### SIDS INITIAL ASSESSMENT PROFILE

<table>
<thead>
<tr>
<th>CAS No(s).</th>
<th>Propylene glycol phenyl ether (PPh)</th>
</tr>
</thead>
<tbody>
<tr>
<td>770-35-4 (major isomer – Secondary Alcohol)</td>
<td></td>
</tr>
<tr>
<td>4169-04-4 (minor isomer – Primary Alcohol)</td>
<td></td>
</tr>
<tr>
<td>41593-38-8 (commercial mixed isomer product)</td>
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</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Propylene Glycol Phenyl Ether (PPh)</th>
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<tbody>
<tr>
<td>Structural Formula</td>
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<tr>
<td>OH</td>
<td></td>
</tr>
<tr>
<td>CH₃-CH-CH-O-(C₆H₅) (major isomer)</td>
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<tr>
<td>(O-C₆H₅)</td>
<td></td>
</tr>
<tr>
<td>CH₃-CH-CH₂- OH (minor isomer)</td>
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### SUMMARY CONCLUSIONS OF THE SIAR

#### Human Health

Propylene glycol phenyl ether (PPh) is rapidly absorbed, distributed throughout the body, metabolized, and eliminated after oral administration. The major routes of elimination are via the urine and feces. The types of metabolites are parent ether conjugates, hydrolyzed propylene glycol, and hydrolyzed alcohol (phenol) conjugates.

Propylene glycol phenyl ether exhibits low acute toxicity by the oral, and inhalation routes. The oral LD50 in rats exceeds 2000 mg/kg (1 death from 10 subjects occurred at this highest dose tested); and the 4-hour inhalation LC50 in rats was greater than 5400 mg/m³ (no deaths). PPh was severely irritating to the eyes but non-irritating to skin in rabbits tested and evaluated according to the Draize criteria. PPh did not cause skin sensitization when tested with guinea pigs by the Buehler method.

In repeated dose-studies ranging in duration from 4 to 26 weeks, few adverse effects were found even at high exposure levels and effects that did occur were mild in nature. In one study, PPh was administered to two generations of rats (25/sex/group) in drinking water for 26 weeks at concentrations of 0, 100, 1000, or 5000 ppm (equivalent to doses of 0, 11.3, 113, or 478 mg/kg-d) (this was a 2-generation reproductive toxicity study also discussed below). Effects were seen only at the highest exposure concentration that manifested as reduced body weights and corresponding reduced food and water consumption. No clinical signs were evident during the course of exposure and no gross or histopathological lesions were seen at autopsy. The NOAEL for this drinking water study with rats was 1000 ppm (113 mg/kg-d) and the LOAEL was 5000 ppm (478 mg/kg-day), based on body weight changes. In another repeated dose test, this time by the dermal route of exposure, rabbits (5/sex/group) received daily applications of PPh 5 days/week for four weeks (19 total applications). A slight increase in platelet counts was found that reached statistical significance in males at the high dose level. Platelet counts in females were unaltered at any dose level. No other parameters were affected other than a local thickening of the skin at the site of application. The increased platelet count in males was considered spurious since no other hematological or clinical chemistry (or any other) parameters corroborated this finding. Thus, the systemic toxicity NOAEL for PPh by the dermal route of exposure in rabbits was the highest dose tested of 1000 mg/kg-day.

In the two-generation reproductive toxicity study discussed above (rats 25 pairs/generation) treated orally with 0, 100, 1000, or 5000 ppm PPh in drinking water, no adverse effects were found on fertility, reproductive...
performance, or on reproductive tissues in parental generations. In offspring, reduced pup weights as well as decreased relative spleen weights and increased relative brain weights and retarded sexual maturation were found at the high dose (but with no effect on reproductive parameters in the F1 generation once they reached sexual maturity). In a developmental toxicity study, PPh was administered daily by gavage to pregnant rabbits (15 per group) over the period of organogenesis at doses of 0, 60, 180, or 540 mg/kg-day. In the dams, the high dose of PPh caused decreased food consumption, decreased body weights, and prostration. No maternal toxicity was seen at the lower dose levels. In fetuses, a statistical increase in the rate of total soft tissue variations was detected (septal heart defect) in the medium and high dose groups. It is possible that this may be considered coincidental because of the low incidence (1 fetus in each group), the common spontaneous occurrence of the variation in this strain of rabbit, and because statistical significance was conferred only due to the unusually low level in the concurrent control group (2.2% fetal incidence and 7.1% litter incidence versus 7.7% and 30.2%, respectively, in the laboratory historical controls). With regard to skeletal variations (predominantly an increase in 13th ribs when combined with other skeletal variations), a statistical increase was detected in the high dose group. This increase in skeletal variations was considered treatment related because the incidence (approximately 10%) exceeded historical control levels. The NOAEL for maternal toxicity was 180 mg/kg-day and the LOAEL was 540 mg/kg-day, based on reduced body weight and clinical signs. The NOAEL for fetal toxicity was 180 mg/kg-day and the LOAEL was 540 mg/kg-day based on the increased incidence of 13th rib buds. PPh exhibits toxicity in the developing rabbit conceptus at high doses that produce toxicity in the dam.

PPh tested negative in the Ames Salmonella assay and also was negative in an in vitro chromosome aberration study with human lymphocytes. In an in vivo mouse bone marrow micronucleus test, mice received two consecutive daily doses of 0, 500, 1000, or 2000 mg/kg-day. The high dose animals had a slightly increased incidence of micronuclei that reached statistical significance in a first assay but did not in a second (although a trend was evident). The study authors attributed this finding to hypothermia, which occurred only in the high dose animals and which has been shown with other chemicals to cause increased micronuclei as a secondary effect from hypothermia. It seems reasonable to conclude that the negative in vitro results and the equivocal in vivo results at a very high dose level that may be due to physiological stress indicate that propylene glycol phenyl ether does not pose a genotoxicity hazard at doses that would likely be encountered in the environment. PPh has not been tested for carcinogenicity.

Environment

The melting point of PPh is 11.4 ºC and the boiling point is 253 ºC. Vapor pressure is 0.029 hPa at 25 ºC and the log octanol-water partition coefficient is 1.5. Finally, water solubility is 10,000 mg/L.

If released into the environment, PPh will distribute primarily to water and soil. The log octanol-water partition coefficient (log Kow) for PPh is 1.50 and the BCF is 0.776 (log BCF = -0.110). Both parameters indicate that PPh will not tend to bioaccumulate up food chains. The Henry’s Law Constant, which indicates propensity to partition from water to air, is low for PPh: 4.36 x 10^-7 atm-m³/mole. Fugacity modeling (Mackay Level III) indicates that PPh is likely to partition roughly equally and predominantly into the soil and water with small to negligible amounts distributing to other environmental compartments (air, sediment, and aquatic biota).

PPh is unlikely to persist in the environment. Once in air, the half-life of PPh due to direct reactions with photochemically generated hydroxyl radicals is estimated to be 3.45 hours. In water, PPh is readily biodegraded under aerobic conditions. In a biodegradation study that measured oxygen depletion, CO₂ production, and organic carbon disappearance (OECD 301F), PPh was “readily biodegradable” by all criteria. In soil, biodegradation also is rapid. When incubated with three soil types for 25 days, PPh degraded rapidly under aerobic conditions and very little under anaerobic conditions. Under aerobic conditions, time to 50% removal usually ranged from 1 to 7 days.

Acute aquatic testing indicates a low order of toxicity for PPh. The acute aquatic toxicity in the Golden Orfe with the 96-hour LC50 was between 215 and 464 mg/L; in the Fathead minnow, the 96-hour LC50 was 280 mg/L (263 mg/L < 95%CL > 297 mg/L). The 48-hour LC50 in daphnia was 370 mg/L (321 mg/L < 95%CL > 431 mg/L). In algae, the 72-hr EC50 was 74.5 mg/L (biomass) and > 100 mg/L (growth rate).

Exposure

In 1999, approximately 16 million pounds (7.3 thousand tonnes) of propylene glycol phenyl ether was produced.
worldwide and this is projected to increase to 18 million pounds (8.2 thousand tonnes) in 2004. Modern production methods result in major isomer content in excess of 85% and minor isomer content less than 15%.

A major use of PPh is as a solvent that facilitates the mixing of aqueous and organic constituents in paints, coatings, and films. PPh is used as a latex coalescent in water-based architectural and industrial coatings and adhesives, a carrier solvent for textile dyes, a solvent for inks in ball point and felt tip pens, stamp pads, and textile printing pastes, and paint remover. Due to its antibacterial properties, PPh also is used in cosmetics and soaps.

During manufacture and transport, occupational exposure potential is low due to the enclosed systems employed. For either occupational or consumer exposure, the most significant likelihood of exposure is by dermal contact or inhalation during application of paints and coatings, or application of materials for which PPh is a solvent or carrier. No occupational or other exposure limits have been established for PPh.

Individuals applying paint or other PPh-containing coatings may be exposed to this propylene glycol ether. Dermal contact through minor spills or usage contact is a source of exposure, as is inhalation from aerosol or vapor generated during application or usage.

Propylene glycol phenyl ether typically enters the environment through slow escape and evaporation from the solvent or coating system used. Spills of such products can also occur during application of coatings. Emissions to the atmosphere or surface water occurring via industrial wastes or effluents during manufacture or processing are limited by predominately enclosed processing and low volatility.

General population exposure also is possible through inhalation of ambient air containing low concentrations of PPh that may be released from industrial processes or through evaporation of coatings or other products containing it.

### RECOMMENDATION

**Environment:** This chemical is currently of low priority for further work.

**Human Health:** This chemical is a candidate for further work.

### RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

**Environment:**
This chemical is currently of low priority for further work because of its low hazard profile.

**Human Health:**
The chemical possesses properties indicating a hazard for human health (eye irritation – which is reversible - and developmental toxicity at high doses associated with maternal toxicity). Based on data presented by the Sponsor country, exposure is controlled in the occupational setting. Due the wide dispersive use, member countries are invited to perform an exposure assessment and if then indicated, a risk assessment, especially for consumers. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

Note: PPh may be evaluated further under the EU Biocides Directive. This will include exposure assessment on operators (occupational) and by-standers (consumers).

Note: the commercial product is commonly referred to as CAS# 770-35-4. CAS# 41593-38-8, which is uncommon, also can refer to the commercial mixed isomer product. However, CAS# 41593-38-8 is rarely used, especially in Europe because it is not listed on EINECS. The commercial product is listed under both CAS #s because modern production methods result in the major isomer content being in excess of 85% and the minor isomer content less than 15%. The major isomer is thermodynamically favored during synthesis and consists of a secondary alcohol configuration.