## APPENDIX M: SUMMARY OF HUMAN HEALTH EFFECTS DATA FOR TRICLOPYR

### Tables from HED Aquatic Uses Risk Assessment 2002

**Table 1. Acute Toxicity of Triclopyr**

| Guideline # | Study Type | MRIDs # | Results | Toxicity Category |
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| **Acute Toxicity of Triclopyr acid, technical grade** | | | | |
| 870.1100 | Acute Oral | 00031940 | LD50 = 729 mg/kg (M); 630 mg/kg (F) | III |
| 870.1200 | Acute Dermal | 00056009 | LD50 > 2000 mg/kg | III |
| 870.1300 | Acute Inhalation | | not available | |
| 870.2400 | Primary Eye Irritation | | not available | |
| 870.2500 | Primary Skin Irritation | | not available | |
| 870.2600 | Dermal Sensitization | | not available | |
| 870.6200 | Acute Neurotoxicity | | not available | |
| **Acute Toxicity of Triclopyr triethylamine salt (TEA)** | | | | |
| 870.1100 | Acute Oral | 41443301 | LD50 = 1847 mg/kg (M& F) | III |
| 870.1200 | Acute Dermal | 41443302 | LD50 > 2000 mg/kg | III |
| 870.1300 | Acute Inhalation | 41443303 | LC50 > 2.6 mg/L | III |
| 870.2400 | Primary Eye Irritation | 41443304 | corrosive | I |
| 870.2500 | Primary Skin Irritation | 41443305 | not irritating | IV |
| 870.2600 | Dermal Sensitization | 41443306 | sensitizer | N/A |
| 870.6200 | Acute Neurotoxicity | | not available | |
| **Acute Toxicity of Triclopyr butoxyethyl ester (BEE)** | | | | |
| 870.1100 | Acute Oral | 40557004 | LD50 = 803 mg/kg (M&F) | III |
| 870.1200 | Acute Dermal | 40557005 | LD50 > 2000 mg/kg | III |
| 870.1300 | Acute Inhalation | 40557006 | LC50 > 4.8 mg/L | III |
| 870.2400 | Primary Eye Irritation | 40557007 | minimally irritating | III |
| 870.2500 | Primary Skin Irritation | 40557008 | not irritating | IV |
| 870.2600 | Dermal Sensitization | 40557009 | sensitizer | N/A |
| 870.6200 | Acute Neurotoxicity | | not available | |
| **Acute Toxicity 3,5,6-trichloro-2-pyridinol (TCP)** | | | | |
| 870.1100 | Acute Oral | 00064938 | LD50 = 794 mg/kg (M); 870 mg/kg (F) | III |
| 870.1100 | Acute Oral (Mouse) | 00043243 | LD50 = 380 mg/kg (M); 415 mg/kg (F) | II |

**Table 2. Toxicity Profile of Triclopyr**

| Guideline No./Study Type | Results |
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| 870.3100<br>90-Day oral toxicity rodents with acid-rat | NOAEL = **5** mg/kg/day in males and females<br>LOAEL = **20** mg/kg/day in males and females based on degeneration of the proximal tubules of the kidneys |
| 870.3100<br>90-Day oral toxicity rodents with ester-rat | NOAEL = **7** mg/kg/day in males and <7 mg/kg/day in females<br>LOAEL = **28** mg/kg/day in males, 7 mg/kg/day based on increased relative kidney weight (M) and decreased red blood cell content, hemoglobin content, and packed cell volume (F). Degeneration of the proximal tubules of the kidneys was seen in males at 70 and 350 mg/kg/day and females at 350 mg/kg/day (HDT). |
| 870.3150<br>183-Day oral toxicity non-rodents-dog | NOAEL **≤ 2.5** mg/kg/day (HDT) in males and females<br>LOAEL > **2.5** mg/kg/day in males and females based on toxicologically non-significant decreased rate of phenolsulfothalein (PSP) due to competition between Triclopyr and PSP for renal excretion. |
| 870.3200<br>21-Day dermal toxicity-rabbit | NOAEL = **1000** mg/kg/day (males and females)<br>LOAEL > 1000 mg/kg/day. Decreased alkaline phosphatase in both sexes of rabbits at 1,000 mg/kg/day and increased absolute and relative liver weight in males at 1,000 mg/kg/day were considered marginal and not of toxicological significance. |
| 870.3700<br>Prenatal developmental with ester-rats | **Maternal** NOAEL = **100** mg/kg/day<br>**Maternal** LOAEL = **300** mg/kg/day based on mortality, clinical signs, necropsy findings, decreased body weight gains, decreased food consumption, increased water consumption, and increased relative kidney and liver weight.<br>**Developmental** NOAEL = **100** mg/kg/day<br>**Developmental** LOAEL = **300** mg/kg/day based on increased incidence of hydrocephalus, cleft palate, microphthalmia/anophthalmia, retinal folds, thin diaphragm/protrusion of the liver, decreased fetal weight and visceral and skeletal anomalies and variants. |
| 870.3700<br>Prenatal developmental with ester-rabbits | **Maternal** NOAEL = **30** mg/kg/day<br>**Maternal** LOAEL = **100** mg/kg/day based on mortality<br>**Developmental** NOAEL = **30** mg/kg/day<br>**Developmental** LOAEL = **100** mg/kg/day based on decreased total live fetuses and increased total fetal deaths, as well as increased fetal and/or litter incidence of skeletal anomalies and variants. |
| 870.3700<br>Prenatal developmental with salt-rabbit | **Maternal** NOAEL = **30** mg/kg/day<br>**Maternal** LOAEL = **100 mg/kg/day** based on mortality, abortions, decreased body weight gain, decreased food efficiency, increased liver and kidney weight.<br>**Developmental** NOAEL = **30** mg/kg/day<br>**Developmental** LOAEL = **100 mg/kg/day** based on decreased live fetuses and increased embryonic deaths due to abortions. |
| 870.3700<br>Prenatal developmental with salt-rat | **Maternal** NOAEL = **100** mg/kg/day<br>**Maternal** LOAEL = **300** mg/kg/day based on mortality<br>**Developmental** NOAEL = **100** mg/kg/day<br>**Developmental** LOAEL = **300** mg/kg/day based on decreased fetal weight, increased fetal and litter incidence of skeletal anomalies, increased fetal incidence of unossified sternebrae. |
| 870.3700<br>Prenatal developmental with acid-rat | **Maternal** NOAEL = **< 50** mg/kg/day<br>**Maternal** LOAEL = **50** mg/kg/day based on increased clinical signs<br>**Developmental** NOAEL = **100** mg/kg/day<br>**Developmental** LOAEL = **200** mg/kg/day based on increase incidence of fetuses and litters with retarded ossification of skull bones, and two litters |

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| | (one fetus per litter) with cleft palate and brachycephaly. |
| 870.3800<br>Reproduction and fertility effects with acid-rat | **Parental/Systemic** NOAEL = **5** mg/kg/day in males and in females<br>**Parental/Systemic** LOAEL = **25** mg/kg/day in males and females based on increased incidence of proximal tubular degeneration in male and female P1 and P2 rats.<br>**Reproductive/Offspring** NOAEL = **5** mg/kg/day in males and females<br>**Reproductive/Offspring** LOAEL = **25** based on increased incidence of F2 pups with exencephaly and ablepharia. |
| 870.4100a<br>228-Day Toxicity Study-dogs | NOAEL = **10** mg/kg/day in males and females<br>LOAEL = **20** mg/kg/day in males and females based on decreased body weight gain (M), decreased hematological parameters (M), changes in clinical chemistry (both sexes), and liver histopathology (both sexes). |
| 870.4100b<br>Chronic toxicity (1 year)-dogs | NOAEL **≤ 5** mg/kg/day in males and females<br>LOAEL > **5** mg/kg/day in males and females based on changes in clinical chemistry which are due not to toxicity, but a physiologic response of the dog based on limited ability of the dog to excrete organic acids at higher plasma concentrations. |
| 870.4300<br>Chronic/Carcinogenicity - rats | NOAEL = **12** mg/kg/day in males ≤ 36 mg/kg/day in females<br>LOAEL = **36** in males, >36 mg/kg/day in females based on marginal increases in proximal tubular degeneration at 6 months.<br>**Increase in adrenal gland pheochromocytoma in males and significant trend ($p<0.05$) for mammary gland adenocarcinomas in females.** |
| 870.4300<br>Carcinogenicity - mice | NOAEL = **84** mg/kg/day in males, 109.5 mg/kg/day in females<br>LOAEL = **143** mg/kg/day in males, 135 mg/kg/day in females based on decreased weight gain<br>**No evidence of carcinogenicity in males, but females had a significant trend ($p<0.05$) for mammary gland adenocarcinomas** |
| 870.5265<br>Gene Mutation | Triclopyr BEE was non-mutagenic when tested up to 5000 ug/plate or cytotoxic levels, in presence and absence of activation, in *S. typhimurium* strains TA98, TA100, TA1535 and TA1537. |
| 870.5300<br>Gene Mutation | In the rec-assay, Triclopyr acid produced no evidence of growth inhibition for the repair competent (H17) or repair deficient (M45) *B. subtilis* bacterial strains when tested up to 2000 ug/disk. |
| 870.5300<br>Gene Mutation | In the host-mediated assay, Triclopyr acid was negative for mutagenicity at doses up to 70 mg/kg in ICR random bred mice when tested against indicator organisms |
| 870.5395<br>In Vivo Cytogenetic assay-rats | Triclopyr acid was negative for chromosomal aberrations in the cytogenetic assay when administered singly or for 5 days to Sprague-Dawley rats up to 70 mg/kg/day. |
| 870.5395<br>In vivo Mouse Micronucleus | Triclopyr BEE was not clastogenic in the mouse micronucleus test up to 600 mg/kg (HDT) |
| 870.5550<br>Unscheduled DNA synthesis | Triclopyr BEE did not cause DNA damage or inducible repair in the rat hepatocyte unscheduled DNA synthesis |
| 870.5550<br>Unscheduled DNA synthesis | Triclopyr acid did not produce any evidence of unscheduled DNA synthesis, as determined by radioactive tracer procedures (nuclear silver grain counts), in rat primary hepatocyte cultures exposed up to cytotoxic levels. |
| 870.5450<br>Dominant lethal assay-mice | Triclopyr acid was negative for the dominant lethal mutagenic effect in treated male rats which were fed for 9 consecutive weeks at doses up to 70 mg/kg/day and mated to virgin females. |
| 870.5450<br>Dominant lethal assay-rats | Triclopyr acid was negative for the dominant lethal mutagenic effect in treated male rats at doses up to 70 mg/kg/day given by oral intubation followed by mating to 2 untreated females per week for 7 weeks |

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| 870.7485<br>Metabolism and pharmacokinetics - rat | In a rat metabolism with C14-triclopyr acid at doses of 3 mg/kg (single, low dose), 3 mg/kg x 14 days (repeated low dose) and 60 mg/kg (high dose), Triclopyr was well absorbed and rapidly excreted at the low dose or repeated low dose. At 60 mg/kg, excretion was decreased between 0-12 hours due to saturation of renal excretion mechanisms (attainment of zero order kinetics). Unmetabolized parent represented >90% of the urinary radioactivity, with the remainder present as primarily TCP. |
| 870.7500<br>Dermal penetration study in humans | In an oral and dermal pharmacokinetics study of Triclopyr in human volunteers, Triclopyr was administered orally and dermally to six human volunteers. More than 80% of the administered dose was found as unchanged Triclopyr in the urine. An average of 1.65% of the dermally applied dose was recovered in the urine and represented dermal penetration of Triclopyr. |
| 52-week mammalian dietary study-beagle dogs (TCP) | A 52-week mammalian dietary study with beagle dogs fed TCP at 0, 3, 12 or 48 mg/kg/day showed treatment-related effects only at the highest dose level. Toxic effects at 48 mg/kg/day (624 ppm) included statistically significant d crease in body weight gain and increases in ALT and ALP. These changes were similar between both sexes. |