Appendix B.

Ecotoxicity Study Summaries

Registrant-Submitted Ecotoxicity Studies

Freshwater Fish: Acute Exposure (Mortality) Studies

Available data indicate that EPTC is slightly toxic on an acute basis to several surrogate freshwater fish species (Table 1). The acute 96-hour median lethal toxicity thresholds (*i.e.*, LC_{50s}) for EPTC range from 14 to 27 mg a.i./L for bluegill sunfish, rainbow trout, cutthroat trout, and lake trout. Fish toxicity studies with EPTC formulations (2.3 - 77.1% a.i.) are also available for consideration in this risk assessment. These studies suggest that the tested formulations and technical grade EPTC exhibit similar toxicity on an acute basis, with 96-hour LC_{50s} ranging from about 16 to 24 mg a.i./L..

Table 1. Freshwater Fish Acute Toxicity Data.

Common Name	%AI	Study parameters	Test Results	MRID	Classification/ Category
Bluegill sunfish *Lepomis macrochirus*	99	96 hour study 10 fish/treatment 0, 0(solvent), 5.6, 10, 18, 32, 56 mg/L. Nominal concentrations used. Static study.	96 HR LC_{50}= 18 (10 - 32) mg/L[2,3]. NOAEC = 5.6 mg/L LOAEC = 10 mg/L based on sublethal effects (at times throughout the study, some fish either at the surface or on the bottom). Mortality and /or loss of equilibrium observed at ≥ 18 mg/L.	00131271	Acceptable/ Slightly toxic[1]
Bluegill sunfish *Lepomis macrochirus*	98.6	96 hour study 10 fish/treatment 0, 0(solvent), 1.8, 4.2, 10, 24, 56 mg/L. Nominal concentrations used. Static study.	96 HR LC_{50} = **14 (10-24) mg/L[2]** NOAEC = 4.2 mg/L LOAEC = 10 mg/L based on sublethal effects (darkened, quiescent and at the surface) and mortality (1 fish). At 24 mg/L and above, 100% mortality.	00144208	Acceptable/ Slightly toxic
Bluegill sunfish *Lepomis macrochirus*	not reported	Mixture of two products: Banvel + Eradicane 6.7 EC (EPTC + R-25788 (inert safener)). 96-hr. acute study. 10 fish/treatment at 0 (control), 56, 100, 180, 320, 580 mg/L (nominal). Assumed static study.	96 hr. LC_{50}: 397.8 (325.7-485.7) mg formulation/L NOAEC: 180 mg/L LOAEC: 320 mg/L based on sublethal effects. Discoloration and abnormal behavior observed at ≥ 320 mg/L.	00027992	Supplemental/ Practically nontoxic for mixture

Table 1. Freshwater Fish Acute Toxicity Data.					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Classification/ Category**
Bluegill sunfish *Lepomis macrochirus*	77.1	Eptam 6E. 20 fish/treatment. Nominal concentrations: 0, 9.9, 13.4, 18.2, 24.2, 32, 42.3 mg/L	96-hr LC_{50}: 22.6 (21.5-24.2) mg formulation/L; 17.4 (16.6 – 18.7) mg a.i./L NOAEC: 18.2 mg/L LOAEC: 24.2 mg/L Mortalities observed at 24.2 mg/L and above. No sublethal effects reported.	00034684	Supplemental/ Slightly toxic for formulation
Bluegill sunfish *Lepomis macrochirus*	47	96-HR Acute fish study. Knoxweed 42 formulation. 20 fish/concentration level. 0, 10, 18, 32, 42, 56 mg/L nominal concentrations in a static bioassay.	96-HR EC_{50}: 24 (17-34) mg formulation/L; 11 (8 – 16) mg a.i./L NOAEC: 10 mg/L LOAEC: 18 mg/L (mortality) Slight loss of equilibrium at ≥ 32 mg/L.	00022361	Acceptable for formulation/ Slightly toxic for formulation
Bluegill sunfish *Lepomis macrochirus*	97.8	Control, solvent control, 5.6, 10, 18, 24, 32, 42, 56 mg/L. 10-20 fish per concentration level. Static study. Nominal concentrations.	LC_{50}: 22.9 (19.3-26.8) mg/L NOAEC: 10 mg/L LOAEC: 18 mg/L based on mortality. At 32 mg/L, fish remained on their sides at bottom of tank.	00021834	Acceptable/ Slightly toxic
Bluegill sunfish *Lepomis macrochirus*	not reported	Eptam 6E. Control, solvent control, 10, 18, 24, 32, 56 mg/L. 10-20 fish per concentration level. Static study. Nominal concentrations.	LC_{50}: 25.4 (23.6 – 27.4) mg formulation/L Slope: 16.08 (9.2 – 22.9) NOAEC: 10 mg/L LOAEC: 18 mg/L based on mortality. At 24 mg/L, fish remained on their sides at bottom of tank.	00021834	Acceptable/ Slightly toxic
Rainbow trout *Onchorhynchus mykiss*	99	96 hour study 10 fish/vessel Mean measured 0, 0 (solvent), 3.2, 5.6, 10, 18, 32 mg/L. Static study	96 HR LC_{50} = 21 (10-32) mg/L NOAEC = 3.2 mg/L LOAEC = 5.6 mg/L based on sublethal effects (fish on bottom). Other sublethal effects observed at higher concentration levels (darkening, loss of equilibrium, at surface). Mortality observed at 18 mg/L and above.	00131272	Acceptable/ Slightly toxic[1]

Table 1. Freshwater Fish Acute Toxicity Data.					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Classification/ Category**
Rainbow trout *Onchorhynchus mykiss*	97.8	Control, solvent control, 10, 18, 21, 24, 32 mg/L. 10-20 fish/concentration level. Static study. Nominal concentrations.	LC_{50}: 19 (17-21) mg/L NOAEC: 10 mg/L LOAEC: 18 mg/L based on mortalities at 18 mg/L and above. Signs of intoxication were observed at ≥ 21 mg/L	00021834	Acceptable/ Slightly toxic
Rainbow trout *Onchorhynchus mykiss*	not reported	Eptam 6E. Control, solvent control, 10, 18, 24, 32, 56 mg/L. 10-20 fish per concentration level. Assumed static study. Nominal concentrations.	LC_{50}: 21 (19-23) mg formulation/L NOAEC: 10 mg/L LOAEC: 18 mg/L based on mortalities at 18 mg/L and above. Signs of intoxication were observed at ≥ 24 mg/L.	00021834	Acceptable/ Slightly toxic for formulation
Rainbow trout *Onchorhynchus mykiss*	2.3	Eptam formulation: 96-HR LC_{50}. 20 fish/concentration level. 0 (assumed), 18, 32, 56, 100, 180 mg/L (nominal). Static study.	LC_{50}>180 mg formulation/L (>4.14 mg/L a.i.). No mortalities were observed.	00025286	Supplemental/ At most, moderately toxic
Rainbow trout *Onchorhynchus mykiss*	47	96-HR Acute fish study. Knoxweed 42 formulation. 10-20 fish/concentration level. 0, 0 (solvent) 10, 18, 32, 42, 56 mg/L nominal concentrations in a static bioassay.	96- HR LC_{50}: 22 (18-27) mg formulation/L; 10 (8 – 13) mg a.i./L NOAEC: 10 mg/L LOAEC: 18 mg/L. Mortality and clinical signs (fish remaining on their sides with an apparent respiration inhibition) at ≥18 mg/L.	00022361	Acceptable for formulation/ Slightly toxic for formulation
Mosquito fish *Gambusia affinis*	77.1	Eptam 6E formulation. 96 hour acute toxicity study. 10 fish/concentration level. 3.16, 10.0, 20.0, 31.6 mg/L. Assumed controls were used and static study (not provided in DER).	96 hr. LC_{50}: 16.4 (13.7 – 19.1) mg formulation/L; 12.6 (10.6 – 14.7) mg a.i./L NOAEC: 10 mg/L LOAEC: 20 mg/L based on signs of toxicity (discoloration, behavior). Test and statistical methodology either poorly described or not provided.	00084743 00108342	Supplemental/ Slightly toxic for formulation
Goldfish *Carassius auratus*	2.3	Eptam formulation. 96-hr. study. 0, 3.2, 10, 18, 32, 56 and 100 mg/L nominal concentrations. 5 fish/concentration level.	96-hr LC_{50}> 100 mg/L (>2.3 mg a.i./L) NOAEL: 2.3 mg a.i./L LOAEL > 2.3 mg a.i./L. No sublethal effects reported.	00025287	Supplemental/ Practically nontoxic for formulation

Table 1. Freshwater Fish Acute Toxicity Data.					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Classification/ Category**
Goldfish *Carassius auratus*	77.1	Eptam 6E formulation. Nominal. Static. Concentration levels based on the amount of total formulation. 0, 21, 24, 28, 32, 37 mg/L. 10 per concentration tested.	96-hr LC_{50}: 26.7 mg formulation/L; 20.6 mg a.i./L NOAEC: 24 mg/L LOAEC: 28 mg/L based on mortality.	00034683	Supplemental/ Slightly toxic
Cutthroat trout *Salmo clarkii* Lake trout *Salvelinus namaycush*	95	96-HR LC_{50} study. No concentrations available in DER. Nominal based on 1999 RED.	Cutthroat trout 96-HR LC_{50}: 17 (15 - 19) mg/L Lake trout 96-HR LC_{50}: 16.2 (14.8 – 17.7) mg/L	40094602	Supplemental/ Slightly toxic

[1]Based on LC_{50} (mg/L): < 0.1 very highly toxic; 0.1-1 highly toxic; >1-10 moderately toxic; >10-100 slightly toxic; >100 practically nontoxic
[2] **Bold** value will be used to calculate risk quotients
[3] Range is 95% confidence interval for endpoint

With regard to potential volatilization of EPTC during the aquatic toxicity tests, the measured test concentrations in a daphnid 48-hour study, 72-hour renewals in a duckweed study, and 96-hour algal studies indicate that EPTC volatilizes from water at levels ranging from 2 to about 50% losses. It is estimated that test concentrations at 96-hours at the end of the fish studies would be 20 to 25 percent less than initial nominal level. Averaging the initial and the predicted final test concentrations, it is estimated that the mean test concentrations are 10 to 13 percent less than nominal test concentrations; thus, fish LC_{50} values are about 10 percent lower than the toxicity values listed above.

Freshwater Fish: Chronic Exposure (Growth/Reproduction) Studies

No freshwater fish chronic studies are available for EPTC. Thus, the potential direct effects to the CRLF in terms of chronic effects (*e.g.*, reproduction, growth) cannot be quantitatively assessed at this time.

Freshwater Invertebrates: Acute Exposure Studies

Available toxicity data indicated that EPTC is slightly to moderately toxic on an acute basis to surrogate freshwater invertebrate species. The acute 48-hour EC_{50s} for EPTC range from 6.49 to 14 mg a.i./L for daphnids. The acute 96-hour EC_{50}s on the technical material for the sowbug and scud (2 studies) are 23, 66 and 23 mg/L, respectively. The 48-hour acute toxicities of the sulfoxide degradate and a mixture of two products, banvel + eradicane 6.7 EC are 22 and 266.5 mg/L, respectively.

Table 2. Freshwater Invertebrate Acute Toxicity Data

Common Name	%AI	Study parameters	Test Results	MRID	Classification/ Category
Water flea *Daphnia magna*	98.4	48-hr static study Treatments: 1.8, 3.2, 5.6, 10, 18, 32, 56, and 100 mg/L. Mean measured concentrations from 1.7 to 93 mg/L.	48-hr LC_{50}**: 6.49 (4.8-8.4) mg a.i./L**[2]. NOAEC: 1.7 mg a.i./L (mean measured). LOAEC: 3.2 mg a.i./L (nominal) based on immobility.	42945601	Acceptable/ Moderately toxic
Water flea *Daphnia magna*	98.6	48-hr static study. Nominal concentrations: 0, 0 (solvent control), 5.6 10, 18, 32,56, 100 mg/L. 20 daphnids/treatment.	48-hr LC_{50}: 14 (12-17)[3] mg a.i./L (nominal). NOAEC: 5.6 mg a.i./L LOAEC: 10 mg a.i./L based on sublethal effects and lethality. No reported sublethal effects.	00144209	Acceptable/ Slightly toxic
Water flea *Daphnia magna*	99	48-HR static study. Mean measured concentrations 0, 0 (solvent), 1.7, 3.6, 6.2, 9.6 mg/L. 20 daphnids/treatment.	48-hr LC_{50}: 7.5 (5.9–9.5) mg a.i./L NOAEC: 3.2 mg/L LOAEC: 5.6 mg/L based on lethality.	00131273	Acceptable/ Moderately toxic
Water flea *Daphnia magna*	98 sulfoxide degradate R078202	48-hr static study (R078202) sulfoxide degradate; measured initial concentrations at 5.6, 10, 18, 32, 57 and 100 mg/L (approx. 4% loss in 48 hours). 20 daphnids/treatment	48-hr LC_{50} = 22 (20-26 mg a.i. /L). Probit slope: 10.74 NOAEC = 10 mg/L LOAEC = 18 mg/L based on immobilization. Sublethal effects not reported	45442201	Supplemental/ Slightly toxic[1]

Table 2. Freshwater Invertebrate Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Classification/ Category**
Water flea *Daphnia magna*	not reported	48-hr static study (assumed). Mixture of two products: Banvel + Eradicane 6.7 EC (EPTC + R-25788). Treatments: 0 (control), 56, 100, 180, 320, 560, 1000 mg/L (nominal); 20 daphnids/treatment.	Test conducted with a mixture of two products. 48-hr LC_{50}: 266.5 (221.7-320.4) mg/L NOAEC: < 100 mg/L	00016546	Supplemental/
Sowbug *Asellus brevicaudus*	95	96-hour static study.	LC_{50}: 23 mg a.i./L	40094602	Supplemental/ Slightly toxic
Scud *Gammarus fasciatus*	95	96-hour static study.	LC_{50}: 66 mg a.i./L	40094602	Supplemental/ Slightly toxic
Scud *Gammarus fasciatus*	95	96-hour static study	LC_{50}: 23 (15 -36) mg a.i./L.	05001497	Supplemental/ Slightly toxic

[1]Based on EC_{50} (mg/L): < 0.1 very highly toxic; 0.1-1 highly toxic; >1-10 moderately toxic; >10-100 slightly toxic; >100 practically nontoxic
[2] **Bold** value will be used to calculate risk quotients
[3] Range is 95% confidence interval for endpoint
[4] Johnson , W.W. and M.T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Department of Interior, Fish and Wildlife Service Resource Publication 137. 98 pp. Washington, D.C.

Freshwater Invertebrates: Chronic Exposure Studies

A life-cycle study with the water flea (*Daphnia magna*) is available to assess the potential chronic risks of EPTC to freshwater invertebrates; study results are summarized in Table 3. An NOAEC of 0.81 mg/L based on a reduction in the number of offspring was established in the study. The 21-day LC_{50} was 3.5 mg/L.

Table 3. Freshwater Invertebrate Chronic Toxicity Data					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Classification /Category**
Water flea *Daphnia magna*	95.6	Static renewal life-cycle test. 10 daphnids/treatment. Treatments (mean measured) were 0 (neg. control), 0 (solvent control), 0.30, 0.47, 0.81, 1.3, 2.7 and 4.2 mg a.i./L.	21-day LC_{50} = 3.5 (2.9-4.3) mg ai./L Slope: 11.065 (3.87 - 18.26) NOAEC (survival): 1.3 mg ai./L. LOAEC (survival): 2.7 mg ai/L. NOAEC (growth): 1.3 mg ai./L. LOAEC (growth): 2.7 mg ai./L. **NOAEC (reproduction): 0.81 mg/L** LOAEC(reproduction): 1.3 mg/L	45075006	Acceptable

[1] **Bold** value will be used to calculate risk quotients

Aquatic Plants: Laboratory Data

Table 4 summarizes test results for three non-vascular and one vascular plant toxicity studies for EPTC. Based on the available data, green algae (*P. subcapitata*) is the most sensitive non-vascular plant species, with an EC_{50} of 1.4 (1.3-1.5) mg a.i./L. The only vascular plant study available identified an EC_{50} of 5.6 (2.9 - 9.3) mg a.i./L for duckweed.

Table 4. Non-target Aquatic Plant Toxicity					
Species	**%A.I.**	**Study Parameters**	**Test Results**	**MRID No.**	**Study Classification**
Green Algae *Pseudokirchneriella subcapitata*	98.4	96-hour study. Treatments (mean-measured): 0 (neg. control), 0 (solvent control), 0.11, 0.22, 0.41, 0.86, 1.6, 3.3, 7.0, and 13 mg a.i./L	4-day EC_{50}: **1.4 (1.3-1.5) mg a.i./L**[1] Probit slope: 10 NOAEC: 0.9 mg a.i./L LOAEC: 1.6 mg a.i./L (based on % inhibition and cell density)	42921202 42899801	Acceptable
Blue-Green Algae *Anabaena flos-aquae*	98.4	5-day study. Treatments (mean-measured): 0.55, 1.2, 2.3, 4.6, 10, 20, 41, 81 mg a.i./L	5-day EC_{50}: 41 mg a.i./L NOAEC: 20 mg a.i./L LOAEC: 41 mg a.i./L (based on cell density)	42883501	Acceptable
Freshwater Diatom *Navicula pelliclosa*	98.4	96-hour study. Treatments (mean-measured): Solvent control, 0.37, 0.67, 1.4, 2.8, 6.0, 11, 22, and 45 mg/L	4-day EC_{50}: 3.9 (3.6 - 4.2) mg a.i./L Probit slope 3.6 NOAEC: 2.8 mg a.i./L LOAEC: 6.0 mg a.i./L (based on % inhibition and cell density)	42921201	Acceptable Supplemental? Check.

Table 4. Non-target Aquatic Plant Toxicity					
Species	**%A.I.**	**Study Parameters**	**Test Results**	**MRID No.**	**Study Classification**
Duckweed *Lemna gibba*	98.4	14-day static renewal study. Treatments (mean-measured):. Control, 0.012, 0.031, 0.092, 0.29, 0.89, 2.9, 9.3, 38.7 mg a.i./L	EC_{50} (biomass): **5.6 (2.9 - 9.3) mg a.i./L**[1] NOAEC (biomass): 0.89 mg a.i./L LOAEC (biomass): 2.9 mg a.i./L EC_{50} (frond no.): 6.7 (2.9 - 9.3) mg a.i./L NOAEC (frond no.): 0.29 mg a.i./L LOAEC (frond no.): 0.89 mg a.i./L	43096001	Acceptable

[1] **Bold** values will be used to calculate risk quotients

Birds: Acute Exposure (Mortality) Studies

EPTC is categorized as practically non-toxic to slightly toxic to birds on acute oral and dietary bases. Table 5 summarizes test results for available acute EPTC toxicity studies for birds. The available acute oral toxicity tests for the mallard duck and bobwhite quail failed to establish a definitive LD_{50} (*e.g.*, mallard duck LD_{50} >1000 mg/kg). A definitive subacute dietary LC_{50} of 20000 ppm was established for the bobwhite quail. Based on available information, it appears that the tested EPTC formulations and mixtures exhibit toxic effects to birds in the same range as EPTC (a.i.).

Table 5. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Study Classification/ Toxicity Category**
Bobwhite Quail *Colinus virginianus*	98.6	Acute oral study 10 birds/sex/dose level 19 day observation period 0 (vehicle), 398, 631, 1000, 1590, 2510 mg total product/kg bw tested.	LD_{50} > 2510 mg a.i./kg bw NOAEL < 398 mg/kg bw LOAEL = 398 mg/kg (reduced food consumption, body weight loss, sublethal effects (lethargy, reduced reactions to external stimuli). Mortality observed at 2510 mg/kg (2 females).	00144280	Acceptable/ Practically non-toxic[1]
Mallard Duck *Anas platyrhynchos*	98.5	Acute oral study 5 birds/sex/dose level 14 day observation period 0 (vehicle), 398, 631, 1000, 1590, 2510 mg/kg bw (adjusted for purity).	LD_{50} > 1000 mg a.i/kg bw NOAEL: 1000 mg/kg LOAEL > 1000 mg/kg. LD_{50} based on the highest concentration which did not cause regurgitation. No effects observed other than regurgitation (1590 and 2510 mg/kg).	00131274	Supplemental/ No more than slightly toxic

Table 5. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Study Classification/ Toxicity Category**
Bobwhite Quail *Colinus virginianus*	97.8	7-day dietary study (3 additional days on basal diet) 10 birds/concentration level (20 at 32,000 ppm) 0 (control), 1000, 1800, 3200, 5600, 10,000, 18,000, 24,000 32,000 ppm (nominal concentrations).	**LC_{50}: 20000 ppm[3]** NOAEC: 1800 ppm LOAEC: 3200 ppm based on inhibition of body weight gain at ≥ 3200 ppm. Mortality observed at ≥ 5600 ppm; slight depression at ≥ 10,000 ppm; ataxia at ≥ 18,000 ppm; pale livers at 18,000 and 24,000 ppm; weight loss around breast area at 24,000 ppm. All birds died at 32,000 ppm; no necropsies were conducted. Birds were 8 weeks old rather than 5-10 days.	00021834	Supplemental/ Practically non-toxic
Bobwhite Quail *Colinus virginianus*	98.5	8-day subacute dietary study: 5 days treated diet with 3 days untreated diet. 10 birds/concentrations. 0, 562, 1000, 1780, 3160, 5620 ppm adjusted to 100% a.i. (nominal).	LC_{50}> 5620 ppm NOAEC: 5620 ppm LOAEC > 5620. No mortality or sublethal effects observed. Slight reduction in group body weight gain for all groups.	00131275	Acceptable/ Practically non-toxic
Bobwhite Quail *Colinus virginianus*	not reported	Eptam 6E formulation (% a.i. not given). 7-day dietary study (3 additional days on basal diet). 10 birds/concentration level. 0 (control), 1000, 1000, 3200, 5600, 10,000, 18,000, 24,000 32,000, 56,000 ppm (nominal concentrations).	LC_{50}: 26000 ppm NOAEC: 5600 ppm LOAEC: 10,000 ppm based on inhibition of body weight gain at ≥ 10,000 ppm; mortality at ≥ 18,000 ppm. Slight depression observed at ≥ 18,000 ppm. Huddling, ataxia and depression observed at ≥ 24,000 ppm. Pale livers and weight loss around breast area at 24,000 and 32,000 ppm. All birds died at 56,000 ppm; no necropsies were conducted. Birds were 8 weeks old rather than 5-10 days.	00021834	Supplemental/ Practically non-toxic

Table 5. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Study Classification/ Toxicity Category**
Bobwhite Quail *Colinus virginianus*	not reported	Mixture of two products: Banvel + Eradicane 6.7 EC (EPTC + R-25788 (inert safener)). % a.i. not provided. 8 Day dietary study 10 birds/concentration level 5 days on treatment, 3 additional days observation 0 (control), 464, 1000, 2150, 4640, 10,000 ppm (nominal concentrations).	LC_{50} > 10,000 ppm NOAEC: 4640 ppm LOAEC: 10,000 ppm based on slight reduction in body weight gain. No clinical signs of toxicity were observed. There was a slight reduction in body weight gain at 10,000 ppm. There were no treatment-related mortalities at any level; mortalities were due to non-treatment related cannibalism.	00016527	Supplemental/ Practically non-toxic
Bobwhite Quail *Colinus virginianus*	47	10-day dietary study. Eptam Knoxweed 42. 10 birds/concentration level. 7 days dietary treatment, 3 days basal diet. 0, 3200, 5600, 10000, 18000, 24000, 32000 ppm.	LC_{50}: 22000 (15714-30800) ppm. NOAEC: 3200 ppm LOAEC: 5600 ppm. Decrease in body weight by day 7 at ≥ 18000 ppm. Toxic signs consisted of depression, ataxia, and huddling at ≥ 24,000 ppm. Pale livers in all surviving birds at 5600 ppm and above; weight loss around breast area at 32000 ppm. Mortality: 0, 0, 1, 0, 4, 7, 5 at 0, 3200, 5600, 10000, 18000, 24000 and 32000 ppm, respectively. Birds were 8 weeks old.	00022361	Supplemental
Mallard Duck *Anas platyrhynchos*	98.5	8-day subacute dietary study: 5 days treated diet with 3 days untreated diet. 10 birds/concentrations. 0, 562, 1000, 1780, 3160, 5620 ppm adjusted to 100% a.i. (nominal).	LC_{50} > 5620 ppm NOAEC: 3160 ppm LOAEC: 5620 based on decrease in body weight gain and food consumption. No mortality or other sublethal effects observed. Reduction in group body weight gain at 5620 ppm.	00131276	Acceptable/ Practically non-toxic
Mallard Duck *Anas platyrhynchos*	98.6	8-day subacute dietary study: 5 days treated diet with 3 days untreated diet. 10 birds/concentrations. 0, 562, 1000, 1780, 3160, 5620 ppm adjusted to 100% a.i. (nominal).	LC_{50}> 5620 ppm NOAEC: 1000 ppm LOAEC: 1780 based on decrease in body weight gain. No mortality or other sublethal effects observed. Reduction in group body weight gain at ≥ 1780 ppm.	00144207	Acceptable/ Practically non-toxic

Table 5. Avian Acute Toxicity Data					
Common Name	**%AI**	**Study parameters**	**Test Results**	**MRID**	**Study Classification/ Toxicity Category**
Mallard Duck *Anas platyrhynchos*	---	Mixture of two products: Banvel + Eradicane 6.7 EC (EPTC + R-25788 (inert safener)). % a.i. not provided. 8 Day dietary study 10 birds/concentration level 5 days on treatment, 3 additional days observation 0 (control), 464, 1000, 2150, 4640, 10,000 ppm (nominal concentrations).	LC_{50} > 10,000 ppm NOAEC: 4640 ppm. LOAEC: 10,000 ppm based slight reduction in body weight gain. No clinical signs of toxicity were observed; however, there was a slight reduction in body weight gain, which was most noticeable at the 10,000 ppm concentration level. There were no mortalities at any level.	00016539	Supplemental/ Practically non-toxic

[1] Based on LD_{50} (mg/kg) <10 very highly toxic; 10-50 highly toxic; 51-500 moderately toxic; 501-2000 slightly toxic; >2000 practically nontoxic

[2] Based on LC_{50} (mg/kg) <50 very highly toxic; 50-500 highly toxic; 501-1000 moderately toxic; 1001-5000 slightly toxic; >5000 practically nontoxic

[3] **Bold** value will be used to calculate risk quotients

Some uncertainty exists about the test concentrations to which the birds were exposed during the dietary tests. EPTC is volatile with a vapor pressure value of 1.6×10^{-2} Torr and the avian feed was not analyzed for concentrations of EPTC. In a laboratory, 40 percent of the EPTC volatilized during a 25-hour study and residue analyses indicate no degradation. In a field study, 73.6 % of EPTC applied by irrigation water volatilized within 52 hours after application. Results from 13 different locations (MN, CO, KY**,** OH, FL**,** 2MS, 5CA) indicate that EPTC dissipated with half-lives between 2 and 56.8 days. The uncertainty about the stability of the test concentrations extends the uncertainty about the toxicity values, since the LC_{50} values are based on test concentrations.

Birds: Chronic Exposure (Growth, Reproduction) Studies

EPTC induced reproductive effects in both bobwhite quail and mallard ducks (Table 6). Effects were observed starting at 593 ppm in the diet and included embryo viability, the number of eggs laid, set and hatched, the number of viable embryos and hatchling survival. Other effects, such as effects on eggs cracked and the proportion of eggs not cracked to eggs laid are not included because they do not relate to CRLF reproduction.

Table 6. Avian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**Test Results**	**MRID**	**Classification**

Table 6. Avian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**Test Results**	**MRID**	**Classification**
Bobwhite Quail *Colinus virginianus*	98.1	Reproduction study 16 pairs per level. Mean-measured concentrations were <25.0 (<LOD, control), 239, 591, and 1490 mg ai/kg diet, respectively.	NOAEC: 591 ppm LOAEC: 1490 ppm based on significant adverse effects on the proportion of eggs set to eggs laid, viable embryos and live embryos.	46554302	Acceptable
Mallard Duck *Anas platyrhynchos*	98.1	Reproduction study. 16 pairs per treatment level. Mean-measured concentrations were <25.0 (<LOD, control), 242, 593, and 1490 mg ai/kg diet, respectively.	NOAEC: **242 ppm**[1] LOAEC: 593 ppm based on a significant reduction in the proportion of viable embryos of eggs set at the 593 and 1490 ppm levels (13 and 21%, respectively). At 1490 mg ai/kg diet, number of eggs laid, eggs set, viable embryos, and live embryos; number hatched; ratios of number hatched to eggs laid and to eggs set; and hatchling survival and the ratio of hatchling survivors to eggs set were adversely affected. Reductions ranged from 24 to 52% of control.	46554301	Acceptable

[1] **Bold** value is the value that will be used to calculate risk quotients

Mammals: Acute Exposure (Mortality) Studies

Table 7 summarizes the available acute mammalian toxicity information for EPTC. Based on the available data, EPTC technical and tested formulations are categorized as slightly toxic at most.

Table 7. Mammalian Acute Toxicity Data

Common Name	%AI	Study parameters	Test Results	MRID	Classification /Category
Laboratory rat *Rattus norvegicus*	Tech	Acute oral study 991, 1427, 2055, 2959, and 5000 mg/kg bw tested 5/sex/dose level 14-day observation period	Acute oral LD_{50}**: 1465 (1290-1663)** mg/kg (M), 1712 (1324-2214) mg/kg (F), 1599 (1294-1976) mg/kg (combined). Dose-related lethargy, salivation, decreased limb tone, and ataxia, persisting to death (within 2 to 4 days) at the higher dosages. Weight loss, hemorrhages/congestion in brain, hemorrhages/erosion in GI tract and hyperemia and/or congestion of lungs and liver were some of the observations recorded.	00157868	Acceptable/ Slightly toxic
Laboratory rat *Rattus norvegicus*	87.8 12.2% inerts PPG 1030	EPA File Symbol: 748-EEE EPTC 7E Acute oral study 508, 807, 1281, 2034, 2632, 3229, 5126 mg/kg	Acute oral LD_{50}: 2322 (1962-2658) mg ai/kg bw (F) slope 2.1; 916 (606-1247) mg ai/kg bw (M) slope 2.3 Recalculated statistics: Acute oral LD_{50}: 845 (618 - 1086) mg/kg bw (M) Slope: 5.3 2272 (1836 – 2606) mg/kg bw (F) Slope: 10.7	00022107	Acceptable/ Slightly toxic
Laboratory rat *Rattus norvegicus*	77.1	Eptam 6E	Acute oral LD_{50}: 1049 mg ai/kg bw (F); 1226 mg ai/kg bw (M)	00024550	Acceptable/ Slightly toxic
Laboratory rat *Rattus norvegicus*	75.39% 13.07% R-33865	Eptam/R-33865 6-IE	LD_{50} (M) = 1324.53 (1163 – 1565) mg/kg Slope: 10.6 LD_{50} (F): 979 (884-1145) mg/kg Slope: 9.0 LD_{50}: 1025 mg ai/kg bw (F); 1323 mg ai/kg bw (M) with 73.4% a.i.	00248776 00117972	Acceptable/ Slightly toxic
Laboratory rat *Rattus norvegicus*	25	Eradicane 25G 5/sex tested at limit dose.	Acute oral LD_{50}: > 5000 mg ai/kg bw (F & M) No mortalities. 9/10 surpassed pre-dose weight by study termination. Clinical signs included piloerection, upward curvature of the spine, and irregular breathing [n=2). No abnormalities were observed upon necropsy.	41831201	Acceptable/ Practically nontoxic

[1] Based on LD_{50} (mg/kg) <10 very highly toxic; 10-50 highly toxic; 51-500 moderately toxic; 501-2000 slightly toxic; >2000 practically nontoxic

[2] **Bold** value is the value that will be used to calculate risk quotients

Mammals: Chronic Exposure (Growth, Reproduction) Studies

Table 8 summarizes two acceptable multi-generation studies are available for EPTC. Frank reproductive effects were not observed in either study. Effects on the parents included decreased body weight, degenerative cardiomyopathy, and renal tubule degeneration. Effects on pups were decreased body weight during the lactation period. Although the NOAEC for pups is higher than the NOAEC for the parents, the effects on the pups were selected as the toxicological endpoint because effects on pup growth are the most relevant for assessing ecological risk to the CRLF.

The sublethal endpoint used to define the action area was selected from a developmental neurotoxicity study. The sublethal effect of concern is a dose-related decrease in absolute brain weight in male pups at post-natal day 63. This study had no NOAEC. In addition to this, it is noted that EPTC tested positively in *in vitro* mouse lymphoma assays (MRIDs 00152454, 00161602), but not in the *in vivo* assays. Therefore, EPTC has intrinsic genotoxicity which was not expressed in either the *in vivo* micronucleus test or the *Drosophila* sex-linked recessive lethal mutation assay.

Table 8. Mammalian Chronic Toxicity Data

Common Name	%AI	Study Parameters	Test Results	MRID	Classification/ Category
Laboratory rat *Rattus norvegicus*	98.4	2-generation reproduction study 30 male and 30 female rats/group at doses of 0, 50, 200, 800 ppm (0, 2.5, 10, 40 mg/kg/day).	Parental systemic NOAEL: 50 ppm (2.5 mg/kg bw/day) LOAEL: 200 ppm (10 mg/kg bw/day) based on decreased body weight and degenerative cardiomyopathy in females. Offspring/Developmental Toxicity NOAEL: 200 ppm (10 mg/kg bw/day) LOAEL: 800 ppm (40 mg/kg bw/day) based on reduced pup body weight during PND 4-21. Reproductive Toxicity NOAEL: 800 ppm (40 mg/kg bw/day) LOAEL: >800 ppm (40 mg/kg bw/day). There were no reproductive effects observed under the conditions of the study.	00161597	Acceptable

Table 8. Mammalian Chronic Toxicity Data					
Common Name	**%AI**	**Study Parameters**	**Test Results**	**MRID**	**Classification/ Category**
Laboratory rat *Rattus norvegicus*	98.6	2-generation reproduction study 15 male and 30 female rats/group at doses of 0, 40, 200, 1000 ppm (0, 1, 2, 10, 50 mg/kg/day).	Parental systemic NOAEL: 200 ppm (10 mg/kg bw/day) LOAEL: 1000 ppm (50 mg/kg bw/day) based on degenerative cardiomyopathy in both sexes and renal tubule degeneration in females. Offspring/Developmental Toxicity NOAEL: 200 ppm (10 mg/kg bw/day) LOAEL: 1000 ppm (50 mg/kg bw/day) based on reduced pup body weight during PND 14-21. Reproductive Toxicity NOAEL: 1000 ppm (50 mg/kg bw/day) LOAEL: >1000 ppm (50 mg/kg bw/day). There were no reproductive effects observed under the conditions of the study.	00043648 00121284 40420408	Acceptable
Laboratory rat *Rattus norvegicus*	98.1	Developmental neurotoxicity study 30/dose at 0, 100, 300 or 1000 ppm (0/0, 7.6/16.4, 21.9/47.9, 67.2/157.3 mg/kg/day).	Maternal NOAEL: 300 ppm (21.9 mg/kg bw/day) LOAEL: 1000 ppm (67.2 mg/kg bw/day) based on piloerection, hunched posture, sides pinched in, decreased body weight, body weight gain and food consumption and increased incidence of whole litter losses. Offspring NOAEL not established. LOAEL: 100 ppm (7.6 mg/kg bw/day) based on dose-related decreases in absolute brain weights in male pups on PND 63.	46319101	Acceptable

MAMMALIAN HAZARD CHARACTERIZATION

The database for EPTC is adequate to assess the toxicology hazard profile. Review of the database revealed treatment-related effects of toxicological concern. Cardiomyopathy and neuronal cell necrosis were observed in studies of varying length of treatment and in different species. EPTC did not produce any significant reproductive and developmental toxicity, and was negative in two oncogenicity studies.

EPTC is a reversible inhibitor of cholinesterase (ChE). Toxicology studies with EPTC did not show any consistent pattern of ChE inhibition among different species, lengths of treatment, or the type of ChE enzyme measured. Inhibition of plasma with dose related increases in RBC and brain ChE inhibition are the typically expected results. In some studies brain ChE activity was inhibited without any effect on either plasma or erythrocyte ChE activities. In other studies, erythrocyte ChE was inhibited with no inhibition of either plasma or brain ChE. Two studies which yielded commonly expected results were a chronic dog oral dosing (capsule) study where plasma, but not other ChE was inhibited, and a rabbit developmental study in which plasma and erythrocyte ChE were inhibited. As a class of compounds, thiocarbamates do not produce consistent ChE inhibition profiles. A study with rats measured the inhibition of ChE by cycloate, butylate, pebulate or vernolate at doses at or near the acute median lethal doses. While vernolate, pebulate and cycloate inhibited plasma, erythrocyte and brain ChE to varying degrees, butylate inhibited plasma ChE only, and EPTC inhibited only erythrocyte and brain ChE but not plasma ChE.

Cardiotoxicity was observed in subchronic and long-term studies, and, in general, the severity and incidence of the lesion increased with increasing dose of EPTC. In 90-day feeding and inhalation studies and in two chronic feeding/oncogenicity studies, all in the rat, histopathological evaluation revealed myocardial degeneration. Additional studies in the rat, revealed myocardial degeneration in adult animals in two separate two-generation reproduction studies. In two chronic oral dosing studies in the dog, degenerative changes in the cardiac muscle were observed when EPTC was administered in a capsule, but not when administered (at comparable doses) in the diet. In both of the dog studies, electrocardiograms were taken, but only one high-dose male in the capsule study had changes which were described as "potentially" treatment-related.

EPTC, as well as other thiocarbamates (molinate, cycloate, pebulate, vernolate and butylate), have toxic effects on the central and peripheral nervous systems. With EPTC, there was an increased incidence and severity of neuronal necrosis/degeneration in both the central and peripheral nervous systems of both rats and dogs. In the neurotoxicity studies in the rat, dose-related increases in the incidence of neuronal necrosis were observed in the brains after acute and subchronic exposure to EPTC. The acute delayed neurotoxicity study in the hen, however, did not reveal any delayed neurotoxicity. In both of the combined chronic toxicity/oncogenicity studies in the rat and in the chronic (capsule) study in the dog, treatment related neuromuscular lesions were observed. In all of these studies hindquarter weakness was observed, and at necropsy evaluation, atrophy and degeneration of the skeletal muscle was observed. In the dog study, the lesions were described as Wallerian-type degeneration in the spinal cords and various peripheral nerves.

The developmental and reproductive toxicity of EPTC was evaluated. Studies in the rat and rabbit showed developmental and reproductive toxicity only in the presence of maternal or parental toxicity. In a prenatal developmental toxicity study in rats, developmental toxicity (in part, decreased fetal body weight and decreased litter size, but effects were attributed to maternal stress) was seen in the presence of marked maternal toxicity (increased mortality and decreased body weight). In a developmental toxicity study in rabbits, developmental toxicity (decreased fetal body weight) was again seen in the presence of marked maternal toxicity (in part, decreased body weight and increased mortality). In a two-generation reproduction study in rats, effects in the offspring were observed only at or above treatment levels which resulted in parental toxicity. However, even though there does not appear to be any concern about the reproductive or developmental toxicity of EPTC based on the studies available, the neurotoxic effects (neuronal necrosis and degeneration) warrant the need for a developmental neurotoxicity study, and therefore the retention of the 10X safety factor, as required by the Food Quality Protection Act (FQPA).

Update: a developmental neurotoxicity study has been submitted and reviewed. The dose/concentration levels tested were 0, 100, 300, or 1000 ppm (equivalent to 0/0, 7.6/16.4, 21.9/47.9, and 67.2/157.3 mg/kg/day [gestation/lactation]). The maternal LOAEL is 1000 ppm (67.2 mg/kg/day) based on clinical signs (piloerection, hunched posture, sides pinched in); decreased body weight, body weight gain, and food consumption; and increased incidence of whole litter losses. The maternal NOAEL is 300 ppm (21.9 mg/kg/day). The offspring LOAEL is 100 ppm (to 7.6 mg/kg/day; LDT) based on dose-depended decreases in absolute brain weights in male pups on PND 63 at all dose levels. An offspring NOAEL was not established. This study is classified **Acceptable** and may be used for regulatory purposes, however it does not satisfy the guideline requirement for a developmental neurotoxicity study in rats (OPPTS 870.6300, §83-6); OECD 426 (draft) at this time pending a comprehensive review of all available positive control data.

EPTC is not carcinogenic. Oncogenicity studies in both the rat and mouse did not indicate that exposure to EPTC resulted in an increased incidence of neoplastic lesions. EPTC has intrinsic genotoxicity which was not expressed in either the *in vivo* micronucleus test or the Drosophila sex-linked recessive lethal mutation assay. This is supported by lack of a carcinogenic effect in long-term studies and no genetic component in reproduction and developmental studies.

The metabolism of EPTC was evaluated in rats using ^{14}C-labeled EPTC. EPTC was rapidly absorbed and excreted; there was very little bioaccumulation. Most of the radioactivity appeared in the urine with markedly lower amounts in the feces and exhaled air. No sex differences were noted in the absorption, tissue distribution and excretion of EPTC.

In dermal absorption studies with EPTC and other thiocarbamates, EPTC was found to rapidly evaporate (volatilize) from warm skin. Based on a dermal absorption study in the rat which utilized a charcoal impregnated filter to capture vapors lost from the skin, absorption of EPTC was determined to be 5% at 10 hours. Although adequate dermal

absorption studies were available, HED recommended that a 21-day dermal toxicity study in the rat be performed with technical EPTC. A 21-day dermal toxicity would better define the toxicity of EPTC by the dermal route.

Acute Toxicity

Results of acute toxicity studies, primary eye and dermal irritation studies and dermal sensitization study with EPTC technical material are summarized in Table 1. EPTC is moderately toxic (Toxicity Category III) via the oral and dermal routes and in a primary eye irritation study in rabbits, the technical was found to be slightly irritating (Toxicity Category III). EPTC is most toxic via the inhalation route (Toxicity Category II).

Table 9. Acute Toxicity of EPTC, Technical

Study Type	Animal	Results	Tox Cat	MRID No
81-1: Acute Oral	Rat	LD_{50} Male 1465 (1290-1663) mg/kg Female 1712 (1324-2214) mg/kg Combined 1599 (1294-1976) mg/kg	III	00157868
81-2: Acute Dermal	Rabbit	LD_{50} Male > 2000 mg/kg Female > 2000 mg/kg	III	00157869
81-3: Acute Inhalation	Rat	LC_{50} Combined 1.39 (0.97-2.00) mg/L	II	00157870
81-4: Primary Eye Irritation	Rabbit	PIS (24hr) = 2.2 Reversed within 3 days	III	00157871
81-5: Primary Dermal Irritation	Rabbit	PII = 1.4	IV	00157872
81-6: Dermal Sensitization	Guinea Pig	Very slight sensitizer	N/A	00157873
		Weak sensitizer (Magnusson-Kligman)	N/A	41709201

Table 10. Subchronic, Chronic and Other Toxicity Table		
Guideline No./ Study Type	**MRID No. Classification /Doses**	**Results[a]**
870.3100 90-Day oral toxicity - rat	MRID 00144651 Acceptable EPTC (98.4%) at 0, 18/3, 36/15, 72, or 120 mg/kg/day	Systemic NOAEL: 3 mg/kg bw/day Cholinesterase NOAEL: 72 mg/kg bw/day in females and 120 mg/kg bw/day in males. Systemic LOAEL: 15 mg/kg bw/day; decreased body weight and body weight gain and increased incidence of cardiomyopathy in both sexes. Cholinesterase LOAEL = 120 mg/kg bw/day (inhibition of plasma ChE in females). Not established in males.
870.3150 90-Day oral toxicity in dogs (feeding)	MRID 00150327 Acceptable EPTC (98.4%) at 0, 200, 600, or 1800 ppm (equivalent to 0, 5, 15 or 45 mg/kg/day)	Systemic NOAEL: 600 ppm (15 mg/kg/day) in males and 1800 ppm (45 mg/kg/day) in females. Cholinesterase NOAEL: 600 ppm (15 mg/kg/day) in males and 1800 ppm (45 mg/kg/day) in females. Systemic LOAEL: 1800 ppm (45 mg/kg/day; excessive salivation and decreased body weight in males). Not established in females. Cholinesterase LOAEL: 1800 ppm (45 mg/kg/day; inhibition of plasma cholinesterase in males). Not established in females
870.3465 90-Day inhalation toxicity	MRID 00154784 Acceptable whole body chamber to aerosolized (particle size, MMADar = 2.8 μm) EPTC (98.6%) at concentrations of 0, 8.3, 58 or 290 mg/m^3, six hr/day, 5 days/week	NOAEL: 8.3 mg/m^3 LOAEL: 58 mg/m^3 based on clinical signs (ocular irritation, chromodacyorrhea, and alopecia), decreased food consumption and brain ChE inhibition in males, and increased prothrombin time in females).
870.3700a Prenatal developmental in rats	MRID 00138919 Acceptable Gavaged with EPTC (assumed 100%) at doses of 0 (vehicle, corn oil), 30, 100, or 300 mg/kg/day on gestation days (GD) 6 through 15	Maternal NOAEL: 100 mg/kg/day Maternal LOAEL: 300 mg/kg/day (lethality, decreased body weight, body weight gain, corrected body weight gain, and food consumption Developmental NOAEL: 100 mg/kg/day Developmental LOAEL: 300 mg/kg/day (decreased fetal body weight, decreased litter size, increased resorptions, increased incidence of omphalocle and increased incidence of unossified sternebrae)

Table 10. Subchronic, Chronic and Other Toxicity Table		
Guideline No./ Study Type	**MRID No. Classification /Doses**	**Results[a]**
870.3700b Prenatal developmental in rabbits	MRID 40442302 Acceptable EPTC (97.6%) at 0, 10.3, 75.8, or 568 mg/kg/day from GD 7 through 19	Maternal Systemic NOAEL: 75.8 mg/kg/day Maternal Cholinesterase NOAEL: Not established Maternal LOAEL: 568 mg/kg/day based on decreased body weight and food consumption, mortality and clinical signs (loose stools, hematuria, salivation, stained nose or lip, wet fur coat and loss of appetite/anorexia). Maternal Cholinesterase LOAEL: 10.3 mg/kg/day (inhibition of serum cholinesterase) Developmental NOAEL = 75.8 mg/kg/day Developmental LOAEL = 568 mg/kg/day based on reduced fetal body weights
870.3800 Reproduction and fertility effects	MRID 0012128, 40420408 Acceptable EPTC (98.6%) at dietary levels of 0, 40, 200, or 1000 ppm (calculated doses: 0, 2, 10, or 50 mg/kg/day).	Parental NOAEL: 200 ppm (10 mg/kg/day) Parental LOAEL: 1000 ppm (50 mg/kg/day), based on degenerative cardiomyopathy in males and females and renal tubule degeneration in females Offspring NOAEL: 200 ppm (10 mg/kg/day) Offspring LOAEL: 1000 ppm (50 mg/kg/day) based on decreased pup weight during postnatal day 14 to 21 Reproductive NOAEL: 1000 ppm (50 mg/kg/day) Reproductive LOAEL: Not established
870.3800 Reproduction and fertility effects	MRID 00161597 Acceptable EPTC (98.4%) at dietary levels of 0, 50, 200, or 800 ppm (calculated doses: 0, 2.5, 10, or 40 mg/kg/day)	Parental/Systemic NOAEL: 50 ppm (2.5 mg/kg/day) Parental/Systemic LOAEL: 200 ppm (10 mg/kg/day) in males and females, based on decreased body weight/body weight gain and cardiomyopathy Offspring NOAEL: 200 ppm (10 mg/kg/day) Offspring LOAEL: 800 ppm (40 mg/kg/day) based on decreased mean pup weight during lactation days 4 to 21 Reproductive NOAEL: 800 ppm (40 mg/kg/day) Reproductive LOAEL: Not established
870.4300 Combined chronic toxicity/ carcinogenicity study in rats	MRID 00145004, 00145311 Acceptable EPTC (purity not given) in diet at 0, 5.01, 25.0, or 125.8 mg/kg/day in males and 4.97, 24.8, or 124.8 mg/kg/day in females	NOAEL: 5 mg/kg/day. LOAEL: 25 mg/kg/day in both sexes (decreased body weight and increased incidences of myocardial and neuromuscular lesions). No increase in neoplastic lesions.

Table 10. Subchronic, Chronic and Other Toxicity Table		
Guideline No./ Study Type	**MRID No. Classification /Doses**	**Results[a]**
870.4300 Combined chronic toxicity/ carcinogenicity study in rats	MRID 40215001 Unacceptable for chronic (no NOAEL established); acceptable for carcinogenicity. EPTC (98.4%) in diet at dose levels of 0, 9, 18, 36, or 72 mg/kg/day	NOAEL: not established. LOAEL: 9 mg/kg/day (decreased body weights and body weight gains and accelerated appearance of cardiomyopathy in both sexes; decreased food efficiency in females.
870.4100b Chronic toxicity dogs (capsule)	MRID 40442301 Acceptable EPTC (97.6%) administered in capsules at 0, 1, 8 or 60 mg/kg/day for one year	Systemic NOAEL: 8 mg/kg/day Cholinesterase NOAEL: 8 mg/kg/day LOAEL: 60 mg/kg/day (decreased body weight gain in males and peripheral/central nervous system degeneration and skeletal/cardiac muscle degeneration in both sexes) Cholinesterase LOAEL: 60 mg/kg/day (decreased plasma ChE)
870.4100b Chronic toxicity dogs (feeding)	MRID 00161595 Unacceptable (LOAEL not achieved) EPTC (98.4% in diet at 0, 200, 600, or 1800 ppm (equivalent to 0, 5.6, 17.3, or 48.5 mg/kg/day in males and 0, 6.1, 17.4 or 54.7 mg/kg/day in females) for 1 year	NOAEL: 1800 ppm (48.5 mg/kg/day, males; 54.7 mg/kg/day, females) LOAEL: Not established.
870.4300 Carcinogenicity mice	MRID 00161596 Acceptable EPTC (98.5%) at concentrations of 0, 200, 600 or 1800 ppm (approximately 0, 30, 90, or 270 mg/kg/day in males and females) for 78 weeks	NOAEL: 600 ppm (90 mg/kg/day) LOAEL: 1800 ppm (270 mg/kg/day) based on decreased body weight and food consumption No evidence of increased incidence of neoplasms.

Table 10. Subchronic, Chronic and Other Toxicity Table		
Guideline No./ Study Type	**MRID No. Classification /Doses**	**Results[a]**
870.6100 Acute delayed neurotoxicity in the hen	MRID 00150325 Acceptable Hens dosed with EPTC (98.4%) at 4674 mg/kg (LD_{50}) and observed for 21 days. Surviving hens redosed with EPTC and observed for an additional 21 days. Negative (corn oil) and positive (TOCP, 500 mg/kg) control groups included in the study.	No EPTC-treated hens lost weight, became subdued and/or unsteady. All surviving hens recovered by day 7. At termination of the study, no histopathological evidence of neurotoxicity was observed in the EPTC-treated hens. All TOCP-treated hens, however, exhibited ataxia, which became progressively worse over time. Neuropathological evaluation of the TOCP-treated hens had significant neurological degeneration in one or more spinal cord levels, as well as peripheral nerves.
870.6200a Acute neurotoxicity screening battery	MRID 43039701, 43297401 Acceptable EPTC (98.4%) by gavage at doses of 0 (vehicle only, 100% corn oil), 200, 1000, or 2000 mg/kg.	NOAEL: not established in males and established at 200 mg/kg in females LOAEL: 200 mg/kg in males (neuronal cell necrosis in the brain) and 1000 mg/kg in females (clinical signs, death, and neuronal cell necrosis in the brain)
870.6200b Subchronic neurotoxicity screening battery	MRID 43230901 Acceptable EPTC (98.4%) at 0 (basal diet), 500, 1000, or 2500 ppm (0, 7.9, 39.4, or 193 mg/kg/day, males; 0, 8.8, 43.5, or 205 mg/kg/day, females) for 13 weeks	NOAEL: 100 ppm (7.9 mg/kg/day, males; 8.8 mg/kg/day, females). LOAEL: 500 ppm (39 mg/kg/day, males; 44 mg/kg/day, females) based on decreased body weight gain and relative brain weight in females and neuronal necrosis in the brain in males and females)
870.6300 Developmental neurotoxicity	MRID 46319101 Acceptable EPTC (98.1%) in the diet to pregnant rats from gestation day (GD) 7 to lactation day (LD) 23 at nominal doses of 0, 100, 300, or 1000 ppm (equivalent to 0/0, 7.6/16.4, 21.9/47.9, and 67.2/157.3 mg/kg/day [gestation/lactation])	Maternal NOAEL: 300 ppm (21.9 mg/kg/day) Maternal LOAEL: 1000 ppm (67.2 mg/kg/day) based on clinical signs (piloerection, hunched posture, sides pinched in); decreased body weight, body weight gain, and food consumption; and increased incidence of whole litter losses Offspring NOAEL: Not established Offspring LOAEL: 100 ppm (to 7.6 mg/kg/day; LDT) based on dose-depended decreases in absolute brain weights in male pups on PND 63 at all dose levels

Table 11. Mutagenicity Studies

Study	Results
Escherichia coli Reverse Gene Mutation Assay MRID No.: 00152451	Negative with / without S9 activation at 10 - 500 µg/plate
Escherichia coli Reverse Gene Mutation Assay MRID No.: 00152452	Negative with / without S9 activation at 0.001 - 5.0 µL/plate
Mouse Lymphoma Assay MRID No.: 00152454	Negative without S9 activation at 0.0125 - 0.15 µL/mL, and slightly mutagenic effect with S9 activation at 0.005 - 0.06 µL/mL.
Mouse Lymphoma Assay MRID No.: 00161602	Negative without S9 activation Positive with S9 activation
Drosophila melanogaster Sex-Linked Recessive Lethal Mutations MRID No.: 00153248	Negative for inducing sex-linked recessive lethals
In vitro Chinese Hamster Ovary (CHO) Cell Chromosome Aberration Assay MRID No.: 00161601	Negative with/without S9 activation
Mouse Lymphoma Chromosomal Aberration Assay MRID No.: 00142895, 00152455	Negative without S9 activation at 0.0125 - 0.15 µL/mL and with S9 activation at 0.005 - 0.06 µL/mL
Mouse Micronucleus Assay MRID No.: 00159391	Negative at MTD (55% lethality))
Bacillus subtilis Rec-Assay MRID No.: 00152451	Negative without S9 activation at 1 to 100% (v/v), with S9 activation not evaluated.
Unscheduled DNA Synthesis MRID No.: 00161600	Negative

Terrestrial Invertebrates: Acute Exposure (Mortality) Studies

Table 12 summarizes the terrestrial invertebrate toxicity information available for EPTC. The available acute toxicity studies on honey bees indicated that EPTC is practically non-toxic to terrestrial invertebrates.

Table 12. Terrestrial Invertebrate Acute Toxicity Data

Common Name	%AI	Study parameters	Test Results	MRID	Classification /Category
Honey bees *Apis mellifera*	87	EPTC plus safener 72-HR Acute contact toxicity test 0, 48, 72 µg ai/bee	72 hour contact LD_{50} > 72.5µg a.i./bee. No stomach poison effect. Mortality rate at 72 µg ai/bee was 2.5%.	00142894	Acceptable/ Practically non-toxic
Honey bees *Apis mellifera*	Tech.	48-HR Acute contact toxicity test. Bell jar vacuum duster used to expose bees to pesticide. Large study with multiple pesticides tested.	At 12.09 µg/bee, mortality was 5.91%. No other details were available. No other details provided. **LD_{50}>12.09 µg/bee.**	00036935	Supplemental
Honey bees *Apis mellifera*	--	Newly emerged worker bees fed 0, 10, 100, 1000 ppm in sugar syrup solution. Toxicity measured by the number of days for mortality in half the test group.	No effects up to 100 ppm. At 1000 ppm, there was a significant decrease in the half-life of test bees. Relatively non-toxic at rates up to 1000 ppm in sugar syrup. No other details provided.	00071149	Supplemental

[1] Based on LD_{50} (mg/kg) <10 very highly toxic; 10-50 highly toxic; 51-500 moderately toxic; 501-2000 slightly toxic; >2000 practically nontoxic

[2] **Bold** value is the value that will be used to calculate risk quotients

Toxicity to Terrestrial Plants

The results of the Tier II seedling emergence and vegetative vigor toxicity tests on non-target plants are summarized below in **Table 13.**

Table 13. Non-target Terrestrial Plant Seedling Emergence and Vegetative Vigor Toxicity (Tier II) Data

Crop	Type of Study Species	NOAEC [EC_{05}] (lb ai/A)	EC_{25} (lb ai/A)	Most sensitive parameter	Slope
Seedling Emergence					
Monocots	Corn *Zea Mays*	7.4 7.4	>7.4 >7.4	Seedling emergence Dry weight	N.D.
	Wild oats *Avena fatua*	7.4 [0.0578] 0.017	>7.4 > 0.231 < 0.925 0.10	Seedling emergence Dry weight Phytotoxicity	N.D.
	Winter wheat *Triticum aestivum*	7.4 [0.14] 0.029	>7.4 0.23 0.18	Seedling emergence Dry weight Phytotoxicity	4.26±0.826
	Purple nutsedge *Cyperus rotundus)*	0.17 0.0144	0.27 0.015	Seedling emergence Dry weight	1.13±0.425
Dicots	Carrot *Daucus carota*	7.4 >0.6<7.4 [>7.4]	>7.4 >7.4 >7.4	Seedling emergence Dry weight Phytotoxicity	-1.80±2.55
	Soybean *Glycine max*	7.4 [0.42]	>7.4 1.8	Seedling emergence Dry weight	1.54±0.461
	Sugar beet *Beta vulgaris*	7.4 [1.8]	>7.4 3.5	Seedling emergence Dry weight	3.23±1.73
	Oilseed rape *Brassica napus*	7.4 [4.0]	>7.4 6.2	Seedling emergence Dry weight	5.14±10.5
	Morning glory *Ipomea hederacea*	7.4 [0.035] 0.23	>7.4 0.26 1.1	Seedling emergence Dry weight Phytotoxicity	1.10±0.206
	Velvet leaf	7.4 [0.076] 0.17	>7.4 >0.925 < 3.7 0.53	Seedling emergence Dry weight Phytotoxicity	0.780±1.48
Vegetative Vigor					
Monocots	Corn *Zea Mays*	>3.7 <7.4 [0.087]	>3.7 < 7.4 >7.4	Dry weight Phytotoxicity	N.D.
	Wild oats *Avena fatua*	0.925 [0.31]	3.5 2.1	Dry weight Phytotoxicity	3.96±1.09
	Winter wheat *Triticum aestivum*	0.925 [0.087]	2.9 0.22	Dry weight Phytotoxicity	2.33±0.740
	Purple nutsedge *Cyperus rotundus)*	[3.4] [4.8]	5.9 6.98	Dry weight Phytotoxicity	4.06±2.61
Dicots	Cocklebur *Xanthium strumarium*	[4.9]	>7.4	Dry Weight	4.60±8.91
	Soybean *Glycine max*	0.925 [0.41]	4.7 3.0	Dry weight Phytotoxicity	2.95±0.855
	Sugar beet *Beta vulgaris*	[2.6]	6.7 2.2	Dry weight Phytotoxicity	2.33±2.66
	Oilseed rape *Brassica napus*	[>3.7 < 7.4] 7.4	>3.7 < 7.4 >7.4	Dry weight Phytotoxicity	N.D.
	Morning glory *Ipomea hederacea*	[3.0] [1.4]	5.9 13	Dry weight Phytotoxicity	3.23±2.13
	Velvet leaf	[0.085] [0.023]	2.0 7.4	Dry weight Phytotoxicity	0.704±0.370