1986) and a teratology study (Research Triangle Institute, 1986) in rats. Both the studies used purified 2,3,4,6-tetrachlorophenol (99% pure) suspended in olive oil.

In the teratology study, pregnant rats were administered by gavage with 0, 25, 100 or 200 mg/kg/day 2,3,4,6-tetrachlorophenol in olive oil daily on days 6-15 of gestation. Body weight gain, food consumption and clinical signs of toxicity were recorded during the gestation period. Rats were sacrificed on gestation day 20; gross pathology, liver and gravid uterine weight and status of uterine contents were recorded. Fetuses were removed, weighed and examined for malformations.

Results of this study indicated the only statistically significant adverse effect in the high-dose group (200 mg/kg/day): reduced maternal weight gain (corrected to exclude weight of uterine contents) as contrasted with controls. No significant maternal effects were noted at 25 or 100 mg/kg/day dosage group. Embryo-fetal growth and prenatal viability were not adversely affected by tetrachlorophenol exposure, nor was there any definitive evidence of an effect of the compound on fetal morphological development.

Based on data presented above, the 25 mg/kg/day dosage represents the subchronic NOAEL for 2,3,4,6-tetrachlorophenol; by applying an uncertainty factor of 1000 to this NOAEL, an RfD of 0.025 mg/kg/day or 0.03 mg/kg/day can be derived.

__I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF – 1000: 10 interspecies and 10 for intraspecies variability to the toxicity of this chemical in lieu of specific data and 10 for extrapolation of a subchronic effect level to its chronic equivalent.

MF – None

__I.A.4. Additional Studies/Comments (Oral RfD)

Previously an RfD of 0.01 mg/kg/day was verified on 7/8/85 based on a 55-day oral study (Hattula et al., 1981) in which Wistar rats were administered daily with 0, 10, 50 and 100 mg/kg/day 2,3,4,6-tetrachlorophenol by gavage (10 rats/group). This study reported body weight changes and organ histopathology at doses higher than 10 mg/kg; the NOAEL identified in this study was 10 mg/kg/day. This study, however, used commercial grade compound which contains substantial proportion of contaminants such as pentachlorophenol and dioxins. Additionally, this study used few number of animals and the duration of the study was only 55 days.

Schwetz et al. (1974) evaluated potential effects of both commercial grade and purified 2,3,4,6-tetrachlorophenol on embryo-fetal development following gavage dosing of pregnant Sprague-Dawley rats on gestational days 6 through 15. Based upon an earlier range finding study, doses of 10 and 30 mg/kg/day of both grades of tetrachlorophenol were examined in this teratology study. Administration of either grade of the compound resulted in no evidence of maternal toxicity, resorptions, fetal body weight or fetal crown-rump length. The only fetal anomaly that was increased at 30 mg/kg/day was delayed ossification of the skull bones, an effect that was interpreted as a developmental delay, not teratogenicity. The lower dose (10 mg/kg/day) in this study produced subcutaneous edema in exposed fetuses that was considered a chance alone incidence. The subcutaneous edema was not observed in the high-dose group. The issues related to both these studies, discussed above, call into question the validity of the data to derive an RfD.

__I.A.5. Confidence in the Oral RfD

Study – High
Database – Medium