APPENDIX J. Ecological Effects Data

I. Toxicity to Terrestrial Organisms

Acute toxicity to terrestrial animals is categorized using the classification system shown below (U.S. EPA, 2004). Toxicity categories for terrestrial plants have not been defined.

Categories of acute toxicity for avian and mammalian studies.		
Toxicity Category	**Oral LD_{50}**	**Dietary LC_{50}**
Very highly toxic	< 10 mg/kg	< 50 ppm
Highly toxic	10 - 50 mg/kg	50 – 500 ppm
Moderately toxic	51 - 500 mg/kg	501 - 1000 ppm
Slightly toxic	501 - 2000 mg/kg	1001 - 5000 ppm
Practically non-toxic	> 2000 mg/kg	> 5000 ppm

a. Avian, Acute and Subacute

One acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of permethrin to birds. The preferred test species are mallard duck (waterfowl) and bobwhite quail (upland gamebird). Guideline 71-1 is fulfilled for avian species, and results of these studies are tabulated in **Table J.1**.

Table J.1. Avian acute oral toxicity.

Species	% a.i.	LD_{50} (mg a.i. /kg-bw)	Study period length	Toxicity category	Identification number, date	Study classification[a]
Mallard duck *(Anas platyrhynchos)*	95.7	>4,640	24 hrs	Practically non-toxic	MRID 00112938 July 21, 1975	Acceptable
Mallard duck *(Anas platyrhynchos)*	94.4	>2,000	14 days	Practically non-toxic	MRID 41888401 1991	Acceptable
Mallard duck *(Anas platyrhynchos)*	Tech	>9,869 (male) >10,327 (female)	21 days	Practically non-toxic	MRID 00042142 1977	Acceptable
Ring-necked pheasant (*Phasianus colchicus)*	Tech	>13,534	24 hrs	Practically non-toxic	MRID 00042121 1977	Acceptable
Ring-necked pheasant (*Phasianus colchicus)*	Tech	>13,740 (male) >15,345 (female)	21 days (male) 21 days (female)	Practically non-toxic	MRID 00042121 1977	Acceptable

Table J.1. Avian acute oral toxicity.						
Species	**% a.i.**	**LD_{50} (mg a.i. /kg-bw)**	**Study period length**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Japanese quail (*Coturnix coturnix*)	Tech	>20,000 (male) >15,517 (female)	24 hrs	Practically non-toxic	MRID 00042120 1977	Supplemental
Starling (*Sturnus vulgaris*)	Tech	>42,706	24 hrs	Practically non-toxic	MRID 00042144 1977	Supplemental
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline						

The results of the acute oral toxicity studies (MRID 00112938, 41888401, 00042142, 00042121, 00042120, 00042144) available for permethrin indicate that it can be classified as practically non-toxic to avian species on an acute oral basis with LD_{50} values for mallard ducks (*Anas platyrhynchos*), Japanese quail (*Coturnix coturnix*), starlings (*Sturnus vulgaris*), and ring-necked pheasants (*Phasianus colchicus*) ranging from >2,000 to >42,706 mg a.i./kg-body weight. Based on all of the acute oral toxicity studies, mallard ducks were the species tested at the lowest concentrations; therefore, for the purposes of this assessment they were considered the "most sensitive species tested" with LD_{50} values ranging from >2000 to >10,327 (for females; >9,869 mg a.i./kg-body weight for males) mg a.i./kg-diet. While the LD_{50} value of >9,869 mg a.i./kg-body weight for mallard duck males was considered the most sensitive acute oral toxicity endpoint for all tested avian species, it should be noted that no treatment-related mortality was observed.

Two subacute dietary studies using the TGAI are required to establish the toxicity of permethrin to birds. The preferred test species are mallard duck and bobwhite quail. Results of these tests are tabulated in **Table J.2**.

Table J.2. Avian subacute dietary toxicity.					
Species	**% a.i.**	**LC_{50} (mg a.i./kg-diet)[a]**	**Toxicity category**	**Identification number, date**	**Study classification[b]**
Mallard duck *(Anas platyrhynchos)*	95.7	>10,000	Practically non-toxic	MRID 00112939 July 21, 1975	Acceptable
Mallard duck *(Anas platyrhynchos)*	93.4	>5,200	Practically non-toxic	MRID 41888403 1991	Acceptable
Mallard duck *(Anas platyrhynchos)*	92	>23,000	Practically non-toxic	ACC 227722 1978	Acceptable

Table J.2. Avian subacute dietary toxicity.					
Species	**% a.i.**	**LC_{50} (mg a.i./kg-diet)[a]**	**Toxicity category**	**Identification number, date**	**Study classification[b]**
Northern bobwhite quail *(Colinus virginianus)*	93.4	>5,200	Practically non-toxic	MRID 41888402 1991	Acceptable
Northern bobwhite quail *(Colinus virginianus)*	95.7	>10,000	Practically non-toxic	MRID 00072845 July 21, 1975	Acceptable
Japanese quail (*Coturnix japonica*)	92	>23,000	Practically non-toxic	MRID 00042123 March 5, 1976	Supplemental
Ring-necked pheasant (*Phasianus colchicus)*	92	>23,000	Practically non-toxic	MRID 00043733 January 1976	Acceptable

[a]5-day dietary exposure followed by additional 3-day observation period.
[b]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.

The results of the sub-acute dietary toxicity studies (MRID 00112939, 41888403, 41888402, 00072845, 00042123, and 00043733, and ACC.# 227722) available for permethrin indicate that it can be classified as practically non-toxic to avian species on an acute dietary basis with LC_{50} values for mallard ducks (*Anas platyrhynchos*), Northern bobwhite quail (*Colinus virginianus*), Japanese quail (*Coturnix japonica*), and ring-necked pheasants (*Phasianus colchicus*) ranging from >5,200 to >23,000 mg a.i./kg-diet. Based on all of the sub-acute dietary toxicity studies, bobwhite quail were the species tested at the lowest concentrations; therefore, for the purposes of this assessment they were considered the "most sensitive species tested" with LC_{50} values ranging from >5,200 to >10,000 mg a.i./kg-diet. While the LC_{50} value of >10,000 mg a.i./kg-diet for bobwhite quail was considered the most sensitive sub-acute dietary toxicity endpoint for all tested avian species, it should be noted that no treatment-related mortality was observed.

b. Avian, Chronic

Avian reproduction studies using the TGAI are required for permethrin because the following conditions are met: (1) birds may be subject to repeated or continuous exposure to the pesticide, especially preceding or during the mating season; (2) the pesticide is stable in the environment to the extent that potentially toxic amounts may persist in animal feed; and (3) the pesticide is stored or accumulated in plant or animal tissues. The preferred test species are mallard duck and bobwhite quail. Results are tabulated in **Table J.3**.

Table J.3. Avian reproductive toxicity.					
Species	**% a.i.**	**NOAEC/ LOAEC (mg a.i./kg-diet)**	**Observed Effects**	**Identification number, date**	**Study classification[a]**
Northern bobwhite quail *(Colinus virginianus)*	92.4	25/ >25	No Effect	MRID 00110671 1976	Acceptable
Northern bobwhite quail *(Colinus virginianus)*	95.2	500 />500	No Effect	MRID 42322901 1992	Acceptable
Mallard duck *(Anas platyrhynchos)*	92.4	25 / >25	No Effect	MRID 00110670 Dec 2, 1976	Acceptable
Mallard duck *(Anas platyrhynchos)*	95.2	125 / 500	Overall decrease in egg production (↓13.2%) at 500 mg/kg-diet; not statistically significant but correlated with an apparent increase in the number of hens with a regressing ovary.	MRID 42322902 1992	Acceptable
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.					

Four avian reproduction studies with mallard ducks (*Anas platyrhynchos*) and Northern bobwhite quail (*Colinus virginianus*) have been submitted to the Agency for permethrin (MRID 00110670, 00110671, 42322901, and 42322902). In three of the four studies (MRID 00110670, 00110671, 42322901), there were no observed adverse effects on any of the endpoints including food consumption, number of eggs laid, eggs cracked, egg shell thickness, viable embryos, live three-week embryos, normal hatchlings, 14-day-old survivors and offspring body weight. While the one study with bobwhite quail (MRID 42322901) established a NOAEC at the highest tested concentration of 500 mg a.i./kg-diet (LOAEC>500 mg a.i./kg-diet), the other two studies that evaluated effects on bobwhite quail (MRID 00110671) and mallards (MRID 00110670) only tested up to 25 mg a.i./kg-diet (NOAEC=25 mg a.i./kg-diet, LOAEC>500 mg a.i./kg-diet).

In the fourth avian reproduction study with permethrin and mallard ducks (MRID 42322901), there was a decrease in food consumption and an overall decrease in egg production (↓13.2%) at 500 mg a.i./kg-diet; although these effects were not statistically significant, they were associated with an apparent increase in the number of hens with a regressed ovary (8 hens in the 500 mg a.i./kg-diet treatment group compared to 2 in control). Although the effects were not statistically significant, given the magnitude of effects, the associated increase in occurrences of regressed ovaries, and the acknowledgment by the study authors that the effects may be treatment-related, the NOAEC and LOAEC for this study have been set at 125 and 500 mg

a.i./kg-diet, respectively. The results of this study indicate that permethrin may have adverse effects on avian reproduction at higher levels of exposure.

c. Mammals, Acute and Chronic

Typically, mammalian toxicity data from the Agency's Health Effects Division (HED) are used to approximate toxicity to mammals. However, wild mammal toxicity tests may be required on a case-by-case basis, depending on the results of the lower tier studies such as acute and sub-acute testing, intended use pattern, and pertinent environmental fate characteristics. No studies evaluating toxicity to wild mammal species have been submitted by the registrants for permethrin. However, additional laboratory data were available from the open literature, as well as from HED, and have been considered as surrogate data for mammalian wildlife for the purposes of this risk assessment. A summary of acute and chronic laboratory mammalian data, including data submitted by registrants as well as published in the open literature, is provided below in **Table J.4**.

Table J.4. Mammalian toxicity.

Species	% a.i.	Test type	Toxicity value and affected endpoints	Identification number, date	Study classification[a]
Rat (*Rattus norvegicus*)	96	Acute Oral LD_{50}	LD_{50} = 8,900 mg/kg/ bw	279-GNRU 1978	NA
Rat (*Rattus norvegicus*)	94 25:75, cis:trans	Acute Oral LD_{50}	LD_{50} = 152 mg/kg-bw [b]	Cantalamessa 1993 (ECOTOX Ref. # 74863)	Supplemental
Rat (*Rattus norvegicus*)	TGAI; % a.i. not reported	Acute Oral LD_{50}	LD_{50} = 2280 mg a.i./kg-bw for females LD_{50} = 3580 mg a.i./kg-bw for males	MRID 242899	Acceptable
Rat (*Rattus norvegicus*)	92	Acute Oral LD_{50}	LD_{50} = 570 mg a.i./kg-bw for females LD_{50} = 703 mg a.i./kg-bw for males	MRID 44707301	Acceptable
Rat (*Rattus norvegicus*)	94 - 98 cis:trans 40:60	Chronic, 3-generation reproductive study	Systemic toxicity NOAEL =1,000 ppm (50 mg/kg/day) tremors in F0, F1, F2. No reproductive effects (NOAEL >2,500 ppm.	MRIDs 92142092, 120271, 92142037.	Acceptable
Rat (*Rattus norvegicus*)	93.9 cis:trans 38:62	Developmental Toxicity	NOAEL = 50 mg/kg/day LOAEL = 150 mg/kg/day (decrease fetal wt; ↓3.2% from controls; $p \leq 0.05$)	MRID 40943603	Acceptable

Table J.4. Mammalian toxicity.					
Species	**% a.i.**	**Test type**	**Toxicity value and affected endpoints**	**Identification number, date**	**Study classification[a]**
Beagle dogs	92.5 cis:trans 32:60	Chronic oral toxicity study	NOAEL = 100 mg/kg/day LOAEL = 1000 mg/kg/day Based on neurological clinical signs (tremors, uncoordinated gait, nervousness and convulsions, also excessive salivation and vomiting) and decreased body weight gain (37% and 33% less than control for males and females, respectively) in the high-dose group.	MRID 0129600	Acceptable
Mouse (*Mus musculus*)	94	Reproduction and Growth	NOAEL= 2.77 mg/kg-bw/day (~55.44 mg/kg-diet) [c] LOAEL = 5.59 mg/kg-bw/day (~111.8 mg/kg-diet) [c] Decreased maternal body weight gain during gestation (↓57% from controls) and lactation (↓187% from controls), increased # of dead pups (↑64% from controls), decreased # of live pups (↓10% from controls), and decreased body weight gain of pups (↓52% from controls) at 9.8 mg/kg-bw/day	Farag *et al.* 2006 (ECOTOX Ref. # 100119)	Supplemental

[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline; NA: not available
[b] This LD_{50} is based on the 24-hour LD_{50} value of 340.5 mg/kg-bw reported in the study for 8-day old rats but was scaled to be representative of the assumed typical test organism, a 350g laboratory rat, for use in T-REX.
[c] The NOAEL and LOAEL values are based on the values of 4.9 and 9.8 mg/kg-bw, respectively, reported in the study for mice but were scaled to be representative of the assumed typical test organism, a 350g laboratory rat, for use in T-REX.

There is one registrant submitted acceptable rat acute oral toxicity study discussed in the HED chapter of the Reregistration Eligibility Decision Document (RED) for permethrin (Dated April 4th 2006; DP Barcode D324993). The reported laboratory rat LD_{50} value for the technical active ingredient of permethrin for females was 2280 mg a.i./kg-bw (3580 mg a.i./kg-bw for males)(MRID 242899); no other information was discussed. In addition to the data used and reported by HED, an LD_{50} value of 8900 mg a.i./kg-bw for acute oral toxicity of the technical active ingredient of permethrin to laboratory rats was reported in the EFED chapter of the RED for permethrin (Dated April 5th 2006; DP Barcode D326784); no additional information could be found in the chapter or in the EFED files (No MRID; Document Reference No. 279-GNRU, 1978). Based on these reported laboratory rat LD_{50} values, permethrin is practically non-toxic to small mammals on an acute oral basis.

Following the completion of the EFED and HED chapters written for the RED in 2006, additional acceptable acute oral toxicity data with the technical active ingredient of permethrin

(92% a.i.) have been submitted to the Agency (MRID 44707301). The reported laboratory LD_{50} value for the technical active ingredient of permethrin for female Sprague-Dawley rats (6-8 weeks old) in this study was 570 mg a.i./kg-bw (703 mg a.i./kg-bw for males; 614 mg a.i./kg-bw combined)**.** Based on this reported laboratory rat LD_{50} value, permethrin is classified as slightly toxic to small mammals on an acute oral basis.

In addition to the registrant data, more sensitive acceptable acute toxicity data considered for quantitative risk estimation purposes for mammals were identified in the open literature. *Cantalamessa* (1993; ECOTOX Ref # 74863) reported 24-hour LD_{50} values of 340.5 (95% CL = 308.8-375.6), 399.0 (95% CL = 346.1-460.0), 471.0 (95% CL = 384.5-577.0), and 1500.0 (95% CL = 938.0-2345.3) mg/kg-bw for 8-day old, 16-day old, 21-day old, and adult Wistar rats. LD_{50} values and associated confidence intervals were determined by using ten animals per dose level, with individuals in four or more dose levels being exposed to permethrin (25:75, cis:trans, 94% purity) dissolved in corn oil via gavage. At least two separate experiments were used to evaluate pyrethroid lethality, and the reported LD_{50} values represent the average of the two separate experiments. Based on the range of reported laboratory rat LD_{50} values from this study, permethrin can be classified as moderately toxic to slightly toxic to small mammals on an acute oral basis.

In the HED chapter of the RED for permethrin (Dated April 4th 2006; DP Barcode D324993) one registrant-submitted acceptable/guideline three generation reproduction study (MRID 92142092, 120271, 92142037) with rats was discussed. In this study, permethrin (purity, 94.0-98.8%) was administered to groups of 12 male and 24 female Wistar rats in the diet at concentrations of 0, 500, 1000, or 2500 ppm (0, 25, 50, and 125 mg/kg/day, respectively, using a standard conversion factor of 0.05). The LOAEL for systemic toxicity is 2500 ppm (125 mg/kg/day) based on tremors observed in the F0 females, and the F1 and F2 males and females. The systemic toxicity NOAEL is 1000 ppm (50 mg/kg/day). The reproductive toxicity NOAEL is ≥2500 ppm (125 mg/kg/day) and the reproductive toxicity LOAEL is not identified. The NOAEL for offspring growth and development is ≥2500 ppm (125 mg/kg/day) and the offspring LOAEL is not identified. However, one of the major deficiencies noted for this study was a lack of homogeneity and stability of the compound in the test diets, suggesting that the estimated exposure levels may be unreliable.

In addition to the three generation reproduction study, the other studies that were discussed in the HED RED chapter that demonstrated adverse effects on growth or reproduction of mammals at more sensitive quantifiable levels was an acceptable/guideline prenatal developmental study with rats (MRID 40943603) and an acceptable/guideline chronic oral toxicity study with dogs (MRID 00129600). In the developmental study, 24 presumed pregnant Wistar rats per group were administered 0 (corn oil carrier), 15, 50, or 150 mg/kg/day of permethrin (93.9% a.i.; 38 cis:62 trans isomers) by gavage on gestation days (GD) 7-16, inclusive. The maternal toxicity NOAEL and LOAEL were 50 mg/kg/day and 150 mg/kg/day, respectively, based on clinical signs of toxicity and decreased body weight gain (↓18-88% from controls; $p \leq 0.05$) and food consumption. The developmental toxicity NOAEL and LOAEL were 50 mg/kg/day and 150 mg/kg/day, respectively, based on decreased fetal body weight (↓3.2% from controls; $p \leq 0.05$). However, mean litter weight of the 150 mg/kg/day group was 3% (n.s.)

greater than that of the controls. Therefore, the reduced fetal body weights were considered a questionable toxic response.

In the chronic oral toxicity study, permethrin (92.5% a.i., cis/trans 32.3/60.2) was administered to beagle dogs (6/sex/group) in corn oil by gelatin capsule at dose levels of 0, 5, 100, or 1000 mg/kg/day for one year. There were no mortalities but neurological clinical signs (tremors, uncoordinated gait, nervousness and convulsions, also excessive salivation and vomiting) were observed in the high-dose group. At the high-dose, decreased body weight gain (37% and 33% less than control for males and females, respectively) and decreased food consumption (increased food left uneaten) were reported. Therefore, the systemic toxicity NOAEL and LOAEL for this study are 100 and 1000 mg/kg/day, respectively, based on clinical neurotoxic signs and decreased body weight gain and food consumption.

No other relevant studies of sufficient detail or with more sensitive endpoints were found in the EFED files. Only one additional study of limited utility for the purposes of this risk assessment was found in the EFED files. This laboratory study conducted with white mice (*Mus musculus*), evaluated the effects of cotton treated with the formulation Damminix (7.4% a.i.; to be used as small rodent nesting material in woodlots to control disease-transmitting) used as nest material on the survivability of neonates born in the nests, and the ability of those exposed mice to reproduce successfully when they became adults. Pregnant mice formed nests of the treated cotton, and their offspring lived in these nests for 21 days, until they were weaned, were separated into groups, and mated. No significant effects were noted on any parameter, suggesting that neonatal mice are not affected by Damminix-treated nesting material, and can reproduce successful when they reach adulthood.

In addition to the registrant data, more sensitive acceptable reproduction toxicity data considered for quantitative risk estimation purposes for mammals were identified in the open literature. *Farag et al.* (2006; ECOTOX Ref # 100119) reported a NOAEL of 4.9 mg/kg-bw/day in mice based on increased number of dead pups, decreased number of live pups, decreased body weight and body weight gain in pups, and decreased maternal body weights. While no significant effects were noted in the lowest test group of 4.9 mg/kg-bw/day as compared to the control, significant adverse effects were noted in both the 9.8 mg/kg-bw/day and 19.6 mg/kg-bw/day treatment groups. At the LOAEL of 9.8 mg/kg-bw/day, maternal body weight gain decreased during gestation (↓57% from controls) and lactation (↓187% from controls), the number of dead pups increased (↑64% from controls), the number of live pups decreased (↓10% from controls), and body weight gain of pups was decreased (↓52% from controls).

The study design should be carefully considered when interpreting the results and conservative nature of the experiment. In particular, it should be noted that sixty 10-week old mice (30 males and 30 females) at each treatment level were given permethrin (40:60, cis:trans, 94% purity) by gavage at dose levels of 0 (corn oil), 4.9, 9.8, and 19.6 mg/kg-bw/day before mating for 5 days a week for 4 weeks. Typically, the 2-generation reproduction studies with rats that are submitted to the Agency expose rats via treated feed; the dosing regime in this study with mice represents one that is intensified as compared to what the Agency normally receives. The gavage route of administration potentially influences the metabolism and toxicity of a test compound, and may increase or decrease its toxicity compared to dietary administration. It

generally is predicted to increase the toxicity of a compound compared to dietary administration because of the bolus dose and rapid absorption of the compound from the small intestine. In addition, although similar to the other acute and chronic studies (other than the three-generation rat study) discussed for permethrin, corn oil was used as a carrier, and may enhance the bioavailability of permethrin. While the results of this study are likely reflective of a conservative exposure scenario, the degree to which they are representative of actual high-end exposure scenarios encountered in the wild is uncertain. Additional data available for mammals can be found in **APPENDIX I** (Health Effects Division (HED) Data Tables for Permethrin).

d. Terrestrial Insects, Honeybee Acute

A honey bee acute contact study using the TGAI is required for permethrin because its use on cotton will result in honey bee exposure. The acute contact LD_{50}, using the honey bee, *Apis mellifera*, is an acute contact, single-dose laboratory study designed to estimate the quantity of toxicant required to cause 50% mortality in a test population of bees. The TGAI is administered by one of two methods in an acute test: whole body exposure to technical pesticide in a non-toxic dust diluent; or, topical exposure to technical pesticide via micro-applicator. The median lethal dose (LD_{50}) is expressed in micrograms of active ingredient per bee (µg a.i./bee). Results of this test are tabulated below (**Table J.5**). Toxicity category descriptions for honey bee acute contact toxicity are the following (Atkins, 1981):

If the LD_{50} is *less than 2* µg a.i./bee, then the test substance is *highly toxic*.
If the LD_{50} is *2 to less than 11* µg a.i./bee, then the test substance is *moderately toxic.*
If the LD_{50} is *11* µg a.i./bee or *greater*, then the test substance is *practically non-toxic.*

The acute oral LD_{50}, using the honey bee, *Apis mellifera*, is an acute oral, single-dose laboratory study designed to estimate the quantity of toxicant required to cause 50% mortality in a test population of bees. The TGAI is administered by feeding bees the technical pesticide in a sugar and water (and possibly solvent) solution using a feeding tube inserted into a cage. The LD_{50} is expressed in micrograms of active ingredient per bee (µg a.i./bee). Results of this test are tabulated in **Table J.5**. The Office of Pesticide Programs (OPP) does not have a categorization scheme for acute oral toxicity to honey bees. However the following acute oral toxicity categorization scheme based on ICBB (1985) categorization is provided for informational purposes:

If the LD_{50} is greater than 100 µg a.i./bee, then the test substance is *virtually non-toxic*.
If the LD_{50} 10–100 µg a.i./bee, then the test substance is *slightly toxic*.
If the LD_{50} 1–10 µg a.i./bee, then the test substance is *moderately toxic*.
If the LD_{50} less than 1.0 µg a.i./bee, then the test substance is *highly toxic*.

A honey bee foliar residue toxicity study is required on an end-use product for any pesticide intended for outdoor application when the proposed use pattern indicates that honey bees may be exposed to the pesticide and when the formulation contains one or more active ingredients having an acute contact honey bee LD_{50} which falls in the moderately toxic or highly toxic range. Usually, pesticides toxic to honey bees require precautionary labeling specific to bees on all end-use formulations and registrants are required to submit data in accordance with

Guideline 141-2 (Honey Bee Toxicity of Residues on Foliage). The purpose of this guideline study is to develop data on the residual toxicity to honey bees. Bee mortality determinations are made from bees exposed to treated foliage harvested at various time periods after treatment. The available study on foliar residue toxicity for permethrin is listed in **Table J.5**.

Table J.5. Honey bee acute toxicity.

Species	Type of study	% a.i.	48-hour LD_{50} (µg a.i./bee)	Category	Identification number, date	Study classification[a]
Honey bee (*Apis mellifera*)	Acute Contact	Tech	0.05	Highly toxic	MRID 00045044 1975	Supplemental
Honey bee (*Apis mellifera*)	Acute Contact	NR	0.16	Highly toxic	MRID 00045046 1975	Supplemental
Honey bee (*Apis mellifera*)	Acute Contact	93.1	0.024	Highly toxic	MRID 42674501 1993	Acceptable
Honey bee (*Apis mellifera*)	Acute Oral	Tech	0.19	Highly toxic	MRID 00045044 1975	Supplemental
Honey bee (*Apis mellifera*)	Acute Oral	93.1	0.13	Highly toxic	MRID 42674501 1993	Acceptable
Honey bee (*Apis mellifera*)	Foliar Residue	25WP	<0.2 lb a.i./acre (97-100% mortality at this application rate)	Highly toxic	MRID 42009301 1991	Acceptable

[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.

The only Agency guideline terrestrial invertebrate tests are for honey bees (*Apis mellifera*). A total of six studies include acute contact, acute oral, and acute contact with treated foliage LD_{50} values for permethrin technical grade active ingredient (TGAI) and formulated permethrin and honey bees (MRID 00045044, 00045046, 42674501, 42009301). The acute contact LD_{50} values range from 0.024 (with TGAI) to 0.16 µg a.i./bee (with formulation), the acute oral LD_{50} ranges from 0.13 to 0.19 µg a.i./bee (both with TGAI), and the single treated foliage study (treated with formulation Ambush 25W) reports an LD_{50} value of < 0.2 lb a.i./A. Based on these results, permethrin is classified as 'highly toxic' to honey bees on an acute exposure basis.

e. Terrestrial Invertebrates, Toxicity to Beneficial and other Non-Target Insects

In addition to the guideline studies with honey bees, a number of other older studies with terrestrial invertebrates and formulated permethrin are available to the Agency; however, many of the studies have little information reported and the results presented below are presented as they are in the studies. Several studies were submitted to show the effects of permethrin on non-target insects, primarily wasps and mites that are natural predators or parasites of the target insects for the pesticide. These studies include acute contact and foliar residue exposures and are summarized in **Table J.6**. The results of these studies indicate that permethrin is highly toxic to beneficial and other non-target insects.

One acute contact 5-day study with various species of parastitic wasps (MRID 05009995) demonstrates a range in sensitivity of the five tested species ((*Apanteles sp.*, *Opius bruneipus*, *Telenomus remus*, *Copidosoma truncatellum*, and *Diglyphus intermedius*), with mortality ranging from 0% to 85% at 0.1 lb a.i./A, and 40% to 100% at 0.2 lb a.i./A. A study with alkali bees (*Nomia melanderi*) exposed to foliage treated with formulated permethrin reported mortality ranging from 25% to 78% at rates ranging from 0.5 oz. a.i./A to 2 o.z. a.i./A, respectively (NR 1975). Another study with alfalfa leafcutter bees (*Megachile rotundata pacifica*), exposed to foliage treated with formulated permethrin reported mortality ranging from 24% to 88% at rates ranging from 0.5 oz. a.i./A to 2 o.z. a.i./A, respectively (ICI US1975). In other studies with mites (*Amblyseium fallacis*), convergent ladybeetles (*Hippodamia convergens*), and predatory mites (*Metaseiulus occidentalis*) acutely exposed to formulated permethrin, LD_{50} values ranging from <0.5 to 15.5 ppm a.i. were reported (MRID 00045048, 05009995, 00045048, ICI US 1975, ICI US 1976, ICI US NR). These laboratory studies indicate that permethrin is highly toxic to terrestrial invertebrates at rates equal to or below the maximum allowed on current labels, or concentrations well below what can be expected to be found in the environment following use of permethrin according to current labels.

Table J.6. Non-target insect toxicity.

Species	% a.i.	Test type	Test result	Identification number, date	Study classification[a]
Parasitic wasp (*Apanteles sp.*)	3.2EC	Acute, 5 day contact	100% mortality at 0.2 lb a.i./A 17% mortality at 0.1 lb a.i./A	MRID 05009995 1975	Supplemental
Parasitic wasp (*Opius bruneipus*)	3.2EC	Acute, 5 day contact	43% mortality at 0.2 lb a.i./A 0% mortality at 0.1 lb a.i./A	MRID 05009995 1975	Supplemental
Parasitic wasp (*Telenomus remus)*	3.2EC	Acute, 5 day contact	90% mortality at 0.2 lb a.i./A 13% mortality at 0.1 lb a.i./A	MRID 05009995 1975	Supplemental

Table J.6. Non-target insect toxicity.

Species	% a.i.	Test type	Test result	Identification number, date	Study classification[a]
Parasitic wasp (*Copidosoma truncatellum*)	3.2EC	Acute, 2 day contact	100% mortality at 0.2 lb a.i./A 85% mortality at 0.1 lb a.i./A	MRID 05009995 1975	Supplemental
Parasitic wasp (*Diglyphus intermedius*)	3.2EC	Acute, 5 day contact	40% mortality at 0.2 lb a.i./A 55% mortality at 0.1 lb a.i./A	MRID 05009995 1975	Supplemental
Mite (*Amblyseium fallacis*)	25EC	Acute	100% mortality at 0.5 ppm	MRID 00045048 1975	Supplemental
Mite (*Amblyseium fallacis*)	Ambush	Acute	LC_{50} <1 ppm	ICI US 1976	Supplemental
Mite (*Amblyseium fallacis*)	Form.	Acute, dip test	LC_{50} <0.5 ppm	ICI US NR	Supplemental
Convergent ladybeetle (*Hippodamia convergens*)	Form.	Contact	LD_{50} <3.9 ppm	MRID 05009995 1975	Supplemental
Convergent ladybeetle (*Hippodamia convergens*)	Form.	Treated foliage	LD_{50} = 15.5 ppm	MRID 05009995 1975	Supplemental
Alfalfa leafcutter bee (*Megachile rotundata pacifica*)	NR	Caged with treated foliage	48-hour LD_{50} = 0.16 µg a.i./bee	ICI US 1975	Supplemental
Predatory mite (*Metaseiulus occidentalis*)	Ambush	Acute	LD_{50} <2.0 ppm	ICI US Aug/Sep 1976	Supplemental
Predatory mite (*Metaseiulus occidentalis*)	25 EC	Acute, contact	LD_{90} = 1–5 ppm	MRID 00045048 1975	Supplemental
Predatory mite (*Metaseiulus occidentalis*)	Form.	Acute, dip test	LD_{50} = <1 ppm	ICI US NR	Supplemental
Alkali bee (*Nomia melanderi*)	NR	Caged with treated foliage	48-hour LD_{50} = 0.16 µg a.i./bee	NR 1975	Supplemental

[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.

In addition to the above laboratory studies, a number of field studies examining the toxicity of permethrin to ladybird beetles (*C. undecimpunctata* and *Coccinella septempunctata*) (ICI US NR), hover flies (Syrphidae) (ICI US NR), six-spotted thrips (*Scolothrips sexmaculatus*) (ICI US 1976), hemipteran predators (*Geocoris pallens*, *Orius tristicolor*,and *Nabis americoferris*) (NR 1976), and earthworms (*Lumbricus and Allolobophora spp*.) and unnamed spiders, mites and collembola were available to the Agency. Again, however, the utility of these studies for risk assessment purposes is limited because very little information was reported in the available files. Spray application of permethrin to oil rape seed resulted in significant reductions in ladybird beetles were observed at rates as low as 15 ppm. Spray application of permethrin at rates as low as 31.2 ppm caused a reduction in the numbers of hover fly larvae, and at 125 ppm no larvae survived. A field 8-spray program on a 10 day interval with an 25% EC of permethrin applied to cotton caused a significant reduction in the numbers at all rates tested (0.8, 1.6 and 3.2 oz) in all hemipteran predators, with populations temporarily eliminated. Lastly, earthworm populations were slightly reduced (non-statistically significant) when exposed to permethrin at levels of 11 lb a.i./A, but not at 1.1 lb a.i./A. Overall, these studies show that applications of formulated permethrin are likely to reduce the numbers and possibly eliminate populations of invertebrates. The results of these studies are shown in **Table J.7**.

Table J.7. Terrestrial invertebrate field toxicity testing.

Species	% a.i.	Test type	Test result	Identification number, date	Study classification[a]
Seven spot ladybird (*Coccinella septempunctata*) and Eleven spot ladybird (*C. undecimpunctata*)	NR	Field application to oil seed rape	Significant reduction in numbers at rates of 15 ppm and higher, 24 h post-treatment.	ICI US NR	Supplemental
Hover flies (Syrphidae)	NR	Field, spray application	All rates of 31.2 ppm and above ceased a reduction in the numbers of larvae and no larvae observed at 125 ppm.	ICI US NR	Supplemental
Six-spotted thrips (*Scolothrips sexmaculatus*)	25	Field, 8-spray program on a 10-day interval with PP557 25% EC and PP383 25% EC applied to cotton.	No significant reduction in numbers at 8 days post-treatment at 3.2 oz a.i./A.	ICI US 1976	Supplemental

Table J.7. Terrestrial invertebrate field toxicity testing.					
Species	**% a.i.**	**Test type**	**Test result**	**Identification number, date**	**Study classification[a]**
Hemipteran predators (*Geocoris pallens*) (*Orius tristicolor*) (*Nabis americoferris*)	25	Field, 8-spray program on a 10-day interval with PP557 25% EC and PP383 25% EC applied to cotton.	Significant reduction in numbers at all rates tested (0.8/1.6 and 3.2 oz); populations temporarily eliminated.	NR 1976	Supplemental
Earthworms (Lumbricus and Allolobophora spp.) and unnamed spiders, mites and collembola	NR	Spray application	Slight decrease (non-statistically significant) in earthworm populations at 5 kg a.i./A, no effect at 0.5 kg a.i./A.	ICI US 1975	Supplemental
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.					

f. Terrestrial Plants

No data have been submitted to the Agency to evaluate the effects of permethrin on terrestrial plants because historically, terrestrial plant toxicity studies and associated risk analysis of plants were not required for registration of a pesticide unless it met specific use and pesticide classification criteria which would trigger potential concerns. In addition to the lack of registrant-submitted data, no studies demonstrating significant adverse effects of permethrin to any terrestrial plant have been identified in the open literature. Although a number of studies involving terrestrial plants and permethrin were identified in the open literature, none of these studies provide reliable estimates of toxicity that may be used in this risk assessment. Reasons that these studies were deemed unacceptable for use include, but are not limited to, the following reasons: there were no observed effects at any test level but did not test up to the maximum allowable rate, there were no controls, they were efficacy studies in which observed effects were confounded by the presence of an insect pest complex, there were severe methodology limitations inhibiting the achievement of definitive conclusions.

II. Toxicity to Freshwater Animals

Toxicity to fish and aquatic invertebrates is categorized using the system shown below (U.S. EPA, 2004). Toxicity categories for aquatic plants have not been defined.

Categories of acute toxicity for aquatic animals.	
LC_{50} (ppm)	**Toxicity Category**
< 0.1	Very highly toxic
> 0.1 - 1	Highly toxic

> 1 - 10	Moderately toxic
> 10 - 100	Slightly toxic
> 100	Practically nontoxic

a. Freshwater Fish, Acute

Two freshwater fish toxicity studies using the TGAI are required to establish the acute toxicity of permethrin to fish. The preferred test species are rainbow trout (coldwater sp.) and bluegill sunfish (warmwater sp.). Results of these tests are tabulated below in **Table J.8**.

Table J.8. Freshwater fish acute toxicity.

Species	% a.i.	96-Hour LC_{50} (ppb)	Toxicity category	Identification number, date	Study classification[a]
Bluegill sunfish *(Lepomis macrochirus)*	95.7	2.52	Very highly toxic	MRID 00110663 June 21, 1976	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	100	6.1	Very highly toxic	MRID 00110657 November 1974	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	95.7	6.8	Very highly toxic	MRID 00043263 December 1979	Supplemental
Bluegill sunfish *(Lepomis macrochirus)*	Tech	0.79	Very highly toxic	MRID 00042128 January 1976	Supplemental
Bluegill sunfish *(Lepomis macrochirus)*	94.4	13.3	Very highly toxic	EPA Beltsville 2343 May 23, 1978	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91.4	13.5	Very highly toxic	EPA Beltsville 1127 May 16, 1978	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	5.0[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	24EC	10.8	Very highly toxic	ESI 1976	Supplemental
Bluegill sunfish *(Lepomis macrochirus)*	24EC	13	Very highly toxic	MRID 00110705 1977	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	10EC	24	Very highly toxic	MRID 42584004 1992	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	38.5	9	Very highly toxic	EPA Beltsville 2356 June 21, 1978	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	38.4	33.4	Very highly toxic	ACC 096699 1978	Supplementary
Bluegill sunfish *(Lepomis macrochirus)*	38.5	6.8[b]	Very highly toxic	MRID 40098001 1986	Acceptable

Table J.8. Freshwater fish acute toxicity.					
Species	**% a.i.**	**96-Hour LC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Bluegill sunfish *(Lepomis macrochirus)*	91	4.5[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	8.0[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	7.1[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	5.6[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	7.6[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	7.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	13.0[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	91	6.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Bluegill sunfish *(Lepomis macrochirus)*	Technical	6.8	Very highly toxic	MRID 00043263 1991	Core
Bluegill sunfish *(Lepomis macrochirus)*	21	32	Very highly toxic	MRID 00097445 1991	Supplementary
Rainbow trout *(Oncorhynchus mykiss)*	95	9.8	Very highly toxic	MRID 00110657 November 1974	Acceptable
Rainbow trout *(Oncorhynchus mykiss)*	94	5.3	Very highly toxic	MRID 00043265 December 1979	Supplemental
Rainbow trout *(Oncorhynchus mykiss)*	Tech	2.1	Very highly toxic	MRID 00042126 1976	Supplemental
Rainbow trout *(Oncorhynchus mykiss)*	91	4.1[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss*)	91	2.9[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss*)	91	6.0[b]	Very highly toxic	MRID 40098001 1986	Acceptable

Table J.8. Freshwater fish acute toxicity.					
Species	**% a.i.**	**96-Hour LC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Rainbow trout *(Oncorhynchus mykiss*)	91	7.0[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss*)	91	8.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss*)	91	4.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss*)	91	5.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss*)	91	4.1[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Rainbow trout *(Oncorhynchus mykiss)*	24EC	56	Very highly toxic	MRID 00042132 May 1977	Supplemental
Rainbow trout *(Oncorhynchus mykiss)*	26.2	32	Very highly toxic	MRID 43740601 March 24, 1995	Acceptable
Rainbow trout *(Oncorhynchus mykiss)*	10 EC	72	Very highly toxic	MRID 42584003 1992	Acceptable
Rainbow trout *(Oncorhynchus mykiss)*	38.4	20.9	Very highly toxic	MRID 00110657 1978	Supplemental
Coho Salmon *(Oncorhynchus kisutch)*	Tech	17	Very highly toxic	MRID 00072846 June 1976	Acceptable
Atlantic salmon *(Salmo salar*)	Tech	1.5	Very highly toxic	MRID 00083085 June 1976	Acceptable
Brook trout (*Salvelinus fontinalis*)	92.5	3.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Brook trout (*Salvelinus fontinalis*)	Tech	3.9	Very highly toxic	MRID 00042127 March 1977	Supplemental
Brook trout (*Salvelinus fontinalis*)	57 EC	5.2[b]	Very highly toxic	MRID 40098001 1986	Supplemental
Brook trout (*Salvelinus fontinalis*)	13EC	2.3[b]	Very highly toxic	MRID 40098001 1986	Supplemental
Fathead minnow (*Pimephales promelas*)	91	5.7[b]	Very highly toxic	MRID 40098001 1986	Acceptable

Table J.8. Freshwater fish acute toxicity.					
Species	**% a.i.**	**96-Hour LC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Fathead minnow (*Pimephales promelas*)	38.5 EC	5.7[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Fathead minnow (*Pimephales promelas*)	Tech	3	Very highly toxic	MRID 00042129 1976	Acceptable
Channel catfish (*Ictalurus punctatus*)	91	7.2[b]	Very highly toxic	MRID 40098001 1986	Acceptable
Channel catfish (*Ictalurus punctatus*)	Tech	5.4	Very highly toxic	MRID 00043735 June 1976	Acceptable
Carp (*Cyprinus carpio*)	Tech	15	Very highly toxic	ES-F2 1976	Supplemental

[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.
[b]In all cases for MRID 40098001, toxicity values are based on static exposure and nominal test concentrations.

The acute toxicity studies available to the Agency demonstrate that permethrin can be classified as very highly toxic to freshwater fish, with LC_{50} values ranging from 0.79 to 72 µg a.i./L for a number of different species. The studies also demonstrate that both the technical grade active ingredient and formulated permethrin share a very similar range of toxicity, with LC_{50} values ranging from 0.79 to 17.0 µg a.i./L for permethrin TGAI, and from 2.3 to 72.0 µg a.i./L for formulated permethrin.

b. Freshwater Fish, Chronic

A freshwater fish early life-stage test using the TGAI is required for permethrin because the end-use product may be applied directly to water or is expected to be transported to water from the intended use site (i.e., cotton), and because the following conditions are met: permethrin is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity, studies on aquatic invertebrates showed reproductive effects (daphnid 21-day LOEC = 0.56 ppb), pesticide is persistent in water (e.g., half-life = 37 days in aerobic soil study). The submitted data are listed in **Table J.9**.

Table J.9. Freshwater fish chronic toxicity.					
Species	**% a.i.**	**NOAEC/ LOAEC (ppb)**	**Endpoints affected**	**Identification number, date**	**Study classification[a]**

Table J.9. Freshwater fish chronic toxicity.					
Species	**% a.i.**	**NOAEC/ LOAEC (ppb)**	**Endpoints affected**	**Identification number, date**	**Study classification[a]**
Fathead minnow (*Pimephales promelas*) Full Life Cycle Test (egg to egg)	95.7	0.30 / 0.41	Full life cycle exposure resulted in significant reduction in number of fry surviving to 30 days. Only 3-8% of fry survived exposure to 0.41 ppm, compared to 85-95% in controls. No Effect on adult growth or number of eggs produced.	MRID 00110666 1977	Acceptable
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.					

Only a single acceptable life-cycle study on fathead minnows (*Pimephales promelas*) was available to the Agency to evaluate the effects of chronic exposure to permethrin (95.7% a.i.) on freshwater fish (MRID 00110666). The study demonstrated that chronic exposure to concentrations as low 0.41 µg a.i./L has the potential to cause reproductive toxicity. A significant reduction in the number of surviving fry at 0.41 µg a.i./L relative to the controls was observed (8% vs. 85-95% survival). However, no other adverse effects were noted on growth or number of eggs produced.

c. Freshwater Invertebrates, Acute

A freshwater aquatic invertebrate toxicity test using the TGAI is required to establish the toxicity of permethrin to aquatic invertebrates. The preferred test species is the water flea, *Daphnia magna*. Submitted results of acute toxicity tests with freshwater invertebrates are tabulated in **Table J.10**.

Table J.10. Freshwater invertebrate acute toxicity.					
Species	**% a.i.**	**48-Hour EC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Waterflea *(Daphnia magna)*	Tech	0.32	Very highly toxic	MRID 00043736 October 1976	Acceptable
Waterflea (*Daphnia magna*)	Tech	0.58	Very highly toxic	MRID 00110662 October 26, 1977	Acceptable
Waterflea (*Daphnia magna*)	95.7	0.04	Very highly toxic	MRID 00043736 December 1975	Acceptable
Waterflea *(Daphnia magna)*	94.4	0.7	Very highly toxic	EPA Beltsville 2420 July 8, 1979	Acceptable
Waterflea (*Daphnia magna*)	91	1.26 [b]	Very highly toxic	MRID 40098001 1986	Supplemental
Waterflea (*Daphnia magna*)	95.7	7.2	Very highly toxic	MRID 00110663 June 21, 1976	Acceptable

Table J.10. Freshwater invertebrate acute toxicity.					
Species	**% a.i.**	**48-Hour EC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Waterflea (*Daphnia magna*)	25EC	0.76	Very highly toxic	MRID 00110662 October 26, 1977	Acceptable
Waterflea (*Daphnia magna*)	25EC	1.31	Very highly toxic	MRID 00042139 1977	Supplemental
Waterflea (*Daphnia magna*)	26.2	3.3	Very highly toxic	MRID 43740602 1995	Acceptable
Waterflea (*Daphnia magna*)	10EC	9.9	Very highly toxic	MRID 42584002 1992	Acceptable
Mayfly (*Hexagenia bilineuta*)	97	0.100	Very highly toxic	MRID 00047040 September 9, 1980	Acceptable
Crayfish (*Procambarus blandingii*)	89.1	210	Very highly toxic	MRID 00042136 1977	Supplemental
Scud (*Gammarus pseudolimnaeus*)	91	0.17[b,c]	Very highly toxic	MRID 40098001 1986	Acceptable
Midge *(Chironomus plumosus)*	91	0.56 [b]	Very highly toxic	MRID 40098001 1986	Supplemental
Pond snail (*Lymnaea stagnalis*)	25EC	<25, 000	Cannot be determined	MRID 00042141 1986	Supplemental
Scud (*Hyalella azteca*)	100	0.0212	Very highly toxic	Anderson *et al.*2006 (ECOTOX Ref. # 90039)	Supplemental

[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.
[b]In all cases for MRID 40098001, toxicity values are based on static exposure and nominal test concentrations.
[c]96-hour LC50

The acute toxicity studies available to the Agency demonstrate that permethrin can be classified as slightly toxic to very highly toxic to freshwater invertebrates, with EC_{50} values ranging from 0.039 to <25,000 µg a.i./L. The studies also demonstrate that while the technical grade active ingredient can be classified as highly toxic to very highly toxic, with EC_{50} values ranging from 0.039 to 210 µg a.i./L, formulated permethrin is classified as slightly toxic to very highly toxic, with EC_{50} values ranging from 0.76 to <25,000 µg a.i./L.

In addition to the standard acute guideline studies mentioned above for freshwater invertebrates, an additional study examining the effects of acute exposure of *Daphnia* ephippia to permethrin was submitted (MRID 00110662). In this study, ephippia were exposed to permethrin TGAI at levels ranging from 0.001 to 100 mg a.i./L for 48 hours. After the exposure period, the eggs were rinsed and allowed to hatch in uncontaminated tap water. Time from exposure to hatching ranged from 4-5 days. The EC_{50} value for number of first instars hatched was calculated twice based on two runs of the experiment, and were reported as 34 µg a.i./L and 108 µg a.i./L. The results of this study are presented below in **Table J.11**.

In addition to the aforementioned acute mortality studies with freshwater invertebrates, an additional study was identified in the open literature which reported a more sensitive EC50 value (Anderson et al, 2006; ECOTOX Ref. # 90039). This study was conducted to determine the

toxicity of permethrin to the baetid mayfly *Procloeon sp.*, the amphipod *Hyalella azteca*, and the midge *Chironomus dilutus*. The determined 48-h (*Procloeon sp.*) and 96-h (*H. azteca* and *C. dilutus*) EC_{50} values for the mayfly, amphipod, and midge were 0.0896, 0.0212, and 10.45 µg a.i./L, respectively. Specifically, the estimated EC_{50} value for Hyalella is of interest because it is more sensitive than the most sensitive toxicity value from the other studies available to the Agency. Although this EC_{50} is the most sensitive toxicity value available for freshwater invertebrates, it was estimated based on static, nominal test concentrations, and therefore, still likely underestimates toxicity. In addition, it should be noted that although *Hyalella* is considered a benthic organism, this toxicity study was performed using water-only exposures. This study has been reviewed and is considered acceptable for quantitative use within the context of this risk assessment.

d. Freshwater Invertebrate, Chronic

A freshwater aquatic invertebrate life-cycle test (Guideline 72-4) using TGAI is required for permethrin since the end-use product may be transported to water from the intended use site, and the following conditions are met: (1) permethrin presence in water is likely to be continuous or recurrent; (2) aquatic acute LC_{50} or EC_{50} are less than 1 mg/L (i.e. 0.04 ppb, MRID 00043736) or (3) the EEC in water is equal to or greater than 0.01 of any acute EC_{50} or LC_{50} value. Physiochemical properties indicate cumulative effects, and permethrin is persistent in water (i.e., half-life 37 days aerobic soil metabolism). The preferred test species is *Daphnia magna*. The available test data for freshwater invertebrate chronic toxicity is listed in **Table J.11**.

Table J.11. Freshwater aquatic invertebrate chronic toxicity.

Species	% a.i.	NOAEC/ LOAEC (ppb)	Endpoints Affected	Identification number, date	Study Classification
Waterflea (*Daphnia magna*)	98.6	0.039/0.084	Reproduction and growth LOAECS in ppb for neonates produced (0.084), daphnid survival (0.34), growth as a function of weight (>340), and growth in length (0.084) (21 days)	MRID 43745701 May 12, 1995	Acceptable
Waterflea *(Daphnia magna*)	94.4	0.28 / 0.56	Reproduction Total production of young per adult daphnid and adult survival (28 days)	EPA Beltsville TN 2420 July 8, 1979	Supplemental
Waterflea (*Daphnia magna*)	Tech	EC_{50} = 70	Reproduction (EC_{50} calculated for eggs)	MRID 00110662 October 26, 1977	Supplemental

There are a total of two chronic exposure studies with permethrin involving freshwater invertebrates. These two guideline life-cycle studies with waterfleas (*Daphnia magna*) report NOAEC values ranging from 0.039 to 0.28 µg a.i./L. The first study (MRID 43745701; used TGAI-98.6% a.i.) reported the NOAEC and LOAEC as 0.039 and 0.084 µg a.i./L, respectively, based on 14% and 4% reductions in the number of young produced per female and length, respectively. Decreased adult survival was also observed at 0.34 µg a.i./L. In the second life cycle study (EPA Beltsville TN 2420, 1979; used TGAI-94.4% a.i.), total production of young per adult and adult survival were decreased by 13% and 4%, respectively, at 0.56 µg a.i./L. The NOAEC was reported as 0.28 µg a.i./L.

e. Ecosystem Field Study

The results of one registrant-submitted study field study with aquatic organisms was available for permethrin (MRID 00042134) and is presented in **Table J.12**,. In the study, researchers monitored a 5-acre pound for unspecified amount of time prior to spraying a 5-acre cotton field adjacent to it with two formulations of permethrin (Pounce and Ambush; % a.i. not reported). The two formulations were alternately applied at a single rate of 0.2 lb a.i./acre on 5 rows of cotton each time by ground spray equipment, every five days, for seventeen total applications. Fish, crayfish, mussels, zooplankton and macroinvertebrate populations were monitored bimonthly for five months following the application period. Samples of fish, crayfish, mussels, water, and sediment from the pond and soil from the cotton field were collected for residue analysis. Although no treatment-related effects were noted in fish, crayfish, mussel, or zooplankton populations, aquatic insect populations decreased by 79% following a significant rainfall after permethrin applications (unclear, but around the 9^{th} or 10^{th} application). Water sampled from the pond after the drop in macro-invertebrate abundance contained 0.05 - 0.11 µg a.i./L permethrin. The populations of insects did not increase until a month a half after the decline and almost a month after the final application. Tissue analyses showed 0.06 mg a.i./kg-bw permethrin in crayfish samples, 0.03 mg a.i./kg-bw in mussel, and no detectable levels in fish samples.

Any definitive conclusions are difficult to draw from this study due to poor experimental design, a lack of control pond data, the fact that the water level in the pond was maintained by pumped well water, and the inability to perform any statistical analyses.
However, the results of this experiment do suggest the potential for toxic effects to aquatic invertebrates as a result of permethrin use at a rate similar to those allowed under current labels. The occurrence of macro-invertebrate population decline after a heavy rainfall following treatment, suggests the potential for off-site transport of permethrin to aquatic systems via erosion/runoff at concentrations that could be harmful to aquatic organisms. The potential effects may include food chain interruption and removal of biomass. The potential for of-site transport is also supported by the fact that permethrin soil concentrations near the pond were higher than those further away from the pond. Under aerial application conditions and higher ratios of treated land surface to water surface, the potential for increased levels of contamination and intensified toxic effects would be expected to be even higher.

Table J.12. Aquatic ecosystem field study.					
Species	% a.i.	Endpoints Affected	Description	Identification number, date	Study Classification[a]

Table J.12. Aquatic ecosystem field study.					
Species	**% a.i.**	**Endpoints Affected**	**Description**	**Identification number, date**	**Study Classification[a]**
Fish: Tilapia (*Tilapia* sp.), goldfish (*Carassius auratus*), golden shiners (*Notemigonus crysoleucas*), channel catfish (*Ictalurus puntatus*), brown bullheads (*Ictalurus melas*), white perch (*Morone americana*), largemouth bass (*Micropteus salmoides*), Leoggleeye (*Lepomis gulosus*), green sunfish (*Lepomis cyanellus*), bluegill (*Lepomis macrochirus*), red swamp crayfish (*Procanibarus clarkii*) Crayfish (*Procambarus blandingii* Freshwater mussels (Leptodea sp.) Macroinvertebrates: Whirlygig beetles (Gyrinidae), water striders (Gerridae and Veliidae), mayflies (Ephemeroptera), damselflies (Coenagrionidae), dragonflies (Libellulidae) Zooplankton (Rotifera, copepod and cladocera)	0.2 lb a.i./acre	Mortality	Permethrin was applied to a 5-acre cotton field adjacent to a pond. Fish and invertebrate populations in pond were monitored after application. No fish, mussel or crayfish deaths were reported, but quantitative data not shown. Reductions in macroinvertebrate and zooplankton populations observed. Permethrin was found in tissue samples of mussels (0.03 ppm) and crayfish (0.06 ppm) from the pond.	MRID 00042134 October 20, 1977	Supplemental
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline					

III. Toxicity to Estuarine and Marine Animals

a. Estuarine and Marine Fish, Acute

Acute toxicity testing with estuarine/marine fish using the TGAI is required for permethrin because the end-use product is expected to reach this environment because of its use in coastal counties (i.e., cotton use). The preferred test species is the sheepshead minnow *(Cyprinodon variegatus)*. The submitted tests on the acute toxicity of permethrin to estuarine and marine fish are tabulated in **Table J.13**.

Table J.13. Estuarine/marine fish acute toxicity.					
Species	**% a.i.**	**96-Hour LC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Inland silversides (*Menidia beryllina*)	Tech	6.2	Very highly toxic	MRID 41134801 March 23, 1989	Supplemental
Inland silversides (*Menidia beryllina*)	94.6	6.6	Very highly toxic	MRID 41874901 May 18, 1989	Acceptable
Sheepshead minnow *(Cyprinodon variegatus)*	93	7.8	Very highly toxic	MRID 40228401 1987	Supplemental
Sheepshead minnow *(Cyprinodon variegatus)*	10EC	>300	Very highly toxic	MRID 42608201 1992	Supplemental
Atlantic Silverside *(Menidia menidia*)	93	2.2	Very highly toxic	MRID 40228401 EPA 1987	Supplemental
Striped mullet (*Mugil cephalus*)	93	5.5	Very highly toxic	MRID 40228401 EPA 1987	Supplemental
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.					

The acute toxicity studies available to the Agency demonstrate that permethrin can be classified as highly toxic to very highly toxic to estuarine/marine fish, with LC_{50} values ranging from 2.2 to >300 µg a.i./L. The studies also demonstrate that while the technical grade active ingredient can be classified as very highly toxic, with LC_{50} values ranging from 2.2 to 7.8 µg a.i./L, formulated permethrin is classified as highly toxic to estuarine/marine fish with a single reported LC_{50} value of >300 µg a.i./L.

b. Estuarine and Marine Fish/ Chronic

The Agency has requested the estuarine/marine fish life-cycle test (Guideline 72-5) using the TGAI of permethrin. The preferred test species is the sheepshead minnow (*Cyprinodon variegatus*). The study was requested for the following reasons:

(1) The pesticide is intended for use such that its presence in water is likely to be continuous or recurrent.
(2) FIFRA requires a fish life-cycle test for any pesticide if the aquatic acute LC_{50} or EC_{50} is less than 1 ppm. The reported LC_{50} for permethrin for the sheepshead minnow (*Cyprinodon variegatus*) is 7.8 ppb (MRID 40228401).

Only a single early life-stage study with sheepshead minnows (*Cyprinodon variegatus*) was available to the Agency to evaluate the effects of chronic exposure to permethrin (93% a.i.) on estuarine/marine fish (NR 1994) (**Table J.14)**. The study demonstrated that chronic exposure to concentrations as low 10 µg a.i./L has the potential to cause reduced survival. However, a

NOAEC could not be established because effects were seen at the lowest tested concentration of 10 µg a.i./L (NOAEC < 10µg a.i./L) and no other information was reported.

Table J.14. Estuarine/marine fish chronic toxicity.

Species	% a.i.	NOAEC/ LOAEC (ppb)	Endpoints affected	Identification number, date	Study classification[a]
Sheepshead minnow *(Cyprinodon variegatus)*	93	<10 /10	Reduced survival (28 days)	NR 1994	Supplemental

[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline

c. Estuarine and Marine Invertebrates, Acute

Acute toxicity testing with estuarine/marine invertebrates using the TGAI is required for permethrin because the end-use product will be used in coastal counties (i.e., cotton). The preferred test species are mysid shrimp and eastern oyster. Results of these tests are tabulated in **Table J.15**.

Table J.15. Estuarine/marine invertebrate acute toxicity.

Species	% a.i.	96-hour LC_{50}/EC_{50} (ppb)	Toxicity category	Identification number, date	Study classification[a]
Mysid *(Americamysis bahia)*	93	0.019	Very highly toxic	MRID 40228401 1978	Supplemental
Mysid *(Americamysis bahia)*	93	0.046	Very highly toxic	MRID 40228401 1978	Supplemental
Mysid *(Americamysis bahia)*	93	0.02	Very highly toxic	MRID 40228401 1978	Supplemental
Mysid *(Americamysis bahia)*	90.8	0.075	Very highly toxic	MRID 43492902 October 1986	Acceptable
Brown Shrimp (*Penaeus aztecus*)	89	0.34	Very highly toxic	MRID 00042135 May 1977	Acceptable
Pink Shrimp (*Penaeus duorarum*)	93	0.22	Very highly toxic	MRID 40228401 1978	Supplemental
Pink Shrimp (*Penaeus duorarum*)	95.7	0.35	Very highly toxic	MRID 00110660 December 1975	Acceptable
Pink Shrimp (*Penaeus duorarum*	3.2 EC	0.51	Very highly toxic	MRID 00110661 December 1975	Acceptable
Fiddler Crab (*Uca pugilator*)	95.7	2.39	Very highly toxic	MRID 00110660 December 1975	Acceptable
Fiddler Crab (*Uca pugilator*)	89	2.65	Very highly toxic	MRID 00042135 May 1977	Supplemental
Fiddler Crab (*Uca pugilator*)	3.2 EC	7.6	Very highly toxic	MRID 00110661 December 1975	Acceptable
Stone Crab (*Menippe mercenaria*)	93	0.018	Very highly toxic	MRID 40228401 1978	Supplemental
Pacific Oyster (*Crassostrea gigas*)	Tech	>1050	Moderately toxic	MRID 00042140 December 1977	Supplemental

Table J.15. Estuarine/marine invertebrate acute toxicity.					
Species	**% a.i.**	**96-hour LC_{50}/EC_{50} (ppb)**	**Toxicity category**	**Identification number, date**	**Study classification[a]**
Pacific Oyster (*Crassostrea gigas*)	10EC	6500b	Moderately toxic	MRID 42723301 1992	Acceptable
Eastern Oyster (*Crassostrea virginica*)	95.7	>536	Highly toxic	MRID 00110660 December 1975	Supplemental
Eastern Oyster (*Crassostrea virginica*)	95.7	>407	Highly toxic	MRID 00110660 December 1975	Supplemental
Eastern Oyster (*Crassostrea virginica*)	93	>1000	Moderately toxic	MRID 40228401 EPA 1978	Supplemental
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline [b]48-hour EC50					

The acute toxicity studies available to the Agency demonstrate that permethrin can be classified as moderately toxic to very highly toxic to estuarine/marine invertebrates, with EC_{50} values ranging from 0.018 to 6500 µg a.i./L. It should be noted that permethrin generally appears to be less toxic to bivalves (Eastern and Pacific oysters; *Crassostrea virginica* and *Crassostrea gigas*) than other estuarine/marine invertebrates; EC_{50} values ranged from >407 to 6500 µg a.i./L and 0.018 to 7.6 µg a.i./L for bivalves and the rest of the estuarine/marine invertebrates, respectively. The studies also demonstrate that both the technical grade active ingredient and formulated permethrin can be classified as moderately toxic to very highly toxic, with EC_{50} values ranging from 0.018 to >1050 µg a.i./L and 0.51 to 6500 µg a.i./L, respectively.

d. Estuarine and Marine Invertebrates, Chronic

An estuarine/marine invertebrate life-cycle toxicity test using the TGAI is required for permethrin because the end-use product is expected to transport to an estuarine/marine environment from the intended use site (i.e., cotton), and the following conditions are met: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) any aquatic acute LC_{50} or EC_{50} is less than 1 mg/L (e.g., mysid EC_{50} = 0.075 ppb, MRID 43492902); (3) the EEC in water is equal to or greater than 0.01 of any acute LC_{50} or EC_{50} value or (4) studies of other organisms indicate that the reproductive physiology of fish and/or invertebrates may be affected, physiochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g., half-life of 37 days aerobic soil metabolism). The preferred test species is mysid shrimp. The results of the available study are tabulated in **Table J.16**.

Table J.16. Estuarine/marine invertebrate life-cycle toxicity.					
Species	**% a.i.**	**NOAEC/ LOAEC (ppb)**	**Endpoints affected**	**Identification number, date**	**Study classification[a]**
Mysid (*Americamysis bahia*)	95	0.011/0.024	Mortality	MRID 41315701 March 1989	Supplemental

Table J.16. Estuarine/marine invertebrate life-cycle toxicity.					
Species	**% a.i.**	**NOAEC/ LOAEC (ppb)**	**Endpoints affected**	**Identification number, date**	**Study classification[a]**
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline					

There is only one chronic exposure study with permethrin (95% a.i.) involving estuarine/marine invertebrates (MRID 41315701) available to the Agency. This life-cycle study with mysids (*Americamysis bahia*) reports NOAEC and LOAEC values of 0.011 and 0.024 µg a.i./L, respectively, based on a 20% increase in mortality at the LOAEC relative to the control. While no adverse effects on growth were noted based on adult body weight (length measurements were not taken), the effects of chronic exposure to permethrin on reproduction of mysids could not be evaluated in this study due to significant study limitations (*i.e.*, poor reproductive performance of controls). Therefore, the utility of this study for risk assessment purposes is severely limited.

IV. Toxicity to Aquatic Plants

Only one study examining the toxicity of permethrin to non-vascular aquatic plants was initially available to the Agency (MRID 40228401). This study involving technical permethrin (93% a.i.) and the marine diatom (*Skeletonema costatum*) reports an EC_{50} value of 92 µg a.i./L However, no NOAEL, raw data, or additional information were reported.

Only two other studies establishing EC_{50} values for non-vascular plants were identified in the open literature. The first (Stratton *et al.*, 1980; ECOTOX Ref # 4684) laboratory toxicity assay was conducted to determine the effects of permethrin on the growth (yield and rate), $^{14}CO_2$ uptake, and acetylene reduction of the blue-green alga, *Anabaena inequalis*. The study determined the EC_{50} of permethrin towards growth yield, growth rate, photosynthesis (uptake of $^{14}CO_2$ and $NaH^{14}CO_3$), and acetylene reduction to be 1.6, 5.0, >100 and >100 mg a.i./L, respectively. However, no NOAEL or raw data were reported.

The second open literature study (Walsh and Alexander, 1980; ECOTOX Ref # 5297) was conducted to evaluate methodologies of marine algal bioassays and to determine the effects of permethrin on the marine alga, *Skeletonema costatum*. EC_{50} values and their 95% confidence intervals were calculated on a Digital Equipment Corporation PDP11/45 computer by moving average method. The 96-hour static toxicity test yielded growth EC_{50} values of 68 and 72 µg a.i./L, based on cell counts and absorbance, respectively. However, no NOAEL or raw data were reported. The results of the available studies are tabulated in **Table J.17**.

No acceptable data from registrant-submitted studies or the open literature on the toxicity of permethrin to aquatic vascular plants were available to the Agency for this assessment.

Table J.17. Aquatic plant toxicity				
Species	**% a.i.**	**EC_{50} (ppb)**	**Identification number, date**	**Study classification[a]**

Table J.17. Aquatic plant toxicity				
Species	**% a.i.**	**EC_{50} (ppb)**	**Identification number, date**	**Study classification[a]**
Marine diatom (*Skeletonema costatum*)	93	92	MRID 40228401 1986	Acceptable
Blue-green alga (*Anabaena inequalis*)	Not available	1600, 5000, >100,000 and >100,000 for growth yield, growth rate, photosynthesis, and acetylene reduction, respectively	Stratton *et al.,* 1980; ECOTOX Ref # 4684	Supplemental
Marine diatom (*Skeletonema costatum*)	Not available	68 and 72 based on cell counts and absorbance, respectively	Walsh and Alexander, 1980; ECOTOX Ref # 5297	Supplemental
[a]Acceptable: study satisfies guideline; Supplemental: study is scientifically sound, but does not satisfy guideline.				

V. Toxicity to Aquatic-phase Amphibians

A number of studies involving amphibian toxicity testing and permethrin were identified in the open literature and are summarized below. None of these studies provide reliable estimates of toxicity that may be used quantitatively in this risk assessment; however they do provide some information regarding the hazard of permethrin to amphibians.

Dwyer et al 2005 (ECOTOX Ref. # 81380) compared boreal toad (*Bufo boreas boreas)* larvae sensitivity to the sensitivity of fish for permethrin. However, significant limitations of these data severely hinder their utility for quantitative risk assessment purposes. For instance, toxicity estimates for the boreal toad are based on static nominal concentrations and there is considerable variability in the measured concentrations taken only from the stock solutions relative to the nominal, the concentration of the co-solvent (acetone) in the study is not stated, wild-caught frogs with an unknown exposure history were used, the developmental stage of the test larvae was not stated and it is unknown whether the stage is matched across treatments, and test animal weight was expressed as the average of 20 animals. Particularly, reliance on the nominal concentrations is problematic and toxicity estimates are unacceptably uncertain due to permethrin's low solubility (5.5 µg a.i./L), high k_{oc}, and propensity to sorb. However, in spite of these limitations the study may be useful for qualitative purposes to demonstrate that boreal toad larvae were less sensitive than the tested fish species to permethrin (96-hr LC_{50}>10 µg a.i./L).

Jolly et al 1978 (ECOTOX Ref. # 5181) evaluated the acute toxicity of permethrin on crayfish (*Procambarus clarkii*), channel catfish (*Ictalurus punctatus*), largemouth bass (*Micropterus salmoides*), mosquito fish (*Gambusia affinis*), and bullfrogs (*Rana catesbeiana*). While the study may be useful for qualitative risk assessment purposes, serious design issues and uncertainties make it unacceptable for quantitative use. In particular, wild-caught frogs with an unknown exposure history were used, the actual formulation tested is not stated and its potential inert ingredients are unknown, it is unknown whether the estimated toxicity endpoints are corrected for percent active ingredient, it is unclear whether the toxicity endpoints are based on measured exposure concentrations, and larvae 6 - 8 mm in length were use. Because larvae of 6-8

mm in length were used, and bullfrog larvae reported in open literature are 10 mm in length, it suggests that the animals are close to being newly hatched and it is possible that they still have their yolk sac. Subsequently, this may have affected the extent to which they uptake chemicals in the water, and toxicity could be significantly underestimated. In addition, potentially relying on nominal concentrations is problematic due to permethrin's low solubility (5.5 µg a.i./L), high k_{oc}, and propensity to sorb. Therefore, toxicity estimates are unacceptably uncertain. However, the study does provide information on the relative toxicity of the permethrin formulated product to bullfrogs under these test conditions; compared to newly hatched crayfish (96 hr LC_{50} = 0.39 µg/L), bullfrog larvae are 18,000X less sensitive (96-hr LC_{50}=7033 µg /L).

Thurston et al 1985 (ECOTOX Ref. #12004) evaluated the relative acute toxicity of permethrin to a variety of freshwater animals, including Bullfrog tadpoles (*Rana catesbiana*), under standardized test conditions for the purposes of determining the extent to which a single species might be used as a surrogate for others. A number of study limitations include: the amount of solvent (dimethylformamide) used was not reported and it is not clear whether a solvent control was evaluated; although concentrations were measured, recovery of the chemical was not reported; the number of tadpoles tested per treatment was not reported; the loading rate was not reported; and tadpoles had a considerable range in sizes (2 - 5 g), their developmental stages as tadpoles likely varied considerably, and it is unknown whether the stages were matched across treatments. These deviations and the lack of description of some significant details on design, hinder the use of this study for quantitative risk assessment purposes. However, the study does provide information on the relative toxicity of the permethrin to bullfrogs under these test conditions. The bullfrog was less sensitive to permethrin relative to most other species tested; the 96-hr LC_{50} values for bullfrog larvae, goldfish (*Carassius auratus*), waterfleas (D*aphnia magna*), rainbow trout (*Oncorhynchus mykiss*), and bluegill sunfish (*Lepomis macrochirus*) were 115 µg a.i./L (95% CI: 53.8 - 245 µg a.i./L), >228 µg a.i./L , <1.4 µg a.i./L, 5 µg a.i./L, and 5 µg a.i./L, respectively.

Johansson et al 2006 (ECOTOX Ref. #88266) investigated the effects of acute exposure to permethrin on survival and development of the tadpoles of the common frog, *Rana temporaria*, and assessed the influence of chronic exposure. In the 3-day acute study, tadpoles at a Gosner stage 25 were exposed to permethrin concentrations of 2, 8, and 32 µg a.i./L under presumably static conditions; concentrations were selected based on a previously reported LC_{50} of 2.5 µg a.i./L. In the chronic study, tadpoles were exposed to 0, 0.1, and 1 µg a.i./L permethrin from 6-hrs post fertilization until metamorphosis under static renewal conditions (every 72 hours). Response variables included growth (body length, tail length, wet weight), survival, age at metamorphosis and growth rate (body weight at metamorphosis divided by the number of days required to complete metamorphosis).

In the acute study, permethrin showed no effect of concentration on growth measurements ($p>0.09$). There was a weak but significant effect of permethrin concentration on survival ($p=0.0026$), and it appeared that survival was reduced by roughly 20% at the highest test concentration (32 µg a.i./L). In the chronic study, permethrin had a significant effect on size at metamorphosis (body weight $p=0.017$; tail length $p=0.0068$; wet weight $p=0.0018$) and the metamorphs gradually increased in size with increasing pesticide concentration. No effect of permethrin on either survival or age at metamorphosis was observed; however, weight showed a

distinct and sharp increase across increasing concentrations of permethrin. Control animals were roughly 0.85 g, while animals in the 0.1 and 1 µg a.i./L treatments were 0.9 and roughly 1.1 g, respectively.

The limitations of this study that hinder its utility for risk assessment purposes include: a very high loading rate of tadpoles (exceeded the recommended rate of 1 tadpole/L) for the acute study and for the early part of the chronic study; test organisms were fed during the acute study and it may have reduced the amount of permethrin in solution and confidence in exposure estimates; and wild-caught frogs with an unknown exposure history were used. At most, this study does offer that survival may be adversely affected following a 3-day acute exposure period, while growth may be positively correlated with increasing permethrin concentrations following chronic exposure from 6-day post-fertilization through metamorphosis.

The objective of Berril et al (ECOTOX Ref. # 2850) was to evaluate the effects of exposure of tadpoles and embryos of five amphibian species to permethrin to determine behavioral effects. Species tested included the leopard frog (*Rana pipiens*), green frog (*R. clamitans*), wood frog (*R. sylvatica*), American toad (*Bufo americanus*), and the spotted salamander (*Ambystoma maculatum*). However, wild-caught frogs with an unknown exposure history were used, the purity of permethrin was not reported, all exposure concentrations were reported as nominal, no concentrations were measured, loading rates were very high, test conditions were very poorly described, river water was used as dilution water and the exposure to other chemicals is unknown, and it is not clear whether eggs were dejellied in order to conduct the exposure studies of embryos and if so, what the procedure was to accomplish this task. Particularly, reliance on the nominal concentrations is problematic and toxicity estimates are unacceptably uncertain due to permethrin's low solubility (5.5 µg a.i./L), high k_{oc}, and propensity to sorb. The only notable results of the study are that permethrin exposure under the conditions tested had transient effects on growth and may have decreased survival at 50 and 100 µg a.i./L. Subsequently, due to an extreme number of uncertainties and significant study limitations, it is not possible to put any observed effects into context for this risk assessment and they will not be discussed further.

The objective of Yasmeen and Nayccmunnisa 1992 (ECOTOX Ref. # 100130) was to look at acetylcholine esterase, choline acetylase, and calmodulin in the brains of *Rana cyanphlictis*. However, wild-caught frogs with an unknown exposure history were used, only a single nominal concentration of 0.25 mg /L was tested and it was unclear whether the concentrations were corrected for percent active ingredient of the tested formulation 25% a.i.), inert ingredients in the formulation were unknown, loading rates, measured concentrations, and water quality were not discussed, it was not clear whether there was any true replication of test groups, the methods of quantification of enzyme activity had a low sensitivity (polyacrylamide gel electrophoresis was used along with gel densitometry), enzyme activity was not normalized to protein content, and methods of measuring protein content were not reported. Subsequently, due to significant study limitations, it is not possible to put any observed effects into context for this risk assessment and they will not be discussed further.

While Fort et al 1999 (ECOTOX Ref. # 89641) exposed embryos of *Xenopus laevis* to pond water and sediment contaminated with multiple chemicals including permethrin, the contribution of the various chemical to the observed toxicity is uncertain. Therefore, the utility of this study comes from the portion in which physicochemical characterization of the causes of abnormal frog embryo–larval and limb development was performed using the frog embryo teratogenesis assay—*Xenopus* (FETAX). In this portion of the study, specific compounds, including permethrin, were subsequently identified within the complex mixture fractions from the pond and sediment and tested by dilution in a control solution and native reference water using both the 4- and 30-d treatment protocols. The 4-day assays suggest that permethrin could be a teratogen and cause potential adverse effects on gut and neural development (EC_{50}=59.4 µg a.i./L; minimum concentration to inhibit growth at p<0.05 was 50 µg a.i./L; LC_{50}=693 µg a.i./L) in blastula-stage embryos. The extended portion of the study observed no effects of permethrin on limb development. However, addition to inadequate characterization of exposure of test subjects (*e.g.*,no information on test concentrations), the results of the study are problematic due to relatively high loading rates and the use of static renewal. Since larvae do not develop at the same rate, the presumption is that some larvae were exposed for longer periods of time than others. The study was conducted under static renewal with 48 hour water changes, potentially resulting in poor water quality given the loading rate of 10 larvae/L (the recommended loading is 1 per Liter). Therefore, the utility of this study for quantitative risk assessment purposes is severely limited.

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