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# Final Report on the Safety Assessment of Propylene Glycol Stearate and Propylene Glycol Stearate Self-Emulsifying

**Propylene Glycol Stearates (PGS) are a mixture of the mono- and diesters of triple-pressed stearic acid and propylene glycol and are used in a wide variety of cosmetic products.**

**Studies with $^{14}C$-labeled PGS show that it is readily metabolized following ingestion. In rats, the acute oral LD50 has been shown to be approximately 25.8 g/kg. The raw ingredient produced no significant dermal toxicity, skin irritation, or eye irritation in acute tests with rabbits. Subchronic animal studies produced no evidence of oral or dermal toxicity. Propylene glycol monostearate was negative in in vitro microbial assays for mutagenicity.**

**In clinical studies, PGS produced no significant skin irritation at concentrations up to 55% nor skin sensitization on formulations containing 2.5%. Photo-contact allergenicity tests on product formulations containing 1.5% PGS were negative.**

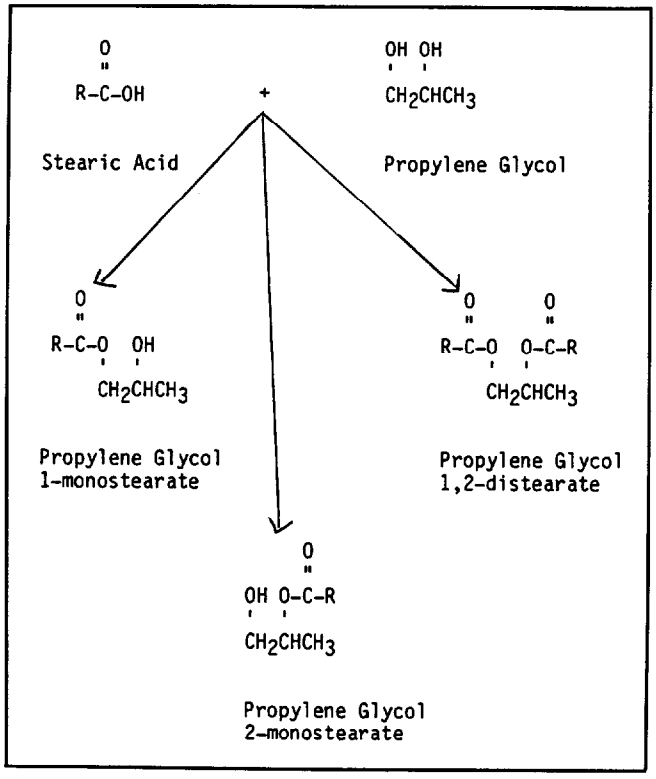
**From the available information, it is concluded that Propylene Glycol Stearates are safe as cosmetic ingredients in the present practices of use.**

## CHEMISTRY

### Composition

#### Propylene Glycol Stearate

Propylene Glycol Stearate (PGS) is a mixture of the 1,2-propanediol mono- and diesters of stearic and palmitic acids in which the monoester, propylene glycol monostearate, predominates. It is produced by reacting propylene glycol and triple-pressed stearic acid under elevated temperatures in the presence of a catalyst. The general reaction is as follows:




where (R-C-) is the acyl moiety corresponding to the mixture of fatty acids in commercial stearic acid.[1-6]

One manufacturer reported that triple-pressed stearic acid consists of 42.5 ± 3% stearic acid, 47 ± 3% palmitic acid, and lesser amounts of several other fatty acids.[7] The Cosmetic, Toiletry and Fragrance Association (CTFA) Cosmetic Ingredient Chemical Description[8] for stearic acid includes the following as component fatty acids:

| | |
|---|---|
| Octadecanoic Acid (stearic) | 39%-95% |
| Hexadecanoic Acid (palmitic) | 5%-50% |
| 9-Octadecanoic Acid (oleic) | 0%-5% |
| Tetradecanoic Acid (myristic) | 0%-3% |
| Heptadecanoic Acid (margaric) | 0%-2.5% |
| Eicosanoic Acid (arachidic) | 0%-2% |
| Pentadecanoic Acid | 0%-1% |

PGS, then, is a mixture of the three chemical structures shown above with the esterified acyl moiety (R-C-) representing a complex blend of fatty acyl components. The total monoester content is not less than the minimum concentration claimed by the vendor.[4] One manufacturer reported that PGS normally

**TABLE 1.** Analyses of Four Commercial Samples of PGS.[a]

| | *Sample number* | | | |
|---|---|---|---|---|
| | *1* | *2* | *3* | *4* |
| PG monoesters | | | | |
| PGP[c] | 27.8[b] | 17.2 | 14.3 | 7.3 |
| PGS | 19.5 | 35.3 | 11.1 | 62.9 |
| Other (includes myristates and oleates) | 4.1 | 1.5 | 3.1 | 2.3 |
| Total monoesters | 51.4 | 54.0 | 28.5 | 72.5 |
| PG diesters | | | | |
| PGPP | 15.1 | 4.6 | 20.1 | 1.5 |
| PGPS | 24.5 | 16.9 | 34.5 | 4.8 |
| PGSS | 6.9 | 18.5 | 13.1 | 21.2 |
| Other (includes myristates and oleates) | 2.1 | 3.0 | 2.8 | 0.1 |
| Total diesters | 48.6 | 43.0 | 70.5 | 27.6 |

[a]Data from Ref. 10.
[b]All values are percentage of total.
[c]P, palmitate; S, stearate.

contains 52%–58% monoester;[9] another reported 45%–55%.[7] In this regard, Sahasrabudhe and Legari[10] analyzed four commercial samples of PGS. Their quantitative data, presented in Table 1, represent percentages of the total sample. Differences from 100% account for unreacted fatty acids. Decouzon and Naudet[11] and Johns and Pepper[12] also performed chemical analyses of PGS; their results are shown in Table 2.

### Propylene Glycol Stearate SE

Propylene Glycol Stearate SE (PGS-SE) is a self-emulsifying grade of PGS that contains some sodium and/or potassium stearate.[3] PGS is modified by addition of potassium hydroxide and additional stearic acid such that the resulting product contains 5%–6% of the potassium salt of triple-pressed stearic acid and 7%–10% by weight of free triple-pressed stearic acid.[7,13] The published scientific literature does not often distinguish between PGS and PGS-SE, and information available for PGS may apply to PGS-SE.

**TABLE 2.** Analyses of Two Samples of PGS.[a]

| | *Ref. 11* | *Ref. 12* |
|---|---|---|
| Monoester | 52.0[a] | 75.3 |
| primary | 35.4 | |
| secondary | 16.6 | |
| Diester | 25.4 | 24.2 |

[a]All values are percentage of total.

## Chemical and Physical Properties

PGS and PGS-SE are white to cream-colored, waxy solids that have a slight, characteristic, fatty odor and taste. They are marketed in the form of beads or flakes.[2,4,5-7,14]

PGS is soluble in such organic solvents as alcohols, mineral or fixed oils, hot cottonseed oil, peanut oil, isopropyl myristate, benzene, chloroform and other chlorinated hydrocarbons, ether, acetone, and ethyl acetate. It is insoluble in water, propylene glycol, glycerine USP, PEG 400, and 70% sorbitol. PGS may be dispersed in hot water with the aid of a small amount of soap or other suitable surface active agent.[2,4,6,15,16] PGS-SE contains such a soap component.

Propylene glycol 1-monostearate is quite surface active. It is adsorbed at the oil/water interface, and it forms a thick plastic film under the proper conditions of concentration and temperature.[17] PGS produces more weakly organized, amorphous emulsions than do polyol esters.[18]

A racemic 80:20 mixture of propylene glycol 1-monostearate and propylene glycol 2-monostearate shows four different polymorphic modifications of crystalline structure. Detailed discussions of PGS crystalline structure have been published.[19,20]

The measured values and commercial specifications for other chemical and physical properties of PGS and PGS-SE are listed in Table 3.

Methods for the commercial and laboratory syntheses of PGS and PGS-SE have been described.[1,7,9,10,13,21-26]

Neither PGS nor PGS-SE absorbed UV-B light between 280 and 320 nm.[27]

## Reactivity

Lorant[28] described the high temperature decomposition of PGS. From 135° to 238°C, PGS lost $H_2O$. At 310°C, the ester linkage was broken, and free myristic acid was detected.

No other information was found concerning the chemical or physical reactivity of PGS or PGS-SE.

## Analytical Methods

Methods used to analyze PGS are described in the Food Chemicals Codex.[4]

PGS can be positively identified by matching infrared absorption data to standard IR spectra.[2]

Johns and Pepper[12] described gel chromatographic and titration techniques for the determination of the monoester content of PGS-SE. Column and gas-liquid chromatographic methods for the analysis of propylene glycol fatty acid esters were reported by Sahasrabudhe and Legari.[10] Fluorine magnetic resonance has also been used for the quantitative analysis of PGS.[29]

## Impurities

The stearic acid used in the commercial manufacture of PGS and PGS-SE may contain unreported amounts of 9-hexadecenoic acid and 9,12-octadecanoic acid. Unsaponifiable material may be present at concentrations up to 0.3%, and

**TABLE 3.** Chemical and Physical Properties of PGS and PGS-SE.

| *Ingredient* | *Melting pt.* | *Acid value* | *Sapon value* | *Iodine value* | *Hydroxyl value* | *Loss in drying* | *Residue on ignition* |
|---|---|---|---|---|---|---|---|
| PGS | 30°–40°C[a] | 20 max[b,c] | 165–175[b] | 0.5 max[b,d,e] | 150–170[f] | 2% max[a] (1 g, 105°C, 1 hr) | 1% max[a] |
| | 45°C[f] | 8 max[a] | 157–178[a] | 3 max[f] | | | 0.1%[f] |
| | 44°–45°C[g] | 2 max[f] | 155–165[f] | 1.0 max[h,i] | | | |
| | 33.5°–38.5°C[d] | 5.0 max[h,e] | 165–191[h] | | | | |
| | 36.38°C[i] | 3.0 max[d] | 171–183[d] | | | | |
| | 35°–38°C[e] | | 181–191[e] | | | | |
| PGS-SE | 40°C[d] (softening pt.) | 20 max[j,d] | 165–175[j,d] | 1.0 max[j,k] | 80–110[k] | | |
| | 60°C[k] (approx.) | 16–20[k] | 165–174[k] | 0.5 max[d] | | | |

[a]Data from Ref. 5.
[b]Data from Ref. 2.
[c]Data from Ref. 4.
[d]Data from Ref. 30.
[e]Data from Ref. 16.
[f]Data from Ref. 6.
[g]Data from Ref. 14.
[h]Data from Ref. 1.
[i]Data from Ref. 9.
[j]Data from Ref. 13.
[k]Data from Ref. 7.

some grades of stearic acid may contain up to 0.07% glyceryl monostearate. Butylated hydroxytoluene (BHT) may be added as a preservative.[8]

The limits of impurities for PGS and PGS-SE are listed in Table 4. The potassium salt of stearic acid and free stearic acid are not considered to be impurities in PGS-SE, as they are added purposefully at the time of manufacture. Trace quantities of neutralized catalyst may remain in the finished product; the catalyst used is deemed proprietary.[9] There are no diluents, solvents, or additives present.[1,7,9,13]

## USE

### Purpose and Extent of Use in Cosmetics

PGS produces a "waxy, occlusive, water insoluble film" when applied to the skin.[31] The major uses of PGS and PGS-SE in cosmetics are as emulsifiers, emollients, texturizers, lubricating agents, and viscosity builders. They are generally included at concentrations of 0.5%–5% in lotions and 1%–10% in creams. The potassium stearate component of PGS-SE provides for greater emulsifying power.[7,14,16,30-32]

Table 5 lists product types and the number of product formulations containing PGS or PGS-SE as reported by the Food and Drug Administration (FDA) in 1976. Although an analysis by product type was not available for the 1979 FDA data, the 1979 totals for all product categories are listed in Table 5 for comparison to the 1976 figures.

The cosmetic product formulation computer printout which is made available by the FDA is compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.[33] Ingredients are

**TABLE 4.** Impurities.

| *Ingredient* | *Free propylene glycol* | *Free stearic acid* | *Water* | *Arsenic (as As)* | *Heavy metals (as Pb)* |
|---|---|---|---|---|---|
| PGS | 3.0% max[a,b] | 2.5% max[a] | 3.0% max[b] (normally less than 1.0%) | 3 ppm max[c] | 10 ppm max[c] |
| | 1.5% max[c] | 1.5% max[b]<br>0.5%[d] (assayed) | | | |
| PGS-SE | 1.5% max[e,f] | not considered impurity | 2.0% max[f] | | |

[a]Data from Ref. 1.
[b]Data from Ref. 9.
[c]Data from Ref. 4.
[d]Data from Ref. 12.
[e]Data from Ref. 13.
[f]Data from Ref. 7.

**TABLE 5.** Product Formulation Data.[a]

| Product category[b] | Total no. containing ingredient | No. product formulations within each concentration range (%)[b] | | | | | |
|---|---|---|---|---|---|---|---|
| | | Unreported concentration | >10–25 | >5–10 | >1–5 | >0.1–1 | ≤0.1 |
| *Propylene Glycol Stearate* | | | | | | | |
| Bath preparations | 1 | – | – | – | 1 | – | – |
| Eyebrow pencil | 7 | – | 7 | – | – | – | – |
| Eye shadow | 63 | – | – | – | 51 | 12 | – |
| Eye lotion | 13 | – | – | – | 13 | – | – |
| Mascara | 7 | – | – | – | 7 | – | – |
| Other eye makeup preparations | 3 | – | – | – | 3 | – | – |
| Colognes and toilet waters | 1 | – | – | – | – | 1 | – |
| Sachets | 4 | – | – | – | 4 | – | – |
| Hair conditioners | 1 | – | – | – | 1 | – | – |
| Hair rinses (noncoloring) | 4 | – | – | – | – | 4 | – |
| Hair shampoos (noncoloring) | 1 | – | – | – | 1 | – | – |
| Blushers (all types) | 36 | – | – | – | 31 | 5 | – |
| Makeup foundations | 28 | – | – | 9 | 18 | 1 | – |
| Leg and body paints | 15 | – | – | – | 15 | – | – |
| Lipstick | 3 | – | 2 | – | 1 | – | – |
| Makeup bases | 141 | – | – | 1 | 138 | 2 | – |
| Rouges | 3 | – | – | 1 | 2 | – | – |
| Other makeup preparations (not eye) | 6 | – | – | 2 | 4 | – | – |
| Manicuring preparations | 1 | – | – | 1 | – | – | – |
| Shaving cream (aerosol, brushless, and lather) | 1 | – | – | – | 1 | – | – |
| Skin cleansing preparations (cold creams, lotions, liquids, and pads) | 4 | – | – | – | 4 | – | – |
| Face, body, and hand skin care preparations (excluding shaving preparations) | 28 | – | – | – | 14 | 14 | – |
| Hormone skin care preparations | 2 | – | – | – | 2 | – | – |
| Moisturizing skin care preparations | 22 | – | – | – | 18 | 4 | – |
| Night skin care preparations | 2 | – | – | – | 2 | – | – |
| Other skin care preparations | 2 | – | – | – | 1 | 1 | – |
| Suntan gels, creams, and liquids | 2 | – | – | – | 1 | 1 | – |
| 1976 TOTALS | 401 | – | 9 | 14 | 333 | 45 | – |
| 1979 TOTALS[c] | 226 | – | 1 | 4 | 184 | 36 | 1 |
| *Propylene Glycol Stearate SE* | | | | | | | |
| Eye shadow | 15 | – | – | – | 15 | – | – |
| Tonics, dressings, and other hair grooming aids | 1 | – | – | – | 1 | – | – |
| Blushers (all types) | 12 | – | – | – | 12 | – | – |
| Makeup foundations | 2 | – | – | – | 2 | – | – |
| Makeup bases | 76 | – | – | – | 76 | – | – |

**TABLE 5.** (Continued.)

| Product category[b] | Total no. containing ingredient | No. product formulations within each concentration range (%)[b] | | | | | |
|---|---|---|---|---|---|---|---|
| | | Unreported concentration | >10–25 | >5–10 | >1–5 | >0.1–1 | ≤0.1 |
| Other makeup preparations (not eye) | 5 | – | – | – | 5 | – | – |
| Shaving cream (aerosol, brushless, and lather) | 1 | – | – | – | 1 | – | – |
| Skin cleansing preparations (cold creams, lotions, liquids, and pads) | 1 | – | – | – | – | – | 1 |
| Face, body, and hand skin care preparations (excluding shaving preparations) | 6 | – | 1 | – | 4 | 1 | – |
| Moisturizing skin care preparations | 7 | – | – | – | 6 | 1 | – |
| Skin lighteners | 3 | – | – | – | 3 | – | – |
| Other skin care preparations | 1 | – | – | – | 1 | – | – |
| Suntan gels, creams, and liquids | 1 | – | – | – | 1 | – | – |
| 1976 TOTALS | 131 | – | 1 | – | 127 | 2 | 1 |
| 1979 TOTALS[c] | 161 | 19 | – | 7 | 134 | – | 1 |

[a]Data from Ref. 34.

[b]Preset product categories and concentration ranges in accordance with federal filing regulations (21 CFR 720.4).

[c]Data from Ref. 35.

listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the true, effective concentration found in the finished product; the effective concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to tenfold error in the assumed ingredient concentration.

In 1976, PGS and PGS-SE were reported as ingredients in a total of 401 and 131 cosmetic formulations, respectively. PGS was reported at concentrations up to 25%; one product contained between 10% and 25% PGS-SE, while all others contained less than 5%. The 1979 FDA data show some significant changes in the reported uses of PGS and PGS-SE. Only one formulation contained PGS at the 10%–25% level, and PGS-SE was reported at concentrations no higher than 10%.

Products containing PGS or PGS-SE are applied to all areas of the skin, hair, nails, and mucous membranes. Most prevalent uses include application to the face and around the eye (Table 5).

Formulations containing PGS or PGS-SE are applied as many as several times a day and remain in contact with the skin for various periods of time following each application. Daily or occasional use may extend over many years (Table 5).

### Noncosmetic Uses

In the pharmaceutical industry, PGS serves as an emulsifying agent and fatty base for suppositories and rectal ointments.[36-39] It is classified as an inactive ingredient in topical analgesic, antirheumatic, otic, burn, and sunburn treatment/prevention products.[40]

In foods, propylene glycol mono fatty acid esters are used as emulsifiers and stabilizers either alone or in combination with mono- and diglycerides.[4,10] PGS has been used in the United States since 1958 because it improves the texture, softness, and "keeping quality" of several foods. The literature describes its use in such foods as macaroni,[41] mashed potatoes,[42] massecuites,[43] milk fat emulsions,[44] fats and oils, cheese, frozen dairy desserts, imitation dairy products, gelatins and puddings, sweet sauce, alcoholic and nonalcoholic beverages, and baked goods.[25] It is used at concentrations up to 12.0% in edible fats and oils.[25]

The average U.S. daily human consumption of PGS from all food sources was calculated to be 16, 24, 94, and 43 mg/kg of body weight for the age groups 0–5 months, 6–11 months, 12–23 months, and 2–65+ years, respectively. The estimated maximum possible daily intakes for these same age groups were 20, 167, 181, and 77 mg/kg of body weight, respectively. These figures are thought to be considerably overstated, owing to cumulative overestimations in the calculation process.[25]

## BIOLOGICAL PROPERTIES

### General Effects

Under contract with the FDA, a group of scientists designated the Select Committee on Generally Recognized as Safe (GRAS) Substances evaluated the safety of PGS for food use. In a final report, this group concluded that the scientific literature from 1920 through 1973 presents no evidence that "demonstrates or suggests reason to suspect" that PGS poses a hazard to the public when it is used in foods "at levels that are now current or that might reasonably be expected in the future."[25] PGS is currently considered GRAS under the provisions of Sections 172.856, 182.4505, and 582.4505 of the CFR.[33] These regulations concern multipurpose food additives and emulsifying agents destined for human or animal consumption.

The Joint FAO/WHO Expert Committee on Food Additives has also evaluated propylene glycol esters of fatty acids for human oral ingestion. Evaluation was based on the content of propylene glycol, for which they established an acceptable daily intake of up to 25 mg/kg body weight.[45]

### Secondary Effects

When used as a lipophilic emulsifier in pharmaceutical ointments and gels, PGS has been shown either to stimulate or to inhibit the release of different drugs as measured by both in vitro and in vivo assays.[46-50]

## Absorption, Metabolism, Storage, and Excretion

Balls and Matlack[51] studied the in vitro hydrolysis of fatty acid esters, including propylene glycol monostearate, in the presence of pancreatic lipase. The compound was shown to be hydrolyzed to the extent of about 80% in 15 hours at 40°C. Similarly, steapsin hydrolyzed 70% of propylene glycol distearate in vitro at 30°C in 18 hours.[52]

Propylene glycol monostearate (PGMS) is readily hydrolyzed in vivo, and the propylene glycol (PG) and stearic acid (S) moieties enter their respective metabolic pathways.[25] Through the use of isotopically labeled compounds, the hydrolysis, absorption, and metabolism of propylene glycol distearate (PGDS) were studied in rats and found to be similar to those of the glyceryl esters of stearic acid. PGDS was synthesized as $^{14}$C-carbonyl-labeled or as propylene glycol-1-$^{14}$C. The rate of uptake, course, and fate of the two fragments of the molecule were traced independently. In addition, a comparative study was made through the use of a mixture of glyceride esters of labeled stearic acid and through the use of labeled free propylene glycol and stearic acid.[52,53]

Oral administration of the labeled PGDS to rats resulted in intestinal hydrolysis to PGMS, PG, and S. Cannulation of intestinal lymphatics demonstrated the appearance of radioactivity from PGDS in the lymph. This radioactivity was comparable to that which appeared in the lymph after rats were fed labeled glyceryl stearate esters. Only small amounts of PG, and no PGMS or S, were detected in the lymph. It was concluded that the absorption mechanism for PGDS is similar to that for the glyceryl stearate esters.[53]

After labeled (*) PG*DS, PGDS*, PG plus S*, and PG* plus S were orally administered to rats, a variety of measurements were made. The rate of absorption was determined by the residual radioactivity of gastrointestinal tract extracts. The total absorption of PGDS in the rat was found to be 33% of the administered dose in 8 hours. Labeled stearic acid was 33% absorbed in 3 hours, while propylene glycol was absorbed at an even greater rate (94% in 5 hours). These findings would indicate that the initial limiting factor governing PGDS absorption is the hydrolysis of the ester linkage. This holds true for the first 3 hours, after which the governing factor is the rate of absorption of the stearic acid moiety. The propylene glycol moiety was completely absorbed after 72 hours, leaving behind a more slowly absorbed stearic acid.[52]

Approximately 6% of the total dose or 19% of the absorbed dose of PGDS* was excreted in the urine in 72 hours. Only 0.4% of the radioactivity was excreted from PG*DS, indicating the origin of urinary excretory products to be derived largely from the stearate portion of the molecule. No explanation was offered for this relatively large urinary excretion. PG plus S did not give similar results. The metabolism of the stearic acid portion of PGDS is therefore different from free stearic acid given in the presence of propylene glycol. About 94% of the absorbed PG moiety of PGDS was utilized in oxidative respiration, as evidenced by the $^{14}CO_2$ excretion in a 72-hour period. The mechanism by which propylene glycol is utilized, by oxidation to lactic acid and subsequent conversion to pyruvate, has been thoroughly described in the literature. Approximately 51% of the stearate moiety of PGDS was also metabolized to $Co_2$.[52]

## Animal Toxicology

### Acute Studies

*Oral Toxicity*

*Propylene Glycol Stearate:* The acute oral toxicity of PGS was evaluated in one study on the undiluted ingredient,[54] in three studies on the ingredient diluted in solvent,[55-57] and in five studies on product formulations containing PGS.[58-62] In each study, young adult albino rats were fasted overnight and administered a single dose of the test sample by gastric intubation. They were then allowed free access to food and water for two weeks. The results and other details of these studies are summarized in Table 6. From the most definite of these data, the acute oral LD50 of PGS in rats was 25.8 g/kg.

*Propylene Glycol Stearate SE:* The acute oral toxicity of PGS-SE was evaluated in one study on the undiluted ingredient[65] and one study on the ingredient diluted in corn oil.[64] The results and other details of these studies are summarized in Table 6. From these data, the acute oral LD50 of PGS-SE in rats is greater than 32.0 g/kg.

*Dermal Toxicity*

A makeup foundation product formulation containing 2.5% PGS was tested for acute dermal toxicity on ten rabbits. A 2 g/kg sample of the product was applied to the clipped intact and abraded trunk of each animal and held in contact with the skin for 24 hours under occlusion. The product was found to be "nontoxic" under the conditions of the test.[59]

*Primary Skin Irritation*

*Propylene Glycol Stearate:* The potentials for primary skin irritation caused by undiluted PGS,[66-68] 55% PGS in an unnamed solvent,[55,69] 30% PGS in propylene glycol,[56] and two product formulations containing PGS[59,62] were evaluated using the Draize rabbit skin patch test technique. In each study, 0.5 ml samples were applied and occluded for 24 hours, after which time the patch sites were graded for erythema and edema on the Draize scale. The results and other details of these studies are summarized in Table 7. The undiluted ingredient produced no or only mild skin irritation. When PGS was diluted to 55% in an unnamed solvent or to 30% in propylene glycol, the test showed minimal to mild irritation. Product formulations containing PGS produced no or only minimal skin irritation.

*Propylene Glycol Stearate SE:* Undiluted PGS-SE was tested according to the Draize rabbit skin patch test technique in two studies.[70,71] The results and other details of these studies are summarized in Table 7. PGS-SE produced minimal skin irritation.

*Eye Irritation*

*Propylene Glycol Stearate:* The Draize rabbit eye irritation procedure or a modification of the test was used to evaluate undiluted PGS,[56,72,73] 55% PGS in

**TABLE 6.** Acute Oral Toxicity.

| *Ingredient* | *Conc. (%)* | *Dose* | *Dose of ingredient (adj. for dilution)* | *No. of rats* | *LD50 (adjusted for dilution)* | *Comment* | *Ref.* |
|---|---|---|---|---|---|---|---|
| PGS | 100 | 5.0 g/kg | 5.0 g/kg | 10 | >5.0 g/kg | No deaths. | 54 |
| | 55 (in unnamed solvent) | 5.0 g/kg | 2.75 g/kg | 5 | >2.75 g/kg | | 55 |
| | 30 (in propylene glycol) | –[a] | – | 20 | 2.3 g/kg | Doses administered not reported. | 56 |
| | unreported conc. in propylene glycol | – | 1.0–32.0 g/kg | 5 at each of 8 dose levels | 25.8 g/kg | No effects at 1.0 and 2.0 g/kg; unkempt coats for 12–16 hours at 4.0 and 8.0 g/kg; lethargy, staggering gait, impaired locomotion, and unkempt coats at 16.0, 20.0, 25.0, and 32.0 g/kg; 2 animals died on day 2 at 25.0 g/kg, and all 5 died on day 1 at 32.0 g/kg; survivors at 25.0 g/kg appeared normal by day 4. | 57 |
| | 3.5 (in makeup foundation formulation) | 15.9 g/kg | 0.56 g/kg | 5 | – | LD50 not reached with doses administered | 58 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | 2.5 (in makeup foundation formulation) | 5.0 g/kg | 0.12 g/kg | 10 | – | LD50 not reached with doses administered. | 59 |
| | 1.5 (in blusher product formulation) | 21.5 g/kg | 0.32 g/kg | 5 | – | LD50 not reached with doses administered. | 60 |
| | 1.5 (in makeup foundation formulation) | 20 ml/kg | 0.3 g/kg | 10 | – | No deaths; no toxic effects. | 61 |
| | 1.5 (in moisturizing liquid makeup formulation) | 15.0 g/kg | 0.22 g/kg | 5 | – | LD50 not reached with doses administered. | 62 |
| PGS-SE | 100 | 10 g/kg | 10 g/kg | 10 | >10 g/kg | No deaths. | 63 |
| | 50 (in corn oil) | 2.0–64.0 g/kg | 1.0–32.0 g/kg | 5 at each of 6 dose levels | >32.0 g/kg | No deaths; no effects at 2–8 g/kg; unkempt coats, white feces, and diarrhea at 16 g/kg; nasal hemorrhage, white feces, diarrhea, lethargy, and unkempt coats at 32–64 g/kg; all animals appeared normal by day 9. | 64 |

[a]No data.

**TABLE 7.** Primary Skin Irritation.

| *Ingredient* | *Conc. (%)* | *No. of rabbits* | *Primary irritation index (max = 8.0)* | *Comments* | *Ref.* |
|---|---|---|---|---|---|
| PGS | 100 | 6 | 0.0 | No signs of irritation. | 66 |
| | 100 | 6 | 0.0 | No signs of irritation. | 67 |
| | 100 | 6 | 1.38 | Mild irritation; some edema and definite erythema. | 68 |
| | 55 (in unnamed solvent) | 18 | 0.44 | Minimal irritation. | 55 |
| | 55 (in unnamed solvent) | 9<br>9<br>9<br>9 | 1.1<br>1.1<br>1.2<br>1.3 | Three test batches plus PGS control; mild irritation. | 69 |
| | 30 (in propylene glycol) | 6 | 0.4 | Minimal irritation. | 56 |
| | 2.5 (in makeup foundation formulation) | 6 | 0.0 | No signs of irritation. | 59 |
| | 1.5 (in moisturizing liquid makeup formulation) | 9 | 0.39 | Minimal irritation | 62 |
| PGS-SE | 100 | 6 | 0.25 | Minimal irritation. | 70 |
| | 100 | 2 | 0.5 | Minimal irritation. | 71 |

an unnamed solvent,[55,69] and five product formulations containing PGS.[58-62] In each study, a 0.1 ml sample was instilled into one eye of each rabbit with no subsequent washing; some rabbits received a water wash either two or four seconds after instillation as noted in Table 8. Treated eyes were examined and graded on the Draize eye irritation scale at 1, 2, 3, 4, and 7 days. The results and other details of these studies are summarized in Table 8. The undiluted ingredient produced only minimal eye irritation which cleared by day 3. The diluted ingredient and product formulations containing PGS also produced no more than minimal transient irritation.

*Propylene Glycol Stearate SE:* Undiluted PGS-SE was tested according to a modification of the Draize rabbit eye irritation procedure in which some animals received a water wash after instillation. The results and other details of this study are summarized in Table 8. Undiluted PGS-SE produced minimal transient eye irritation which cleared by day two.[65]

### *Intraperitoneal Injection*

The recorded lethal dose for intraperitoneal injection of PGS into mice is 200 mg/kg.[74]

### Subchronic Studies

*Oral Toxicity*

Rats in groups of 48 were fed for 13 weeks on diets containing 0%, 1.5%, 3.36%, or 7.52% PGS with mono- and diglycerides added to bring the total fat content to 7.52%. The groups showed no significant differences with respect to growth, relative organ weight (adrenals, gonads, heart, kidneys, liver, spleen, brain), histology, blood glucose, BUN, plasma cholesterol, plasma glutamate-pyruvate transaminase, hemoglobin, hematocrit, white cell count, white cell differential count, clotting time, or urinalyses.[75]

*Dermal Toxicity*

A moisturizing liquid product formulation containing 2.2% PGS was tested in a subchronic dermal toxicity study on weanling female albino rats. Doses of 0.8 ml/kg were applied to the shaved dorsal areas of the backs of 15 animals five times a week for 13 weeks. Routine hematology, serum chemistry, and urinalysis were performed at 7 and 13 weeks; necropsy and histopathology were also performed at 13 weeks. All animals survived to the end of the 13-week exposure period. Minimal skin irritation was noted sporadically, but there were no changes in gross appearance or behavior. Statistically significant differences (as compared to controls) in BUN, hemoglobin, hematocrit, RBC count, serum glucose, and kidney weight were considered toxicologically insignificant because all the values fell within normal limits for the testing laboratory.[76]

*Skin Sensitization*

The Landsteiner and Jacobs guinea pig sensitization technique was used to determine the sensitization potential of PGS-SE. The backs and flanks of two white male guinea pigs were clipped free of hair, and a 0.1% suspension of PGS-SE in physiological saline was injected intracutaneously three times a week until a total of ten injections had been made. The first injection consisted of 0.05 ml, while the remaining nine were 0.1 ml each. A challenge injection of 0.05 ml was made two weeks after the tenth sensitization injection. The challenge site was evaluated 24 hours later and compared with similar readings taken after the first injection. No reactions indicative of sensitization occurred in this strictly limited experiment.[77]

### Chronic Studies

A preparation containing 50% stearyl propylene glycol hydrogen succinate, 17% propylene glycol monostearate, and lesser amounts of other propylene glycol derivatives was incorporated into the diets of 30 rats, 10 per group, at levels of 2.5%, 5%, and 10% for six months. It was reported that no evidence of gross or histological pathology was attributable to the mixture. The same mixture was fed at levels of 5% and 10% in the diet to groups of four dogs for six months. There were no signs of toxicity.[78]

### Special Studies

Propylene glycol monostearate was evaluated for mutagenic activity in a series of in vitro microbial assays with and without metabolic activation. Plate

**TABLE 8.** Draize Eye Irritation.

| Ingredient | Conc. (%) | No. of rabbits | Ocular irritation index (max = 110) | | | | | Comments | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| | | | Day 1 | Day 2 | Day 3 | Day 4 | Day 7 | | |
| PGS | 100 | 3 unwashed | 0 | 0 | 0 | 0 | 0 | No irritation. | 72 |
| | | 6 washed | 0 | 0 | 0 | 0 | 0 | No irritation; 3 washed after 2 seconds and 3 washed after 4 seconds. | |
| | 100 | 6 | 0.33 | 0.33 | 0 | 0 | 0 | One rabbit showed slight conjunctival redness. | 73 |
| | 100 | 3 | 4.0 | 4.0 | 0 | 0 | 0 | Minimal irritation. | 56 |
| | 55 (in unnamed solvent) | 6 | 3.0 | 0 | 0 | 0 | 0 | Three test batches plus PGS control; minimal irritation. | 69 |
| | | 6 | 5.0 | 0 | 0 | 0 | 0 | | |
| | | 6 | 1.0 | 1.0 | 0 | 0 | 0 | | |
| | | 6 | 3.0 | 0 | 0 | 0 | 0 | | |
| | 55 (in unnamed solvent) | 6 | 1.0 | 0 | 0 | 0 | 0 | Test batch plus PGS control; minimal transient irritation. | 55 |
| | | 6 | 3.0 | 0 | 0 | 0 | 0 | | |
| | 3.5 (in makeup foundation formulation) | 3 | 4.0 | 0 | 0 | 0 | 0 | Minimal transient irritation. | 58 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2.5 (in makeup foundation formulation) | 6 | 0 | 0 | 0 | 0 | 0 | No irritation | 59 |
| | 1.5 (in makeup foundation formulation) | 3 unwashed | 0 | 0 | 0 | 0 | 0 | No irritation. | 61 |
| | | 6 washed | 0 | 0 | 0 | 0 | 0 | No irritation; 3 washed after 2 seconds and 3 washed after 4 seconds. | |
| | 1.5 (in moisturizing liquid makeup formulation) | 6 | 1.0 | 0 | 0 | 0 | 0 | Minimal transient irritation. | 62 |
| | 1.5 (in blusher product formulation) | 3 | 0 | 0 | 0 | 0 | 0 | No irritation. | 60 |
| PGS-SE | 100 | 3 unwashed | 0.67 | 0 | 0 | 0 | 0 | Minimal transient irritation in unwashed eyes. | 65 |
| | | 6 washed | 0 | 0 | 0 | 0 | 0 | No irritation in washed eyes; 3 washed after 2 seconds and 3 washed after 4 seconds. | |

tests, nonactivated suspension tests, and activated suspension tests with *Salmonella typhimurium* (strains TA-1535, TA-1537, TA-1538) were all negative; nonactivated and activated suspension tests with *Saccharomyces cerevisiae* (strain D4) were also negative. It was concluded that propylene glycol monostearate was not mutagenic in the assays employed.[79]

## Clinical Assessment of Safety

### Propylene Glycol Stearate

*Primary Skin Irritation*

A 24-hour occlusive patch test procedure was used to evaluate the primary skin irritation caused by 55% PGS in an unnamed solvent on 80 subjects,[80] and by 5% PGS in mineral oil on 100 subjects.[56] Product formulations containing 1.5%–3.5% PGS were also tested on a total of 237 subjects.[58,60,81,82] The results and other details of these studies are summarized in Table 9. PGS at 55% produced at most a barely perceptible skin irritation in some subjects (PII = 0.03 out of 4.0); 5% PGS in mineral oil produced no irritation. Product formulations containing 1.5%–3.5% PGS produced up to mild irritation, most probably by virtue of the other ingredients present in the formulations.

*Cumulative Skin Irritation*

A controlled use test was conducted on a foundation makeup formulation containing 2.5% PGS. A group of 24 women panelists used the formulation once per day for 28 consecutive days. They were then patch tested to the product 48 hours after the completion of the use period to determine sensitization potential. No irritation was demonstrated during the use portion of the study. A mild to moderate erythema demonstrated by two subjects at challenge was judged to be product-related, although the offending ingredient could not be identified.[59]

**TABLE 9.** Clinical 24-Hour Single Insult Patch Tests with PGS.

| *Test material* | *PGS conc. (%)* | *No. of subjects* | *Results* | *Ref.* |
|---|---|---|---|---|
| PGS | 55 (in unnamed solvent) | 80 | PII = 0.03 (max = 4.0); barely perceptible erythema in 5 subjects. | 80 |
| PGS | 5 (in mineral oil) | 100 | "Negative." | 56 |
| Makeup foundation | 3.5 (in product formulation) | 100 | "Negative." | 58 |
| Moisturizing liquid | 2.2 (in product formulation) | 19 | PII = 0.08 (max = 4.0); one subject with mild and one with barely perceptible erythema. | 81 |
| Blusher | 1.5 (in product formulation) | 100 | "Negative." | 60 |
| Moisturizing liquid | 1.5 (in product formulation) | 18 | PII = 0.50 (max = 4.0); scores ranged from 0.5 to 2.0 in 9 subjects. | 82 |

*Skin Sensitization*

Several product formulations containing PGS have been tested for human skin sensitization on a total of 4084 subjects using a variety of testing methods. These studies included one Schwartz–Peck Prophetic Patch Test[83] on a product formulation containing 2.5% PGS,[59] four repeat insult patch tests on product formulations containing 1.5%–2.5% PGS,[59,61,84,85] and two controlled use tests on product formulations containing 1.5% PGS.[61,85] The results and other details of these studies are summarized in Table 10. Of the 4084 subjects reported in Table 10, there were no reactions indicative of sensitization to PGS.

*Photo-Contact Allergenicity*

A foundation formulation containing 1.5% PGS was tested for photo-contact allergenicity on 28 subjects. Applications of 0.1 ml/cm$^2$ under an occlusive patch, followed by irradiation with three times the minimal erythema dose from a Xenon Solar Simulator (150 W; UVA and UVB region 290–400 nm), were repeated twice a week for three weeks. A 24-hour challenge patch was made adjacent to the induction patch sites ten days after the last induction exposure. This was followed by irradiation for three minutes from the light source fitted with a Schott WG345 filter to eliminate UVB radiation. One nonirradiated and one no-product site served as controls. It was concluded that the product produced no indication of phototoxicity or photoallergy.[61]

**TABLE 10.** Clinical Skin Sensitization Tests on Product Formulations Containing PGS.

| *Test method* | *PGS conc. (%)* | *No. of subjects* | *Results* | *Ref.* |
|---|---|---|---|---|
| Schwartz–Peck (1944) Prophetic Patch Test; included open patch, closed patch, and ultraviolet test conditions. | 2.5 in product formulation | 299 | No reactions | 59 |
| Repeat insult (10×) with challenge after 2-week rest; included open patch, closed patch, and ultraviolet test conditions. | 2.5 in product formulation | 151 | No reactions | 59 |
| Repeat insult (9×) with challenge after 2-week rest; closed patch. | 2.2 in product formulation (50% aqueous dispersion for induction patches 3 to 9 and challenge) | 115 | No reactions | 84 |
| Repeat insult (9×) with 2 consecutive 48-hour challenge patches after 2-week rest; closed patch on upper back. | 1.5 in product formulation | 213 | No "significant reactions" | 61 |
| Repeat insult (9×) with 2 consecutive 48-hour challenge patches after 2-week rest; closed patch on upper back. | 1.5 in product formulation | 3034 (Summary of multiple tests) | No confirmed sensitization to PGS | 85 |
| Use Test; procedure not reported. | 1.5 in product formulation | 247 (Summary of multiple tests) | No confirmed sensitization to PGS | 85 |
| Use Test; procedure not reported. | 1.5 in product formulation | 25 | No reactions | 61 |

A procedure identical to the one described above was used to test a foundation formulation containing 1.5% PGS in several studies, the results of which were available only in summary form. There were no confirmed photoallergic reactions in a total of 228 subjects.[85]

### Propylene Glycol Stearate SE

No clinical data were available for PGS-SE. Since the chemical components of PGS-SE that distinguish it from PGS (sodium and/or potassium stearate and free stearic acid) have previously been considered to be safe by this Expert Panel[86] and by the Select Committee on GRAS Substances,[87] and since the literature does not often distinguish between PGS and PGS-SE, the information generally applicable to PGS is considered applicable to PGS-SE in this specific instance.

## SUMMARY

Propylene Glycol Stearate (PGS) is a mixture of the mono- and diesters of triple-pressed stearic acid and propylene glycol. Propylene Glycol Stearate SE (PGS-SE) is a self-emulsifying grade of PGS that contains an additional 5%–6% potassium stearate and 7%–10% free stearic acid. They are used in a wide variety of cosmetic products at concentrations of up to 25% for PGS and up to 10% for PGS-SE (1979 data). PGS is also approved for a variety of pharmaceutical uses and is considered Generally Recognized as Safe (GRAS) for food use.

Studies with $^{14}C$-labeled PGS show that it is readily metabolized following ingestion. In rats, the acute oral LD50 has been shown to be approximately 25.8 g/kg. The raw ingredient produced no significant dermal toxicity, skin irritation, or eye irritation in acute tests with rabbits. Subchronic animal studies produced no evidence of oral or dermal toxicity. A chronic six-month feeding study showed no signs of toxicity when a mixture containing 17% propylene glycol monostearate was incorporated at 10% into the diets of rats and dogs. Propylene glycol monostearate was negative in in vitro microbial assays for mutagenicity.

Although PGS-SE has not been tested as extensively as PGS, it produced no apparent significantly different results in any of the animal tests. The acute oral LD50 in rats is estimated to be greater than 32 g/kg. The ingredient per se produced no significant skin or eye irritation in Draize rabbit irritation tests, and it was not a sensitizer in a guinea pig sensitization test. No other subchronic or chronic studies were available.

In clinical studies, PGS produced no significant skin irritation at concentrations up to 55% in 24-hour single insult skin patch tests. A 28-day controlled use test on a product containing 2.5% PGS demonstrated no cumulative irritation with normal product use but mild to moderate irritation with a challenge skin patch; the offending ingredient was not identified. Several skin sensitization tests on product formulations containing 1.5%–2.5% PGS showed no evidence of sensitization reactions in a total subject population of 4084. Two photo-contact allergenicity tests on product formulations containing 1.5% PGS were negative.

No clinical data were available for PGS-SE. However, the chemical components of PGS-SE that distinguish it from PGS have been considered previously

to be safe, and the information generally applicable to PGS is considered applicable to PGS-SE.

## CONCLUSION

From the available information, the Panel concludes that Propylene Glycol Stearate and Propylene Glycol Stearate SE are safe as cosmetic ingredients in the present practices of use.

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