APPENDIX H: HUMAN HEALTH RISK ASSESSMENT

Toxicity Profile

The EPA (2007A) estimated the degree to which rotenone could cause adverse health effects in humans, and the level or dose at which those effects would occur, evaluating acute, short and intermediate term, and chronic effects. The EPA concluded that "rotenone has high acute toxicity via the oral and inhalation routes of exposure (Category I) and low acute toxicity via the dermal route of exposure (Category IV)," and that "rotenone is not an eye or skin irritant nor is it a skin sensitizer." Table 42 (excerpted from the EPA 2007A), shows the acute toxicity profile for rotenone.

Table 1. Acute toxicity profile of rotenone to humans.

Guideline Number	Study Title	MRID	Results	Toxicity Category
870.1100	Acute oral [rat]	00145496	LD_{50} = 102 mg/kg (M) LD_{50} = 39.5 mg/kg (F)	I
870.1200	Acute dermal [rabbit]	43907501	LD_{50} > 5000 mg/kg	IV
870.1300	Acute inhalation [rat]	42153701	LC_{50} = 0.0212 mg/L (combined) LC_{50} = 0.0235 mg/L (M) LC_{50} =0.0194 mg/L (F)	I
870.2400	Acute eye irritation [rabbit]	42076203	PIS = 3.3 at 1 hr., cleared less than 24 hours	IV
870.2500	Acute dermal irritation [rabbit]	42076204	PIS = 0.08 at 1 hr which decreased to 0 at 72 hours	IV
870.2600	Skin sensitization [guinea pig]	42153702	Not a dermal sensitizer	N/A

LD_{50} = Median Lethal Dose; PIS = primary irritation score

The EPA (2007A) used the toxicological endpoints summarized in Table 43 as part of the human health risk assessment for rotenone. Based on a structure activity relationship and human dermal information, dermal absorption of rotenone was estimated at 10%, while a default factor of 100% was used for inhalation absorption.

Dietary Risk

To estimate acute dietary exposure to rotenone for humans, the EPA (2007A) considered residues in drinking water and food from piscicidal use in fish management. The estimated drinking water concentration (EDWC) was determined to be 200 ppb, which is the solubility limit of rotenone. Estimated exposure from drinking water considered surface water only because rotenone is not expected to reach groundwater, and the estimate is conservative because it assumes water is consumed immediately after treatment with no breakdown or water treatment prior to consumption. Rotenone exposure from food may occur if humans consume fish that survive a treatment, although this type of exposure is unlikely for the general U.S. population.

The EPA estimated acute dietary exposure to rotenone at 0.1117 mg/kg/day, which is 26% less than the acute population adjusted dose (aPAD) of 0.015 mg/kg/day. Since the EPA is concerned when risk estimates exceed 100% of the aPAD, the EPA concluded that acute dietary risk from rotenone is below the level of concern. New mitigation measures required by the EPA will further minimize potential dietary exposure.

To estimate chronic dietary exposure to rotenone, the EPA (2007A) considered residues in drinking water only because chronic exposure from food is not expected due to rotenone's rapid breakdown rate and low potential to bioaccumulate in fish. The EPA also assumed that rotenone could reach drinking water intakes. Based on the chronic toxicity endpoint, the drinking water level of concern (DWLOC) was determined to be 40 ppb for infants and children, which are the most sensitive human subgroups.

Table 2. Rotenone Toxicological Endpoints.

Exposure Scenario	Dose Used in Risk Assessment, Uncertainty Factor (UF)	Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (females 13-49)	NOAEL = 15 mg/kg/day UF = 1000 aRfD = 15 mg/kg/day / 1000 = 0.015 mg/kg/day	 Acute PAD = 0.015 mg/kg/day	Developmental toxicity study in mouse (MRID 00141707, 00145049) LOAEL = 24 mg/kg/day based on increased resorptions
Acute Dietary (all populations)	An appropriate endpoint attributable to a single dose was not identified in the available studies, including the developmental toxicity studies.		
Chronic Dietary (all populations)	NOAEL = 0.375 mg/kg/day UF = 1000 cRfD = 0.375 mg/kg/day / 1000 = 0.0004 mg/kg/day	 Chronic PAD = 0/0004 mg/kg/day	Chronic/onogenicity study in rat (MRID 00156739, 41657101) LOAEL = 1.9 mg/kg/day based on decreased body weight and food consumption in both males and females
Incidental Oral Short-term (1-30 days) Intermediate-term (1-6 months)	NOAEL = 0.5 mg/kg/day	Residential MOE = 1000	Reproductive toxicity study in rat (MRID 00141408) LOAEL = 2.4/3.0 mg/kg/day [M/F] based on decreased parental (male and female) body weight and body weight gain
Dermal Short-, Intermediate- , and Long-Term	NOAEL = 0.5 mg/kg/day 10% dermal absorption factor	Residential MOE = 1000 Worker MOE = 1000	Reproductive toxicity study in rat (MRID 00141408) LOAEL = 2.4/3.0 mg/kg/day
Inhalation Short-term (1-30 days) Intermediate-term (1-6 months)	NOAEL = 0.5 mg/kg/day 100% inhalation absorption factor	Residential MOE = 1000 Worker MOE = 1000	[M/F] based on decreased parental (male and female) body weight and body weight gain
Canter (oral, dermal, inhalation)	Classification: No evidence of carcinogenicity		

UF = uncertainty factor; NOAEL = no observed adverse effect level; LOAEL = lowest observed adverse effect level; aPAD = acute population adjusted does; cPAD = chronic population adjusted dose; RfD = reference dose; MOE = margin of exposure; N/A= Not Applicable

Rotenone is relatively short-lived under typical piscicidal use conditions, dissipating in cold and warm water with half-lives of 20 and 1.5 days, respectively (EPA 2007A). The degradation appears to be driven by aqueous photolysis and hydrolysis and microbial action. Rotenone is also readily neutralized using oxidizing agents such as potassium permanganate ($KMnO_4$), and drinking water treatment such as chlorination, ozonation, or charcoal filtering will further neutralize rotenone. The EPA therefore concluded that no chronic exposures to rotenone will occur where water is neutralized with $KMnO_4$ or treated through a drinking water regimen. However, the EPA also concluded that under limited

circumstances, such as rotenone applied to standing cold water near drinking water intakes with no treatment regimen, rotenone residues in drinking water could exceed the DWLOC (40 ppb) for up to several weeks. To ensure that chronic or sub-chronic exposures to rotenone above 40 ppb will not occur from drinking water, the EPA is requiring registrants to preclude such exposures by either monitoring or prohibiting rotenone use in standing waters with drinking water intakes.

Dermal, Incidental Oral, and Inhalation Risk

Recreational Risk

Although rotenone can be applied in public and private waters, it is only permitted for sale to certified applicators (EPA 2007A). Further, although treatment areas are closed to the public during application, they may be exposed by later recreating in water that was previously treated. The EPA therefore estimated recreational exposure and risk, but only from swimming (dermal and incidental ingestion) because other recreational activities would likely result in significantly less exposure. Recreational risks were calculated through margins of exposure (MOE), which compare estimated exposure to the no observed adverse effect level (NOAEL) in a toxicity study. MOEs $\geq$1,000 indicate that recreational exposure risks to rotenone will not exceed the EPA's LOC for dermal, incidental oral, and inhalation risk.

For short-term risks to adult swimmers on the same day as a 200 ppb application of rotenone, EPA (2007A) determined the dermal and incidental oral MOEs to be 1,600 and 7,000, respectively, neither of which exceeds the EPA LOC of 1,000. However, for short-term risks to toddler swimmers on the same day as a 200 ppb application of rotenone, the EPA (2007A) determined the dermal, incidental oral, and combined non-dietary MOEs to be 970, 850, and 450, respectively, all of which exceed the EPA LOC of 1,000. The EPA therefore estimated it would take three days in 25ºC water for rotenone concentrations to decrease below the LOC (for MOE = 1,000, rotenone concentration = 90 ppb). The EPA is therefore requiring that swimmers not enter rotenone treated areas until exposures are below the LOC.

Occupational Risk

Workers may be exposed while mixing, loading, or applying rotenone or when entering previously treated areas. The EPA (2007A) initially estimated handler risks using a long sleeve shirt, long pants, shoes, socks, no gloves, and no respirator. If these estimates exceed the EPA's LOC, they then estimated how personal protective equipment (PPE; such as additional clothing, chemical-resistant gloves, respirator) and management controls such as enclosed cabs, closed mixing/loading systems, and water-soluble packaging) would lower exposure.

The EPA used the following scenarios to assess risk to occupational handlers for short-term (1 to 30 days) and intermediate-term (1 to 6 months) exposure: mixer/loader, applicator, and mixer/loader/applicator. Exposures were estimated based on application of liquids and wettable powders via helicopter, boat, backpack, and drip bars. The EPA used the Pesticide Handlers Exposure Database (PHED) Version 1.1 (August 1998) to estimate handler exposure, but considers these estimates to be conservative due to several factors (EPA 2007A).

The EPA (2007A) used rotenone's historic maximum labeled concentration (250 ppb; 0.68 lb. ai/A-ft) and solubility limit (200 ppb; 0.54 lb. ai/A-ft) to estimate occupational handler exposure in standing water, as summarized in Table 44. Because many risks exceed the EPA LOC (MOEs < 1,000), the EPA is requiring the maximum labeled treatment concentration to be reduced from 250 ppb to 200 ppb, the use of additional PPE including respirators, and other mitigation measures to reduce occupational exposure.

The EPA (2007A) did not assess risk for occupational activities after rotenone applications because any dermal exposure from collecting dead fish and inhalation exposure from volatilization are expected to be minimal.

Table 3. Rotenone occupational handler risks at 250 ppb and 200 ppb application rates.

Exposure Scenario	Crop or Target	Application Rate[1]	Area Treated Daily (acres)	Combined MOEs[2]							
				Baseline	G + NR	G,DL+ NR	G+80 %R	G,DL + 80%R	G + 90%R	G,DL+90% R	Eng Cont
Mixing/Loading Liquid Concentrates for Helicopter Applications (1a)	Lakes	0.68	10	3.5	290	350	410	530	430	570	1100
	Lakes	0.68	5	7.1	590	710	810	1100	850	1100	2200
	Lakes	0.54	10	4.5	370	450	510	670	540	710	1400
	Lakes	0.54	5	8.9	740	890	1000	1300	1100	1400	2700
Mixing/Loading Liquid Concentrates for Boat Applications (1b)	Lakes	0.68	100	0.35	29	35	41	53	43	57	110
	Lakes	0.68	50	0.71	59	71	81	110	85	110	220
	Lakes	0.54	100	0.45	37	45	51	67	54	71	140
	Lakes	0.54	50	0.89	74	89	100	130	110	140	270
Mixing/Loading Wettable Powders for Boat Applications (2a)	Lakes	0.68	100	0.25	1.7	1.8	4	4.8	4.8	6	84
	Lakes	0.68	50	0.5	3.4	3.7	8	9.5	9.7	12	170
	Lakes	0.54	100	0.31	2.2	2.3	5.1	6	6.1	7.5	110
	Lakes	0.54	50	0.63	4.3	4.6	10	12	12	15	210
Applying Sprays via Helicopter (3)	Lakes	0.68	10	ND	ND	ND	ND	ND	ND	ND	1800
	Lakes	0.68	5	ND	ND	ND	ND	ND	ND	ND	3600
	Lakes	0.54	10	ND	ND	ND	ND	ND	ND	ND	2300
	Lakes	0.54	5	ND	ND	ND	ND	ND	ND	ND	4600
Applying Sprays via Boat Over-surface Boom Equipment (4)	Lakes	0.68	100	48	48	56	66	82	70	88	130
	Lakes	0.68	50	96	96	110	130	160	140	180	380
	Lakes	0.54	100	61	61	70	84	100	88	110	240
	Lakes	0.54	50	120	120	140	170	210	180	220	480
Mixing/Loading/ Applying Liquids with a Backpack Sprayer (using PHED liquid low pressure handwand data (5)	Lakes	0.68	2 acres	0.51	71	77	110	120	110	130	NF
	Lakes	0.54	2 acres	0.51	71	77	110	120	110	130	NF
	Streams	0.000016 lb ai/ft3	10,560 ft long	10	1400	1500	2100	2400	2300	2600	NF
	Streams	0.000013 lb ai/ft3	10,560 ft long	13	1700	1900	2600	3000	2800	3200	NF
Mixing/Loading/ Applying Liquids with Closed System Aspirators (PHED: missing/loading liquid – closed system) (6)	Lakes	0.68	10 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	110
	Lakes	0.68	5 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	220
	Lakes	0.54	10 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	140
	Lakes	0.54	5 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	270
Mixing/Loading/ Applying Liquids with Drip Bars (PHED: mixing/loading liquid) (7)	Streams	0.000016 lb ai/ft3	10,560 ft long	360	30000	36000	41000	53000	43000	57000	110000
	Streams	0.000013 lb ai/ft3	10,560 ft long	440	36000	44000	50000	66000	53000	70000	140000
Mixing/Loading/ Applying Wettable Powders with a Backpack Sprayer (using PHED wettable powder low pressure handwand data) (8)	Lakes	0.68	2 acres	ND	2.6	3	4.8	6.1	5.3	7.1	NF
	Lakes	0.54	2 acres	ND	2.6	3	4.8	6.1	5.3	7.1	NF
	Streams	0.000016 lb ai/ft3	10,560 ft long	ND	53	60	96	120	110	140	NF
	Streams	0.000013 lb ai/ft3	10,560 ft long	ND	65	74	120	150	130	170	NF
Mixing/Loading/ Applying	Lakes	0.68	10 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	84

Wettable Powders with Closed System Aspirators (PHED: mixing/loading liquid closed system) (9)	Lakes	0.68	5 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	170
	Lakes	0.54	10 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	110
	Lakes	0.54	5 acres	N/A	N/A	N/A	N/A	N/A	N/A	N/A	210
Mixing/Loading/ Applying Wettable Powders with Drip Bars (PHED: mixing/loading liquid) (10)	Streams	0.000016 lb ai/ft3	10,560 ft long	250	1700	1800	4000	4800	4900	6000	85000
	Streams	0.000013 lb ai/ft3	10,560 ft long	310	2100	2300	5000	5900	6000	7400	100000
Mixing/Loading/ Applying Wettable Powders via Powder/Sand/Gelatin Paste (11)	Seeps and Springs	There are currently no data to assess this scenario. EPA believes this scenario will result in minimal exposure due to the amount of rotenone used and the fact that this paste is typically mixed in either a lab under a fume hood or by an individual wearing a respirator.									

[1]Lb ai/A-ft unless otherwise noted

[2]G = Gloves; DL= Double Layer (baseline clothing + gloves); NR = No Respirator; R = Respirator; Eng Cont = Engineering Controls; ND = No Data; N/A = Not Applicable; NF = Not Feasible

Risk Characterization

Summary- Conclusion

In summary, rotenone is chemically unstable and rapidly breaks down in the environment to yield water-soluble, non-toxic byproducts. The bodies of vertebrates receiving a sub-lethal dose of rotenone metabolize it to non-toxic excretable substances. Rotenone is not considered to be carcinogenic, and recent experimental findings linking it to Parkinson's disease seem unlikely using EPA-required protocols.

The Re-registration Eligibility Determination for Rotenone (EPA 2007A) therefore concluded that "currently registered uses of rotenone will not pose unreasonable risks or adverse effects to humans or the environment if the requirements for re-registration outlined in this document are implemented." The EPA also concluded the following: "Provided that registrants comply with the requirements of this RED, the EPA believes that rotenone will not present risks inconsistent with FIFRA and that rotenone's benefits to society, including enhanced recreational areas and control of nonnative and invasive species, outweigh the remaining risks." The EPA further concluded that "continued registration of both liquid and wettable powder rotenone products, subject to the requirements of this RED, would provide benefit to society in controlling invasive or unwanted fish species."

Human Health and Ecological Risk

In the comprehensive assessments conducted as part of the rotenone re-registration process, EPA (2007A) concluded that most risks from rotenone are below the EPA level of concern (LOC). However, they also identified potential risks that could pose unreasonable risks or adverse effects to human or ecological health if left unmitigated. As a result, the EPA is requiring registrants and users of rotenone to implement the following risk mitigation measures, which were amended from EPA 2007A:

1. Deactivate with potassium permanganate to ensure that rotenone effects will not spread beyond the treatment area.

2. Encourage users to collect and bury dead fish.

3. Prohibit rotenone from being applied to estuarine/marine environments;

4. The maximum labeled application rate will be reduced from 250 ppb to rotenone's solubility limit of 200 ppb.

5. The Certified Applicator or designee under his/her direct supervision ensures concentrations of rotenone at drinking water intakes are below EPA's LOC (40 ppb).

6. Where appropriate, deactivate effluent with potassium permanganate.

7. Placard treatment areas to prohibit recreational access during treatment, swimming for at least 3 days following treatment, and consumption of dead fish taken from the treatment area.

8. Apply rotenone below the water's surface (except for aerial and backpack sprayer applications).

9. Limit the use of backpack sprayers to only liquid formulations.

10. Require additional personal protective equipment, including air-purifying respirators, protective clothing (coveralls, gloves), and eye protection (splash goggles or face shields).

11. Registrants will update product labels to require these measures.