

ROTENONE - FREQUENTLY ASKED QUESTIONS

What is rotenone?¹

Rotenone is a naturally occurring substance derived from the roots of tropical plants in the bean and pea family that are found primarily in Malaysia, South America, and East Africa. It is derived from ground up plant roots to make a powder formulation or extracted from the roots to make a liquid or crystalline formulation. People have utilized rotenone for centuries to capture fish for food in areas where these plants are naturally found, and it has been used in fisheries management as a piscicide (pesticide that kills fish) in North America since the 1930s. Rotenone affects gill breathing organisms by inhibiting respiration by blocking biochemical pathways of cell metabolism, specifically the reduced nicotinamide adenine dinucleotide (NADH)-dehydrogenase segment of the respiratory chain and resulting in mortality with prolonged exposure. Rotenone has also been used as an insecticide in residential products for control of fleas, ticks, and mites on pets and livestock; and for control of aphids on garden plants. Rotenone was used widely in North America for agricultural use as a botanical insecticide for use in fruit and vegetable crops.

When is it appropriate to use rotenone as a fish removal tool?¹

Fish removal has remained a necessary tool in fisheries management throughout history. Harmful fish species (invasive species, those not native to the area, or those that have expanded beyond their native range with the aid of humans or due to anthropogenic change to the environment), including exotic species (those from a foreign land) can adversely affect wildlife. Harmful aquatic species have contributed to the decline of approximately two-thirds of the threatened or endangered fishes in the U.S. through competition for resources, predation, and hybridization.

In general, rotenone is used as a fish removal tool to meet the following objectives when mechanical removal or habitat or environmental manipulation (e.g., dewatering) is not feasible or effective: 1) altering sport fish populations to improve angler opportunities; 2) conservation of native aquatic species (fish, amphibians, and aquatic reptiles) including those that are listed as threatened or endangered under the Endangered Species Act (ESA); and 3) controlling and mitigating the threat of invasive or pest species that may negatively impact wildlife human health, or cause economic harm.

How and when is rotenone applied?²

Rotenone liquid is typically packaged in 1-, 5-, 30- and 50-gallon containers and powder is typically in 50- and 200-pound containers. Applications are generally made with boats in lakes, reservoirs and ponds, with direct metering into moving water such as streams, and with hand-held equipment such as backpack sprayers in difficult to reach areas. Rotenone may be applied at any time of year, but most applications typically occur during warm months when the compound is more effective and degrades more rapidly. Rotenone is usually applied during low water conditions to limit amount of area treated and piscicide needed. On-site bioassays are performed to identify the lowest effective concentrations for use during the treatment.

What is the reregistration process of rotenone by the Environmental Protection Agency (EPA)?¹

The EPA has regulatory responsibility for the registration and reregistration of pesticides. Every 15 years (or sooner if necessary) the reregistration process is initiated and involves a thorough review based on scientific data to evaluate the potential hazards based on the current registered use, determine the need for additional data to supplement the health and environmental risk assessments, and evaluate criteria to ensure a registered pesticide will have “no unreasonable adverse effects”. The EPA will determine if a pesticide reregistration must be reevaluated if there is new evidence of human and/or environmental risks that were unknown or unable to determine during the initial reregistration process. Rotenone was reregistered by the EPA in 2007 for piscicide use only (EPA 2007). During the reregistration process, the EPA used risk assessments to evaluate the frequency and level of exposure that may occur in humans and ecological receptors upon exposure to rotenone.

How did the EPA determine safe levels of rotenone to be applied?¹

The EPA determined the Level of Concern (LOC) for rotenone concentrations for each potential exposure scenario (e.g., dietary risk, residential and recreational risk, occupational risk), which is 1000 times less than the no observed adverse effect level (NOAEL) for specific exposure routes (EPA 2007). This reflects a 10x uncertainty factor for interspecies extrapolation, a 10x uncertainty factor for intraspecies variation, and a 10x database uncertainty factor because a potentially critical effect (neurotoxicity) cannot be assessed quantitatively with the existing database. When critical factors cannot be assessed quantitatively with the existing database, EPA applies a 10x uncertainty factor to establish exposure limits that ensure the protection of public health and ecological systems. As a result of the reregistration process, the EPA determined the maximum treatment concentration of rotenone for piscicide use to be 200 parts per billion (ppb = $\mu\text{g/L}$).

How much rotenone is used?²

The concentration of active rotenone used to eradicate fish varies with the target species and environmental conditions from 12.5 to 200 ppb; which is 12.5 to 200 parts of rotenone in 1,000,000,000 parts of water (equivalent to 0.07 – 1.1 lb [1.1 – 18 oz] of rotenone in an Olympic-size swimming pool of 666,430 gallons).

How safe is rotenone to the public and applicators?²

Millions of dollars have been spent on research in testing laboratories and environmental monitoring studies to determine the safety of rotenone prior to registration in the U.S. by the EPA and in Canada by the Pest Management Regulatory Agency. Extensive acute (short-term) and chronic (long-term) tests on rotenone have been conducted. Rotenone is not considered a carcinogen (capable of causing cancer), mutagen (capable of causing genetic mutation), teratogen (interferes with normal embryonic development), or reproductive toxin (affects reproductive capabilities). The public will be excluded from treatment areas until rotenone

residues have dissipated to safe levels, and applicators are required to wear additional safety gear to minimize rotenone exposure.

What is a safe level of rotenone exposure?³

The EPA has suggested a safe level for rotenone in drinking water of 40 ppb and a safe level for water contact (e.g. swimming) of 90 ppb. These safe levels assume a conservative worst-case lifetime exposure to rotenone. These are conservative levels since most treatments result in rotenone residues persisting for no longer than a few days to a few months.

How were safe levels of rotenone determined?¹

To determine safe chronic drinking water exposure concentrations for rotenone, the EPA used data from a study where rotenone was administered to rats in concentrations of 0, 7.5, 37.5 and 75 parts per million (ppm or mg/L) daily for two years (equating to 0, 0.375, 1.88, and 3.75 mg/kg/day, respectively)(EPA 2006). Although no mortality or serious abnormalities were observed in any of the treatment groups, male and female rats lost weight in the mid- and high-dose groups. Thus, the lowest observed adverse effect level was 37.5 ppm, so the EPA used the 7.5 ppm as a toxicity end point for chronic oral consumption by humans and applied an additional uncertainty factor which is 1000 times lower than the lowest observed adverse effect level (equating to 0.0004 mg/kg/day or 40 ppb).

For perspective, using estimates reported by Finlayson et al. (2000), the estimated single lethal dose to humans is 300-500 mg/kg body weight. During a rotenone treatment using a concentration of 250 ppb (previous maximum treatment concentration), a 160 lb person would have to drink more than 23,000 gallons of treated water at one sitting to achieve a lethal dose.

The EPA considers chronic risk to humans from rotenone exposure during piscicide applications to be low based on the following reasons: the rapid degradation of rotenone; faster degradation and control of treatment end point by neutralization with potassium permanganate, where appropriate; the cancellation of some application methods (agriculture and residential); new required engineering controls to protect applicators; applications follow piscicide label requirements; and there is adequate signing and public notice or area closures to minimize public exposure to treated waters (EPA 2007).

When can the public access the water after treatment?³

The public will not be allowed in contact with the treated water until rotenone residues have dissipated below 90 ppb. Although the maximum treatment concentration for rotenone is 200 ppb, many treatments will occur at rotenone levels less than 90 ppb and in these cases contact can commence immediately after the treatment process has been completed. The EPA minimizes risks of exposure for swimmers during rotenone treatments by requiring closures (or swimming prohibition) post-treatment until levels are safe for swimming and/or consumption per EPA guidelines.

What is Parkinson's disease (PD) and its relationship to rotenone?²

People with PD have less dopamine producing cells in the brain which typically results in tremors and rigidity. It is a complicated disease likely affected by both genetics and the environment. Published literature over the past ten years indicated that rotenone exposure under certain laboratory conditions could reproduce several symptoms of PD in rodents. Although rotenone is toxic to the nervous system of insects and fish, commercial rotenone products have presented little hazard to humans over many decades of use and are not considered a cause of PD.

Does rotenone use in fisheries management cause PD?³

There is little doubt that rotenone and other chemicals that directly inhibit the mitochondrial energy chain can under certain laboratory exposure conditions reproduce symptoms of PD in animal models. These studies use intravenous (directly into the vein) injections, subcutaneous (below the skin) injections, or intragastric (stomach tube) routes of exposure with the rotenone dissolved in solvents and stabilizers to enhance tissue penetration. The purpose of the animal model studies is often to document possible PD models, not in finding the cause(s) of PD. The laboratory exposures used limit their applicability to humans because they avoid the normal protective measures of the human body through dermal and oral exposure. For example, a two-year long study where rotenone was mixed in the food of rats, using much higher dosages of rotenone, did not produce PD symptoms.

For perspective considering that the maximum treatment concentration of rotenone per the EPA is 200 ppb active rotenone, a 1 kg (2.2 lb) rat would need to be injected with 4 gallons of the 200 ppb rotenone solution daily for 6 weeks to achieve the 3 mg/kg/day concentration used in rotenone model studies. For a typical stream treatment using 50 parts ppb active rotenone, a 70 kg (154 lb) human would have to be injected with 1,109 gallons of 50 ppm rotenone solution daily for 6 weeks to achieve the 3 mg/kg/day concentration as used in the studies.

How are the epidemiological studies of rotenone exposure and PD related to exposure to rotenone used in fisheries management?¹

To date, there are no published studies that conclusively link exposure to rotenone and the development of clinically diagnosed PD. Some correlation studies have found a higher incidence of PD with the occupational (e.g., agricultural use) exposure to pesticides among other factors (e.g., Tanner et al. 2009, 2011), and some have not (e.g., Hertzman 1994; Firestone et al. 2010). It is very important to note that in case-control correlation studies, causal relationships cannot be assumed and some associations identified in odds-ratio analyses may be chance associations. Only one study (Tanner et al. 2011) found an association between occupational rotenone and paraquat use and PD in agricultural workers, primarily farmers. However, there are substantial differences between the methods of application, formulation, and doses of rotenone used in agriculture and residential settings compared with aquatic use as a piscicide, and the agricultural workers interviewed were also exposed to many other pesticides during their careers. Recently, the results of epidemiological studies linking pesticide exposure to PD have been criticized due to high variation among study results, generic categorization of pesticide exposure scenarios,

questionnaire subjectivity, and the difficulty in evaluating the causal factors of PD (Raffaele et al. 2011).

The potential realistic exposure of humans to rotenone during piscicide treatments, as regulated by the EPA (application rate of rotenone used as a piscicide shall not exceed 200 ppb), is not comparable to the dose required to cause the development of PD symptoms in rodents by way of chronic intravenous injections of rotenone into the sub-cutaneous, jugular vein, and substantia nigra. Piscicidal use of rotenone as a restricted use pesticide degrades quickly, is not expected to contaminate groundwater, and restricts human exposure of the treatment area during treatment, all of which make an environmental exposure to rotenone highly unlikely to cause PD or PD-like symptoms (Bové 2005). Overall, the occupational risk for the piscicide use rotenone will be negligible if used at concentrations no higher than the maximum treatment concentration and when certified applicators and professional fishery professionals use the rigorous standard operating procedures developed.

What are the dangers from consuming fish from rotenone treated water?³

Fish killed by rotenone should not be consumed by humans because of concern for salmonella and other bacteriological poisoning that may occur from consuming fish that have been dead for a period of time. The rotenone residues in dead fish carcasses are quickly broken down by physical and biological reactions.

It is possible that piscivorous (fish eating) birds and mammals may feed on dead or dying fish within a treatment area, although piscicide (fish killing) treatment protocols often recommend collection and/or burial of dead or dying fish within a treatment area where practicable. During the EPA's risk assessment process for terrestrial organisms, it was determined that based on rotenone residuals in yellow perch and common carp, a bird or mammal would have to consume thousands of pounds of contaminated fish in one sitting to result in a lethal dose.

How are the effects of rotenone restricted to the treatment site?³

Potassium permanganate, through a chemical reaction called oxidation, deactivates rotenone. Potassium permanganate can be added into the flowing water stream at the point where the effects of rotenone are no longer desired. Potassium permanganate is used worldwide in treatment plants to purify drinking water.

What happens to rotenone after it is applied to the water?²

Rotenone is a compound that breaks down very rapidly in the environment. Rotenone degrades quickly through physical (hydrolysis and photolysis) processes and biological mechanisms. An increase in temperature or sunlight increases the breakdown rate of rotenone.

How long does rotenone persist in water and sediment?²

Numerous monitoring studies have shown that rotenone residues typically disappear within about one week to one month, depending on environmental conditions. The half-life (time required for ½ of material to breakdown) for rotenone varies from about 12 hours to 7.5 days,

and is inversely related to temperature. Rotenone is typically applied when water temperatures are warm to optimize effect on the fish and the breakdown rate in the environment. If necessary, potassium permanganate can be used to speed-up (within 30 minutes) the breakdown of rotenone.

What are the risks of contaminating groundwater?¹

Rotenone is highly insoluble in water and strongly absorbs to soil particles in bottom sediments and to suspended particles in the water column, limiting its mobility and availability to bioaccumulate in organisms. These factors also make rotenone unlikely to leach through soils and reach groundwater, and thorough long-term (10 years post-treatment) monitoring of 80 groundwater wells in treatment areas in California, and short-term monitoring of over 26 wells in California and Montana never detected rotenone, rotenolone, or any formulation products following rotenone treatments (Skaar 2002; Ridley et al. 2007; McMillin and Finlayson 2008). If leaching does occur, rotenone will move vertically through soils typically less than one inch deep (Dawson 1986), making it unlikely to be absorbed by the roots of bank vegetation.

How does rotenone affect aquatic animals?²

Because rotenone is selectively toxic to gill breathing animals, fish are the most sensitive, followed by aquatic invertebrates and gill breathing forms of amphibians. Benthic invertebrates appear less sensitive than planktonic invertebrates, smaller invertebrates typically appear more sensitive than their larger counterparts, and aquatic invertebrates that use gills appear more sensitive than those that acquire oxygen through the skin, or that use respiratory pigments or breathe atmospheric oxygen. Studies have shown that amphibians and invertebrates will repopulate an area after rotenone breaks down.

Will wildlife be affected from consuming water or food containing rotenone?²

Birds and mammals are tolerant of rotenone having natural enzymes in the digestive tract that neutralize rotenone. Birds and mammals that eat dead fish and drink treated water will not be affected. Rotenone does not concentrate in fish tissue, rotenone residues are broken down quickly in the environment, and rotenone is not readily absorbed through the gut of an animal eating the fish or drinking the water. Most fish quickly sink to the bottom of treated water and rapidly decompose making the likelihood of extended exposure through the diet of terrestrial animals very low. This difference in toxicity between fish and birds and mammals coupled with its lack of environmental persistence makes the use of rotenone a good fish management tool.

Will wildlife be affected by the loss of their food supply following a rotenone treatment?²

During rotenone treatments, fish-eating birds and mammals can be found foraging on dying and recently dead fish for up to several days after treatment. Following this abundance of dead fish, a temporary reduction in food supplies may result until fish and invertebrates have been restored. However, most of the affected species are mobile and will seek alternate food sources or forage in other areas. In unique situations like the fledging of young raptors, dead fish may be brought into the treated water body for extended periods of time to provide for an uninterrupted food supply or the timing of the treatments can avoid periods of time when raptors are raising their young.

Will wildlife or livestock be affected by grazing on vegetation along the perimeter of treated waters?

Terrestrial wildlife may be exposed to treatment areas, but are unable to consume enough treated water or vegetation with rotenone residues to reach toxic levels. The EPA did not conduct a risk assessment to evaluate potential risk to birds and mammals from drinking rotenone treated water. However, the EPA studies for the human health risk assessments used rats to determine that the acute dietary exposure (drinking water only) of 200 ppb (maximum application concentration) is below the LOC. Finlayson et al. (2000) estimated that a 0.25 lb (0.113 kg) bird would need to consume 25 gallons of treated water in 24 hours to receive a lethal dose. Similarly for a large mammal, a cow weighing 1,620 lb (735 kg) would have to ingest 4,615 gallons of treated water (at 200 ppb treatment concentration) to reach a median lethal dose (EPA, personal communication).

It is possible that some birds and mammals may consume vegetation bordering stream or lake banks that was sprayed with rotenone during a piscicide treatment by an applicator operating a backpack sprayer unit. A human health and ecological risk assessment for rotenone completed for the U.S. Department of Agriculture, Forest Service, did not analyze this exposure scenario because they determined it irrelevant to aquatic applications (Durkin 2008). The EPA estimated exposure concentrations of rotenone in the form of foliar residues on vegetation (e.g., grass) that may be consumed by wildlife following non-piscicide applications of rotenone before the product registrants withdrew their requests for reregistration for those uses of rotenone; the EPA considered wildlife exposure by way of piscicide applications to rotenone residues on vegetation unlikely.

Does rotenone affect all animals the same?⁴

No. Fish are most susceptible, with rotenone inhibiting a biochemical process at the cellular level making it impossible for fish to use the oxygen absorbed in the blood and needed in the release of energy during respiration. All animals including fish, insects, birds, and mammals have natural enzymes in the digestive tract that neutralize rotenone, and the gastrointestinal absorption of rotenone is inefficient. However, fish (and some forms of amphibians and aquatic invertebrates) are more susceptible because rotenone is readily absorbed directly into their blood through their gills (non-oral route) and thus, digestive enzymes cannot neutralize it.

How many rotenone treatments have been conducted by the Arizona Game and Fish Department (AGFD)?

Since 1990, AGFD has used rotenone as a fish removal tool in 22 waters. Of the rotenone treatments, about 68% (n = 15) treated golf course ponds or stock tanks, 18% were stream treatments (n = 4), and 14% were lake treatments (n = 3).

¹Source: Rotenone Review Advisory Committee Final Report

²Source: American Fisheries Society. 2010. Maintaining North America's healthy native aquatic ecosystems: rotenone's role in eradicating invasive fishes, parasites and diseases. Fish Management Chemicals Subcommittee. <http://www.fisheriessociety.org/rotenone/>

³Source: Original source – American Fisheries Society. 2010. Maintaining North America's healthy native aquatic ecosystems: rotenone's role in eradicating invasive fishes, parasites and diseases. Fish Management Chemicals Subcommittee. <http://www.fisheriessociety.org/rotenone/> and modified with information from the Rotenone Review Advisory Committee Final Report.

⁴Source: Modified from Finlayson, B.J., R. Schnick, R. Cailteux, L. DeMong, W. Horton, W. McClay, C. Thompson, and G. Tichacekl. 2000. Rotenone use in fisheries management: administrative and technical guidelines. American Fisheries Society. Bethesda, Maryland.

Literature Cited

Bové, J., D. Prou, C. Perier, and S. Przedborski. 2005. Toxin-induced models of Parkinson's disease. *NeuroRx* 2:484-494.

Dawson, V. 1986. Absorption/desorption of rotenone by bottom sediments. U.S. Fish and Wildlife Service, National Fisheries Research Laboratory, La Crosse, Wisconsin.

Durkin, P.R. 2008. Rotenone Human Health and Ecological Risk Assessment: FINAL REPORT. USDA Forest Service Contract: AG-3187-C-06-0010, USDA Forest Order Number: AG-43ZP-D-07-0010, SERA Internal Task No. 52-11. Syracuse Environmental Research Associates, Inc. Fayetteville, New York. 152 pages + appendices. Available at: http://www.fs.fed.us/foresthealth/pesticide/pdfs/0521103a_Rotenone.pdf

EPA. 2006. Memorandum: Rotenone: final HED chapter of the registration eligibility decision (RED). PC Code: 071003. DP Barcode: D328478. Washington, D.C.

EPA. 2007. Reregistration eligibility decision for rotenone. EPA 738-R-07-005. Case No. 0255.

Finlayson, B.J., R. Schnick, R. Cailteux, L. DeMong, W. Horton, W. McClay, C. Thompson, and G. Tichacekl. 2000. Rotenone use in fisheries management: administrative and technical guidelines. American Fisheries Society. Bethesda, Maryland.

Firestone, J.A., J.I. Lundin, K.M. Powers, T. Smith-Weller, G.M. Franklin, P.D. Swanson, W.T. Longstreth Jr., and H. Checkoway. 2010. Occupational factors and risk of Parkinson's disease: a population-based case-control study. *American Journal of Industrial Medicine* 53:217-223.

Hertzman, C., M. Wiens, and B. Snow. 1994. A case-control study of Parkinson's disease in a horticultural region of British Columbia. *Movement Disorders* 9(1):69-75.

McMillin, S. and B.J. Finlayson. 2008. Chemical residues in water and sediment following rotenone application to Lake Davis, California 2007. California Department of Fish and Game, Office of Spill Prevention and Response, Pesticide Investigations Unit, OSPR Administrative Report 08-01, Rancho Cordova, California.

Raffaele, K.C., S.V. Vulimiri, and T.F. Bateson. 2011. Benefits and barriers to using epidemiology data in environmental risk assessment. *The Open Epidemiology Journal* 4:99-105.

Ridley , M., J. Moran, and M. Singleton. 2007. Isotopic survey of Lake Davis and the local groundwater. Lawrence Livermore National Laboratory, Environmental Protection Department, Environmental Restoration Division, UCRL-TR-233936.

Skaar, D. 2002. Brief summary of persistence and toxic effects of rotenone. *Montana Fish, Wildlife, and Parks*.

Tanner, C.M., G.W. Ross, S.A. Jewell, R.A. Hauser, J. Jankovic, S.A. Factor, S. Bressman, A. Deligtisch, C. Marras, K.E. Lyons, G.S. Bhudhikanok, D.F. Roucoux, C. Meng, R.D. Abbott, and J.W. Langston. 2009. Occupation and risk of Parkinsonism. *Arch Neurology* 66(9):1106-1113.

Tanner, C.M., F. Kamel, W. Ross, J.A. Hoppin, S.M. Goldman, M. Korell, C. Marras, G.S. Bhudhikanok, M. Kasten, A.R. Chade, K. Comyns, M.B. Richards, C. Meng, B. Priestley, H.H. Fernandex, F. Cambi, D.M. Umbach, A. Blair, D.P. Sandler, and J.W. Langston. 2011. Rotenone, paraquat, and Parkinson's disease. *Environmental Health Perspectives* 119(6):866-872.