented by the following formula, where the x, y, and z values can range from 4 or 5 to over 100:



Because of this branching structure, Polyethylene can be produced with a wide range of molecular weights and branching elements. The number of monomer units in the polymer can vary from small (about 10 to 20 in polyethylene waxes) to very large (over 100,000 for polyethylene of ultrahigh molecular weight).

Physical and Chemical Properties

Table 1 presents the physical and chemical properties of Polyethylene.

Safepharm Laboratories, Ltd. (1997a) tested Polyethylene with an average molecular weight of either 450 or 655 Daltons, finding that neither product was soluble in water. These polymers were described as mainly linear with very little branching, and the manufacturing process had removed all monomers, with no residual ethylene remaining.

Kissin (1999) characterized Polyethylene polymers as shown in Table 2.

Pebsworth (1999) reported the molecular weight of low-density polyethylene, which ranges from waxy products at approximately 500 molecular weight to very tough products at about 60,000 molecular weight. Low-density polyethylene, also known as high-pressure polyethylene, differs from high-density polyethylene and linear low-density polyethylene in that it possesses both long- and short-chain branches along the polymer chain.

This author stated that, traditionally, low-density polyethylene has been described as homopolymer products having a density between 0.915 and 0.940 g/cm^3 (products having a density above 0.940 g/cm^3 are considered to be high-density polyethylenes). In addition, low-density polyethylene has the potential to include a wide range of comonomers that can be polar in nature on the polymer chain. The broad molecular weight distribution in low-density polyethylene is caused by the presence of long branches on the polymer molecule and may have

TABLE 1
Physical and chemical properties of Polyethylene

Molecular weight	198–500,000	Baker Petrolite 2004 NTP Chemical Repository 2001 Lewis 1997
Density	0.910–0.925 g/ml	NTP Chemical Repository 2001
Melting point	85–110°C	NTP Chemical Repository 2001
Flammability (flash point)	221°C	NTP Chemical Repository 2001
Reactivity	Attacked by oxidizing agents such as nitric and perchloric acids, free halogens, benzene, petroleum ether, gasoline and lubricating oils, aromatic and chlorinated hydrocarbons	NTP Chemical Repository 2001
Maximum λ	161.5 nm	IARC 1979
Odor	Odorless	Lewis 1993

TABLE 2
Commercial classification of Polyethylenes (Kissin 1999)

Designation	Acronym	Density (g/cm^3)
High density polyethylene	HDPE	≥0.941
Ultrahigh molecular weight polyethylene[a]	UHMWPE	0.935–0.930
Medium density polyethylene	MDPE	0.926–0.940
Linear low density polyethylene	LLDPE	0.915–0.925
Low density polyethylene[b]	LDPE	0.910–0.940
Very low density polyethylene	VLDPE	0.915–0.880

[a]Linear polymer with molecular weight of over 3×10^6.
[b]Produced in high pressure processes.

molecules that range in length from a few thousand carbons to a million or more carbons.

As molecular weight increases, certain property values of low-density polyethylenes increase as well. These include: melt viscocity, abrasion resistance, tensile strength, resistance to creep, flexural stiffness, resistance to brittleness at low temperature, shrinkage, warpage, and film impact strength. Increased molecular weight results in reduced film transparence, freedom from haze, and gloss; draw-down rate; neck-in and beading; and adhesion. It was noted that molecular weight distributions around an average molecular weight will differ for the two processes, but there will be a definite range in either case, not a single molecular weight (Pebsworth 1999).

According to the Cosmetic, Toiletry, and Fragrance Association (CTFA), as supplied to the cosmetics industry, weight average molecular weight, number average molecular weight, and polydispersity may be given (CTFA 2004d). The number average molecular weight of a given polymer sample is determined by taking the sum of each of the polymer molecular masses multiplied by the number of polymer molecules at that molecular mass. That total is divided by the total number of polymer molecules in the sample to yield the number average molecular weight.

The weight average molecular weight is the sum of the fraction of the total sample mass represented by each type of polymer multiplied by the molecular mass of each type. Polydispersity is determined by the ratio of the weight average molecular weight to the number average molecular weight. The higher the value for polydispersity, the wider the range of molecular weights represented in the sample. Table 3 provides values for these parameters from two suppliers (CTFA 2004d).

In yet another characterization of Polyethylene supplied to the cosmetics industry for use as an abrasive, Induchem specified a molecular weight range (weight average or number average not stated) of 60,000 to 70,000 and particle size of 10 to 800 μm (CTFA 2004c).

Information from Baker Petrolite (2004) indicated that Polyethylenes used in the cosmetics industry have number average molecular weights (Mn) as low as 300 to 400. This company's trade name Polyethylene, PERFORMALENE 400, is a polymer where the molecular mass distribution may have portions as low as 198. The data on PERFORMALENE 400 polyethylene showed no indication of toxicity, irritation or sensitization, therefore a molecular weight limitation was not considered to be suitable in this case. Molecular weights are not normally included in the quality control tests used for specifications, and are also subject to some variation depending upon the testing technique. Baker Petrolite recommends using the value of 198 as the lower limit of PERFORMALENE 400 polyethylene number average molecular weight distribution.

Additional data (CTFA 2005) indicated that a supplier sells Polyethylene to the personal care industry with a molecular weight of 104,000 to 109,000.

TABLE 3
Polyethylene molecular weights and polydispersity data (CTFA 2004c)

Value	Supplier A	Supplier B
Weight average molecular weight (Mw)	152,500	70,200
Number average molecular weight (Mn)	15,600	9,300
Polydispersity (Mw/Mn)	9.8	7.5

Method of Manufacture

Lewis (1997) stated that the preparation of Polyethylene varies. Cross-linked Polyethylene (XLPE) can be made by irradiating linear polyethylene or by using a cross-linking agent, such as an organic peroxide (e.g., benzoyl peroxide catalyst). Low-density (branched) Polyethylene is formed by the oxygen catalyzed polymerization of ethylene or by applying pressures of 100 to 300 psi at less than 100°C. High-density (linear) Polyethylene is prepared using a metallic catalyst to polymerize ethylene.

Cottom (1999) stated that Polyethylene waxes are synthetic waxes. Low-molecular-weight polyethylenes possessing wax-like properties are produced either by high-pressure polymerization or low-pressure (Ziegler-type catalysts) polymerization. Although all the products have the same general structure, the processes yield products with distinctly different properties. Some polyethylenes have moderately low densities as a result of the branching that occurs during the polymerization. Molecular weight distributions also vary widely among the different processes, as does the range of molecular weights available.

Kissin (1999), in the *Kirk-Othmer Encyclopedia of Chemical Technology*, described methods of manufacture that include polymerization (1) in supercritical ethylene at a high ethylene pressure and temperature above the polyethylene melting point (110°C to 140°C), (2) in solution or in slurry at 120°C to 150°C, and (3) in the gas phase (no temperature given). The properties of polyethylene are maintained by controlling the density, molecular weight, and molecular weight distribution, or by cross-linking. Polyethylene resins are produced either in radical polymerization reactions or in catalytic polymerization reactions.

Analytical Methods

Various methods have been used to identify Polyethylene (IARC 1979). Ultraviolet, visible, and infrared spectrometries have been employed to identify polyethylene in paper coatings. Infrared spectrometry has also been used in textiles. Identification can be accomplished by examining the pyrolysis products of Polyethylene by polarography of bromo or nitro derivates; thin-layer chromatography; combining ultraviolet

analysis, color-forming reactions, and thin-layer chromatography; mass spectrometry; and gas chromatography.

Impurities

IARC (1979) stated that ethylene in the United States is 99.9% pure with impurities including ethane, propylene, carbon dioxide, carbon monoxide, sulfur, hydrogen, acetylene, water, and oxygen.

Sheftel et al. (2000) stated that catalyst (ash contents) from production of high-density (low-pressure) Polyethylene can be reduced to 0.002% to 0.003% by washing. Safepharm Laboratories, Ltd. (Safepharm 1997a) stated that the Polyethylene they tested contained no residual ethylene and that the manufacturing process had removed all monomers.

Information regarding Polyethylene from Baker Petrolite (2004) affirmed that their products (PERFOMALENE polyethylenes) do not use any organic peroxides as catalysts. It was also reported that their process was designed to remove the proprietary catalysts that they use. The data submitted on irritation, sensitization, and an Ames test were from studies using typical batches of commercial products. If there were any residual materials that promoted adverse effects, the tests would have been expected to show some indication.

A safety data sheet for evaluation of cosmetic ingredients provided indicated that Polyethylene is a pure component containing 100% active ingredient and no solvents, preservatives, antioxidants, or additives (CTFA 2004c). This data sheet also showed that there is no known residue from manufacturing.

Another company (CTFA 2004d) reported one product with a value of 1200 ppm of carbon hydrogen compounds (C6–C11) and that their Polyethylene waxes (number weight molecular weights between 3000 and 11,000) are free of aromatic solvents. A third company (CTFA 2004d) stated that their Polyethylene is produced using a slurry process in which no organic peroxides were used. The reported number average molecular weight was 957.

USE

Cosmetic

Polyethylene is used in a wide range of cosmetic product types. As shown in Table 4, current industry reports to the Food and Drug Administration (FDA) include 717 uses (FDA 2002b). For each product type, Table 4 gives the total number of products reported to FDA (in parentheses in the first column). For eyeliner products, for example, of the total of 548 products reported, 297 contained Polyethylene.

Table 4 also gives the results of an industry survey (CTFA 2004a) of current use concentrations—overall the use concentration ranged from 0.09% to 24%. That same survey also provided some data on the physical form of Polyethylene as a function of product type containing which.

Noncosmetic

Food Packaging

Schwope et al. (1987) stated that both High-Density Polyethylene (HDPE) and Low-Density Polyethylene (LDPE) are among the most widely used food-packaging materials, both as a film and in containers. When used in food packaging, Polyethylene is regularly compounded with antioxidants to reduce thermal degradation, antiblocking agents to prevent film sticking, and slip additives to reduce friction.

In the Code of Federal Regulations (21CFR177.1600-177.1620), the FDA recognizes the safety of carboxyl-modified, chlorinated, and fluorinated Polyethylenes as a food-contact surface.

Medical Products

The medical uses of Polyethylene include dentistry, plastic stents in the treatment of malignant biliary structures (Catalano et al. 2002), microsutures used in gynecology microsurgery (Gomel et al. 1980), intrauterine contraceptive devices (Ober et al. 1970), strips in breast augmentations (Roberts and Taylor 1990), and orthopedic implants (FDA 1996).

FDA Center for Devices and Radiological Health (CDRH) mandates biocompatibility testing of materials to be implanted, including Polyethylene. Under the provisions of the FDA Modernization Act of 1997, CDRH established guidance on the recognition and use of consensus standards (FDA 1998a).

Under this provision, CDRH has recognized the ISO 10993 series of standards as the basis for biocompatibility testing (FDA 1998a, 1998b, 2002a). Relevant to the use of Polyethylene in cosmetic products, the tests listed below are routinely performed on all medical devices containing Polyethylene requiring premarket approval:

- Cytotoxicity—in accordance with ISO 10993-5, extracts are tested for ability to cause cell lysis or toxicity and compared with negative and positive controls.
- Sensitization—in accordance with ISO 10993-10, guinea pig maximization test.
- Irritation—in accordance with ISO 10993-10, rabbit acute intracutaneous reactivity.
- Toxicity—in accordance with ISO 10993-11, acute systemic toxicity in the mouse.
- Pyrogenicity—in accordance with ISO 10993-11, temperature rise in rabbits over a 3-h observation period.

Accordingly, all medical grade Polyethylene considered in premarket approval applications by CDRH has been found safe for implantation according to these criteria (FDA 1998a, 1998b, 2002a). CDRH's findings on premarket approval applications are prepared in a summary of safety and effectiveness data. One such example for an implantable device containing Polyethylene is a cardiac ablation catheter (premarket approval application number P000020) approved November 29, 2000 (FDA 2000).

TABLE 4
Frequency of use, use concentrations, and physical form of Polyethylene in cosmetics as a function of product categories

Product category (total number of formulations) (FDA 2002b)	Number of products with ingredient (FDA 2002b)	Concentration of use (%) (CTFA 2004a)	Physical form of Polyethylene (CTFA 2004a)
Baby products			
Baby lotions, oils, powders, and creams (60)	1	3	Powder
Other baby products (34)	—	3	Powder
Bath products			
Bath soaps and detergents (421)	4	0.3–8	Not stated
Other bath preparations (196)	10	4–18	Powder or not stated
Eye products			
Eyebrow pencils (102)	16	6	Not stated
Eyeliners (548)	297	6–10	Small ball or not stated
Eye shadow (576)	20	9–24	Powder, small ball, or not stated
Eye makeup remover (100)	6	5–10	Powder or not stated
Mascara (195)	39	3–8	Not stated
Other eye makeup preparations (152)	4	3–16	Powder or wax
Fragrance products			
Fragrance powders (273)	7	—	—
Perfumes	—	5	Not stated
Other fragrance preparations (173)	1	3	Not stated
Noncoloring hair products			
Hair conditioners (651)	1	—	—
Hair tonics, dressings, etc. (598)	4	2	Not stated
Hair-coloring products			
Hair bleaches (120)	2	—	—
Other hair-coloring preparations (55)	1	—	—
Makeup			
Blushers (245)	23	2–10	Powder, small ball, wax, or not stated
Face powders (305)	25	5–10	Powder, small ball, or not stated
Foundations (324)	23	2–11	Powder, small ball, or not stated
Leg and body paints (4)	—	3–8	Not stated
Lipsticks (962)	67	3–16	Powder, small ball, wax, or not stated
Makeup bases (141)	7	—	—
Rouges (28)	4	8–20	Not stated
Makeup fixatives (20)	3	3	Not stated
Other makeup preparations (201)	20	0.2–11	Powder or not stated
Nail care products			
Nail polish and enamel (123)	—	0.09	Not stated
Other manicuring preparations (55)	—	3	Not stated
Personal hygiene products			

(Continued on next page)

TABLE 4
Frequency of use, use concentrations, and physical form of Polyethylene in cosmetics as a function of product categories
(Continued)

Product category (total number of formulations) (FDA 2002b)	Number of products with ingredient ingredient (FDA 2002b)	Concentration of use (%) (CTFA 2004a)	Physical form of Polyethylene (CTFA 2004a)
Underarm deodorants (247)	—	7	Not stated
Other personal cleanliness products (308)	12	5–10	Not stated
Skin care products			
Skin cleansers (775)	55	2–11	Powder or not stated
Depilatories (34)	—	5	particles (abrasive)
Face and neck creams, lotions, powder, and sprays (310)	5	1–10	Powder, small ball, or not stated
Body and hand creams, lotions, powder, and sprays (840)	12	2–16	Powder or not stated
Moisturizers (905)	12	5–10	Not stated
Night creams, lotions, powder, and sprays (200)	3	—	—
Paste masks/mud packs (271)	11	4	Not stated
Other skin care preparations (725)	18	0.6–5	Powder or not stated
Suntan products			
Suntan gels, creams, and liquids (131)	2	0.5–8	Powder or not stated
Indoor tanning preparations (71)	—	3	Not stated
Other suntan preparations (38)	2	5	Not stated
Total uses/ranges for Polyethylene	**717**	**0.09–24**	

According to Induchem, there is no difference between medical-grade and cosmetic-grade Polyethylene (CTFA 2004c).

Other Uses

Polyethylene containers are used for packaging of materials such as cosmetics, flammable and combustible liquids, and pharmaceuticals. Figge and Freytag (1980) determined that Polyethylene is suitable for packaging cosmetics. Polyethylene is used in agricultural fields or greenhouses as a tarp to contain fumigants in soil to reduce emissions into the atmosphere (Papiernik and Yates 2002). Polyethylene is also used in wire and cable coatings and insulations, as well as pipe and molded fittings (Lewis 1997).

According to Kissin (1999), uses of Polyethylene resins include many film grades of low-density polyethylene, high-density polyethylene, and linear low-density polyethylene for bags and packaging; coatings for paper, metal, wire, and glass; household and industrial containers such as bottles for different fluids like water, food products, detergents, and liquid fuels, etc.; toys; and various types of piping and tubing.

According to Cottom (2004), major uses of polyethylenes include hot-melt adhesives for applications requiring high temperature performance, additives to improve the processing of plastics, slip and rub additives for inks and paints, and cosmetic applications. Some by-product polyethylene waxes have been recently introduced. Uses include additives for inks and coatings, pigment dispersions, plastics, cosmetics, toners, and adhesives.

GENERAL BIOLOGY

Absorption, Metabolism, Distribution, and Excretion

Most studies of the effects of Polyethylene were done using implantation, so data normally found in this section is included in the following section.

Cellular and Tissue Response—Biocompatibility

Bing (1955) summarized early research on tissue reaction to Polyethylene and carried out a series of experiments to confirm past results.

Polyethylene film balls (7 mm diameter) were implanted intraperitoneally in four rats that were subsequently killed after 11 days, 39 days, 3 and 4 months. In each rat, a capsule of connective tissue was observed. Leukocytes, macrophages, and very few giant cells were found surrounding the area of the implant in the rat killed after 11 days. The 3- and 4-month implantations had little inflammatory reaction.

Small pieces of Polyethylene film were also implanted intraperitoneally into four rats that were killed at the same intervals. Again, the Polyethylene was surrounded by fibrous tissue; however, in contrast to the reaction to the Polyethylene ball, there were many foreign-body giant cells surrounding the film.

Pieces of Polyethylene mesh woven from 0.7 mm thick threads at 1 to 3 mm apart were implanted subcutaneously and intraperitoneally in five rats. Animals were killed at 5, 19, about 45, and about 100 days. The Polyethylene, in each case, was

surrounded by connective tissue and polymorphonuclear leucocytes, macrophages, and a few giant cells (Bing 1955).

In a longitudinal study, Gomel (1980) investigated the histologic reaction to nonabsorbable polyethylene sutures (10-0 in weight) in the bicornuate uterus of a New Zealand white rabbit. Sutures were placed in several rows on each uterine horn. After 24 days, the right uterine horn was removed and after 80 days, the left horn was removed. Segments of tissue containing the sutures were trimmed, fixed in formalin, sectioned, and stained. Two reactions were determined; degree of mononuclear histiocyte infiltration and multinucleated giant cell reaction.

After 24 days, histiocyte infiltration varied from none to marked in the 10 samples, with an average of moderate. There were no multinucleated giant cell reactions. After 80 days, all samples showed some histiocyte infiltration, ranging from minimal to moderate while four of the ten samples had giant cells (Gomel 1980).

Rodrigo et al. (2001) investigated the biological effect of Polyethylene particles of different sizes on human osteoblastic cells isolated from the trabecular bone of 17 osteoarthritic patients. Ten osteoblastic marker secretion samples were obtained from subjects aged 68 $\pm$ 7 years. Seven osteocalcin expression samples came from patients aged 65 $\pm$ 5 years. Polyethylene particles of two different sizes (<30 and 20 to 200 μm) were used. The osteoblastic samples were cultured in three different flasks; with <30-μm particles, 20-to 200-μm particles, and a control flask not treated with Polyethylene. Osteoblastic function was evaluated.

Small (<30 μm) Polyethylene particles were shown to have a greater effect on osteoblastic function markers than larger particles (20 to 200 μm). Evidence of inhibition of both osteoblast proliferation and collagen synthesis was observed.

The seven osteocalcin samples were tested in four flasks, two with <30-μm particles and two controls without Polyethylene. The small Polyethylene particles increased osteocalcin expression and secretion, which may be responsible for osteoclast bone resorption, leading to reduced orthopedic implant stability (Rodrigo et al. 2001).

Rodrigo et al. (2002) examined the hypothesis that Polyethylene and other implant materials may cause alteration in osteoblastic function, resulting in bone loss around the implant. The study focused on the effects of high density Polyethylene on interleukin-6 (IL-6) expression in human osteoblastic cells. Cytokines, such as IL-6, are the most important components in cell proliferation, osteoclast formation, and the stimulation of osteoclasts to resorb adjacent bone. Increased release of cytokines can lead to osteolysis in patients with Polyethylene prosthetics. Human osteoblastic cells, obtained from trabecular bone explants of 15 osteoarthritic patients aged 65 $\pm$ 5 years, were incubated with high-density Polyethylene particles (<5 μm).

Polyethylene increased the expression and secretion of IL-6 in human osteoblastic cells (Rodrigo et al. 2002).

Noting that macrophages are often found in the inflamed membrane that commonly surrounds Polyethylene orthopedic implants, Xing et al. (2002) assessed the effect of polyethylene particle phagocytosis on the viability of mature human monocyte-derived macrophages (MDMs). The Polyethylene used has characteristics similar to that of ultra-high molecular weight Polyethylene. Three healthy volunteers (no detailed information was provided) contributed blood, which was centrifuged to isolate monocytes. Particles of high-density polyethylene (HDPE, size 4 to 10 μm) were suspended in soluble type I collagen. The MDMs were incubated in a collagen control, as well as in the collagen-HDPE substrata for 31 days.

Initial contact (seen as early as 2 h after incubation) of the MDMs with the HDPE particles did not cause a toxic effect. After 24 h, most of the particles were associated with the cells, revealing that phagocytosis of the particles had occurred. The HDPE particles did not change the cell viability, as evidenced by similar viability in the control macrophages. The cells associated with particles were activated, rather than necrotic. This was evidenced further at 31 days. The test cells were more viable and had higher DNA values than the control cells.

The authors concluded that phagocytosis of HDPE particles by MDMs prolongs the macrophages' survival, and the authors speculated that this may explain the chronic inflammation surrounding Polyethylene orthopedic implants (Xing et al. 2002).

ANIMAL TOXICOLOGY

Acute Toxicity

Lefaux (1968) stated that attempts to determine the lethal dose (LD_{50}) of low-pressure Polyethylene were unsuccessful. The rats could not be given more than 7.95 g/kg and at this level, the animals did not show signs of poisoning; their weights and histopathological examinations were normal.

Safepharm Laboratories, Ltd. (1997a) investigated the acute oral toxicity of Polyethylene (average molecular weight of 450) in 10 male and female Sprague-Dawley CD strain rats (201 to 223 g). The rats were fasted and then given a single oral dose of Polyethylene as a suspension in arachis oil BP at a dose of 2000 mg/kg body weight. The animals were observed for 14 days and then killed and underwent necropsy.

During the experimental period, no rats died or had signs of systemic toxicity; they did show an expected gain in bodyweight. Necropsy revealed no abnormalities. The LD_{50} was determined to be greater than 2000 mg/kg body weight (Safepharm Laboratories, Ltd. 1997a).

Subchronic Toxicity

Lefaux (1968) fed male and female rats diets of 1.25%, 2.50%, and 5.00% Polyethylene for 90 days. No adverse effects were seen and the molecular weight of polyethylene was not specified for the study.

Dermal Irritation and Sensitization

As noted earlier, Baker Petrolite (2004) stated that their trade name Polyethylene, PERFORMALENE 400, showed no indication of toxicity, irritation, or sensitization.

Dermal Irritation

Safepharm Laboratories, Ltd. (1997b) tested the acute dermal irritation of Polyethylene (average molecular weight of 450) on three New Zealand white rabbits weighing 2.77 to 2.94 kg and 12 to 16 weeks old. Each rabbit was clipped free of fur from the dorsal flank area the day before testing. Polyethylene (0.5g) was administered with 0.5 ml of distilled water to the skin and occluded with a 2.5-cm^2 patch. Four hours after application, the patch was removed and the area was examined 1, 24, 48, and 72 h later. Polyethylene caused a primary irritation index of 0.0, according to the Draize index. No corrosive effects were noted.

Safepharm Laboratories, Ltd. (1997f) also tested the acute dermal irritation of Polyethylene with an average molecular weight of 655 utilizing the same procedure described above. Three New Zealand white rabbits, aged 12 to 16 weeks and weighing 2.40 to 2.75 kg, were tested. Erythema and eschar formation, as well as edema, were evaluated on a scale of 0 to 4. Polyethylene caused slight erythema at one treated site at the 24-h observation. No irritation was observed at the other two treated sites and no corrosive effects were noted during the study. The primary irritation index was calculated as 0.2 and Polyethylene was classified as a mild irritant.

Dermal Sensitization

Safepharm Laboratories, Ltd. (1997d) tested the sensitization potential of Polyethylene (average molecular weight of 450) on 34 female albino Dunkin Hartley guinea pigs (299 to 364 g, 8 to 12 weeks old). The left flank of each animal was clipped of hair. The test group had a cotton lint patch saturated with 50% Polyethylene (*w*/*w*) in arachis oil BP applied to the left flank for 6 h. Guinea pigs in the control group underwent the same procedure with vehicle alone. The first induction was followed by two more inductions at the same site on days 7 and 14, for a total of three 6-h exposures. Twenty-four hours after each induction, erythema and edema were measured on a scale of 0 to 4. On day 28 of the experimental period, the right flank of each guinea pig was clipped. The same day, a challenge patch saturated with 50% Polyethylene (*w*/*w*) in arachis oil BP was applied to the left flank for 6 h. Also, a patch with 25% Polyethylene (*w*/*w*) in arachis oil BP was applied to the right flank. Patches were removed after 6 h and erythema and edema was quantified 24 and 48 h later. No reactions were observed after any of the inductions or after the challenge. Polyethylene did not cause sensitization in any of the guinea pigs tested.

Ocular Irritation

Safepharm Laboratories, Ltd. (1997c) tested the acute eye irritation potential of Polyethylene (average molecular weight of 450) on three New Zealand white rabbits weighing 3.00 to 3.18 kg and ages 12 to 16 weeks old. Approximately 66 mg (0.1 ml) of the solid test material was placed in the conjunctival sac of the right eye and the eyelids were held together for about a second. The left eye of each rabbit was left untreated and served as a control. The rabbits' eyes were assessed at 1, 24, 48, and 72 h, as well as 7 days following treatment. Redness, chemosis, and discharge of the conjunctivae were scored, with a maximum score of 20. The iris irritation was scored for a maximum score of 10; also, the degree and area of opacity of the cornea were scored, for a maximum score of 80.

Corneal effects were seen in only one treated eye; diffuse corneal opacity was observed at 24 and 48 h after treatment. Inflammation of the iris was seen in only one treated eye at 24- and 48-h observations. At 1 h after treatment, moderate conjunctival irritation was noted in all treated eyes. At 24 h, moderate and minimal conjunctival irritation was seen in one and two treated eyes, respectively. Moderate conjunctival irritation was observed in one treated eye at 48 h, which decreased in severity to minimal at the 72-h observation. All treated eyes appeared normal at 48 h and 7 days after application. Polyethylene caused a maximum group mean score of 11.0 and was classified as a mild irritant (Safepharm Laboratories, Ltd. 1997c).

Safepharm Laboratories, Ltd. (1997g) also investigated the acute eye irritation potential of Polyethylene with an average molecular weight of 655. Three New Zealand white rabbits weighing 2.50 to 2.83 kg and 12 to 16 weeks old were tested. Approximately 55 mg (0.1 ml) of the solid test material was placed in the conjunctival sac of the right eye and the eyelids were held together for about a second. The left eye of each rabbit was left untreated and served as a control. The rabbits' eyes were assessed at 1, 24, 48, and 72 h, as well as 7 days following treatment. Redness, chemosis, and discharge of the conjunctivae were scored, with a maximum score of 20. The iris irritation was scored for a maximum score of 10; also, the degree and area of opacity of the cornea were scored, for a maximum score of 80. The total irritation score could range from 0 to 110.

Diffuse corneal opacity was observed in one treated eye at both the 24- and 48-h observations. All treated eyes displayed moderate conjunctival irritation 1 h after treatment. At the 24-h observation, one and two treated eyes suffered from moderate and minimal conjunctival irritation, respectively. Minimal conjunctival irritation was observed in all treated eyes at 48 h and in only one eye at 72 h. All treated eyes appeared normal at the 72-h and 7-day observations. Polyethylene produced a maximum group mean score of 11.7 and was classified as a mild irritant to the rabbit eye (Safepharm Laboratories, Ltd. 1997g).

New Zealand white rabbits were tested with 0.1 ml of a product containing 13% (w/v) polyethylene beads (CTFA 2004b). OECD method 405 was utilized for the study. After 1 h, the maximum ocular score was 8/110 with resolution after 48 h. No corneal abrasions were observed. No further details were provided.

GENOTOXICITY

FDA (1996) has reported on the cytotoxic potential of breakdown products from biomaterials, including Polyethylene. Medical grade Polyethylene was incubated for various times, up to 8 weeks under several model physiologic conditions. Although Polyester urethane breakdown products were cytotoxic, spot tests for mutation induction in *Salmonella* and induction of the SOS response in *Escherichia coli* yielded no measurable genotoxic effect.

Safepharm Laboratories, Ltd. (1997e) investigated the mutagenicity of Polyethylene with an average molecular weight of 450 using *Salmonella typhimurium* strains TA1535, TA1537, TA98, and TA100 as well as *E. coli* WP2uvrA$^-$. Each strain was tested at concentrations of 1, 10, 30, 100, 300, and 1000 μg/plate. Aliquots of 0.1 ml of one of the bacterial cultures were dispensed into test tubes, followed by 2.0 ml of molten, trace histidine/tryptophan, supplemented top agar, 0.05 ml of the test material formulation, vehicle (toluene) or positive control and either 0.5 ml of S9 mix or phosphate buffer. The contents of the test tubes were mixed and evenly distributed on Vogel-Bonner Minimal agar plates. All of the plates were incubated at 37°C for 48 h.

Polyethylene did not increase the mutation frequency above background in any strain at any concentration. No toxicity was observed in any strain of bacteria used (Safepharm Laboratories, Ltd. 1997e).

CARCINOGENICITY

In its 1979 assessment, the International Agency for Research on Cancer (IARC) could not, due to lack of data, draw a conclusion on the carcinogenic effects of Polyethylene on humans (IARC 1979). In 1987, IARC listed Polyethylene as a group 3 agent, all of which are "not classifiable as to carcinogenicity in humans" due, most commonly, to inadequate evidence of carcinogenicity in humans and inadequate or limited evidence in experimental animals (IARC 1987).

Solid State Carcinogenesis

Due to the extensive medical use of Polyethylene, there are numerous studies on the solid state carcinogenic effect of Polyethylene, particularly in rats. Selected studies are described below.

Bering et al. (1955) investigated tumor incidence in rats after implantation of pure Polyethylene. Wistar and Hisaw (originally from Wistar stock) rats were used, 50 of each strain and equal numbers of each sex. An additional 50 Hisaw rats were used as a control group; however, of the original 150 rats, 59 were victims of cannibalism, leaving 91 surviving rats. Of the remaining rats, 28 were controls (14 female, 14 male), and of the test subjects, 37 were Hisaw strain (20 female, 17 male), and 26 were Wistar strain (13 female, 13 male). Pure Polyethylene squares (1.5 to 2 cm^2) were aseptically implanted subcutaneously in the abdominal wall and subgaleally over cranial defects in the test subjects. The control group was subjected to an identical surgical procedure. All surviving rats were killed 25 months after the surgery.

Sixteen tumors developed in the test group. Eight were considered unrelated to the Polyethylene; seven were breast tumors and one was a hepatocarcinoma. Of the eight tumors resulting from the Polyethylene, six were found in the abdomen and two in the skull. Seven of the tumors appeared in the Hisaw strain rats, whereas only one developed in the Wistar rats. Tumors developed in five female test rats and three males. Five rats of the control group also developed tumors: four in the breast and one carcinoma of the bowel. A 12.7% incidence of fibrosarcoma in the test rats was reported (Bering et al. 1955).

Oppenheimer et al. (1961) evaluated the carcinogenic effects of powdered Polyethylene and compared these results to those of Polyethylene films. Glass coverslips (1.8 cm diameter) were imbedded subcutaneously in the right and left abdominal walls of ninety Wistar rats. After 4 months, four test groups were created by either removing the coverslip or leaving it in and/or introducing glass or Polyethylene powder into the pocket created by the glass coverslip. These four groups were Polyethylene powder with coverslip, glass powder with coverslip, Polyethylene without coverslip, glass powder without coverslip. The two control groups included subjects with and without cover slips, all without powder. Although not directly stated, groups were most likely made up of 15 rats in each of the six groups.

Those with Polyethylene powder and the coverslip remaining developed five tumors whereas those with Polyethylene but without the coverslip developed only one tumor. In the glass powder and coverslip group, six tumors occurred, whereas in the glass powder without coverslip group, no tumors developed. The control group with the coverslip had six tumors and those with the coverslip removed developed no tumors. The authors concluded that implantation of Polyethylene powder does not produce tumors, thus plastics do not chemically invoke carcinogenesis. Rather, they stated that tumor production is a physical reaction to imbedded plastic films (Oppenheimer et al. 1961).

Nakamura et al. (1994) compared the tumorgenicity of medical-grade Polyethylene and poly-L-lactide (PLLA) plates. One hundred and forty-five male KBL Wistar rats were used; they were 11 weeks old and averaged 400 g in weight. Implants of Polyethylene and PLLA were prepared, sized at 20 $\times$ 10 $\times$ 1 mm, and inserted subcutaneously in the back skin. Fifty were implanted with PLLA, 50 with Polyethylene, 30 controls underwent a sham operation, and 15 were used for sequential harvesting of PLLA plates. After 24 months, any survivors were killed and examined.

In the PLLA group, tumors occurred in 22 rats (2 were ectopic and unrelated to the implants) and in the Polyethylene group, 23 developed tumors (2 of these were unrelated to the implants). The control group had no tumors (Nakamura et al. 1994).

CLINICAL ASSESSMENT OF SAFETY

Case Reports

Two cases were discussed by Smahel et al. (1977) on the long-term reaction to Polyethylene strips implanted for breast augmentation. In each case, the fibrin-covered strips were closely packed and were 1.5 to 2 mm wide, up to 1 mm long and 0.07 mm thick. The first case was a 44-year-old woman who had the operation 11 years earlier. She had been healthy until she had fallen on her left breast, and later, her right breast. After the trauma, both breasts were enlarged and deformed. On histological examination dense collagen fibers containing histiocytes surrounded each breast capsule. Between the Polyethylene strips were numerous macrophage and giant cells containing clear vacuoles or amorphous material, signifying the breakdown of Polyethylene.

In the second case, a 34-year-old woman had her augmentation 7 years earlier. Since the surgery, her breasts had been hard and deformed. On histological examination Polyethylene strips were surrounded by dense collagenous tissue and sporadic macrophages and giant cells, indicating a prolonged interaction (Smahel et al. 1977).

Roberts and Taylor (1990) reported a case of adenocarcinoma of the breast associated with Polyethylene strips used for augmentation. A woman who had a bilateral breast augmentation at 25 years of age developed difficulties at 58 years of age. There was no family history of breast disease. She was experiencing discomfort in the right axillary tail and examination revealed a fullness in this area. A sonomammogram detected two small benign nodules, which did not change over the following the 4-month examination period. However, 9 months later, the patient returned with increased discomfort and a more prominent lump. Aspiration cytology revealed malignant cells and a mastectomy was performed. The tumor appeared to be developing next to a fibrous capsule surrounding the Polyethylene strips. On histological examination a ductal carcinoma had passed through the fibrous capsule and came in contact with the Polyethylene strips.

Occupational Exposure Case Reports

Akhmetova (1977) evaluated the eyes of workers at factories producing synthetic ethyl alcohol and high-pressure Polyethylene. The most prominent substances, found at the maximum allowable concentration (MAC; 50 mg/m^3), were unsaturated hydrocarbons of the ethylene series. Eyes of 229 workers, age 20 to 40, were examined and compared to those of 173 workers who did not come into contact with workplace toxicants. Forty percent of the test group showed signs of hyperemia of the palpebral conjunctiva, which was more predominant in full-time permanent workers. The average gauges of the retinal vessels was significantly larger in exposed workers at Polyethylene factories than the control group. The diameter of the vessels increased after a year and then peaked after 4 to 5 years of exposure. Workers in the Polyethylene industry had an average intraocular pressure of 11.9 $\pm$ 0.31 mm Hg compared to controls at 13.2 $\pm$ 0.18 mm Hg. The authors attributed this decrease to a reduction in the production of aqueous humor.

Czirjak et al. (1987) reported progressive systemic sclerosis in patients exposed to chemicals, one of whom was a synthetic materials–processing artisan believed to have been exposed to Polyethylene and ethylene by inhalation. The 59-year-old woman was exposed to these suspected agents from ages 46 to 55. At 57, her first symptoms appeared and continued, including proximal scleroderma, Raynaud phenomenon, joint involvement, pulmonary manifestation, and esophageal involvement.

An initial report of one brain and five lymphopoietic cancer deaths of employees at a petrochemical plant in Texas prompted a series of epidemiological studies to investigate the possible excessive mortality rate (National Toxicology Program [NTP] 1983). A regional case ascertainment did not show any further deaths but other studies showed that these five cases of lymphopoietic cancer (specifically Hodgkin's disease) deaths were in excess. Further, a case-control study revealed a link between the deaths due to Hodgkin's disease and work in an area of the plant dealing with Polyethylene production. All five cases had, at one time, been assigned to either the high- or low-density Polyethylene areas of the plant. Although this association was established, the author pointed out that the last Hodgkin's disease death occurred in 1966 and despite an increased Polyethylene production at the plant, no further cases were reported.

In a later report, Robinson et al. (1982) noted that workers making Polyethylene are often exposed to the fumes from the thermal degradation of Polyethylene. Among these are some allergens and irritants, including acrolein, formaldehyde, hydrocarbons, carbon monoxide and possible free radicals, and soot.

Clinical Testing

Ober et al. (1968) examined the endometrial morphology of 209 women in whom a variety of Polyethylene intrauterine devices (IUDs) had been implanted. All of the women had been using an IUD from 1 day to 105 months. Ninety-six were asymptomatic, with an average age of 32.3 years. There were 112 symptomatic subjects, with an average age of 32.0 years. Of the 209 samples taken, 200 were viable. Of the 93 asymptomatic subjects, 9.7% had significant lesions, 50.5% showed minor changes, and 40% were normal. Significant lesions were "those biopsies in which a diffuse inflammatory process was detected, as well as those biopsies which revealed other intrinsic endometrial abnormalities."

In the 107 biopsies of symptomatic women 25.2% had significant lesions, 45.8% had minor lesions, and 29% were normal. Two patients had squamous metaplasia of the endometrium and one had atypical glandular hyperplasia. The incidence of the human papillomavirus (HPV) was not evaluated. The authors stated that although conclusions from these results cannot be made, the occurrence of squamous metaplasia suggests that long-term observation of women using polyethylene uterine devices would be beneficial (Ober et al. 1968).

In a later study, Ober et al. (1970) investigated the endometrial changes in women after long-term use of a specific Polyethylene IUD, the Lippes loop. Endometrial biopsy specimens were collected from 393 women who had used the Lippes loop for 18 months or longer. Of the 281 asymptomatic women who used the device for 36 months or more, only 2.5% had significant lesions. Of the 54 symptomatic women who used the device for 18 to 35 months, 20.4% of these had significant lesions. The other 58 who were symptomatic used the device for 36 months or more and 41.4% of them had inflammatory lesions. The authors concluded that the role of squamous metaplasia and the possible development of endometrial neoplasms in women with this Polyethylene IUD could not be assessed from these data.

Dermal Sensitization

In a repeat insult patch test, 201 volunteers were induced with nine consecutive administrations of a rinse-off product containing 13% (*w*/*v*) polyethylene beads (CTFA 2004b). Induction patches were applied for 48 h at a time. There was a rest period of 10 to 14 days between the induction and challenge phases. A challenge patch was applied to the induction site for 48 h and evaluated at 48 and 96 h. At the same time, a 48-h occlusive patch was applied to an untreated site and evaluated at 48 h after application. Irritation was measured on a 0–5 grading scale. No irritation was observed with any of the induction patches. The challenge patch produced a sensitization reaction in one subject with a score of +1; the patch applied to the new site also caused a +1 irritation score. However, a +1 score was not considered clinically significant and the investigators concluded that the product has a low irritation and sensitization potential. No further details were provided.

SUMMARY

Polyethylene is an ethylene polymer used for a variety of purposes in cosmetics, including as an abrasive, adhesive, binder or bulking agent, an emulsion stabilizer, a film former, an oral care agent, and as a nonaqueous viscosity-increasing agent. Polyethylene is also used in food packaging materials and medical products, including prosthetics.

Cellular and tissue responses to Polyethylene, determined as part of implant biocompatibility testing, include fibrous connective tissue build-up around the implant material that varies as a function of the physical form of the impant material. Specific assays for osteoblast proliferation and collagen synthesis demonstrated a reduction as a function of exposure to Polyethylene particles that is inversely related to particle size. The effect of Polyethylene particles on monocyte-derived macrophages, however, had a stimulatory effect, prolonging the survival of these cells in culture.

The LD_{50} for Polyethylene (average molecular weight of 450) in rats (201 to 223 g) was found to be >2000 mg/kg, and in Polyethylene with an average molecular weight of 655, the LD_{50} was determined as >5.0 g/kg. Toxicity testing in rats showed no adverse effects at doses of 7.95 g/kg or at 1.25%, 2.50%, or 5.00% in feed for 90 days.

Dermal irritation studies on rabbits in which 0.5 g of Polyethylene (average molecular weight of 450) was administered in 0.5 ml of water caused no irritation or corrosive effects. When the same procedure was used to test Polyethylene with an average molecular weight of 655, a primary irritation index score of 0.2 was found and Polyethylene was classified as a mild irritant. Polyethylene (average molecular weight of 450) did not cause dermal sensitization in guinea pigs tested with 50% Polyethylene (*w*/*w*) in arachis oil BP. In a repeat insult patch test of 201 volunteers, a product containing 13% Polyethylene beads was tested in a series of nine consecutive administrations. There was no irritation observed with any of the induction patches. Challenge patches produced only a slight response in one subject and the investigators concluded that Polyethylene has a low irritation and sensitization potential.

Polyethylene (molecular weight of 450) was tested as a solid material (66 mg) in the eyes of rabbits. The test substance caused a maximum group mean score of 11.0 and was classified as a mild irritant. All treated eyes appeared normal 48 hours after application. The same procedure, with 55 mg of Polyethylene of average molecular weight of 655 was carried out on white rabbits. The mean maximum group score produced by Polyethylene was 11.7 and it was classified as a mild irritant. All treated eyes appeared normal 72 h after treatment. When white rabbits were tested with 13% Polyethylene beads, the maximum ocular score was 8/110 with resolution after 48 h and no corneal abrasions were observed.

Genotoxicity testing was negative in two bacterial studies. Numerous investigations on the tumor production of Polyethylene implantation have produced mixed results. Polyethylene causes tumors in rats implanted with squares of the test substance; however, testing involving implanting coverslips and powdered Polyethylene suggest that tumors are caused by the physical reaction to imbedded plastic films and not the Polyethylene itself. IARC lists Polyethylene as "not classifiable as to carcinogenicity in humans." No toxicity was observed in any of the strains tested.

There have only been a few cases of reactions to the implantation of Polyethylene in humans. In the three published accounts, Polyethylene strips used for breast augmentation caused increased histological activity around the implant.

There have also been occupational case reports on ocular irritation and systemic sclerosis in workers exposed to Polyethylene. Such workers are also exposed to other irritants.

Clinical testing of intrauterine devices made of Polyethylene failed to conclusively identify statistically significant adverse effects, although squamous metaplasia was observed in treated women.

DISCUSSION

Because of the mostly large size of the Polyethylene polymers used in cosmetics, the Cosmetic Ingredient Review (CIR)

Expert Panel did not expect significant dermal absorption of and systemic exposure to Polyethylene itself.

The Panel was concerned that information on impurities pertaining to residual reactants from the polymerization process were not available. The Panel considered the processes by which low-density Polyethylene is made from the catalyzed polymerization of ethylene. In the United States, ethylene is 99.9% pure. The other 0.1% includes ethane, propylene, carbon dioxide, carbon monoxide, sulfur, hydrogen, acetylene, water, and oxygen. The Panel believed that the concentration of these impurities, or potentially toxic hexanes, in any final polymer would be so low as to not raise toxicity issues. Although it was reported that one process used to cross-link Polyethylene uses an organic peroxide, this process is not currently used, so there is no safety concern regarding the possible presence of organic peroxides. Safety tests of cosmetic-grade Polyethylene have consistently failed to identify any toxicity associated with residual catalyst.

The Panel was concerned that the only genotoxicity data available were nonmammalian, but taking this information in concert with the absence of any chemical carcinogenicity in implant studies suggests no genotoxic mechanism for carcinogenicity. The solid state carcinogenicity effect was not seen as relevant for Polyethylene as used in cosmetics. The available data support the conclusion that Polyethylene is safe for use in cosmetic formulations in the practices of use and concentrations described.

CONCLUSION

The CIR Expert Panel concluded that Polyethylene is safe for use in cosmetic products in the practices of use and concentration as described in this safety assessment.

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