Appendix D: Reviewed Toxicity Data (Registrant and Open Literature)

Summary of Toxicity Value
(Shaded areas are studies used in the risk assessment)

Amphibian Toxicity Study for ETU

Aquatic-phase Amphibians Toxicity Study for ETU

Test Species	Life Stage at Test Start	Test Chemical	Endpoint (mg a.i/L)	ECOTOX Ref/ MRID	Description of Use in Document
South African clawed frog *Venous leaves*	4 days Post fertilization	ETU	4 day- LOAEL = > 1000 (highest tested concentration)	90116	Qualitative

Freshwater Fish Toxicity Studies for mancozeb, maneb and ETU.

Freshwater Fish 96-hr Acute Toxicity - Mancozeb.

Species/ Flow-through or Static	% ai	LC50 (ppb ai)/ (measured/nominal)	Toxicity Category	MRID /Accession No.	Study Classification1
Technical					
Bluegill sunfish *(Lepomis macrochirus)* /static (72 hour)	80.0	3850.0 (nominal)	moderately toxic	000971477	Supplemental
Bluegill sunfish *(Lepomis macrochirus)* /static	80.0	1350.0 (not reported)	moderately toxic	00097173	Supplemental
Bluegill sunfish (*Lepomis macrochirus*) /static	80.0	1540.0 (not reported)	moderately toxic	40118501	Supplemental
Bluegill sunfish (*Lepomis macrochirus*) /static	80.0	2040.0 (measured)	moderately toxic	not reported/Terr. & Aquatic Bio. Lab. Beltsville, MD/1980	Supplemental
Bluegill sunfish (*Lepomis macrochirus*) /flowthrough	81.3	>3600.0 (highest dose tested) (measured)	moderately toxic	45934702	Supplemental
Rainbow Trout (*Salmo gairdneri)*/static	80.0	640.0 (not reported)	highly toxic	not reported/Animal Biology La.b./1977	Supplemental
Rainbow Trout (*Salmo gairdneri)*/static	80.0	460.0 (measured) Probit slope = 4.5 (default) [1]	highly toxic	40118502	Acceptabke
Rainbow Trout (*Oncorhynchus mykiss*)/flowthrough	81.3	910.0 (measured) slope = not reported	highly toxic	45934701	Supplemental
End-Use Product					
Rainbow Trout *(Oncorhynchus mykiss)* /static	37.0	1100.0 (nominal)	moderately toxic	40467501	Supplemental

[1] Raw data unavailable to estimate slope. Used default assumption cited in Urban and Cook (1986).

Freshwater Fish 96-hr Acute Toxicity - Maneb.

Species/ Flow-through or Static	% ai	LC50 (ppb)/ (measured/ nominal)	Toxicity Category	MRID	Study Classification
End-Use Product					
Bluegill sunfish *(Lepomis macrochirus)* /static	80.0 WP	270.0 (mean measured) 170.0 (lowest measured	highly toxic	40749401	Acceptable
Rainbow Trout	80.0	52.0 (lowest	very highly	40706001	Supplemental

Species/ Flow-through or Static	% ai	LC50 (ppb)/ (measured/ nominal)	Toxicity Category	MRID	Study Classification
(Oncorhynchus mykiss) /static	WP	measured 42.0 (based on active ingredient) slope = 2.8 ($p < 0.05$)	toxic		
Bluegill sunfish *(Lepomis macrochirus)* /static	80.0 (Dithane M-22)	979.0 (nominal)	highly toxic	00097240	Supplemental [1]
Bluegill sunfish *(Lepomis macrochirus)* /static	5.6 Tide Maneb	6800.0 (nominal)	slightly toxic	00052557	Supplemental [1]
Bluegill sunfish *(Lepomis macrochirus)* /static	80.0 (DuPont Mannate)	990.0 (nominal)	highly toxic	00090291	Supplemental [1]

[1] Not conducted according to acceptable protocols: the toxicity end points were not based on measured concentrations and/or the information was provided as a reference source with no supporting data or statistical analysis.

Freshwater Fish Early Life-Stage Toxicity - Maneb

Species/Static or Flow-through Study Duration	% ai	NOAEC/LOAEC (ppb)/ (measured/nominal)	Endpoints Affected	MRID	Study Classification
Fathead minnow *(Pimephales promelas)* /flow-through/35 days	87.3	6.1/12 (mean measured) 1	Hatchability, fish survival and length of fry	41346301	Acceptable

Freshwater Fish Early Life-Stage Toxicity Under Flow-through Conditions - Mancozeb Technical

Species/Static or Flow-through Study Duration	% ai	NOAEC/LOAEC (ppb ai)/ (measured/nominal)	Endpoints Affected	MRID/Accession (AC) No.	Study Classification
Fathead minnow *(Pimephales promelas)* /flow-through/35 days	79.3	2.19/4.56 (measured)	Survival and lack of growth effects	43230701	Acceptable

ETU

Acute toxicity of ETU to freshwater fish and invertebrates

Species	Purity	LC_{50}	Toxicity Category	Study	MRID

	(% a.i.)	(ppm/ai)		Classification	
Water flea *Daphnia magna*	99.6	269	Slightly toxic	Acceptable	45910302 or 4602090
Rainbow trout	99.1	>502	Practically nontoxic	Acceptable	45910401 or 46020903

Chronic toxicity of ETU to freshwater invertebrates during a life-cycle toxicity test

Species	Purity (% a.i.)	NOAEC (µg/L)	LOAEC (µg/L)	Endpoints Affected	Study Classification	MRID
Water flea *Daphnia magna*	96.2	2.0	4.1	Adult length, survival, no. young/adult/day	Supplemental	45462901

Freshwater Invertebrate Toxicity Studies for mancozeb, maneb and ETU.

Acute toxicity of mancozeb to freshwater invertebrates

Species/Static or Flow-through/Duration	% ai	LC50/ EC50 (ppb) / (nominal/measured)	Toxicity Category	MRID/Accession (AC) No.	Study Classification1
Technical					
Daphnid *(Daphnia magna)*/static (48 hr.)	80.0	580.0 (nominal) Probit slope = 4.5 (default) [1]	highly toxic	40118503	Acceptable
Daphnid *(Daphnia magna)*static (48 hr.)	82.4	1000.0 (nominal)	highly toxic	40467503	Acceptable

[1] Raw data unavailable to estimate slope. Used default assumption cited in Urban and Cook (1986).

Freshwater Invertebrate Acute Toxicity - Maneb

Species/Static or Flow-through/Duration	% ai	EC50 (ppb)/ (nominal/measured)	Toxicity Category	MRID/Author/ Year	Study Classification
Daphnid *(Daphnia magna)*/ static (48 hr.)	80 WP	310.0(mean measured) 120.0 (lowest measured) slope = 4.2 ($p < 0.05$)	highly toxic	40749402	Acceptable

Acute ETU

Chronic toxicity of ETU to freshwater invertebrates during a life-cycle toxicity test						
Species	**Purity**	**NOAEC**	**LOAEC**	**Endpoints Affected**	**Study**	**MRID**

	(% a.i.)	(µg/L)	(µg/L)		Classification	
Water flea *Daphnia magna*	96.2	2.0	4.1	Adult length, survival, no. young/adult/day	Supplemental	45462901

Freshwater Aquatic Plant Toxicity Studies for mancozeb and maneb.

Non-target Aquatic Plant Toxicity (Tier II) - Mancozeb Technical

Species/duration	% A. I.	EC50/NOAEC (ppb ai)	MRID No.	Classification1
Nonvascular Plants				
freshwater green algae (Pseudokirchneriella subcaptitatum) /120 hrs.	8243	47.0/<22.0 Probit LD50 = 46 95%CI = 41.3-50.1 Probit slope = 4.0 95%CI = 3.4-4.6	43664701	Acceptable
End-Use Formulation				
freshwater green algae (Pseudokirchneriella subcaptitatum) /<120 hrs	7.5 (dimethomorph) 67.7 (mancozeb	19/4.3[1]	43917217	Supplemental[2]
freshwater green algae (Pseudokirchneriella subcaptitatum) /120 hrs	9.0 (dimethomorph/zoxamide) 60.0 (mancozeb	112/28[1]	44283402	Acceptable
Freshwater diatom (*Navicula pelliculosa*)/120hrs.	9.0 (dimethomorph/zoxamide) 60.0 (mancozeb	13.71/2.88[1]	44283402	Acceptable
Freshwater blue-green algae (*Anabaena flosaquae)* 120 hrs.	9.0 (dimethomorph/zoxamide) 60.0 (mancozeb	130/28[1]	44283402	Acceptable

[1]Based on total product concentration.
[2]BDuration of the study was less than the required 120 hours and an inert ingredient control was not included in the test.

Non-target Aquatic Plant Toxicity (Tier II) - Maneb

Species/duration	% A. I.	EC50/NOAEC (ppb ai)	MRID No. Author/year	Classification1
Nonvascular Plants				
freshwater green algae *(*Pseudokirchneriella subcaptitatum) /120 hrs.	87.3	13.4/5.0 (nominal) slope = 4.8 ($p < 0.05$)	40943501	Acceptable

Avian acute and subacute toxicity studies for mancozeb and maneb

Acute oral toxicity of mancozeb to birds.

Species	% ai	LD50 (mg ai/kg)	Toxicity Category	MRID No.	Classification1
English sparrow *(Passer domesticus)* - 10 day study duration	86.0	~1500	slightly toxic	00036094	Supplemental
Mallard Duck *(Anas platyrhynchos)*	86.0	>6400	practically nontoxic	00080716	Supplemental
Japanese Quail *(Coturnix japonica*)	86.0	>6400	practically nontoxic	00080717	Supplemental

Acute oral toxicity of Maneb to birds

Species	% ai	LD50 (mg/kg)	Toxicity Category	MRID/ Author/Year	Classification
Northern bobwhite *(Colinus virginianus)*	86 (doses were adjusted to 100% ai)	>2,150	practically nontoxic	40657001/ D. Fletcher/1988	Acceptable

Avian Subacute Dietary Toxicity - Maneb

Species	% ai	LC50 (ppm)	Toxicity Category	MRID	Study Classification

Bobwhite Quail *(Colinus virginianus*)	assumed to be 100%	>10,000	practically nontoxic	00104264/	Supplemental
Mallard Duck *(Anas platyrhynchos*)	assumed to be 100%	>10,000	practically nontoxic	00098561	Supplemental
Mallard Duck *(Anas platyrhynchos*)	86 (doses were adjusted to 100% ai)	>5,000	practically nontoxic	40657002	Acceptable

Avian chronic toxicity studies for mancozeb and maneb

Chronic avian toxicity information for mancozeb

Species/ Study Duration	**% ai**	**NOAEC/ LOAEC (ppm ai)**	**LOAEC Endpoints**	**MRID No.**	**Classification1**
Northern bobwhite *(Colinus virginianus)* /22 weeks	81.9	125/1000	Hatchling wt., 14-day old survivor wt., & % of 14-day old survivors	44159501	Acceptable
Mallard Duck *(Anas platyrhynchos)* /22 weeks	80.1	125/1000	Reductions in: egg production; early and late embryo viability; hatchability; and offspring weight at hatch and 14-days of age.	41948401	Acceptable
Northern bobwhite *(Colinusvirginianus)* /22 weeks	86.2 - 88.5	300/1000	14-day old survivors wt.	44238001/Johnson, A./1993	Acceptable

Chronic avian toxicity information for maneb

Species/ Study Duration	% ai	NOAEC/ LOAEC (ppm)	LOAEC Endpoints	MRID	Classification
Northern bobwhite *(Colinus virginianus)* /22 weeks	91.0	>500 (highest dose tested)/LAOEC not determined	not determined	43586501	Supplemental1
Mallard Duck *(Anas platyrhynchos)* /22 weeks	91.0	20/100	Reduction in the number of hatchlings as percentages of eggs laid, eggs set, and live 3-week old embryos, and a reduction in the number of 14-day old survivors as a percentage of eggs set.	43586502	Acceptable

Mammalian acute and subchronic toxicity studies for mancozeb and maneb

Mammalian Acute Oral Toxicity - Mancozeb

Species	% ai	LD50 (mg ai/kg)	Toxicity Category)	Affected Endpoints	MRID or Accession (AC) No.
Technical					
laboratory rat (Rattus norvegicus) laboratory mouse *(Mus musculus*)l	80.0	>5,000 (male)	practically nontoxic	mortality	AC259044
laboratory rat (Rattus norvegicus)	72.6	>5,000 (male & female) Probit slope = 4.5 (default)1	practically nontoxic	mortality	00142522
laboratory rat (Rattus norvegicus)	70.0 & 75.0	>5,000	practically nontoxic	mortality	AC254377
End-Use Formulation - Mancozeb					
laboratory rat (Rattus norvegicus)	36.0	>5,000 (male)	practically nontoxic	mortality	AC238564

1 Raw data unavailable to estimate slope. Used default assumption cited in Urban and Cook (1986).

Mammalian Acute Toxicity - Maneb

Species	% ai	Test Type	LD50 (mg/kg)	Toxicity Category)	Affected Endpoints	MRID
Technical						
laboratory rat (Rattus norvegicus) laboratory	not reported	oral - single dose	>5,000	practically nontoxic	mortality	41975601

Mammalian Subchronic Toxicity – Mancozeb

Surrogate Species/ type-duration	% ai	NOAEL/LOAEL (mg/kg/day)	LOAEL Endpoints	MRID or Accession (AC) No.
Laboratory rat (*Rattus norvegicus*)/ feeding-3 months	84.0	9.2417.82 (125/250 ppm) female 14.98/59.92 (250/1000 ppm) male	female - decreased serum thyroxin levels male - body weight decrements, changes in thyroid hormones, changes in liver enzymes, microscopic changes in the liver and thyroids, increased absolute and relative thyroid weights, and increased relative liver weights	00261536
Laboratory mouse (*Mus musculus*)/ feeding-3 months	83.1	18.13/166.9 (100/1000 ppm)	microscopic lesions of thyroid follicular cell hypertrophy or hyperplasia in females and decreased liver MFO enzyme activity in males	AC259888

Mammalian chronic toxicity studies for mancozeb and maneb

Mammalian Developmental and Reproductive Chronic Toxicity - Mancozeb Technical

Species/ Study Duration	% ai	Test Type	NOAEL/LOAEL Toxicity Value (mg/kg/day)	Affected Endpoints	MRID or Accession (AC) No.
laboratory rat (Rattus norvegicus) /not reported	83.0	Developmental	32/128 (□640/2560 ppm) (maternal) 128/512 (□2560/10,240 ppm) (developmental)	mat. - decreased food consumption & body wt. gain dev. - gross developmental defects, central nervous system defects, skeletal defects, cryptorchidism, abortions, increased resporption, and decreased fetal weight	00246663
laboratory rabbit (*Oryctolagus cuniculus*)/not reported	83.0	Developmental	30/80 (990/2,640 ppm) (maternal & developmental)	mat. - abortions, mortality, and clinical signs dev. - abortions	40433001
laboratory rat (Rattus norvegicus) /2 generation	84.0	Reproductive	6.95/68.9 (male) (120/1200 ppm) (parental) ≥69.9/≻69.9 (≥1200/≻1200 ppm) (reproductive)	parental - body weight decrements, increased relative thyroid weights, and increased incidence of thyroid follicular cell hyperplasia reproductive - No adverse offspring effects were attributed to mancozeb. Fecundity and gestation indices; litter sizes; and pup viability, survival, and body weights were all similar among the groups	41365201

Mammalian Developmental and Reproductive Chronic Toxicity - Maneb Technical

Species/ Study Duration	% ai	Test Type	NOAEL/LOAEL Toxicity (mg/kg/day)	Affected Endpoints	MRID
laboratory rat (Rattus norvegicus) /13 weeks	77.9	Feeding	5/24 (80/400 ppm) male 6/30 (80/400 ppm) female	Based on thyroid effects (increased thyroid weights and follicular cell hyperplasia in males) and decreased T4 (thyroxin, a thyroid hormone).	40982601
laboratory rat (Rattus norvegicus) /gestation (days 6-15)	90.4	Developmental	20/100 (400/2,000 ppm)1 (maternal) 20/100 (200/1,000 ppm)1 (developmental)	mat. - based on increased clinical signs (soft stool), decreased body-weight gain and decreased food consumption dev. -based on increased post-implantation (embedding of fertilized egg in uterine lining) loss, increased resorption (total and resorption per dam), and decreased fetal viability	42520001
laboratory rat (Rattus norvegicus) /2-generation	87.3	Reproductive	(75/300 ppm)2 (parental) (300/1,200 ppm)2 (reproductive) (75/300 ppm)2 (fetal)	parental (paternal) - based on a significant increase in lung (both generations) and liver (F1) weight and an increased incidence of diffuse follicular epithelial hypertrophy/hyperplasia (F1) parental (maternal) - based on decreased body weight/body-weight gain and food consumption reproductive - based on delayed vaginal opening in the F1 female offspring fetal - based on slight delay in the startle response in the offspring	42049401

1 ppm conversion based on:
1 mg/kg/day = 20 ppm in adult rats, and 10 ppm in younger rats. (Nelson, 1975)
2 ppm value provided in study review

Terrestrial invertebrate toxicity studies for mancozeb and maneb

Non-target Insect Acute Toxicity - Mancozeb

Species	% ai	LD50 (µg a.i./bee)	Toxicity Category1	MRID	Study Classification 1
Technical					
Honey bee (Apis mellifera)	72.0	> 178.87 (contact)	practically nontoxic	00018842	Acceptable2
End-Use Product					
Honey bee (Apis mellifera)	8.3 (zoxamide) 69.0 (mancozeb)	> 200 (contact)	practically nontoxic	44950504	Acceptable
Honey bee (Apis mellifera)	8.3 (zoxamide) 69.0 (mancozeb)	> 153 (oral)	Virtually nontoxic3	44950504	Supplemental

1 Toxicity category source: 1985. International Commission for Bee Botany Third Symposium on the "Harmonization of methods for testing the toxicity of pesticides to bees".

Non-target Insect Acute Contact Toxicity - Maneb

Species	% ai	LD50 (µg/bee)	Toxicity Category	MRID/Author/ Year	Study Classification
Honey bee (Apis mellifera)	not reported	> 12.09	practically nontoxic	00036935/Atkins *et. al*./1975	Acceptable

Summary of Honey Bee Residue on Foliage - Mancozeb

Species	% ai	LD50 (µg a.i./bee)	Toxicity Category	MRID/Accession (AC) No. Author/Year	Study Classification1
Honey bee *(Apis mellifera)*	72.0	At 0.27 lb ai/A low toxicity from direct application or residue	not applicable	00001949/Johansen, C. and J.Eves/1969	Supplemental2

Summary of Residual and Reproductive Toxicity to *Typhlodromus pyri* - Mancozeb

Species	% ai	LR50a (lb a.i./A)	Affected Endpoints	NOAEC/LOAEC Toxicity Value (lb a.i./A)	Affected Endpoints	MRID/Accession (AC) No. Author/Year	Study Classification1
Predatory or Beneficial Mite *(Typhlodromus pyri)*	81.8	0.1	Mortality	< 0.02/0.02	Reduction in mean number of eggs hatched per female.	45577201/Nienstedt, K and S. Kollmann/2001	Supplemental

a Residue concentration on foliage causing 50% lethality.

Terrestrial plant toxicity studies for mancozeb

Non-target Terrestrial Plant Seedling Emergence Toxicity (Tier I) - Acrobat MZ - Mancozeb and Dimethomorph - End-Use Formulation

Species	% ai Mancozeb/ Dimethomorph	Mancozeb/ Dimethomorph Dose (lbs ai/A)	% Inhibition Response/ Endpoint Affected	MRID No.	Study Classification1
Monocot-Corn	60/9	1.38/0.20	0.0/no parameter affected	44283401	Acceptable
Monocot-Onion	60/9	1.38/0.20	12.0/dry weight	44283401	Acceptable
Monocot-Ryegrass	60/9	1.38/0.20	4.0/height = dry weight	44283401	Acceptable
Monocot-Oat	60/9	1.38/0.20	3.0/height	44283401	Acceptable
Dicot-Cucumber	60/9	1.38/0.20	0.0/no parameter affected	44283401	Acceptable
Dicot-Soybean	60/9	1.38/0.20	4.0/dry weight	44283401	Acceptable
Dicot-Cabbage	60/9	1.38/0.20	1.0/height	44283401	Acceptable
Dicot- Radish	60/9	1.38/0.20	2.0/emergence	44283401	Acceptable
Dicot-Lettuce	60/9	1.38/0.20	0.0/no parameter affected	44283401	Acceptable
Dicot-Tomato	60/9	1.38/0.20	4.0/dry weight	44283401	Acceptable

1 Acceptable (study satisfies guideline). Supplemental (study is scientifically sound, but does not satisfy guideline).

Non-target Terrestrial Plant Vegetative Vigor Toxicity (Tier I) - Acrobat MZ - Mancozeb and Dimethomorph - End-Use Formulation

Species	% ai Mancozeb/ Dimethomorph	Mancozeb/ Dimethomorph Dose (lbs ai/A)	% Inhibition Response/ Endpoint Affected	MRID No.	Study Classification1
Monocot- Corn	60/9	1.38/0.20	2.0/dry weight	44283401	Acceptable
Monocot- Onion	60/9	1.38/0.20	2.0/dry weight	44283401	Acceptable
Monocot- Ryegrass	60/9	1.38/0.20	0.0/no parameter affected	44283401	Acceptable
Monocot- Oat	60/9	1.38/0.20	2.0/height	44283401	Acceptable
Dicot- Cucumber	60/9	1.38/0.20	10.0/dry weight	44283401	Acceptable
Dicot- Soybean	60/9	1.38/0.20	0.0/no parameter affected	44283401	Acceptable
Dicot- Cabbage	60/9	1.38/0.20	0.0/no parameter affected	44283401	Acceptable
Dicot- Radish	60/9	1.38/0.20	5.0/dry weight	442834017	Acceptable
Dicot- Lettuce	60/9	1.38/0.20	3.0/dry weight	44283401	Acceptable
Dicot- Tomato	60/9	1.38/0.20	6.0/dry weight	44283401	Acceptable

1 Acceptable (study satisfies guideline). Supplemental (study is scientifically sound, but does not satisfy guideline).