Hexazinone
Analysis of Risks
to
Endangered and Threatened Salmon and Steelhead

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Summary

Hexazinone is a herbicide registered nationally for control of weeds on agricultural crops and forestry. A Reregistration Eligibility Decision (RED) that includes an ecological risk assessment for aquatic fish, invertebrates, and plants, was issued in September 1994. Hexazinone is practically non-toxic to fishes and practically non-toxic to slightly toxic to freshwater and marine invertebrates. OPP does not categorize toxicity to plants; however, the data indicate that hexazinone is toxic to aquatic plants. The Estimated Environmental Concentrations (EECs) were modeled with a Tier 2 model, PRZM-EXAMS, for current labeled application rates. Acute and chronic risk quotients were calculated from these EECs and the available toxicity values indicate no direct risk to endangered fish and no indirect effect to their food supply of invertebrates. Also, the risk quotients indicate that there are no indirect effects to pacific salmon and steelhead from loss of plant cover. I conclude that hexazinone will not present a direct effect on Pacific salmon and steelhead through acute mortality or long-term sublethal effects and no indirect effects through loss of their food supply or loss of plant cover.

Introduction

This analysis was prepared by the U.S. Environmental Protection Agency (EPA) Office of Pesticides Programs (OPP) to evaluate the risks of hexazinone to 3 Environmentally Significant Units (ESUs) of threatened and endangered Pacific salmon and steelhead (Northern California/Southern Oregon coastal coho salmon, Central Valley California steelhead, and South-central California steelhead).

The general aquatic risk assessment presented in the "Reregistration Eligibility Decision (RED) Hexazinone" issued in September, 1994 was the starting basis for my assessment (Attachment A). This document (US EPA, 1994) is on line at: http://cfpub.epa.gov/oppref/rereg/status.cfm?show=rereg#C.

Problem Formulation - The purpose of this analysis is to determine whether the registration of hexazinone as an herbicide for use on alfalfa and forestry may affect certain threatened and endangered (T&E or listed) Pacific anadromous salmon and steelhead or adversely modify their designated critical habitat.

Scope - This analysis is specific to the following listed Pacific salmon and steelhead and the watersheds in which they occur: Northern California/Southern Oregon coastal coho salmon, Central Valley California steelhead, and South-central California steelhead. It is acknowledged that hexazinone is registered for uses that may occur outside this geographic scope and additional use patterns, and that additional analyses may be required to address other T&E species in the Pacific states as well as across the United States.

Contents

Attachments:

1. Background

Under section 7 of the Endangered Species Act, the Office of Pesticide Programs (OPP) of the U. S. Environmental Protection Agency (EPA) is required to consult on actions that may affect Federally listed endangered or threatened species or that may adversely modify designated critical habitat. Situations where a pesticide may affect a fish, such as any of the salmonid species listed by the National Marine Fisheries Service (NMFS), include either direct or indirect effects on the fish. Direct effects result from exposure to a pesticide at levels that may cause harm.

Acute Toxicity - Relevant acute data are derived from standardized toxicity tests with lethality as the primary endpoint. These tests are conducted with what is generally accepted as the most sensitive life stage of fish, i.e., very young fish from 0.5-5 grams in weight, and with species that are usually among the most sensitive. These tests for pesticide registration include analysis of observable sublethal effects as well. The intent of acute tests is to statistically derive a median effect level; typically the effect is lethality in fish (LC50) or immobility in aquatic invertebrates (EC50). Typically, a standard fish acute test will include concentrations that cause no mortality, and often no observable sublethal effects, as well as concentrations that would cause 100% mortality. By looking at the effects at various test concentrations, a dose-response curve can be derived, and one can statistically predict the effects likely to occur at various pesticide concentrations; a well done test can even be extrapolated, with caution, to concentrations below those tested (or above the test concentrations if the highest concentration did not produce 100% mortality).

OPP typically uses qualitative descriptors to describe different levels of acute toxicity, the most likely kind of effect of modern pesticides (Table 1). These are widely used for comparative purposes, but must be associated with exposure before any conclusions can be drawn with respect to risk. Pesticides that are considered highly toxic or very highly toxic are required to have a label statement indicating that level of toxicity. The FIFRA regulations [40CFR158.490(a)] do not require calculating a specific LC50 or EC50 for pesticides that are practically non-toxic; the LC50 or EC50 would simply be expressed as >100 ppm. When no lethal or sublethal effects are observed at 100 ppm, OPP considers the pesticide will have “no effect” on the species.

Table 1. Qualitative descriptors for categories of fish and aquatic invertebrate toxicity (from Zucker, 1985)

LC50 or EC50	Category description
< 0.1 ppm	Very highly toxic
0.1- 1 ppm	Highly toxic
>1 < 10 ppm	Moderately toxic
> 10 < 100 ppm	Slightly toxic
> 100 ppm	Practically non-toxic

Comparative toxicology has demonstrated that various species of scaled fish generally have equivalent sensitivity, within an order of magnitude, to other species of scaled fish tested under the same conditions. Exceptions are known to occur for only an occasional pesticide, as based on the several dozen fish species that have been frequently tested. Sappington et al. (2001), Beyers et al. (1994) and Dwyer et al. (1999), among others, have shown that endangered and threatened fish tested to date are similarly sensitive, on an acute basis, to a variety of pesticides and other chemicals as are their non-endangered counterparts.

Chronic Toxicity - OPP evaluates the potential chronic effects of a pesticide on the basis of several types of tests. These tests are often required for registration, but not always. If a pesticide has essentially no acute toxicity at relevant concentrations, or if it degrades very rapidly in water, or if the nature of the use is such that the pesticide will not reach water, then chronic fish tests may not be required [40CFR158.490]. Chronic fish tests primarily evaluate the potential for reproductive effects and effects on the offspring. Other observed sublethal effects are also required to be reported. An abbreviated chronic test, the fish early-life stage test, is usually the first chronic test conducted and will indicate the likelihood of reproductive or chronic effects at relevant concentrations. If such effects are found, then a full fish life-cycle test will be conducted. If the nature of the chemical is such that reproductive effects are expected, the abbreviated test may be skipped in favor of the full life-cycle test. These chronic tests are designed to determine a “no observable effect level” (NOEL) and a “lowest observable effect level” (LOEL). A chronic risk requires not only chronic toxicity, but also chronic exposure, which can result from a chemical being persistent and resident in an environment (e.g., a pond) for a chronic period of time or from repeated applications that transport into any environment such that exposure would be considered “chronic”.

As with comparative toxicology efforts relative to sensitivity for acute effects, EPA, in conjunction with the U. S. Geological Survey, has a current effort to assess the comparative toxicology for chronic effects also. Preliminary information indicates, as with the acute data, that endangered and threatened fish are again of similar sensitivity to similar non-endangered species.

Metabolites and Degradates - Information must be reported to OPP regarding any pesticide metabolites or degradates that may pose a toxicological risk or that may persist in the environment [40CFR159.179]. Toxicity and/or persistence test data on such compounds may be required if, during the risk assessment, the nature of the metabolite or degradate and the amount that may occur in the environment raises a concern. If actual data or structure-activity analyses are not available, the requirement for testing is based upon best professional judgement.

Inert Ingredients - OPP does take into account the potential effects of what used to be termed “inert” ingredients, but which are beginning to be referred to as “other ingredients”. OPP has classified these ingredients into several categories. A few of these, such as nonylphenol, can no longer be used without including them on the label with a specific statement indicating the potential toxicity. Based upon our internal databases, I can find no product in which nonylphenol is now an ingredient. Many others, including such ingredients as clay, soybean oil, many polymers, and chlorophyll, have been evaluated through structure-activity analysis or data and determined to be of minimal or no toxicity. There exist also two additional lists, one for inerts with potential toxicity which are considered a testing priority, and one for inerts unlikely to be toxic, but which cannot yet be said to have negligible toxicity. Any new inert ingredients are required to undergo testing unless it can be demonstrated that testing is unnecessary.

The inerts efforts in OPP are oriented only towards toxicity at the present time, rather than risk. It should be noted, however, that very many of the inerts are in exceedingly small amounts in pesticide products. While some surfactants, solvents, and other ingredients may be present in fairly large amounts in various products, many are present only to a minor extent. These include such things as coloring agents, fragrances, and even the printers ink on water soluble bags of pesticides. Some of these could have moderate toxicity, yet still be of no consequence because of the negligible amounts present in a product. If a product contains inert ingredients in sufficient quantity to be of concern, relative to the toxicity of the active ingredient, OPP attempts to evaluate the potential effects of these inerts through data or structure-activity analysis, where necessary.

For a number of major pesticide products, testing has been conducted on the formulated end-use products that are used by the applicator. The results of fish toxicity tests with formulated products can be compared with the results of tests on the same species with the active ingredient only. A comparison of the results should indicate comparable sensitivity, relative to the percentage of active ingredient in the technical versus formulated product, if there is no extra activity due to the combination of inert ingredients. I note that the "comparable" sensitivity must take into account the natural variation in toxicity tests, which is up to 2-fold for the same species in the same laboratory under the same conditions, and which can be somewhat higher between different laboratories, especially when different stocks of test fish are used.

The comparison of formulated product and technical ingredient test results may not provide specific information on the individual inert ingredients, but rather is like a "black box" which sums up the effects of all ingredients. I consider this approach to be more appropriate than testing each individual inert and active ingredient because it incorporates any additivity, antagonism, and synergism effects that may occur and which might not be correctly evaluated from tests on the individual ingredients. I do note, however, that we do not have aquatic data on most formulated products, although we often have testing on one or perhaps two formulations of an active ingredient.

Risk - An analysis of toxicity, whether acute or chronic, lethal or sublethal, must be combined with an analysis of how much will be in the water, to determine risks to fish. Risk is a combination of exposure and toxicity. Even a very highly toxic chemical will not pose a risk if there is no exposure, or very minimal exposure relative to the toxicity. OPP uses a variety of chemical fate and transport data to develop "estimated environmental concentrations" (EECs) from a suite of established models. The development of aquatic EECs is a tiered process.

The first tier screening model for EECs is with the GENEEC program, developed within OPP, which uses a generic site (in Yazoo, MS) to stand for any site in the U. S. The site choice was intended to yield a maximum exposure, or "worst-case," scenario applicable nationwide, particularly with respect to runoff. The model is based on a 10 hectare watershed that surrounds a one hectare pond, two meters deep. It is assumed that all of the 10 hectare area is treated with the pesticide and that any runoff would drain into the pond. The model also incorporates spray drift, the amount of which is dependent primarily upon the droplet size of the spray. OPP assumes that if this model indicates no concerns when compared with the appropriate toxicity data, then further analysis is not necessary as there would be no effect on the species.

It should be noted that prior to the development of the GENEEC model in 1995, a much more crude approach was used to determining EECs. Older reviews and Reregistration Eligibility Decisions (REDs) may use this approach, but it was excessively conservative and does not provide a sound basis for modern risk assessments. For the purposes of endangered species consultations, we will attempt to revise this old approach with the GENEEC model, where the old screening level raised risk concerns.

When there is a concern with the comparison of toxicity with the EECs identified in GENEEC model, a more sophisticated PRZM-EXAMS model is run to refine the EECs if a suitable scenario has been developed and validated. The PRZM-EXAMS model was developed with widespread collaboration and review by chemical fate and transport experts, soil scientists, and agronomists throughout academia, government, and industry, where it is in common use. As with the GENEEC model, the basic model remains as a 10 hectare field surrounding and draining into a 1 hectare pond. Crop scenarios have been developed by OPP for specific sites, and the model uses site-specific data on soils, climate (especially precipitation), and the crop or site. Typically, site-scenarios are developed to provide for a worst-case analysis for a particular crop in a particular geographic region. The development of site scenarios is very time consuming; scenarios have not yet been developed for a number of crops and locations. OPP attempts to match the crop(s) under consideration with the most appropriate scenario. For some of the older OPP analyses, a very limited number of scenarios were available. As more scenarios become available and are geographically appropriate to selected T&E species, older models used in previous analyses may be updated.

Finally, the applicability of the overall EEC scenario, i.e., the 10 hectare watershed draining into a one hectare farm pond, may not be appropriate for a number of T&E species living in rivers or lakes. This scenario is intended to provide a "worst-case" assessment of EECs, but very many T&E fish do not live in ponds, and very many T&E fish do not have all of the habitat surrounding their environment treated with a pesticide. OPP does believe that the EECs from the farm pond model do represent first order streams, such as those in headwaters areas (Effland, et al. 1999). In many agricultural areas, those first order streams may be upstream from pesticide use, but in other areas, or for some non-agricultural uses such as forestry, the first order streams may receive pesticide runoff and drift. However, larger streams and lakes will very likely have lower, often considerably lower, concentrations of pesticides due to more dilution by the receiving waters. In addition, where persistence is a factor, streams will tend to carry pesticides away from where they enter into the streams, and the models do not allow for this. The variables in size of streams, rivers, and lakes, along with flow rates in the lentic waters and seasonal variation, are large enough to preclude the development of applicable models to represent the diversity of T&E species' habitats. We can simply qualitatively note that the farm pond model is expected to overestimate EECs in larger bodies of water.

Indirect Effects - We also attempt to protect listed species from indirect effects of pesticides. We note that there is often not a clear distinction between indirect effects on a listed species and adverse modification of critical habitat (discussed below). By considering indirect effects first, we can provide appropriate protection to listed species even where critical habitat has not been designated. In the case of fish, the indirect concerns are routinely assessed for food and cover.

The primary indirect effect of concern would be for the food source for listed fish. These are best represented by potential effects on aquatic invertebrates, although aquatic plants or plankton may be relevant food sources for some fish species. However, it is not necessary to protect individual organisms that serve as food for listed fish. Thus, our goal is to ensure that pesticides will not impair populations of these aquatic arthropods. In some cases, listed fish may feed on other fish. Because our criteria for protecting the listed fish species is based upon the most sensitive species of fish tested, then by protecting the listed fish species, we are also protecting the species used as prey.

In general, but with some exceptions, pesticides applied in terrestrial environments will not affect the plant material in the water that provides aquatic cover for listed fish. Application rates for herbicides are intended to be efficacious, but are not intended to be excessive. Because only a portion of the effective application rate of an herbicide applied to land will reach water through runoff or drift, the amount is very likely to be below effect levels for aquatic plants. Some of the applied herbicides will degrade through photolysis, hydrolysis, or other processes. In addition, terrestrial herbicide applications are efficacious in part, due to the fact that the product will tend to stay in contact with the foliage or the roots and/or germinating plant parts, when soil applied. With aquatic exposures resulting from terrestrial applications, the pesticide is not placed in immediate contact with the aquatic plant, but rather reaches the plant indirectly after entering the water and being diluted. Aquatic exposure is likely to be transient in flowing waters. However, because of the exceptions where terrestrially applied herbicides could have effects on aquatic plants, OPP does evaluate the sensitivity of aquatic macrophytes to these herbicides to determine if populations of aquatic macrophytes that would serve as cover for T&E fish would be affected.

For most pesticides applied to terrestrial environment, the effects in water, even lentic water, will be relatively transient. Therefore, it is only with very persistent pesticides that any effects would be expected to last into the year following their application. As a result, and excepting those very persistent pesticides, we would not expect that pesticidal modification of the food and cover aspects of critical habitat would be adverse beyond the year of application. Therefore, if a listed salmon or steelhead is not present during the year of application, there would be no concern. If the listed fish is present during the year of application, the effects on food and cover are considered as indirect effects on the fish, rather than as adverse modification of critical habitat.

Designated Critical Habitat - OPP is also required to consult if a pesticide may adversely modify designated critical habitat. In addition to the indirect effects on the fish, we consider that the use of pesticides on land could have such an effect on the critical habitat of aquatic species in a few circumstances. For example, use of herbicides in riparian areas could affect riparian vegetation, especially woody riparian vegetation, which possibly could be an indirect effect on a listed fish. However, there are very few pesticides that are registered for use on riparian vegetation, and the specific uses that may be of concern have to be analyzed on a pesticide by pesticide basis. In considering the general effects that could occur and that could be a problem for listed salmonids, the primary concern would be for the destruction of vegetation near the stream, particularly vegetation that provides cover or temperature control, or that contributes woody debris to the aquatic environment. Destruction of low growing herbaceous material would be a concern if that destruction resulted in excessive sediment loads getting into the stream, but such increased sediment loads are insignificant from cultivated fields relative to those resulting from the initial cultivation itself. Increased sediment loads from destruction of vegetation could be a concern in uncultivated areas. Any increased pesticide load as a result of destruction of terrestrial herbaceous vegetation would be considered a direct effect and would be addressed through the modeling of estimated environmental concentrations. Such modeling can and does take into account the presence and nature of riparian vegetation on pesticide transport to a body of water.

Risk Assessment Processes - All of our risk assessment procedures, toxicity test methods, and EEC models have been peer-reviewed by OPP's Science Advisory Panel. The data from toxicity tests and environmental fate and transport studies undergo a stringent review and validation process in accordance with "Standard Evaluation Procedures" published for each type of test. In addition, all test data on toxicity or environmental fate and transport are conducted in accordance with Good Laboratory Practice (GLP) regulations (40 CFR Part 160) at least since the GLPs were promulgated in 1989.

The risk assessment process is described in "Hazard Evaluation Division - Standard Evaluation Procedure - Ecological Risk Assessment" by Urban and Cook (1986) (termed Ecological Risk Assessment SEP below), which has been separately provided to National Marine Fisheries Service staff. Although certain aspects and procedures have been updated throughout the years, the basic process and criteria still apply. In a very brief summary: the toxicity information for various taxonomic groups of species is quantitatively compared with the potential exposure information from the different uses and application rates and methods. A risk quotient of toxicity divided by exposure is developed and compared with criteria of concern. The criteria of concern presented by Urban and Cook (1986) are presented in Table 2.

Table 2. Risk quotient criteria for direct and indirect effects on T&E fish

Test data	Risk quotient	Presumption
Acute LC_{50}	>0.5	Potentially high acute risk
Acute LC_{50}	>0.1	Risk that may be mitigated through restricted use classification
Acute LC_{50}	>0.05	Endangered species may be affected acutely, including sublethal effects
Chronic NOEC	>1	Chronic risk; endangered species may be affected chronically, including reproduction and effects on progeny
Acute invertebrate LC_{50} [a]	>0.5	May be indirect effects on T&E fish through food supply reduction
Aquatic plant acute EC_{50} [a]	>1[b]	May be indirect effects on aquatic vegetative cover for T&E fish

a. Indirect effects criteria for T&E species are not in Urban and Cook (1986); they were developed subsequently.
b. This criterion has been changed from our earlier requests. The basis is to bring the endangered species criterion for indirect effects on aquatic plant populations in line with EFED's concern levels for these populations.

The Ecological Risk Assessment SEP (pages 2-6) discusses the quantitative estimates of how the acute toxicity data, in combination with the slope of the dose-response curve, can be used to predict the percentage mortality that would occur at the various risk quotients. The discussion indicates that using a "safety factor" of 10, as applies for restricted use classification, one individual in 30,000,000 exposed to the concentration would be likely to die. Using a "safety factor" of 20, as applies to aquatic T&E species, would exponentially increase the margin of safety. It has been calculated by one pesticide registrant (without sufficient information for OPP to validate that number), that the probability of mortality occurring when the LC50 is 1/20th of the EEC is 2.39×10^{-9}, or less than one individual in ten billion. It should be noted that the discussion (originally part of the 1975 regulations for FIFRA) is based upon slopes of primarily organochlorine pesticides, stated to be 4.5 probits per log cycle at that time. As organochlorine pesticides were phased out, OPP undertook an analysis of more current pesticides based on data reported by Johnson and Finley (1980), and determined that the "typical" slope for aquatic toxicity tests for the "more current" pesticides was 9.95. Because the slopes are based upon logarithmically transformed data, the probability of mortality for a pesticide with a 9.95 slope is again exponentially less than for the originally analyzed slope of 4.5.

The above discussion focuses on mortality from acute toxicity. OPP is concerned about other direct effects as well. For chronic and reproductive effects, our criteria ensures that the EEC is below the no-observed-effect-level, where the "effects" include any observable sublethal effects. Because our EEC values are based upon “worst-case” chemical fate and transport data and a small farm pond scenario, it is rare that a non-target organism would be exposed to such concentrations over a period of time, especially for fish that live in lakes or in streams (best professional judgement). Thus, there is no additional safety factor used for the no-observed-effect-concentration, in contrast to the acute data where a safety factor is warranted because the endpoints are a median probability rather than no effect.

Sublethal Effects - With respect to sublethal effects, Tucker and Leitzke (1979) did an extensive review of existing ecotoxicological data on pesticides. Among their findings was that sublethal effects as reported in the literature did not occur at concentrations below one-fourth to one-sixth of the lethal concentrations, when taking into account the same percentages or numbers affected, test system, duration, species, and other factors. This was termed the “6x hypothesis”. Their review included cholinesterase inhibition, but was largely oriented towards externally observable parameters such as growth, food consumption, behavioral signs of intoxication, avoidance and repellency, and similar parameters. Even reproductive parameters fit into the hypothesis when the duration of the test was considered. This hypothesis supported the use of lethality tests for use in assessing acute ecotoxicological risk, and the lethality tests are well enough established and understood to provide strong statistical confidence, which can not always be achieved with sublethal effects. By providing an appropriate safety factor, the concentrations found in lethality tests can therefore generally be used to protect from sublethal effects. As discussed earlier, the entire focus of the early-life-stage and life-cycle chronic tests is on sublethal effects.

In recent years, Moore and Waring (1996) challenged Atlantic salmon with diazinon and observed effects on olfaction as relates to reproductive physiology and behavior. Their work indicated that diazinon could have sublethal effects of concern for salmon reproduction. However, the nature of their test system, direct exposure of olfactory rosettes, could not be quantitatively related to exposures in the natural environment. Subsequently, Scholz et al. (2000) conducted a non-reproductive behavioral study using whole Chinook salmon in a model stream system that mimicked a natural exposure that is far more relevant to ecological risk assessment than the system used by Moore and Waring (1996). The Scholz et al. (2000) data indicate potential effects of diazinon on Chinook salmon behavior at very low levels, with statistically significant effects at nominal diazinon exposures of 1 ppb, with apparent, but non-significant effects at 0.1 ppb.

It would appear that the Scholz et al (2000) work contradicts the 6x hypothesis for acute effects. The research design, especially the nature and duration of exposure, of the test system used by Scholz et al (2000), along with a lack of dose-response, precludes comparisons with lethal levels in accordance with the 6x hypothesis as used by Tucker and Leitzke (1979). Nevertheless, it is known that olfaction is an exquisitely sensitive sense. And this sense may be particularly well developed in salmon, as would be consistent with its use by salmon in homing (Hasler and Scholz, 1983). So the contradiction of the 6x hypothesis is not surprising. As a result of these findings, the 6x hypothesis needs to be re-evaluated with respect to olfaction. At the same time, because of the sensitivity of olfaction and because the 6x hypothesis has generally stood the test of time otherwise, it would be premature to abandon the hypothesis for other acute sublethal effects until there are additional data.

2. Description of hexazinone

a. Chemical overview

- ❑ Common Name: Hexazinone
- ❑ Chemical Name: 3-cyclohexyl-6-(dimethylamino)-1-methyl-Striazine-2,4-(1H,3H)-dione
- ❑ Chemical Family: Triazine-dione
- ❑ Case Number: 0266
- ❑ CAS Registry Number: 51235-04-2
- ❑ OPP Chemical Code: 107201
- ❑ Molecular Weight: 252.3
- ❑ Empirical Formula: $C_{12}H_{20}N_4O_2$
- ❑ Trade and Other Names: Velpar™, Pronone™
- ❑ Basic Manufacturer: DuPont Agricultural Products

Technical hexazinone is a white crystalline solid with a melting point of 113.5 C and a bulk density of 0.61 g/mL. Its solubility in water at 25 C is 2.98 g/100g. Hexazinone solubilities in methanol, acetone, and hexane are 265, 79, and 0.3 g/100 g, respectively.

b. Registered uses

The following is based on the currently registered uses of hexazinone:

- ❑ Type of Agent: Herbicide
- ❑ Classification: General use
- ❑ Summary of Sites:

- Terrestrial Food Crop: Blueberry, pineapple, sugarcane

- Terrestrial Food/Feed Crops:Agricultural rights-of-way/fencerows/hedgerows, pineapple, sugarcane

- Terrestrial Non-Food and Feed Crop: Blueberry, Christmas tree plantations, industrial areas (outdoor), nonagricultural, rights-of-way/fencerows/hedgerows, nonagricultural uncultivated areas/soils, alfalfa, pastures, rangeland, urban areas, drainage systems, forestry

- Public Health: none

- Target Pests: Woody plants and weeds

❑ Formulation Types Registered:

- Technical Grade/Manufacturing-Use Product (MUP): Technical Grade Active Ingredient (98%)

- End-use Product: Emulsifiable concentrate, Granular, Liquid-ready to use, Pelleted/tableted, Soluble concentrate/solid, Water dispersible granules (dry flowable)

❑ Methods of Application:

- Equipment: Aircraft; Backpack sprayer; Band sprayer; Boom sprayer; By hand; Fixed-wing aircraft; Granule applicator; Ground; Hand held sprayer; Hand-carried granule applicator; Handgun; Helicopter; Injection equipment; Knapsack sprayer; Manual granule applicator; Sprayer; Spreader; Stroller boom; Tank-type sprayer; Tree injection equipment; Truck-mounted sprayer

- Method and Rate: Depending on site treated and formulation type, maximum label application rates range from 0.225 - 8 lb ai/acre for spray; 0.5-12 lb ai/acre for soil broadcast treatment, 0.001-0.002 lb ai/1" stem diameter for spot soil treatment, and 0,002-0.004 lb ai/3 ft of plant height for spot soil treatment. These listed rates are the maximum rates identified in the labels. The manufacturer labels, specific to the Pacific Northwest and California, identify the maximum rate for alfalfa application as 1.52 lb ai/acre and forest application as 5.0 lb a.i./A.

- Timing:After bud break; Before bud break; Delayed dormant; Dormant; Early postemergence; Early spring; Early summer; Early tillering; Established plantings; Fall; Foliar; Intercrop; Late postemergence; Late winter; Layby; Postemergence; Postplant; Posttransplant; Prebloom; Preemergence; Preplant; Pretransplant; Ratoon; Seedling stage; Spring; Stubble; Summer; When needed; Winter.

d. Hexazinone usage

According to OPP's Quantitative Use Assessment (QUA) for hexazinone (Table 3) and based on available pesticide survey usage information for the years of 1991 through 2000, an annual estimate of hexazinone's total domestic annual usage averaged approximately 400,000 pounds active ingredient (lb ai) for over 700,000 acre treated. Its largest markets, in terms of total pounds active ingredient, are allocated to alfalfa (63%), woodland (22%), and pasture/rangeland (5%). Crops with a high percentage of total U.S. planted acres treated include nurseries (4%), and alfalfa (2%). Crops with less than 1 percent of the site treated include berries, other hay, landscape, pasture/rangeland, sugarcane, and woodland. See Attachment B for the QUA document.

Table 3. Hexazinone Estimated Usage for Representative Sites (source: QUA Hexazinone 2001)

	Acres			Pounds A.I.	Application Rate
	Planted	Treated			
	1,000		%	1,000	lbs.a.i./A
Alfalfa	25,000	506	2	257	0.5
Berries	100,000	11	<1	10	0.9
Hay, Other	33,000	24	<1	8	0.3
Landscape	30,000	5	<1	10	2.0
Nurseries	400	15	4	10	0.7
Pasture/Rangeland	90,000	77	<1	20	0.2
Sugarcane	1,000	2	<1	1	0.5
Woodland	63,000	80	<1	89	1.1
Total		720		405	

SOURCES: EPA data, USDA, and National Center for Food and Agricultural Policy

The latest information for California pesticide use is for the year 2002 [URL: http://www.cdpr.ca.gov/docs/pur/purmain.htm]. The reported information to the County Agricultural Commissioners includes pounds used, acres treated for agricultural and certain other uses, and the specific location treated. The pounds and acres are reported to the state, but the specific location information is retained at the county level and is not readily available. Table 4 presents hexazinone uses in California for 2002.

Table 4. Use of hexazinone by crop or site in California in 2002

Site	Pounds of Active Ingredient Applied	Number of Applications	Acres Treated
Alfalfa	61,660.90	2,007	120,833.45
Christmas Tree	4.50	3	13.50
Forest, Timberland	40,851.33	403	17,830.40
Landscape Maintenance	5.79		
Non-Outdoor Plants in Containers	24.00		10.50
Oat	3.05	1	8.00
Rangeland	12.00	1	15.00
Regulatory Pest Control	5.74		
Research Commodity	11.00		
Rights of Way	1,072.18		
Structural Pest Control	37.50		
Unknown	10.00	1	20.00
Chemical Total	103,697.97	2,416	

The total pounds of active ingredient in the above table represents the amount of hexazinone applied in the entire state of California. Table 5 represents the amount of hexazinone applied and the number of acres treated in counties of the subject ESUs in California. Less than half (55,789.43 lb ai) of the hexazinone used in California is used in these ESUs where the subject salmon and steelhead occur.

Table 5. Pounds of hexazinone by crop or site in three ESUs in California 2002 (source: http://www.cdpr.ca.gov/docs/pur/purmain.htm).

ESU	Pounds ai	Acres Treated
Alfalfa		
Northern California/Southern Oregon coastal coho[1]	0	0
Central Valley California steelhead[2]	40771.24	66385.54
South-central California Coast steelhead[3]	1038.26	1932
Total	41809.50	68314.54
Forestry		
Northern California/Southern Oregon coastal coho[1]	0	0
Central Valley California steelhead[2]	13979.93	5534.3
South-central California Coast steelhead[3]	0	0
Total	13979.93	5534.3

[1] Counties include Del Norte, Humbolt, Lake, Mendocino, and Trinity.
[2] Counties include Alameda, Amador, Butte, Calaveras, Colusa, Contra Costa, Glenn, Marin, Merced, Nevada, Placer, Sacramento, San Joaquin, San Mateo, San Francisco, Shasta, Solane, Sonoma, Stanislaus, Sutter, Tehama, Tuolumne, Yolo, Yuba.
[3] Counties include Monterey, San Benito, San Luis Obispo, Santa Cruz.

There are limited data available on the amount of hexazinone used in Oregon. The National Pesticide Use Database (http://www.ncfap.org/database/default/htm) provides some information on hexazinone usage in the Pacific Northwest. For alfalfa uses, estimates are provided for Oregon; hexazinone is used on about 14% of alfalfa acreage with a typical rate of 0.523 lb ai/acre. The total amount of hexazinone applied to these acres is 68,003 lb. Table 6 represents the number of acres of alfalfa harvested in the counties in Oregon of the Northern California/Southern Oregon coastal ESU (NASS, Census of Agriculture 2002). There are no estimates provided for forestry use in Oregon.

Table 6. Acres of hexazinone by crop or site in the Southern Oregon ESU (source:NASS Census of Agriculture 2002)

County	Acres Harvested
Alfalfa	
Douglas	1556
Jackson	5895
Josephine	810
Klamath	72491
Total	80752

3. General aquatic risk assessment for endangered and threatened salmon and steelhead

a. Aquatic toxicity of hexazinone

There is a modest amount of aquatic toxicity data on hexazinone. Data submitted to support registration were generated in accordance with Good Laboratory Practice regulations and have been through OPP's rigorous validation requirements for data used in assessments; these data are used in preference to other data.

(1) Toxicity of technical grade hexazinone

The acute toxicity data indicate that technical grade hexazinone is practically non-toxic to both warmwater and coldwater fishes and practically non-toxic to slightly toxic to freshwater and marine invertebrates. Data from the RED and the EFED database are presented in Tables 7 through 11, and the data from AQUIRE is presented in Table 12.

Table 7. Acute toxicity of hexazinone to freshwater fish (source: EFED Pesticide Ecotoxicity Database and RED)

Species	Scientific Name	% ai	96-h LC 50 (ppm)	Toxicity Category
Bluegill Sunfish	*Lepomis macrochirus*	25	238	Practically non-toxic
		97.5	<420	Practically non-toxic
		99	>100	Practically non-toxic
Brook trout	*Salvelinus fontinalis*	99	>100	Practically non-toxic
		90	>100	Practically non-toxic
Fathead minnow	*Pimephales promelas*	97.5	274	Practically non-toxic
Rainbow trout	*Oncorhynchus mykiss*	25	160	Practically non-toxic
		90	>180	Practically non-toxic
		97.5	<420	Practically non-toxic
		99	>180	Practically non-toxic

Table 8. Acute toxicity of hexazinone to freshwater invertebrates (source: EFED Pesticide Ecotoxicity Database and RED)

Species	Scientific Name	% ai	48-h EC50 (ppm)	Toxicity Category
Water flea	*Daphnia magna*	25	110	Practically non-toxic
		95	151.6	Practically non-toxic

Table 9. Acute toxicity of hexazinone to estuarine and marine invertebrates (source: EFED Pesticide Ecotoxicity Database and RED)

Species	Scientific Name	% ai	96-h LC50 (ppm)	Toxicity Category
Crustacea				
Fiddler crab	*Uca pugilatot*	95	>1000	Practically non-toxic
Grass shrimp	*Palaemonetes pugio*	95	78	Slightly toxic
Mollusca				
Eastern Oyster	*Crassostrea virginica*	95	EC50 = 560 (48-h)	Practically non-toxic
			EC50 = 320 (48-h)	Practically non-toxic

Adverse chronic effects on survival or growth of freshwater fish and invertebrates occurred at exposure concentrations of 35.5 ppm of technical hexazinone for fish and 50, 81, and 560 ppm for invertebrates.

Table 10. Chronic toxicity of hexazinone to fish and invertebrates (source: EFED Pesticide Ecotoxicity Database and RED)

Species	Scientific Name	% ai	Duration	Endpoints	NOEL (ppm)	LOEC (ppm)
Fathead minnow	*Pimephales promelas*	98	39d	Fish Length	17	35.5
Water flea	*Daphnia magna*	89.3	21d	Reproduction	20	50
		>98	21d	Survival	29	81

OPP does not categorize toxicity to plants. However, the data indicate that hexazinone is toxic to aquatic plants (table 11).

Table 11. Phytotoxicity of hexazinone to aquatic plant species (source: EFED Pesticide Ecotoxicity Database and RED)

Species	Scientific Name	% ai	NOEL (ppm)	EC50 (ppm)
Blue-green algae	*Anabaena flos-aquae*	100	0.15	0.21
Duckweed	*Lemna gibba*	100	No Data	0.0374
Freshwater diatom	*Navicula pelliculosa*	100	0.0035	0.012
Green algae	*Selenastrum capricornutum*	100	0.004	0.007
Marine diatom	*Skeletonema costatum*	100	0.004	0.012

There are some aquatic toxicity data for hexazinone from EPA's AQUIRE database (http://www.epa.gov/ecotox/). We did not look at the original papers but report the toxicity values for the toxicity test periods that are analogous to the those required by OPP testing requirements as a means of comparison. The AQUIRE reference numbers for each reported value are provided. The data corroborate the toxicity values reported in EFED's database and the hexazinone RED. The range of acute toxicity values for the active ingredient from AQUIRE are 236 to 1964 ppm for freshwater fish compared to >100 to <420 ppm and 110 to >1000 ppm for fish and invertebrates, respectively, from OPP data. Most of the data in AQUIRE are reported from studies conducted with formulated products, however, the types of formulations and percents active ingredient were not reported. Therefore, it is difficult to directly compare these data with those reported by OPP.

Table 12. Summary of acute toxicity data from EPA AQUIRE database

Species	Scientific Name	Test Chemical*	96-h Toxicity (ppm)	Reference
Pink salmon	*Oncorhynchus gorbuscha*	Active	676	13181
			1408	
			236	
Chum salmon	*Oncorhynchus keta*	Active	934	13181
			285	
Coho salmon	*Oncorhynchus kisutch*	Active	923	13181
			246	
Rainbow trout	*Oncorhynchus mykiss*	Active	872	13181
			1964	
			257	
Sockeye salmon	*Oncorhynchus nerka*	Active	925	13181
			317	
Chinook salmon	*Oncorhynchus tshawytscha*	Active	1096	13181
			317	
Mozambique tilapia	*Tilapia mossambica*	Active	380	3296

*Form. = Test was conducted with formulated products. The product composition and percent active ingredient were not given.
Active = Test was conducted with the active ingredient, but the percent hexazinone was not given.

The AQUIRE database is not always reliable regarding the test being with the formulation or the active ingredient; unless the test indicates an active ingredient, it is inputted into AQUIRE as formulation testing. However, we have seen values reported for the technical material in Mayer & Ellersieck (1986) to be reported in AQUIRE as a formulation test We report the information on formulation versus active ingredient, but we need to note that it is not completely reliable.

(2) Toxicity of multiple active ingredient products

There are no known fish toxicity data on hexazinone products that contain other active pesticide ingredients. Table 13 presents fish toxicity data on these ingredients that are formulated with hexazinone. In all combined products hexazinone is the predominant active ingredient. Two products contain sulfometuron methyl. They contain 63.2% hexazinone and

11.8% sulfometuron methyl and 68.6% hexazinone and 6.5% sulfometuron methyl, respectively. Another product contains diuron with amounts of 13.2% hexazinone and 46.8% diuron. This product is only used in Texas and Louisiana on sugarcane; therefore, diuron will have no effect on the three subject ESUs. The data listed in the table below indicate that hexazinone is less toxic than sulfometuron methyl and diuron.

Table 13. Fish toxicity of other pesticide active ingredients in hexazinone products.

Pesticide	Most sensitive species	Lowest LC50 value (ppm)	Reference	Note
Diuron	Cutthroat trout	0.71	EFED	This product only used in TX and LA on sugarcane
Sulfometuron Methyl	Bluegill sunfish, Rainbow trout	12.5	EFED	Both species had same LC50 value

b. Environmental fate and transport

The environmental fate and transport of hexazinone are presented in the RED on pages 21-24. EECs and model inputs are on pages 36-40.

Based on laboratory and field data, hexazinone appears to be persistent and mobile in soil and aquatic environments. Hexazinone will not hydrolyze under normal environmental conditions. The half-life was reported as 82 days for photodegredation on soil, 216 and 1440 days for aerobic soil metabolism, 230 and >1500 days for anaerobic aquatic metabolism and greater than 2 months for aerobic aquatic metabolism. Field and forestry dissipation studies showed that hexazinone had dissipation half-lives of 123 to 154 and 19 to 59 days, respectively. Off-site movement of hexazinone was attributed to leaching and runoff in the field dissipation study.

Hexazinone may be of concern for groundwater and surface water contamination. Hexazinone can contaminate surface waters by spray drift at application and probably for several months post-application via runoff (primarily by dissolution in runoff water). It may be persistent in some receiving surface waters (particularly those with low microbiological activities and long hydrological resident times). Based upon its low soil/water partitioning, it will probably exist primarily dissolved in the water column. Based on the octanol/water coefficient (15), hexazinone is not expected to accumulate in fish. However, supplemental confined rotational crop data indicated that hexazinone does accumulate in crops grown on treated soil. Even though additional data are needed on the mobility of degradates, the data reviewed suggests that the degradates are also persistent and mobile.

c. Incidents

OPP maintains two databases of reported incidents. The Ecological Incident Information System (EIIS) contains information on environmental incidents which are provided voluntarily to OPP by state and federal agencies and others. There have been periodic solicitations for such information to the states and the U. S. Fish and Wildlife Service. The second database is a compilation of incident information known to pesticide registrants and any data conducted by them that shows results differing from those contained in studies provided to support registration. These data and studies (together termed incidents) are required to be submitted to OPP under regulations implementing FIFRA section 6(a)(2).

The Agency has received documented field kills for terrestrial plants (alfalfa, grasses and trees). We are aware of no incident reports of hexazinone for aquatic animals or plants.

d. Estimated and actual concentrations of hexazinone in water

(1) EECs from models

In the environmental risk assessment in the 1994 RED, OPP's Environmental Fate and Effects Division (EFED) derived aquatic EECs from Tier 1 modeling, the GENEEC model. The EECs as reported in the RED are presented in Table 14.

Table 14. EECs expected immediately after application to a six foot deep water body (source: RED).

Use Pattern	Max. Application (lbs ai/A)	EEC Ground Application (ppm)	EEC Aerial Application (ppm)
Terrestrial Feed Crop Use, Alfalfa	1.5	0.0457	0.032
Forestry, Conifer Release	4	0.122	n/a
Forestry	6	0.183	n/a

The residue values in the table above indicate that for the simulations the range of peak aquatic EECs was 0.032 ppm for 1.5 pounds a.i./A to a maximum of 0.183 ppm at 6 pounds a.i./A. Since all of the sites were based on climate and soils relative to the southeastern U.S., and are not likely to be representative of the western U. S., efforts were made by EFED to use more recently developed sites to be more representative of the areas where Pacific salmon and steelhead occur. EFED provided western PRZM-EXAMS results for alfalfa and Christmas trees, the latter used as a surrogate for forestry. The results of this assessment indicate that estimated environmental concentrations from spray applications to alfalfa and forestry are not likely to exceed 0.02503 ppm and 0.03336 ppm, respectively. Values for the loss of hexazinone into surface water are presented in Table 15.

Table 15. Estimated Environmental Concentrations (EECs) for Aquatic Exposure Modeled with PRZM/EXAM.

Crop	Application method	Application Rate (lb ai/acre)	Estimated Environmental Concentration (ppm)			
			Peak	4 day	21 day	60 day
Alfalfa	spray	1.5	0.02503	0.02495	0.02467	0.02379
Forestry	spray	5.0	0.03346	0.03336	0.03301	0.03203

(2) Measured residues in the environment

NAWQA data

Surface water monitoring data for hexazinone are not included in the NAWQA (http://infotrek.er.usgs.gov/servlet/page?_pageid=543&_dad=portal30&_schema=PORTAL30) monitoring programs.

California DPR County Data

Surface water monitoring data for hexazinone are included in the California DPR surface water database (DPR). Table 16 presents a summary of these monitoring data for the California counties in the range of the three ESUs for Pacific salmon and steelhead. A total of 587 samples had 20 detections ranging from 0.000075 ppm to 0.000581 ppm. All of these values are significantly lower than the EECs presented in table 15.

Table 16. California DPR Database Pesticide Residue Concentrations for Surface Waters (1991-2002).

County	Number of Samples	Number of Detects	Maximum Residue (ppm)	Number >0.001ppm
Merced	22	4	0.000075	0
Sacramento	127	0		
San Joaquin	136	5	0.00016	0
Stanislaus	114	3	0.0005	0
Sutter	170	8	0.000581	0
Yuba	18	0		
Total	587	20		0

g. Existing protections

Nationally, there are no specific protective measures for endangered and threatened species beyond the generic statements on the current hexazinone labels. As stated on product labels, it is a violation of Federal law to use a product in a manner inconsistent with its labeling. Labels for hexazinone have the Environmental Hazard Statement:

> "Do Not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwaters. The active ingredient, hexazinone, in this product is known to leach through soil into ground water under certain conditions as a result of agricultural use. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow , may result in ground-water contamination."

California has a county bulletin system. The counties that include hexazinone among the herbicides only have interim protective measures for threatened and endangered terrestrial plants exposed to hexazinone.

h. Discussion and general risk conclusions for hexazinone

In the 1994 RED, RQs for hexazinone did not exceed the fish or invertebrate acute or chronic levels of concern (LOC) for all uses. With respect to indirect effects that hexazinone may have on aquatic plants used as cover by T&E salmon and steelhead, the criteria of concern (RQ > 1.0) for acute effects were exceeded for all uses, based on the tier 1 GENEEC model. RQ values for alfalfa uses ranged from 4.6-6.5 and those for forestry ranged from 220.2-314.6.

Since these numbers raised a concern, more sophisticated Tier 2 PRZM-EXAMS models were run specifically to account for the soil and climate found in California and the PNW.

The risk conclusions in this assessment are based on risk quotients (RQs) derived from the available toxicity data (Tables 7 to 11) and EECs from the PRZM-EXAMS model for currently labeled rates of 1.5 pounds a.i./a and 5 pounds a.i./a. The RQs for fish and invertebrates range from 0.00032 ppm to 0.03301 ppm and are presented in table 17.

Table 17. Risk quotients for freshwater and estuarine fish and invertebrates based on toxicity of the most sensitive species from technical grade testing of the active ingredient (Tables 7 to 11) and EECs modeled (Table 15).

Crop	Peek EEC	Acute FW Fish RQ[1]	Acute FW Invert RQ[2]	Acute Est. Invert RQ[3]	21-day EEC	Chronic FW Invert RQ[4]	60-day EEC	Chronic FW Fish RQ[5]
Alfalfa	0.02503	0.00016	0.00023	0.00032	0.02467	0.00123	0.02379	0.00140
Forestry[6]	0.03346	0.00021	0.00030	0.00043	0.03301	0.00165	0.03203	0.00188

[1] Rainbow trout LC50 = 160 ppm
[2] Water flea EC50 = 110 ppm
[3] Grass shrimp LC50 = 78 ppm
[4] Water flea NOEL = 20 ppm
[5] Fathead minnow NOEL = 17 ppm
[6] In absence of a forest scenario, the Christmas tree scenario was used as a surrogate scenario.

Based solely on the most sensitive species and maximum EECs, the levels of concern for hexazinone are not exceeded for direct acute (RQ > 0.05) or chronic effects (RQ > 1.0) for freshwater and estuarine fish from alfalfa and forestry uses. Likewise the risk quotients for acute risks to invertebrates are less than the level of concern of 0.05. This indicates that hexazinone will have no direct effect on the Pacific salmon and steelhead and no indirect effects with respect to the invertebrate food sources for T&E salmon and steelhead.

Table 18. Risk quotients for aquatic plants based on toxicity of the most sensitive species from technical grade testing of the active ingredient (Tables 7 to 11) and EECs modeled (Table 15).

Crop	Peek EEC	Acute Aquatic Plant RQ*
Alfalfa	0.02503	0.67
Forestry	0.03346	0.89

* Duckweed EC50 =0.0374 ppm

The risk quotients for aquatic plants (Table 18) are less than the level of concern (RQ < 1.0). This indicates that there are no indirect effects to pacific salmon and steelhead from loss of plant cover.

RQ values using the GENEEC model stated in the RED are much higher than those produced using the PRZM-EXAMS model stated in the above table. According to an OPP/EFED environmental engineer who has developed and validated a number of surface water models, the GENEEC model, which is based on sites in Mississippi overpredicts the EECs as compared to PRZM-EXAMS as the former model is more conservative. GENEEC overpredicts to a greater extent in the PNW region than in the southeastern US as there is less total rainfall, and, therefore, less runoff in the PNW. Therefore, the EECs, and hence, the RQs, in the RED are higher than are likely to occur in California and the PNW, but the magnitude of the overprediction cannot be determined.

In both models it is considered that a 10-hectare watershed will be treated with the maximum rate, maximum number of applications, and the minimum intervals between applications. Runoff and drift from this watershed will go into a 1-hectare pond, 2-meters deep. Once again this is a conservative estimate for salmon and steelhead. These fish inhabit fast flowing streams where any contaminants in the water column will move downstream and preclude continued exposure from a single application. Hexazinone products are typically applied once in the winter or spring and as stated in Table 3 in the beginning of this analysis, the typical usage rates are, on average, substantially less than half of the maximum use rate. Therefore, the exposure that the T&E species may encounter may be less than that described by the EECs.

The half-life of hexazinone from aerobic metabolism is greater than two months; however, plant exposure from the one application per year will be minimal due to the water current sweeping the chemical downstream and the low risk (RQ < 1). Samples taken in streams in California (Table 16) indicate a maximum residue that is significantly less than EECs derived for this analysis. Therefore, the risk to aquatic species will not exceed the level of concern.

As discussed in detail above, the poundage of hexazinone used in the PNW and California does not exceed the levels of concern for fish, invertebrates, and plants. Its seasonal treatment applications (once in winter or spring) and low average application rate, indicate that, in my professional judgement, I do not expect the registered uses in the PNW and California to have an effect on aquatic species. I conclude that hexazinone will have no effect on the subject Pacific salmon and steelhead either directly through acute mortality or long-term sublethal effects or indirectly through loss of their food supply or loss of plant cover. Also, hexazinone will have no effect on the critical habitat of these ESUs.

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