Safety Assessment of Polyene Group as Used in Cosmetics

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INTRODUCTION

The 26 ingredients in this report are simple polyolefins that are the polymerization products of vinyl-type monomers. These polyenes are high molecular weight moieties, with very similar structures, properties, and reaction starting materials (monomers). The polyenes function mainly as film formers and/or viscosity increasing agents-nonaqueous in cosmetic products.[1] The ingredients reviewed in this safety assessment are:

Butene/Propylene Copolymer
Butylene/Ethylene Copolymer
Butylene/Ethylene/Propylene Copolymer
Decene/Butene Copolymer
Ethylene/Octene Copolymer
Ethylene/Propylene Copolymer
Hydrogenated Poly(C6-12 Olefin)
Hydrogenated Poly(C6-14 Olefin)
Hydrogenated Poly(C6-20 Olefin)
Hydrogenated Polybutene
Hydrogenated Polydecene
Hydrogenated Polydodecene
Hydrogenated Polyisobutene
Isobutylene/Isoprene Copolymer
Isoprene/Pentadiene Copolymer
Polybutene
Poly(C4-12 Olefin)
Poly(C6-14 Olefin)
Poly(C20-28 Olefin)
Poly(C30-45 Olefin)
Polydecene
Polyethylene
Polyisobutene
Polyisoprene
Polypentene
Polypropylene

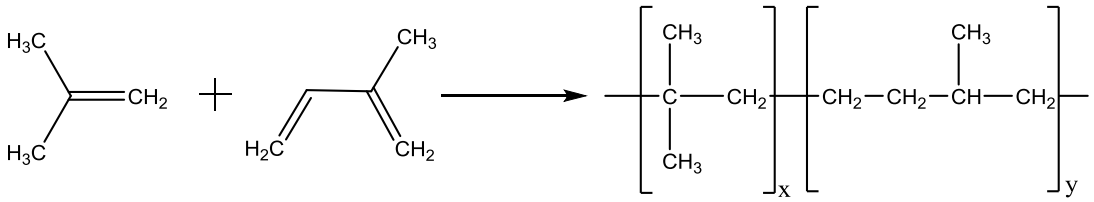
Polybutene (published in 1982), polyethylene (published in 2007), polyisobutene (published in 2008), and hydrogenated polyisobutene (published in 2008) have previously been reviewed by the CIR Expert Panel, which concluded that these ingredients are safe as cosmetic ingredients in the practices of use and concentration as described in each safety assessment.[2-5] Data from these safety assessments are summarized in *italics* in each appropriate section of this report.

Some chemical and toxicological data on hydrogenated polydecene and polybutene in this safety assessment were obtained from robust summaries of data submitted to the European Chemical Agency (ECHA) by companies as part of the REACH chemical registration process. These data summaries are available on the ECHA website.[6,7] The ECHA data summaries included information on analogs (e.g. diisobutylene and triisobutylene for polybutene) for read-across purpose. Where it seems appropriate, those data summaries have been included in this report.

CHEMISTRY

The definitions and CAS registry numbers, where available, of the polyene ingredients are presented in Table 1. Table 2 summarizes available chemical properties, including some information from the original CIR safety assessments of polybutene, polyethylene, polyisobutene, and hydrogenated polyisobutene. Further chemical data on these previously reviewed ingredients can be found in these reports.[2-4]

Polyenes are the polymerization product of vinyl-type monomers (a.k.a. alkenes or olefins). These polyolefins are either homopolymers (e.g., polybutene) or vinyl-type copolymers of two or more monomers (e.g., butene/propene copolymers). The term "vinyl-type copolymers" means that all of the monomers, utilized to make these polymer ingredients, have in common an ethylene unit whose pi electrons are directly involved in the polymerization process. Typically, a catalyst is utilized to initiate the polymerization.[8] There are a large multitude of relevant initiating catalysts, ranging from UV light to Ziegler-Natta-type catalysts, which can result in a range of varied characteristics, such as crystallinity (and resultant hardness). The synthesis of these ingredients is typically carried out in one or more organic solvents, with one or more of these catalysts.



Isobutylene Isoprene Isobutylene/Isoprene Copolymer

Figure 1. An example of polyene synthesis (Isobutylene/Isoprene Copolymer)

For example, formation of polyisoprene occurs by reacting the isoprene monomer in the presence of catalyst in a hydrocarbon solution, usually hexane.[9] The process is stopped with the addition of a terminating reagent. The stabilization of the polymer is often enhanced with the addition of an antioxidant. Subsequent steps in the process include stripping of the solvent, water washing of the polymer to remove catalyst and reagent residues, and finally pressing and formation of a granular product.

These polyene ingredients are high molecular weight, large, inert polymers. While not truly soluble, these ingredients may be swellable in certain organic solvents.

Impurities

Polybutene

Impurities of polybutene include isoparaffins, vinylidene, terminal vinyl structures, chloride, and sulfur containing compounds.[4]

USE

Cosmetic

Table 3 presents the current product formulation use data for polyene ingredients. These ingredients function primarily as film formers and/or viscosity increasing agents-nonaqueous in cosmetic products (Table 1).[1]

According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP), polyethylene has the most reported uses in cosmetic and personal care products, with a total of 2763; the single category with the most reported uses was lipstick with 896.[10] Hydrogenated polyisobutene has the second greatest number of overall uses reported, with a total of 1997; the single category with the most reported uses was lipstick with 841.

In a 2013 Personal Care Products Council use concentration survey, polyethylene had a highest maximum use concentration of 67.6%, which was reported in skin cleansing preparations.[11,12] Hydrogenated polyisobutene had a highest maximum use concentration of 95%, which was reported in lipstick.

In some cases, reports of uses were received from the VCRP, but no concentration of use data were available. For example, hydrogenated C6-14 olefin polymers are reported to be used in 95 formulations, but no use concentration data were available. In other cases, no reported uses were received from the VCRP, but a maximum use concentration was provided in the industry survey. Hydrogenated poly (C6-20 olefin) was not reported in the VCRP database to be in use, but the industry survey indicated that it is used in leave-on formulations at 10%; it should be presumed that hydrogenated poly (C6-20 olefin) is used in at least one cosmetic formulation.

Polyene ingredients with no uses indicated based on the VCRP data or the results of the Council concentration of use survey are listed in Table 4.

Some of these ingredients were reported to be used in pump and aerosol hair sprays, underarm deodorant sprays, face and neck sprays, body and hand sprays, and aerosol suntan products and could possibly be inhaled. For example, hydrogenated polyisobutene was reported to be used in face and neck sprays at a maximum concentration of 8.5%. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles below 10 µm compared with pump sprays.[13-16] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[14,15] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[15] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays.

The polyene ingredients in this safety assessment currently are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU).[17]

Noncosmetic

Many of the polyene ingredients have been approved by the FDA for use as food additives and medical devices. Table 5 lists of many of the regulated uses. Polyethylene and polypropylene are used as negative control materials for International Organization for Standardization (ISO) 10993-6 international standard biological evaluation of medical devices.[18] Ultra high molecular weight polyethylene is the most used biomaterial for the

articulating surface of total joint replacements.[19] Polyisobutene is used in transdermal drug delivery patches and patch adhesives.[20,21] Polyisoprene (*trans*-1,4) is widely used in root canal filling material.[22]

TOXICOKINETICS

Absorption

Hydrogenated Polydecene

A study assessed the absorption potential of undiluted hydrogenated polydecene in male Fischer rats.[6] Groups of 3 rats/time-point received a single or daily (for 15 days) oral gavage dose of 30, 210, or 1500 mg radiolabeled hydrogenated polydecene. Tissues and body fluids were sampled at 0.08, 0.25, 0.5, 1, 2, 4, 8, 24, 48, 72, 120, and/or 168 h post-dosing. With all 3 dose levels, very little of the administered dose was absorbed. What was absorbed was found in the liver, fat, lymph nodes, kidney and spleen. The majority of the test compound was excreted into the feces without being absorbed (> 92%). Urinary excretion was low (< 1%), and very little of the dose was recovered in the bile (0.01%).

Biocompatibility

Polyethylene

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.[2] 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.

TOXICOLOGICAL STUDIES

Single Dose (Acute) Toxicity

Oral – Non-Human

Polybutene

When tested for acute oral toxicity in albino rats, concentrations of polybutene ranging from 15% to 75% were relatively harmless (average molecular weight not specified).[4]

In acute oral toxicity studies in rats, the LD_{50}s of polybutene analogs diisobutylene and triisobutylene were > 2000 mg/kg/body weight each in rats.[7] No mortalities were observed in either study of the single concentration tested.

The LD_{50}s of polybutene analogs di-n-butene, tributene, and tetrabutene (containing 30% pentabutene) in rats were > 10,000 mg/kg each.[7] In the study of di-n-butene at necropsy, 1 animal had partial thickening of the forestomach and another had partial hyperemia of the small intestine membrane. No mortalities were observed in any of these studies.

Polyethylene

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.[2]

Hydrogenated Polyisobutene

Acute oral toxicity testing with mice caused no deaths with a maximum of 89.608 g/kg of a hydrogenated polyisobutene mixture.[3] Oral toxicity using a single dose of 5 g/kg hydrogenated polyisobutene caused no deaths in rats in several studies; however, lethargy and wetness in the anogenital area after dosing was observed. The authors of these studies also concluded that the LD_{50} is greater than 5.0 g/kg body weight. The average molecular weight was reported to be 900 in one of the studies.

Hydrogenated Polydecene

In an acute oral toxicity study in Sprague-Dawley rats (5 rats/sex), the LD_{50} was > 5000 mg/kg undiluted hydrogenated polydecene (average molecular weight not specified).[6]

Hydrogenated Polydodecene

In an acute oral toxicity study in 5 Sprague-Dawley rats of each sex, the LD_{50} was > 5000 mg/kg undiluted hydrogenated polydodecene (average molecular weight not specified).[6]

Inhalation – Non-Human

Polybutene

Polybutene produced no abnormalities in rats during an 18.5 mg/L inhalation exposure.[4]

The LC_{50} of the polybutene analog diisobutylene in albino rats was > 4185 ppm (19,171 mg/m^3) after a 4-hour, single, whole-body exposure.[7] No mortalities or overt signs of toxicity were observed.

Hydrogenated Polydecene

In an acute inhalation study, the LC_{50} for hydrogenated polydecene was > 5.2 mg/L when tested in 6 male and 6 female Sprague-Dawley-derived rats (average molecular weight not specified).[6] The rats were exposed for 4 h via nose-only exposure. No mortalities were observed, and no significant clinical signs were observed during and after the exposure period. No treatment-related signs of toxicity were observed at necropsy.

The combined LC_{50} for the dimer of hydrogenated decene (analog of hydrogenated polydecene) was 1.17 mg/L (CI = 0.94 to 1.46 mg/L) when tested in groups of 5 male and female Sprague-Dawley rats.[6] The rats were exposed to aerosol/vapor of the test material for 4 h at concentrations of 0.77, 0.94, 1.1, 1.4, or 5.1 mg/L. All animals treated with 5.1 mg/L died within 2 days. Two to 5 females each from all the remaining treatment groups died. No males in the 0.77 or 0.94 dose groups died, but 2 males each in the remaining dose groups died. Clinical signs included dyspnea and nasal discharge. Body weight gain was reduced in the first week, but within normal parameters the second week. Treatment-related effects of the lung were observed during gross necropsy of only the animals that died during the study. Microscopic lesions in the lung were observed in all of the high-dose animals (no further details).

In another acute inhalation study of the dimer of hydrogenated decene, the LC_{50} could not be determined when tested in 5 male and 5 female Sprague-Dawley rats via whole body inhalation.[6] The animals were tested at 5 mg/L. Nine of the 10 treated animals died within 3 days. Clinical signs included reduced activity, increased respiration rate, respiratory sounds, labored breathing, irregular breathing, muzzle and abdominal staining, partially closed eyes, hunched back, and lying on the side. In the one female that survived treatment, all respiratory signs were normal by day 5, but muzzle staining persisted until day 9. A marked loss in body weight was observed through day 4. At necropsy, the surviving female had absolute and relative lung and trachea weights greater than the controls. The heart appeared to be affected (no further details). In the animals that died following treatment, treatment-related increases in respiratory findings were observed (no further details).

Hydrogenated Polydodecene

In an acute inhalation toxicity study, the LC_{50} for hydrogenated polydodecene was > 5.06 mg/L when tested in 5 Sprague-Dawley rats of each sex (average molecular weight not specified).[6] The rats were exposed nose-only for 4 h. Clinical signs observed after removal from the exposure chamber included wet fur, hunched posture, piloerection, increased respiration rate, ptosis, and isolated incidents of decreased respiration rate and red/brown stain on the head. One hour after exposure, the only observable clinical signs included hunched posture, piloerection, and increased respiration rate. By day 2 post-exposure, all animals had recovered and appeared to be normal. There were no treatment-related changes observed in body weight. No treatment-related signs of toxicity were observed at necropsy.

Dermal – Non-Human

Polybutene

In acute dermal toxicity tests, polybutene in formulations produced no abnormalities or irritation in rabbits and had an LD_{50} greater than 10.25 g/kg (average molecular weight not specified).[4]

The LD_{50} of the polybutene analog diisobutylene in rats exposed to the test material under occlusive patches for 24 h was > 2000 mg/kg.[7] No mortalities or overt signs of toxicity were observed.

Hydrogenated Polydecene

In an acute dermal toxicity study of the undiluted dimer of hydrogenated decene (analog of hydrogenated polydecene), the LD_{50} value was estimated to be > 3000 mg/kg when tested in 2 male and 2 female New Zealand White rabbits (average molecular weight not specified).[6] The rabbits received 3000 mg/kg test material on clipped

skin on the back and the test site was occluded for 24 h. The remaining test material was removed. Skin reactions observed at 24 h post-patch removal included pale red erythema and slight to mild edema. By day 14, only slight edema and desquamation were observed. One female rabbit died on day 9 of the observation period. The rabbit was observed to be emaciated prior to death. No other clinical, behavioral, or systemic signs of toxicity were observed. No treatment-related signs of toxicity were observed at necropsy.

Hydrogenated Polydodecene

The LD_{50} for undiluted hydrogenated polydodecene was > 2000 mg/kg in an acute dermal toxicity study in 5 male and 5 female Sprague-Dawley rats (average molecular weight not specified).[6] The rats were exposed to a single occluded dose of 2000 mg/kg test material for 24 h on 37 cm^2 clipped skin. The test material was removed at the end of the treatment period. No clinical signs of toxicity or skin irritation were observed. Body weight appeared unaffected by treatment and there were no treatment-related signs of toxicity observed at necropsy.

Repeated Dose Toxicity Studies

Oral – Non-Human

Polybutene

A 2-year chronic oral toxicity study of polybutene (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.[4] 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 (75% concentrate) in Beagle dogs, it was found by the authors that daily oral administration of polybutene 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. Average molecular weights of polybutene were not specified in these studies.

Polyethylene

Toxicity testing in rats showed no adverse effects to polyethylene at doses of 7.95 g/kg or at 1.25%, 2.50%, or 5.00% in feed for 90 days.[2] The average molecular weight of polyethylene was not specified in this study.

Hydrogenated Polydecene

In a 90-day oral toxicity study, groups of 20 male and 20 female Sprague-Dawley rats received hydrogenated polydecene in polyethylene glycol via gavage at dose levels of 0, 100, 500, or 1000 mg/kg bw/day for 91 days (average molecular weight not specified).[6] The toxicity of the test material was examined in F_1 generation rats following a reproduction study where the test material was administered in an in utero phase (F_0 generation). This study is described in the Reproductive and Developmental Toxicity section. The F_1 generation rats of each dose group, including the vehicle control, had minor gastrointestinal effects (no further details provided). Transient changes in body weight, body weight gain, feed consumption, hematology, and organ weights were observed but not considered to be treatment-related. A significant increase in prothrombin time was observed in males of the 1000 mg/kg/day dose group, but no corresponding decreases in platelets or macroscopic or microscopic changes were observed. Thus, this result was not considered biologically significant. No treatment-related changes in clinical chemistry, mortality, or ophthalmology were observed. The no observed adverse effect level (NOAEL) was determined to be 1000 mg/kg/day.

In another 90-day oral toxicity study of hydrogenated polydecene, 10 F-344 rats/sex/dose received the test material in their diet at dose levels of 0, 1000, 7000, or 50,000 ppm (equivalent to 77.5, 553.7, and 4159.4 mg/kg/day, respectively, in males and 85.5, 611.5, and 4619.9 mg/kg/day, respectively, in females).[6] Average molecular weight was not specified. An additional 5 rats per sex were administered control or 50,000 ppm for 13 weeks and left untreated for the following 4 weeks to examine recovery. No mortalities were observed during the course of the study. Clinical signs of toxicity observed in the 50,000 ppm group included oily and ungroomed coats, soft feces, and brown staining. Hair loss occurred at a greater incidence in the treated animals when compared to controls. Oily coats continued through the first week of the recovery period, particularly in females receiving 50,000 ppm; during recovery weeks 2-4, they appeared ungroomed and exhibited hair loss. Soft feces were also occasionally observed in the 7000 ppm females. Although there was a slight increase in feed consumption in the

high-dose group compared to controls (8% in males and 10% in females) that continued through the recovery period, there was no effect observed on either body weight or feed efficiency. There were slight (<5%), but significant increases in erythrocyte counts, hemoglobin, and packed cell volume in 7000 and 50,000 ppm males. The increase in hemoglobin was dose-related. There was also a slight (6%), but significant, increase in platelet counts in high-dose males and females. None of these effects were observed at the end of the recovery period. No treatment-related effects were noted in the bone marrow. Absolute and relative liver weights in treated males were slightly lower, however, at the end of the reversibility period the liver weights were comparable to controls. There were no treatment-related effects noted in clinical chemistry, urinalysis, gross pathology, or histopathology. The NOAEL for this 90-day study of hydrogenated polydecene was determined to be 50,000 ppm (4159.4 mg/kg/day in males and 4619.9 mg/kg/day in females).

In a 4-week dietary toxicity study in rats, the NOAEL for hydrogenated polydecene was 6245 mg/kg/day in males and 6771 mg/kg/day in females (average molecular weight not specified).[6] The test material was administered to F-344 rats (5 sex/dose) in the diet for four weeks at concentrations of 0, 8000, 20,000, or 50,000 ppm (equivalent overall mean daily intakes were 1039, 2538, or 6245 mg/kg/day for males and 995, 2481, or 6771 mg/kg/day for females). No clinical signs of toxicity or mortality were observed in any rats during the study. Overall body weight gain and feed consumption of females in the 50,000 ppm dose group was higher than the controls. A dose-dependent decrease in mandibular lymph node weights (absolute and relative to body weight) was observed in males and females; however, these results were statistically significant only for 50,000 pm females but were not considered adverse effects since there were no other findings. Gross necropsy, histopathology, and microscopic findings did not reveal any significant treatment-related findings.

Hydrogenated Polydodecene

In an oral repeated dose toxicity study, the trimer of hydrogenated dodecene (an analog of hydrogenated polydodecene) in arachis oil was administered once daily by gavage to three groups each of 10 male and 10 female Sprague-Dawley Crl:CD® (SD) IGS BR strain rats.[6] This study is described in the Reproductive and Developmental Toxicity section. Dose levels were 50, 250, or 1000 mg/kg/day. Another group of 10 male and 10 female rats received the vehicle alone to serve as a control. During the dosing period, one mortality each were observed in the control and 250 mg/kg/day dose groups. These deaths were not treatment-related. No signs of clinical toxicity or effects on behavorial and functional performance, sensory reactivity, body weight, or feed and water consumption were observed following treatment with the test material. No significant treatment-related effects were observed in the hematological and clinical chemistry assessments or during the gross pathology examination. The NOAEL for the oral administration of the trimer of hydrogenated dodecene in this oral rat study was 1000 mg/kg/day.

Another repeated dose oral toxicity study of the trimer of hydrogenated dodecene in rats determined the NOAEL to be 1000 mg/kg/day.[6] The test material was administered by oral gavage to 5 Sprague-Dawley CD rats/sex/dose at dose levels 0 or 1000 mg/kg body weight/day for 28 consecutive days. An additional 2 satellite groups (0 and 1000 mg/kg/day) were also maintained without treatment for 14 days following the end of the dosing period. Treatment-related effects in mortality, clinical signs, body weight, feed consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology were not observed.

Dermal – Non-Human

Polybutene

Polybutenes did not affect hepatic or skin enzymatic activities in rats following once daily treatments for 6 days (average molecular weight not specified).[4]

REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY

Polybutene

No teratogenic effects were found when polybutene was fed to rats at 1% or 10% in the diet for six months.[4] *A three-generation reproductive study in Charles River albino rats that ingested polybutene 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. Average molecular weights were not specified in these studies.*

Hydrogenated Polydecene

The reproductive effects of hydrogenated polydecene were studied in rats that received the test material via oral gavage (average molecular weight not specified).[6] (See 90-day repeated dose study of hydrogenated polydecene in Sprague-Dawley rats described in the above Repeated Dose Toxicity section). Groups of 30 male and 30 female Sprague-Dawley rats received 0, 100, 500, or 1000 mg/kg bw/day hydrogenated polydecene in polyethylene glycol daily for 4 weeks prior to mating and through mating. At the end of mating, males were sacrificed. Females were treated through gestation and until lactation day 21. No treatment-related effects were observed on clinical signs, body weight, or gross pathology in the parental generation or in the pups through lactation day 21. There were no treatment related effects on reproduction or pup viability. The NOAEL for parental systemic effects, parental reproductive effects, and offspring effects in this one generation rat study is 1000 mg/kg bw/day.

Hydrogenated Polydodecene

The reproductive effects of the trimer of hydrogenated polydodecene (analog of hydrogenated polydodecene) were studied in one generation of rats that received the test material via gavage.[6] (See repeated dose study of the trimer of hydrogenated polydodecene in Sprague-Dawley rats described in the above Repeated Dose Toxicity section). Groups of 24 male and 24 female Sprague-Dawley rats received 0, 50, 250, or 1000 mg/kg/day of the test material in arachis oil daily. Two non-treatment related mortalities occurred during the study, one in the control group and the other in the 250 mg/kg/day dose group. No treatment-related effects were observed on clinical signs, body weight, feed and water consumption, or fertility and mating performance in the parental rats. Hematological and clinical chemistry measurements were within normal parameters. No treatment-related effects on offspring growth or development were observed. Litter sizes were comparable to controls in all dose groups. No adverse effects were observed during gross necropsy or histopathological examination. The NOAEL for adult toxicity and reproductive and development toxicity in this rat study is 1000 mg/kg/day.

GENOTOXICITY

In vitro

Polyethylene

Genotoxicity testing of polyethylene was negative in two bacterial studies.[2] Average molecular weights were not specified in these studies.

Polyisobutene

In a study to determine the ability of various insulating fluids to induce transformation in the Syrian hamster embryo (SHE) cell transformation assay and to enhance 3-methylcholanthrene (MCA)-induced transformation of C3H/10T1/2 cells, a low-viscosity polyisobutene-based oil did not induce transformation activity and was slightly cytotoxic.[3] In the two-stage transformation assay of C3H/10T1/2 cells, the polyisobutene oil had promoter activity. Average molecular weights werenot specified in these studies.

Hydrogenated Polydecene

Hydrogenated polydecene was not mutagenic in a reverse gene mutation assay in *Salmonella typhimurium* strains TA1535, TA1537, TA98, and TA100 and *Escherichia coli* strain WP2uvrA (average molecular weight not specified).[6] The test material was incorporated in emulsions with sorbitan stearate and polysorbate 60 at concentrations of 156.25, 312.5, 625, 1250, 2500, or 5000 μg/plate, with and without metabolic activation using the pre-incubation method. The positive controls yielded expected results.

In reverse mutation assays, *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 were treated with hydrogenated polydecene at concentrations up to 10 mg/plate (average molecular weight not specified).[6] The positive controls yielded expected results. Hydrogenated polydecene was not mutagenic with or without S9 metabolic activation at all tested doses.

Hydrogenated Polydodecene

The genotoxic potential of the trimer of hydrogenated polydodecene (an analog of hydrogenated polydodecene) was assayed in a chromosome aberration study using human lymphocyte cultures in 2 experiments.[6] In the first experiment, the test material was cultured at concentrations of 0, 39, 78.1, 156.25, 31 2.5, 625, 1250, 2500 and 5000 μg/mL. In the second experiment, the test material was cultured at concentrations of 625, 1250, 2500 and 5000μg/mL for 20 hours or 1250, 2500, and 5000 μg/mL for a 44 hour harvest time. All experiments

were conducted in duplicate, with and without S9 metabolic activation. Cytotoxicity was not observed in a range finding test conducted prior to the main assay at concentrations ≤ 5000 µg/ml. The test material did not induce chromosomal aberrations or polyploidy cells, with or without metabolic activation. Positive controls, ethyl methanesulfonate in the absence of S9, and cyclophosphamide in the presence of S9, yielded expected results. The authors concluded that the trimer of hydrogenated polydodecene was not clastogenic to human lymphocytes in vitro when tested at concentrations ≤ 5000 µg/mL.

In a mammalian cell gene mutation assay (HGPRT locus), Chinese hamster ovary (CHO) cells cultured in vitro were exposed to the trimer of hydrogenated polydodecene in ethanol at concentrations of 0, 313, 625, 1250, 2500, or 5000 µg/mL with and without metabolic activation for 4 hours.[6] In the range-finding test, relative cloning frequencies (RCEs) ranged from 97% to 73% for doses ranging from 0.5 to 5000 µg/mL without metabolic activation. RCEs were 122% to 80% for the same dose range with metabolic activation. RCEs in the first mutation assay were 92% to 77% and 111% to 89% for doses ranging 313 to 5000 µg/mL with and without metabolic activation, respectively. The activated portion of the first mutation assay was repeated and RCE was 100% to 71% for the same dose range. In the confirmatory assay, the RCEs among the test material-treated cultures ranged from 50% to 23% and 89% to 52% for the concentrations of 313 to 5000 µg/mL with and without metabolic activation, respectively. A significant response was observed at 625 µg/mL when compared to the solvent control data in the repeat definitive mutation assay with activation; however, the increase was not significant when it was compared to the historical, cumulative solvent control data. The same was true at 2500 µg/mL, with activation, in the confirmatory mutation assay. The increase in the number of mutants was not significant when compared to historical, cumulative solvent control data. The response seen in the definitive mutation assay at 625 µg/mL was not reproduced in the confirmatory assay. Controls were within the historical negative control values. The trimer of hydrogenated polydodecene was not mutagenic in this mammalian cell gene mutation assay.

CARCINOGENICITY

Polyethylene

Numerous investigations on the tumor production of polyethylene implantation have produced mixed results.[2] 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." Average molecular weights were not specified.

Polyisobutene

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 (average molecular weight 250) appeared to reduce the number of 7,12-dimethylbenz[a]anthracene (DMBA)-induced tumors.[3]

Polypropylene

IARC determined that polypropylene is not classifiable as to its carcinogenicity to humans (Group 3).[23]

IRRITATION AND SENSITIZATION

Irritation

Dermal – Non-Human

Polybutene

In primary skin irritation studies, polybutene in formulations produced no abnormalities or irritation in rabbits at concentrations up to 15%; however, mild irritation was observed at concentrations greater than 15%.[4] Average molecular weights were not specified.

Polyethylene

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.[2] 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.

Hydrogenated Polyisobutene

A skin irritation study in six rabbits using four patches each containing 0.5 g/patch of a hydrogenated polyisobutene mixture caused no reactions in any of the animals on intact or abraded skin.[3] The primary irritation index was 0.0. There was a primary irritation index score of 1.8 for rabbits treated with undiluted hydrogenated polyisobutene on the intact or abraded skin. Rabbits dosed dermally with 0.5 ml hydrogenated polyisobutene) on intact and abraded skin exhibited a primary irritation index of 0.38; not a dermal irritant. In a similar study, hydrogenated polyisobutene produced a primary irritation index of 0.96; also not a dermal irritant. Average molecular weights were not specified in these studies.

Hydrogenated Polydecene

In a primary skin irritation study, 6 New Zealand White rabbits were treated with 0.5 mL of hydrogenated polydecene on clipped or abraded skin (average molecular weight not specified).[6] The test sites were then occluded. At 24 h, any remaining test material was washed off and the animals were observed for skin reactions at 24 and 72 h. At 24 h, slight erythema was observed in 4 of the abraded sites and 5 of the intact sites. Slight edema was observed on 3 of the abraded sites. Edema was observed at an abraded site at the end of the treatment. All effects had reversed 2 days post-exposure. After 72 h, the mean erythema score was 0.42 for both the intact and abraded skin. The mean edema score after 72 h was 0.17 for intact skin and 0.08 for abraded skin. Based on these results, the study authors calculated a primary dermal irritation index of 0.5 for hydrogenated polydecene and concluded that it was not a primary irritant or corrosive when applied dermally to rabbits.

A similar study of 0.5 ml hydrogenated polydecene assessed the primary skin irritation potential in 6 female New Zealand White rabbits (average molecular weight not specified).[6] The mean erythema score for intact skin over 72 h was 0.75, while the mean erythema score for the same time period was 0.67. The mean edema score for intact and abraded skin over 72 h was 0.25 and 0.08, respectively. All rabbits had very slight to well-defined erythema on both intact and abraded sites and slight edema on 3 intact and 1 abraded site s at the end of treatment. There was no difference in severity between intact and abraded sites. Two days after treatment, only 1 abraded site still had evidence of slight erythema. The primary dermal irritation index was calculated to be 0.9 and the authors of the study concluded that hydrogenated polydecene was not a primary irritant or corrosive when applied dermally to rabbits.

The trimer of hydrogenated decene (an analog of hydrogenated polydecene) was considered to be a mild irritant following the Draize classification system, but the EU classification system indicated it was non-irritating.[6] Groups of 3 New Zealand White rabbits were dermally exposed to 0.5 ml of undiluted test material on 2.5 cm^2 areas that were semi-occluded for up to 4 h. In the preliminary rabbit tested, the compound was applied for 3 min and 1 h to test for corrosivity. Animals were observed for 7 days. No treatment-related changes in body weight were observed. Very slight erythema and edema were observed in 1 rabbit through 72 h. At 72 h, the skin had lost its elasticity and flexibility. At 7 days, slight desquamation was observed. No effects were observed in the other 2 rabbits.

Dermal – Human

Polybutene

Human primary irritation tests of a formulation containing 20% polybutene produced no irritation.[4] *The average molecular weight was not specified.*

Hydrogenated Polyisobutene

No primary skin irritation was produced in a 72-h primary skin irritation patch test study with 100% hydrogenated polyisobutene in 25 male and female participants.[3] There was no irritancy observed in humans during a 24-h single-insult patch test with a lip gloss containing 66.11% hydrogenated polyisobutene. Average molecular weights were not specified in these studies.

In a study to analyze the effects of hydrogenated polyisobutene on skin moisturization, no adverse effects were reported when 10 female subjects were treated with a single application of a formulation containing 8% of the test material.[24] The average molecular weight of hydrogenated polyisobutene was not specified.

Hydrogenated Polydecene

In a study of formulations with differing ratios of polyols and oils on skin moisturization and skin surface roughness in 98 subjects, no adverse effects were reported following exposure to formulations containing

hydrogenated polydecene with equal amounts of cetylethylhexanoate and pentaerythrityl tetraehtylhexanoate tested at total concentrations up to 35%.[25] The average molecular weight of hydrogenated polydecene was not specified.

Ocular – Non-Human

Polybutene

Rabbits suffered only minimal eye irritation when polybutenes were instilled into the eyes with and without washouts.[4] Average molecular weights were not specified.

Polyethylene

Polyethylene (molecular weight of 450) was tested as a solid material (66 mg) in the eyes of rabbits.[2] 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.

Polyisobutene

Irritant and corrosive effects were examined using a single instillation of polyisobutene into rabbit eyes.[3] 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. The average molecular weight was not specified.

Hydrogenated Polyisobutene

When 0.1 ml 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.[3] The authors determined that hydrogenated polyisobutene is not an eye irritant. Another study of 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 7-day eye irritation study on rabbits using 0.1 ml hydrogenated polyisobutene produced no eye irritation in any of the washed or unwashed rabbit eyes. An unknown concentration of hydrogenated polyisobutene instilled into the right eyes of six rabbits produced a score of 1 on the Draize scale. No other effects were observed. Average molecular weights were not specified in these studies.

Hydrogenated Polydecene

In a primary eye irritation study in New Zealand White rabbits, 0.1 ml of undiluted hydrogenated polydecene was instilled into the conjunctival sac of the right eye of each animal (3/sex; average molecular weight not specified).[6] Eyes were not rinsed. Animals then were observed for 72 h. No corneal lesions or iris changes were observed in any of the animals. Conjunctival changes included mild erythema in 5 of the 6 rabbits that were still present in 3 of the rabbits at 72 h and swelling occurred in 3 of the rabbits. None of the rabbits had any discharge. Individual total scores over the three time points for all changes observed ranged from 0 to 4 out of a possible score of 110. The authors concluded that hydrogenated polydecene was not an ocular irritant.

In another ocular study of 9 male New Zealand White rabbits, 0.1ml hydrogenated polydecene was instilled into the conjunctival sac of one eye while the other eye served as control (average molecular weight not specified).[6] Treated eyes were examined for ocular irritancy at 1, 24, 48, and 72 h post-treatment. Both eyes of 3 of the 9 treated rabbits were rinsed with distilled water and the rinsed eyes were examined for ocular irritancy at 1, 24, 48, and 72 h. None of the rabbits exhibited corneal lesions or iris changes. In the unrinsed eyes, moderate to severe conjunctival redness with oily residue was noted at 1 h. By 24 h, there was only slight redness and the eye was clear by 48 h. In the rinsed eyes, there was no to slight conjunctival redness 1 h after treatment with oily residue around the eye; the eyes were clear by 24 h. The study authors concluded that hydrogenated polydecene was moderately irritating.

Ocular – Human

Hydrogenated Polyisobutene

Three shades of coded cosmetic foundations/concealer products, two containing an unspecified concentration of hydrogenated polyisobutene and one containing 4% hydrogenated polyisobutene, were examined

for signs of ocular irritation when used at least once a day for 29 days by 59 subjects.[3] There were no adverse reactions reported. Average molecular weights were not specified.

Mucous Membrane – Non-Human

Polybutene

Polybutene produced no irritation or signs of systemic toxicity when applied to the vaginas of rabbits.[4] Average molecular weight was not specified.

Sensitization

Dermal – Non-Human

Polyethylene

Polyethylene (average molecular weight of 450) did not cause dermal sensitization in guinea pigs tested with 50% polyethylene (w/w) in arachis oil BP.[2]

Hydrogenated Polyisobutene

Hydrogenated polyisobutene was intradermally injected in an area of the skin on the back and flanks of guinea pigs.[3] 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. Average molecular weights were not specified in these studies.

Hydrogenated Polydecene

Hydrogenated polydecene was not a dermal sensitizer in a guinea pig maximization test at concentrations up to 10% v/v (average molecular weight not specified).[6] After an initial range finding test, hydrogenated polydecene was administered intradermally to 10 male and 10 female Hartley guinea pigs at 5.0% v/v in mineral oil. One week after the intradermal induction, treatment groups were induced by topical application of the 10% v/v test material in mineral oil for 48 hours. Fourteen days following topical induction, all animals received a 10% v/v test material in mineral oil challenge application at naïve sites. In addition to test material administration, additional groups of 20 animals also received vehicle control and 1-chloro-2, 4-dinitrobenzene (DNCB) as positive control.

One female in the test group exhibited abnormal gait, flaccid body tone and tremors on day 9 of the study and then was found dead on day 10 of the study. The death was not considered treatment-related by the study authors. No signs of skin irritation, edema, or erythema were observed in any of the remaining male or female treatment or vehicle control group animals throughout the study period. No other signs of clinical toxicity were noticed following administration of the test material. Animals that received the positive control experienced expected results. The individual and group mean body weights for both male and female guinea pigs were found to be similar to those of the vehicle controls through the study period.[6]

In a dermal maximization study of hydrogenated polydecene in corn oil, 20 Dunkin-Hartley guinea pigs were treated with 6 intradermal injections of the test material (2 injections at 50% aqueous Freund's Complete Adjuvant, 2 injections of 100% test material, and 2 injections of 100% test material in 25% aqueous Freund's Complete Adjuvant).[6] Control group animals were treated with 6 intradermal injections (2 injections of 50% aqueous Freund's Complete Adjuvant, 2 injections vehicle, and 2 injections of the vehicle in 25% aqueous Freund's Complete Adjuvant). On test day 6, no irritation was observed so the test sites were treated with 0.5 ml of 10% sodium lauryl sulfate. On test day 7, each test group animal was treated with a topical application of the test material for 48 h. The control group received vehicle only. On test day 20, animals were challenged with 100% hydrogenated polydecene via topical application. During the challenge, 2 test group animals exhibited positive responses (details not provided) to the test material. No positive responses were observed in the control animals. A rechallenge was conducted using 50% and 100% hydrogenated polydecene. A positive response was observed in one animal exposed to 100% hydrogenated polydecene. The authors concluded that hydrogenated polydecene was not a dermal sensitizer in this maximization study. Average molecular weight of hydrogenated polydecene was not specified.

Hydrogenated polydecene was not a dermal sensitizer in a sensitization study in 10 male Hartley guinea pigs (average molecular weight not specified).[6] The animals were patched with a Webril pad containing 0.5 ml hydrogenated polydecene on the midline of the back. A positive control group were patched with DNCB. A challenge dose of 0.5 ml of the test material and the positive control was administered 2 weeks after the final

sensitization dose. Eight of the 10 animals in the treated group had slight erythema and edema. All animals in the positive control group also exhibited slight erythema and edema.

In a delayed contact hypersensitivity study in 10 male and 10 female Hartley guinea pigs treated with a dimer of hydrogenated decene (an analog of hydrogenated polydecene), sensitization by the test material was not induced.[6] The guinea pigs were induced with 3 occlusive exposures of 5% w/v test material in spectrum oil for a duration of 6 h for 3 weeks. Following a 2 week rest period, the test animals and a naïve control group were challenged with 5 % w/v of the test material in spectrum oil. The animals were scored for skin sensitizing reactions at 24 and 48 h following the challenge phase. The primary challenge resulted in a grade 1 response (details not provided).

In another dermal sensitization study of the dimer of hydrogenated decene, 10 male and 10 female Hartley guinea pigs were tested according the Magnusson-Kligman maximization test protocol.[6] The animals were intradermally induced with 5% of the test material in mineral oil. A negative control group was induced with vehicle alone and a positive control group received DNCB. The animals were topically challenged with 10% of the test material. No signs of skin irritation, edema, or erythema were observed in any of treated animals or vehicle control group animals throughout the study period. No other signs of clinical toxicity were noticed following administration of the test material. The individual and group mean body weights for male and female guinea pigs were found to be similar to those of the vehicle controls through the study period. In this study, the dimer of hydrogenated decene was not a dermal sensitizer.

The trimer of hydrogenated decene (an analog of hydrogenated polydecene), in propylene glycol was a slight sensitizer according to an local lymph node assay (LLNA).[6] The stimulation indices were 1.56, 1.89, and 3.54 for the test concentrations of 25%, 50%, and 100%, respectively. EC_3 values were not provided.

Dermal – Human

Polybutene

Repeated insult patch tests of 3.1-50% polybutene in formulations produced, at most, minimal irritation in a small percentage of the test population.[4] The products tested produced no irritation or sensitization. Average molecular weights were not specified.

Polyethylene

In a repeat insult patch test of 201 volunteers, a product containing 13% polyethylene beads was tested in a series of nine consecutive administrations.[2] 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. The average molecular weight of polyethylene was not specified in this study.

Hydrogenated Polyisobutene

Repeat-insult patch tests performed to evaluate the primary irritancy/sensitization potential of formulaitons containing 1.44% or 4% hydrogenated polyisobutene in 54 male and female subjects found no reactions greater than slight erythema.[3] 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. Average molecular weights were not specified.

Phototoxicity

Polybutene

Photo patch tests of formulations with concentrations ranging from 15% to 50% polybutene produced no reactions.[4] Average molecular weights were not specified.

Hydrogenated Polyisobutene

The phototoxic potential of cosmetic foundations/concealer products containing 4% hydrogenated polyisobutene or 1.44% hydrogenated polyisobutene, and a blank patch under UVA light source (320 to 400 nm) was studied in 26 fair-skinned volunteers.[3] No significant reactions were reported. Formulations containing 1.44% or 4% 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. Average molecular weights were not specified.

Comedogenicity

Polyisobutene

The comedogenic potential of polyisobutene was studied using adult New Zealand White rabbits.[3] 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. The average molecular weight of polyisobutene was not specified.

CLINICAL STUDIES

Polyethylene

There have only been a few cases of reactions to the implantation of polyethylene in humans.[2] 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.

SUMMARY

Data from earlier CIR safety assessments on polybutene, polyethylene, polyisobutene, and hydrogenated polyisobutene have not been summarized here. Only new data are summarized below.

The polyenes function mainly as film formers and/or viscosity increasing agents-nonaqueous in cosmetic products. Polyethylene has the most reported uses in cosmetic and personal care products, with a total of 2763; the single category with the most reported uses was lipstick with 896. Hydrogenated polyisobutene has the second greatest number of overall uses reported, with a total of 1997; the single category with the most reported uses was lipstick with 841.

In a survey of use concentrations conducted by the Personal Care Products Council, polyethylene had a highest maximum use concentration of 67.6%, which was reported in skin cleansing preparations. Hydrogenated polyisobutene had a highest maximum use concentration of 95%, which was reported in lipstick.

Many of the polyene ingredients have been approved by the FDA for use as food additives and in medical devices.

An oral study that assessed the absorption potential of undiluted hydrogenated polydecene in rats found that the majority of the test compound was excreted into the feces without being absorbed (> 92%). Urinary excretion was low (< 1%), and very little of the dose was recovered in the bile (0.01%).

In acute oral toxicity studies in rats, the LD_{50}s of diisobutylene and triisobutylene were > 2000 mg/kg/body weight each in rats. The oral LD_{50}s of di-n-butene, tributene, and tetrabutene (containing 30% pentabutene) in rats were > 10,000 mg/kg each. The oral LD_{50} values for undiluted hydrogenated polydecene and undiluted hydrogenated polydodecene were > 5000 mg/kg in rat studies.

In acute inhalation studies, the LC_{50} of diisobutylene vapor in albino rats was > 4185 ppm (19,171 mg/m^3) after a 4- hour, single, whole-body exposure. The LC_{50} for an aerosol of hydrogenated polydecene was > 5.2 mg/L in rats. The combined LC_{50} for the dimer of hydrogenated decene was 1.17 mg/L in rats. In another acute inhalation study of the dimer of hydrogenated decene, the LC_{50} could not be determined in rats tested at 5 mg/L because 9/10 animals died within 3 days of administration of the test material. The LC_{50} for hydrogenated polydodecene was > 5.06 mg/L.

Acute dermal studies of diisobutylene and hydrogenated polydodecene found the LD_{50} values > 2000 mg/kg in rats. In a rabbit study, the dermal LD_{50} value for the dimer of hydrogenated decene was > 3000 mg/kg.

No adverse effects were observed in oral repeated dose studies of hydrogenated polydecene, with the NOAELs determined to be 1000 mg/kg/day in one 90-day rat study and over 4000 mg/kg/day in another. In a 4 week oral repeated dose study, the NOAEL for hydrogenated polydecene was 6245 mg/kg/day in males and 6771 mg/kg/day in females. Gross necropsy, histopathology, and microscopic findings did not reveal any significant treatment-related findings. The NOAEL for the oral administration of the trimer of hydrogenated dodecene in two respective oral repeated dose toxicity studies in rats was 1000 mg/kg/day. Treatment-related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology were not observed in either study.

In rat reproductive studies of hydrogenated polydecene and the trimer of hydrogenated polydodecene, the NOAELs for parental systemic and reproductive effects and for offspring were 1000 mg/kg body weight/day for the respective studies. No treatment-related effects were observed on clinical signs, body weight, or gross pathology in the parental generation or in the pups. There were no treatment related effects on reproduction or pup viability.

Hydrogenated polydecene at concentrations up to 10 mg/plate was not mutagenic in Ames assays, with or without metabolic activation. The trimer of hydrogenated polydodecene was not clastogenic to human lymphocytes nor was it mutagenic in CHO cells (HGPRT locus assay) in vitro when tested at concentrations up to 5000 µg/mL.

IARC determined that polypropylene is not classifiable as to its carcinogenicity to humans (Group 3).

Hydrogenated polydecene and the trimer of hydrogenated decene were not primary irritants or corrosives in several rabbit studies. In a study to analyze the effects of hydrogenated polyisobutene on skin moisturization in humans, no adverse effects were reported in subjects treated with a single application of a formulation containing 8% of the test material. No adverse effects were reported following exposure to formulations containing hydrogenated polydecene with equal amounts of cetylethylhexanoate and pentaerythrityl tetraehtylhexanoate tested at total concentrations up to 35% in a study in human subjects.

One primary eye irritation study in rabbits found undiluted hydrogenated polydecene not to be an ocular irritant, while another study found the material to be moderately irritating.

Hydrogenated polydecene was not a dermal sensitizer in guinea pig maximization tests at concentrations up to 100%. The dimer of hydrogenated decene was not a dermal sensitizer in one guinea pig maximization study and was given a grade 1 response in another. The trimer of hydrogenated decene in propylene glycol was a slight sensitizer according to an LLNA. The stimulation indices were 1.56, 1.89, and 3.54 for the test concentrations of 25%, 50%, and 100%, respectively.

DATA NEEDS

Clarification on the method of manufacture and types and concentrations of impurities, including residual monomers, initiators, and catalysts, found in cosmetic-grade polyene ingredients is desired. The average molecular weights of the polyenes used in personal care products is also desired. Additional toxicological data that would help the CIR Expert Panel assess the safety of the use of these ingredients in cosmetics is always welcomed.

TABLES AND FIGURES

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1]
(The idealized copolymer structures herein present a depiction of block copolymers only for the sake simplicity and are not intended to suggest that block is the dominant form)

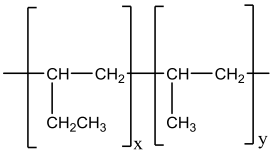
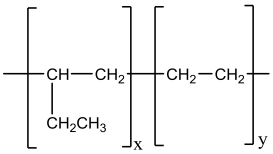
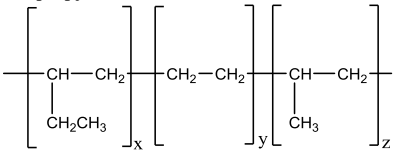
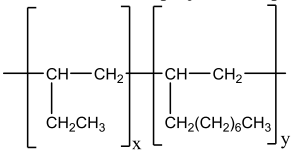
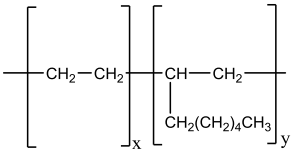
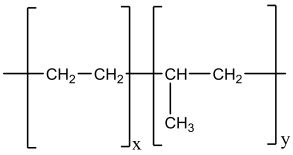
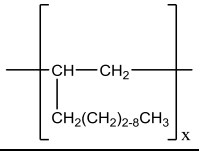
Ingredient CAS No.	Definition & Structure	Function(s)
Butene/Propylene Copolymer 29160-13-2	Butene/Propylene Copolymer is a copolymer of butene and propylene monomers. 	film formers; slip modifiers; viscosity increasing agents-nonaqueous
Butylene/Ethylene Copolymer	Butylene/Ethylene Copolymer is a copolymer of butylene and ethylene monomers. 	viscosity increasing agents-nonaqueous
Butylene/Ethylene/Propylene Copolymer	Butylene/Ethylene/Propylene Copolymer is a copolymer of butylene, ethylene and propylene monomers. 	film formers
Decene/Butene Copolymer	Decene/Butene Copolymer is a polymer of butene and decene monomers. 	viscosity increasing agents-nonaqueous
Ethylene/Octene Copolymer	Ethylene/Octene Copolymer is a copolymer of ethylene and 1-octene monomers. 	film formers; viscosity increasing agents-nonaqueous
Ethylene/Propylene Copolymer 9010-79-1	Ethylene/Propylene Copolymer is the copolymer of ethylene and propylene monomers. 	film formers; viscosity increasing agents-nonaqueous
Hydrogenated Poly(C6-12 Olefin) 68037-01-4	Hydrogenated Poly(C6-12 Olefin) is a series of low molecular weight polymers of olefin monomers, each containing 6 to 12 carbon atoms. 	skin-conditioning agents-occlusive; viscosity increasing agents-nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1]
(The idealized copolymer structures herein present a depiction of block copolymers only for the sake simplicity and are not intended to suggest that block is the dominant form)

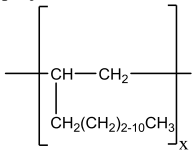
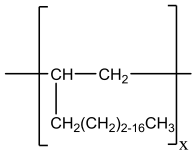
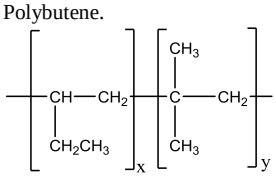
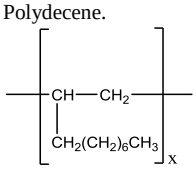
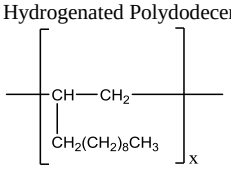
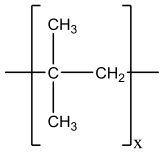
Ingredient CAS No.	Definition & Structure	Function(s)
Hydrogenated Poly(C6-14 Olefin) 68037-01-4	Hydrogenated Poly(C6-14 Olefin) are a series of low molecular weight polymers of olefin monomers, each containing 6 to 14 carbon atoms. 	skin-conditioning agents-occlusive; viscosity increasing agents-nonaqueous
Hydrogenated Poly(C6-20 Olefin) 69430-35-9	Hydrogenated Poly(C6-20 Olefin) is a polymer synthesized from hydrogenated C6-20 olefins. 	epilating agents
Hydrogenated Polybutene	Hydrogenated Polybutene is the end-product of the controlled hydrogenation of Polybutene. 	viscosity increasing agents-nonaqueous
Hydrogenated Polydecene 68037-01-4	Hydrogenated Polydecene is the end-product of the controlled hydrogenation of Polydecene. 	fragrance ingredients; hair conditioning agents; skin-conditioning agents-emollient; skin-conditioning agents-misc.; solvents
Hydrogenated Polydodecene	Hydrogenated Polydodecene is the hydrogenated homopolymer of Dodecene. 	binders; hair conditioning agents; skin-conditioning agents-emollient; solvents; viscosity increasing agents-nonaqueous
Hydrogenated Polyisobutene 68937-10-0	Hydrogenated Polyisobutene is the polymer that conforms generally to the formula: 	skin-conditioning agents-emollient; viscosity increasing agents-nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1]
(The idealized copolymer structures herein present a depiction of block copolymers only for the sake simplicity and are not intended to suggest that block is the dominant form)

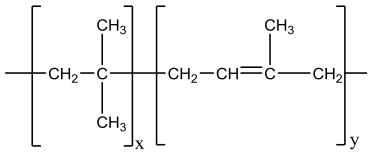
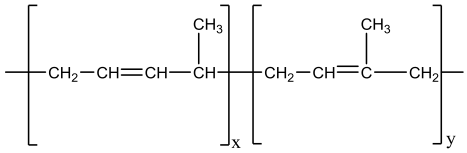
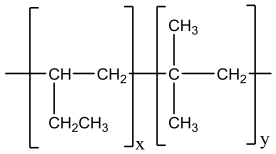
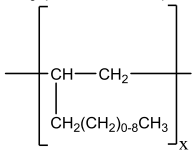
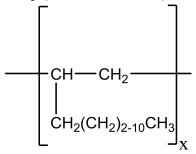
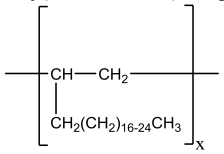
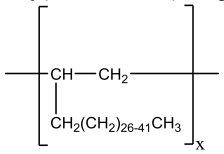
Ingredient CAS No.	Definition & Structure	Function(s)
Isobutylene/Isoprene Copolymer 9010-85-9	Isobutylene/Isoprene Copolymer is a copolymer of isobutylene and isoprene monomers. 	viscosity increasing agents-nonaqueous
Isoprene/Pentadiene Copolymer	Isoprene/Pentadiene Copolymer is a copolymer of isoprene and 1,3-pentadiene monomers. 	viscosity increasing agents-nonaqueous
Polybutene 9003-28-5 9003-29-6	Polybutene is the polymer formed by the polymerization of a mixture of iso- and normal butenes. 	binders; epilating agents; viscosity increasing agents-nonaqueous
Poly(C4-12 Olefin)	Poly(C4-12 Olefin) is a polymer synthesized from C4-12 olefins. 	skin-conditioning agents-occlusive
Poly(C6-14 Olefin)	Poly(C6-14 Olefin) is a polymer synthesized from C6-14 olefins. 	viscosity increasing agents-nonaqueous
Poly(C20-28 Olefin) 64743-02-8	Poly(C20-28 Olefin) is a polymer synthesized from C20-28 olefins. 	binders; film formers; skin-conditioning agents-occlusive; surface modifiers; viscosity increasing agents-nonaqueous
Poly(C30-45 Olefin)	Poly(C30-45 Olefin) is a polymer synthesized from C30-45 olefins. 	film formers

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1]
(The idealized copolymer structures herein present a depiction of block copolymers only for the sake simplicity and are not intended to suggest that block is the dominant form)

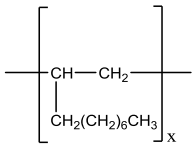
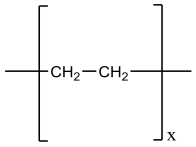
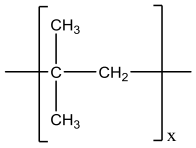
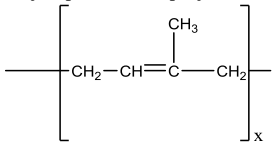
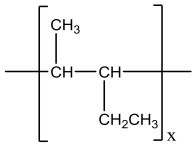
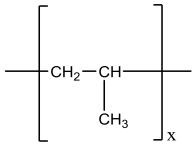
Ingredient CAS No.	Definition & Structure	Function(s)
Polydecene 25189-70-2 37309-58-3	Polydecene is the polymer formed by the polymerization of decene. It conforms to the formula: 	skin-conditioning agents-occlusive
Polyethylene 9002-88-4	Polyethylene is a polymer of ethylene monomers that conforms generally to the formula: 	abrasives; adhesives; binders; bulking agents; emulsion stabilizers; film formers; oral care agents; viscosity increasing agents-nonaqueous
Polyisobutene 9003-27-4	Polyisobutene is the homopolymer of isobutylene that conforms generally to the formula: 	binders; film formers; viscosity increasing agents-nonaqueous
Polyisoprene 9003-31-0	Polyisoprene is the polymer of isoprene that conforms generally to the formula: 	viscosity increasing agents-nonaqueous
Polypentene 9078-70-0	Polypentene is the polymer formed by the polymerization of pentene. It conforms to the formula: 	film formers; viscosity increasing agents-nonaqueous
Polypropylene 9003-07-0	Polypropylene is a polymer of propylene monomers that conforms generally to the formula: 	bulking agents; viscosity increasing agents-nonaqueous

Table 2. Physical and chemical properties of polyenes

Property	Value	Reference
Polybutene		
Physical Form	Light colored, nondrying, sticky viscous liquid	[4]
Solubility	Insol. in water, sol. in hydrocarbon and chlorinated hydrocarbon solvents	[4]
Melting point ^{o}C	124-130	[4]
Density g/cm^3	0.92	[4]
Polyethylene		
Odor	odorless	[2]
Molecular Weight g/mol	198-500,000	[2]
Melting point ^{o}C	85-110	[2]
Flammability (flash point) ^{o}C	221	[2]
Density g/cm^3	0.910-0.925	[2]
Maximum λ (nm)	161.5	[2]
Polyisobutene		
Physical Form	White to yellowish or pale rubbery solid	[3]
Odor	Slight rubber/petroleum odor	[3]
Molecular Weight g/mol	900 minimum	[3]
Flash point ^{o}C	165	[3]
Solubility	Insol. in water	[3]
Specific gravity g/cm^3	0.92	[3]
Hydrogenated Polyisobutene		
Physical Form	Clear liquid	[3]
Odor	Odorless	[3]
Molecular Weight g/mol	350 minimum	[3]
log K_{ow}	13.27	[3]
Solubility	Negligible in water	[3]
Boiling point ^{o}C	35	[3]
Freezing point ^{o}C	Below -30	[3]
Specific gravity at 20 ^{o}C (g/cm^3)	0.819-0.830	[3]

Table 2. Physical and chemical properties of polyenes

Hydrogenated Polydecene		
Physical Form at 20 ^{o}C and 1013 hPa	Clear liquid	[6]
Odor	Odorless	[6]
log K_{ow}	> 6.5	[6]
Solubility in water at 20 ^{o}C (mg/l)	< 0.1	[6]
Vapor pressure at 20 ^{o}C	< 0.545	[6]
Freezing point ^{o}C at 1013 hPa	-57	[6]
Specific gravity at 15.6 ^{o}C (g/cm^{3})	0.82 to 0.83	[6]

Table 3. Frequency (2014) and concentration of use (2013) according to duration and type of exposure for polyene ingredients.[10-12]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Butylene/Ethylene Copolymer		**Butylene/Ethylene/Propylene Copolymer**		**Decene/Butene Copolymer**		**Ethylene/Propylene Copolymer**	
Totals[†]	**1**	**1.5**	**14**	**4.5**	**3**	NR	**100**	**0.0063-12.5**
Duration of Use								
Leave-On	1	NR	14	4.5	3	NR	100	0.0063-12.5
Rinse Off	NR	1.5	NR	NR	NR	NR	NR	2
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	2	NR	1	NR	7	0.0063-4
Incidental Ingestion	1	NR	8	NR	2	NR	68	0.0097-12.5
Incidental Inhalation-Spray	NR	NR	1a	NR	NR	NR	4; 6[a]; 1[b]	0.11; 0.21[a]
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	1; 1[b]	NR
Dermal Contact	NR	1.5	5	4.5	NR	NR	29	0.0063-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	3	2
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	1	1.5	8	NR	2	NR	68	0.0097-12.5
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Ethylene/VA Copolymer		**Hydrogenated Poly(C6-14 Olefin)**		**Hydrogenated C6-14 Olefin Polymers**[c]		**Hydrogenated Poly(C6-20 Olefin)**	
Totals[†]	**70**	**0.002-8**	**18**	**0.25-58**	**96**	**NR**	**NR**	**10**
Duration of Use								
Leave-On	66	0.002-2.1	18	58	92	NR	NR	10
Rinse Off	4	8	NR	0.25-1	4	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	17	0.83-2.1	NR	NR	13	NR	NR	NR
Incidental Ingestion	10	0.21	8	58	6	NR	NR	10
Incidental Inhalation-Spray	2; 8[a]; 6[b]	NR	3[a]; 3[b]	NR	15[a]; 25[b]	NR	NR	NR
Incidental Inhalation-Powder	1; 6[b]	NR	2; 3[b]	NR	25[b]	NR	NR	NR
Dermal Contact	36	0.08-8	10	NR	90	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	0.25-1	NR	NR	NR	NR
Nail	16	0.002-2	NR	NR	NR	NR	NR	NR
Mucous Membrane	10	0.21	8	58	6	NR	NR	10
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 3. Frequency (2014) and concentration of use (2013) according to duration and type of exposure for polyene ingredients.[10-12]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Hydrogenated Polydecene		**Hydrogenated Polyisobutene**		**Polybutene**		**Poly (C30-45 Olefin)**	
Totals[†]	**743**	**0.005-59**	**1997**	**0.00055-95**	**1718**	**0.1-82.4**	**1**	**0.6-26.1**
Duration of Use								
Leave-On	710	0.035-59	1950	0.001-95	1703	0.1-82.4	1	0.6-26.1
Rinse Off	33	0.005-49	47	0.00055-51	15	8-20	NR	NR
Diluted for (Bath) Use	NR	35	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	76	2-38	221	0.09-67.7	220	0.5-13.1	NR	NR
Incidental Ingestion	184	5.2-59	841	0.29-95	1254	6-82.4	NR	NR
Incidental Inhalation-Spray?[2, 5]	16; 213[a]; 108[b]	1.8-42; 0.88-5[a]	10; 189[a]; 220[b]	0.048-31; 0.53-58.9[a]	2; 12[a]; 8[b]	0.1; 20[a]	NR	26.1
Incidental Inhalation-Powder?[4,5]	4; 108[b]	0.9-10.5	42; 220[b]	1-4	11; 8[b]	0.92-4	NR	NR
Dermal Contact	514	0.035-49	1112	0.001-93	391	0.1-73	1	0.6-26.1
Deodorant (underarm)	NR	2-13.8	4	NR	NR	NR	NR	NR
Hair - Non-Coloring	42	0.005-36	14	0.00055-58.9	4	NR	NR	NR
Hair-Coloring	NR	1-11	3	0.048-20	NR	NR	NR	NR
Nail	1	NR	7	23-68.5	NR	8	NR	NR
Mucous Membrane	184	5.2-59	847	0.29-95	1259	6-82.4	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Polydecene		**Polyethylene**		**Polyisobutene**		**Polyisoprene**	
Totals[†]	**154**	**0.098-47.9**	**2763**	**0.0097-67.6**	**290**	**0.24-40**	**29**	**0.098-47**
Duration of Use								
Leave-On	127	0.098-47.9	2374	0.0097-52.6	275	0.24-40	26	0.098-47
Rinse Off	27	25	388	0.05-67.6	15	1.1-3.5	3	1.8
Diluted for (Bath) Use	NR	NR	1	10	NR	NR	NR	NR
Exposure Type								
Eye Area	9	0.098-6	773	0.06-21	101	0.45-36.3	2	0.49-47
Incidental Ingestion	73	10.2-47.9	896	0.0097-18.9	48	6-40	3	2-12.2
Incidental Inhalation-Spray?[2,5]	1; 11[a]; 8[b]	NR	17; 111[a]; 69[b]	0.5-52.6; 0.47-12[a]	6; 37[a]; 24[b]	5.5-7; 0.5[a]	9[a]; 6[b]	NR
Incidental Inhalation-Powder?[4,5]	7; 8[b]	NR	84; 69[b]	4-30	4; 24[b]	NR	3; 6[b]	NR
Dermal Contact	63	0.098-25	1753	0.03-67.6	174	0.24-36.3	26	0.098-47
Deodorant (underarm)	NR	NR	3	9.6-12.1; 1.6[d]	NR	NR	NR	NR
Hair - Non-Coloring	2	NR	16	0.26-6	5	NR	NR	NR
Hair-Coloring	16	NR	2	5-6	NR	NR	NR	NR
Nail	NR	NR	24	0.42-15	NR	NR	NR	NR
Mucous Membrane	73	10.2-47.9	1093	0.0097-18.9	48	6-40	3	1.8-12.2
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 3. Frequency (2014) and concentration of use (2013) according to duration and type of exposure for polyene ingredients.[10-12]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Polypropylene							
Totals†	**22**	**0.05-68.6**						
Duration of Use								
Leave-On	18	0.05-68.6						
Rinse Off	4	0.2-66						
Diluted for (Bath) Use	NR	NR						
Exposure Type								
Eye Area	5	0.4-68.6						
Incidental Ingestion	NR	4						
Incidental Inhalation-Spray?[2,5]	2[a]; 6[b]	NR						
Incidental Inhalation-Powder?[4,5]	6[b]	2.8						
Dermal Contact	18	0.05-66						
Deodorant (underarm)	NR	NR						
Hair - Non-Coloring	NR	NR						
Hair-Coloring	NR	NR						
Nail	1	NR						
Mucous Membrane	1	4-66						
Baby Products	NR	NR						

NR = Not reported.

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

[a.] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.

[b.] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c.] Hydrogenated C6-14 Olefin Polymers is a synonym for Hydrogenated Poly(C6-14 Olefin). The VCRP database has entries for both names.

[d.] 1.6% in an aerosol underarm deodorant.

Table 4. Polyene ingredients with no reported uses.[10-12]

Butene/Propylene Copolymer
Ethylene/Octane Copolymer
Hydrogenated Polybutene
Hydrogenated Polydodecene
Isobutylene/Isoprene Copolymer
Isoprene/Pentadiene Copolymer
Poly (C4-12 Olefin)
Poly(C6-14 Olefin)
Poly(C20-28 Olefin)
Polypentene

Table 5. FDA approved uses of polyenes

Ingredients	Regulation	CFR Reference
isobutylene/isoprene copolymer; polyethylene; polyisobutene	Food additives permitted for direct addition to food for human consumption – chewing gum base	21 CFR172.615
hydrogenated polyisobutene; isobutylene/isoprene copolymer; polybutene; polyethylene; polyisobutene; polyisoprene; polypropylene; hydrogenated polybutene;	Adhesives approved for use as indirect food additives	21 CFR175.105
polybutene; polyisobutene; polyisoprene;	Pressure-sensitive adhesives approved for use as indirect food additives	21 CFR175.125
hydrogenated polyisobutene; polybutene; polyethylene; polyisobutene; polypropylene; hydrogenated polybutene	Resinous and polymeric coatings - adhesives and components of coatings approved for use as indirect food additives	21 CFR175.300
hydrogenated polybutene	Components of paper and paperboard in contact with aqueous and fatty foods approved for use as indirect food additives	21 CFR176.170
isobutylene/isoprene copolymer; polybutene; polyethylene; polyisobutene; polyisoprene; hydrogenated polybutene	Components of paper and paperboard in contact with dry food approved for use as indirect food additives	21 CFR176.180
polyethylene	Defoaming agents used in coatings approved for use as indirect food additives	21 CFR176.200
polyethylene	Defoaming agents used in the manufacture of paper and paperboard approved for use as indirect food additives	21 CFR176.210
polyethylene; polyisobutene; polypropylene	Cellophane approved for use as indirect food additives	21 CFR177.1200
ethylene/propylene copolymer; isobutylene/isoprene copolymer; polyisobutene	Approved for use in closures with sealing gaskets for food containers – indirect food additives	21 CFR177.1210
isobutylene/isoprene copolymer; polyisobutene	Isobutylene polymers approved for use as indirect food additives	21 CFR177.1420
butylene/ethylene/propylene copolymer; ethylene/octene copolymer; ethylene/propylene copolymer; polyethylene; polypropylene	Olefin polymers approved for use as indirect food additives	21 CFR177.1520
butylene/ethylene copolymer;	Poly-1-butene resins and butene/ethylene copolymers approved for use as indirect food additives	21 CFR177.1570
ethylene/propylene copolymer; isobutylene/isoprene copolymer; polybutene; polyethylene; polyisoprene	Rubber articles intended for repeated use approved for use as indirect food additives	21 CFR177.2600
polybutene; polyethylene; polyisobutene; hydrogenated polybutene	Lubricants with incidental food contact approved as indirect food additives (addition to food not to exceed 10 ppm for polybutene, hydrogenated polybutene, and polyethylene; for use only as a thickening agent in mineral oil lubricants in polyisobutene)	21 CFR178.3570
polyisobutene; hydrogenated polybutene	Plasticizers in polymeric substances approved as indirect food additives	21 CFR178.3740
polyethylene	Reinforced wax approved for use as indirect food additives	21 CFR178.3850
hydrogenated polybutene	Release agents approved for use as indirect food additives	21 CFR 178.3860
polyisobutene; hydrogenated polybutene	Surface lubricants used in the manufacture of metallic articles approved for uses as indirect food additives	21 CFR178.3910
polypropylene	Packaging materials for use during the irradiation of prepackaged foods	21 CFR179.45
polyethylene	Polyethylene – approved as a food additive permitted in feed and drinking water of animals	21 CFR573.780
polypropylene	Intercardiac patch or pledget – cardiovascular device	21 CFR 870.3470
polyethylene	Ear nose and throat devices – prostheses of the ear and mandible	21 CFR874.3430; .3450; .3495; .3620; .3695; .3880; .3930

Table 5. FDA approved uses of polyenes

Ingredients	Regulation	CFR Reference
polypropylene	Nonabsorbable polypropylene surgical suture - general and plastic surgery device	21 CFR878.5010
polypropylene	Approved use as a finger joint polymer constrained prosthesis – orthopedic device	21 CFR888.3230
polyethylene	Approved use as bone cap; ankle joint prosthesis, elbow joint prosthesis; finger joint prosthesis; hip joint prosthesis; knee joint prosthesis; shoulder joint prosthesis; wrist join prosthesis-orthopedic devices	21 CFR888.3000; .3100; .3110; .3120; .3150; .3160; .3200; .3220; .3310; .3340; .3350; .3353; .3358; .3390; .3490; .3500; .3510; .3520; .3530; .3535; .3540; .3550; .3560; .3565; .3640; .3650; .3660; .3670; .3680; .3800; .3810
polybutene; polypropylene	Tolerances and exemptions for pesticide chemical residues in food – polymers; exemptions from the requirement of a tolerance	40 CFR180.960
polybutene	Tolerances and exemptions for pesticide chemical residues in food – polybutenes; exemption from the requirement of a tolerance	40 CFR180.1037

References

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