

membranes. The overall SAR rating for human health is low/moderate concern.

The SAR did note a concern for solvent neurotoxicity, i.e., neurotoxic effects that can occur due to "high" and/or "prolonged" dermal and inhalation exposures to organic solvents. It should be noted that the inclusion of the phrase "solvent-type neurotoxicity" in the SAR assessment does not necessarily indicate chemical-specific concerns. By including this statement those performing the SAR assessment are acknowledging that the chemical is a member of a class of chemicals that can exhibit solvent neurotoxicity.

C. Conclusions

The Agency used two sources of information to determine the toxicity of propylene carbonate: The 12 toxicity studies submitted by the petitioner and reviewed by the Agency, and a SAR assessment. The two sources of data support each other. However, results of the SAR Assessment are a type of predicted data based in part on surrogate data. There is actual data generated using propylene carbonate as the test substance, and actual data has precedence over predicted data.

The Agency reviewed a propylene carbonate developmental toxicity study in the rat with a maternal no observed adverse effect level (NOAEL) of 1,000 milligrams/kilogram/day (mg/kg/day) and a maternal lowest observed adverse effect level (LOAEL) of 3,000 mg/kg/day based on mortality, clinical signs and decreased food consumption. In the same study, the developmental NOAEL is 3,000 mg/kg/day and the developmental LOAEL is 5,000 mg/kg/day based on an increase in skeletal variations. In a propylene carbonate 13-week rat feeding study the NOAEL is equal to or greater than 5,000 mg/kg/day, the highest dose tested. A LOAEL was not identified in that study, but it would be even greater than 5,000 mg/kg/day. It is noted that each of these NOAELs is equal to or greater than 1,000 mg/kg/day. As a matter of practice, for both the developmental and the 13-week toxicity study, the Agency does not encourage testing above 1,000 mg/kg/day. The lack of effects at 1,000 mg/kg/day is considered adequate to define the toxicity, without pushing the dose levels higher until effects are apparent.

The SAR assessment judged propylene carbonate to be of low/moderate concern. It did not identify any carcinogenic concerns. One identified concern was for possible irritation to mucous membranes. This concern would involve the dermal and

inhalation exposure routes and would be addressed through the use of protective equipment such as gloves and respirators, not through establishment of tolerance exemptions.

A concern predicted by the SAR, based on its structural chemistry and chemical class, is for possible solvent neurotoxicity from exposure to propylene carbonate. As previously explained, this statement acknowledges that propylene carbonate is a member of a class of chemicals that can exhibit solvent neurotoxicity. However, the propylene carbonate data base includes a 13-week inhalation toxicity study in the rat with a neurotoxicity evaluation. Based on its review and evaluation of this inhalation toxicity study, the Agency determined that there was no evidence of neurotoxicity potential.

The SAR also indicated a concern for developmental toxicity at high dose levels. However, the Agency reviewed a propylene carbonate developmental toxicity study in the rat with a maternal NOAEL of 1,000 mg/kg/day and a maternal LOAEL of 3,000 mg/kg/day based on mortality, clinical signs and decreased food consumption. In the same study, the developmental NOAEL is 3,000 mg/kg/day and the developmental LOAEL is 5,000 mg/kg/day based on increase in skeletal variations.

Considering the NOAELs of greater than 1,000 mg/kg/day for the propylene carbonate toxicity studies and the overall judgement of low/moderate concern from the SAR assessment, propylene carbonate is of low toxicological concern.

IV. Aggregate Exposures

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

Over 1 million pounds of propylene carbonate are either produced or imported per year. Some of this propylene carbonate production is used as a chemical intermediate, in the production of other chemicals. Propylene carbonate has been approved by the Food and Drug Administration for use as an indirect food additive as a component of adhesives. According to 21 CFR 175.105, propylene carbonate can be a component of an adhesive used as part of "articles intended for use in packaging, transporting, or holding

food." Propylene carbonate is also used in cosmetics. Information on the internet (Huntsman website) indicates that propylene carbonate is used in tub and tile cleaners, hard surface and floor cleaners that could be used in and around the home.

The Agency has used various screening-level models to estimate some of the existing levels of exposure, and those that could occur as a result of establishing this tolerance exemption. To assure protectiveness, these estimates are deliberately intended to over-estimate exposure as shown in the following Table 2:

TABLE 2.—SCREENING-LEVELS OF EXPOSURE USING PROPYLENE CARBONATE

Type of Exposure	Exposure Level
Dietary - Food (as a result of application to crops)	Acute exposure: Less than 1 mg/kg/day at 95th percentile chronic exposure: Less than 1 mg/kg/day
Dietary - Drinking Water	Acute exposure: Much less than 1 mg/kg/day Chronic exposure: Much less than 1 mg/kg/day
Residential (as a result of using a cleaning product)	Approximately 6 mg/kg/day
Residential (as a result of using a laundry detergent)	Approximately 1 mg/kg/day
Residential (as a result of application to a lawn)	Less than 1 mg/kg/day

With one exception all of the screening-level exposure estimates are in the range of or less than 1 mg/kg/day. The existing studies for propylene carbonate yielded NOAELs that were equal to or greater than 1,000 mg/kg/day. The screening-level exposure estimates are orders of magnitude lower than these NOAELs. Even considering the reported uses, the use of propylene carbonate as an inert ingredient should result in human exposure far below any dose level that could possibly produce an adverse effect.

V. Cumulative Effects from Substances with a Common Mechanism of Toxicity

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency