A ~~Toxicological~~ Review of the Aquatic Herbicides Aquamaster® and Rodeo®[1]

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Increasing public awareness of the ~~adverse~~ potential effects of pesticide use has been growing over the past several decades. Environmentalists are now raising red flags when pesticides are used, and are demanding proactive assessments of the potential impacts of pest management activities. What has not been widely recognized is the magnitude of difference between the highly publicized persistent toxicity of many insecticides and the relative non-toxicity of glyphosate based herbicides, such as Aquamaster® and Rodeo®.

This paper reviews current risk assessments, bioassay toxicity tests, and other studies performed on Aquamaster®-and Rodeo® herbicides, to establish confidence in the use of these herbicides as sound and environmentally protective techniques for the management of invasive aquatic plant species. Toxicity assessments of glyphosate, the active ingredient in Aquamaster® and Rodeo® brand herbicdes, its major metabolite - amino methyl-phosphonic acid (AMPA), and potential supplemental surfactants (R-11 or nonylphenolethoxylate (NPE), polyethoxylated alkylamine (POEA), LI 700) are reviewed separately[Separately? Where?] to gain insight into potential toxicity of these components, and guide surfactant selection. [other than one acute study AMPA is never discussed and the only surfactant mentioned is POEA]

Introduction

One hundred thirty-six invasive plant species are listed as noxious weeds by the State of California. These weed species are categorized according to a statewide assessment of the importance of the pest, the likelihood that eradication or control efforts would be successful, and the present distribution of the pest within the state. The California Department of Food and Agriculture (CDFA) uses herbicides as a part of its integrated weed management programs for control and eradication of noxious weeds. Among the 136 plant species designated as noxious weeds for the state of California, *(check #)* weed species are emergent vegetation, or establish around aquatic habitats. These fast growing species impair waterways and compromise wetland habitats. However, because their leaves are above water, they are prime subjects for foliar applied herbicide control.

Purple loosestrife (*Lythrum salicaria*) is an invasive wetland perennial that is capable of developing monospecific stands along water edges, which choke out native vegetation and restrict wildlife access to water. There is currently a purple loosestrife *alert* in California as CDFA and other resource agencies try to eradicate this weed and prevent its spread into central and southern parts of the state. Herbicide application is the most effective and widely used management technique in the control of this noxious weed.

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[1] Aquamaster and Rodeo are trademarks of Monsanto Company and DowAgrosciences, respectively.

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To minimize potential toxicity to non-target aquatic organisms, a careful selection of herbicide is required. Glyphosate-based herbicides like Aquamaster® (Monsanto Company, St. Louis MO) and Rodeo® (DowAgrosciences, Indianapolis, IN) are excellent choices because the active ingredient, while soluble in water, tends to bind tightly to sediment, suspended particulates, organic matter and soil, becoming essentially unavailable to plants or other aquatic organisms. Glyphosate does not bioaccumulate, in terrestrial or aquatic animals (Giesy et al. 2000). Herbicidal effects are therefore limited to foliar contact. Glyphosate rapidly dissipates from surface waters and soil microflora readilyquickly biodegrades glyphosate into AMPA and CO_2 (Gardner & Grue 1996). AMPA, an intermediate metabolite [refered to as a major metabolite earlier] also undergoes rapid degradation to CO_2 in soil and water (Rueppel et al 1977).

How Aquamaster® and Rodeo® herbicides work

Aquamaster® or Rodeo® herbicide is applied by direct spray to foliage. Glyphosate is assimilated by leaves and other green plant tissue and is rapidly translocated within the phloem throughout the plant. Glyphosate acts by preventing the plant from producing the essential amino acids tryptophan, tyrosine, and phenylalanine. This reduces the production of protein within the plant, and inhibits plant growth (Herbicide Handbook, 1994; Glyphosate Pesticide Fact Sheet, USDA). This mode of action for glyphosate is a biochemical pathway not found in animals, thus contributing to the low risk from the labeled uses of glyphosate. The addition of a surfactant to any glyphosate-based formulation including Rodeo® or and Aquamaster® reduces reduces the spray's surface tension on plant leaves and facilitates the penetration of glyphosate through cuticular waxes on target plants.

Glyphosate

Glyphosate-based weed control products are among the most widely used broad-spectrum herbicides in the world because they are highly efficacious, cost effective, practically non-toxic, and quickly biodegrade rapidlyreadily in the environment. Formulations of glyphosate including Rodeo® and Aquamaster® have been extensively investigated for their potential to produce adverse effects in non-target organisms. Governmental regulatory agencies, international organizations, and others have reviewed and assessed the available scientific data for glyphosate formulations and independently judged their safety to be of minimal risk to the environment (Agriculture Canada 1991; USEPA 1993; WHO 1994).

Since its development in the 1970's, there have been no documented cases of adverse effects on fish or aquatic invertebrates associated with glyphosate use for the control of aquatic weeds (Geisy et al. 2000). Several field studies have investigated effects of aquatic weed control applications on aquatic animals (Solberg and Higgins 1993; Findlay and Jones 1996; Simenstad et al. 1996; Linz et al 1997). No measurable increases in effects on density, abundance, or survival of aquatic invertebrates have been reported from the direct effects of glyphosate in field studies (Haag 1986; Henry et al. 1991; Gardner & Grue 1996; Simenstad et al. 1996; Linz et al. 1999).

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Toxicological Effects

Numerous tests to study the toxicity of glyphosate herbicides have been conducted on ~~rats~~rodents, dogs, ~~mice, rabbits, mallards, bobwhite (~~birds~~)~~, fish, aquatic invertebrates and aquatic vegetation. Glyphosate is poorly absorbed from the digestive tract and is excreted largely unchanged by mammals (EXTOXNET database, Cornell Univ). ~~It is therefore not surprising that almost all available toxicity data show glyphosate-based herbicides to be practically non-toxic to mammals.~~

The smaller the amount of the chemical required to kill 50% of the test organisms in the toxicity bioassay (LC_{50}), the more toxic the chemical is. The acute oral LD_{50} value for glyphosate in rats is 5,600 mg/kg. Other oral LD_{50} values for glyphosate are 1,538 mg/kg to greater than 10,000 mg/kg for mice, rabbits, and goats (Extoxnet database, University of Cornell; National Library of Medicine 1992; Monsanto Company 1985~~, *WHY USE THIS OLD REF? WHAT ABOUT WILLIAMS ET AL., 2000 OR EVEN THE US EPA RED 1993, WHO, 1994; THE EU 2002; ETC.)*~~. In contrast, a highly toxic compound might have an LC_{50} between 0.1 and 1 mg/kg for aquatic animals, and 50 to 500 mg/kg for birds. See the Table 1 for the toxicity classifications for aquatic and avian species. ~~[*CONFUSING GOING FROM MAMMALIAN ACUTE TOXICITY TO AQUATIC AND AVIAN TOXICITY – THE TOXICITY CLASSIFICATIONS FOR MAMMALS ARE DIFFERENT]*~~

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Table 1. Toxicity Classification For Aquatic and Avian Species (Giesy et al. 2000)

U.S. EPA Toxicity Classifications[a]	European Toxicity Classification[b] (Aquatic)	Acute aquatic LC_{50} or EC_{50} (mg/L)	Avian dietary LC_{50} (mg/kg)
Practically nontoxic	--	>100	>5000
Slightly toxic	Harmful	>10, ≤ 100	>1000, ≤ 5000
Moderately toxic	Toxic	>1, ≤ 10	>500, ≤ 1000
Highly toxic	Very toxic	≥ 0.1, ≤ 1	>50, ≤ 500
Very highly toxic	Very toxic	<0.1	≤ 50

Subchronic and Cchronic toxicity studies have been performed with rats, dogs, mice and rabbits lasting from 21 days to two years. ~~With few exceptions there were no t~~Few treatment-related ~~gross or cellular~~ changes ~~found by~~were observed in these studies and were confined to the high-doses tested ~~(Monsanto 1985~~US EPA RED, 1993). Based on lack of evidence of carcinogenicity in male and female rats and mice the U.S. EPA classified glyphosate as a Group E chemical, negative for carcinogenicity in humans. No treatment-related effects on fertility were noted in a two-generation rat reproduction study at high doses up to 2134 mg/kg/day ~~, nor were any systemic effects noted in adult rats.~~

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No observable effects level (NOEL) and lowest effects level (LEL) are toxicity reference values (TRVs) used in wildlife exposure assessments to calculate the hazard quotient (which is a measure of risk) for a particular chemical of concern. ~~A NOEL of 10 mg/kg/day, and an LEL of 30 mg/kg/day were derived for glyphosate from the Monsanto study (1985) due to increased incidence of unilateral renal tubular dilation in third generation male pups (USEPA Integrated Risk Information System (IRIS) database).~~ *THE IRIS DATABASE IS **COMPLETELY OUTDATED** FOR GLYPHOSATE IT WAS LAST REVISED IN 1990 AND IS CURRENTLY UNDERGOING REVISION. THE NEW CHRONIC RAT AND NEW 2 GEN RAT REPRO THAT WERE SUBMITTED FOR THE RE-REGISTRATION AND INCLUDED IN THE US EPA 1993 RED SUPERCEDE THE STUDIES MENTIONED IN IRIS AND ARE THE STUDIES THE US EPA CURRENTLY USES IN IT'S RISK ASSESSMENTS. IN ADDITION AS THESE EFFECTS WERE NOT SEEN IN THE MORE RECENT STUDY THE US EPA IN THE RED PAGE 16 STATES THAT THEY HAVE CONCLUDED THAT THESE FINDINGS WERE SPURIOUS AND NOT RELATED TO GLYPHOSATE TREATMENT.*

~~Other t~~Toxicological data for Rodeo® include: Oral LD_{50} rat>5000 mg/kg; Dermal LD_{50} rabbit >5000 mg/kg; 4-h Inhalation LC_{50} rat >1.3 mg/L; Skin irritation rabbit, none; Skin sensitivity in guinea pig, none; Eye irritation in rabbit, none (Herbicide Handbook 1994). *WHAT OTHER TOXICOLOGY DATA FOR RODEO? WHAT ABOUT AQUAMASTER DATA? WHY IS THIS IN A SECTION ON GLYPHOSATE TOXICITY?*

Glyphosate is only slightly toxic to wild birds, and practically non-toxic to fish. LC_{50} values for both mallards and bobwhite quail are greater than 4,500 ppm (Forest Service 1984, Giesy et al. 2000). The acute LC_{50} values for fish exposed to Roundup® (glyphosate-based formulation with POEA surfactant added), glyphosate as IPA salt, AMPA, and POEA are listed in Table 2. *WHAT IS THE BASIS/INTENT FOR INCLUDING THE ROUNDUP FORMULATION AND OTHER SUBSTANCES HERE? COULDN'T ONE CONSIDER "GLYPHOSATE AS IPA SALT" – RODEO – IT ISN'T UNTIL A LATER SECTION THAT THE COMPOSITION OF RODEO IS EVEN INDICATED – NOTHING ABOUT AQUAMASTER – WHICH IS BASICALLY THE SAME THING AS RODEO – THIS IS NEVER DISCUSSED.*

Table 2. LC_{50} Values for fish exposed to components of the herbicide Roundup.

Test Compound	Test Species	LC_{50} Values
Roundup®	Rainbow trout	8.2 mg/L (NOEL is 6.4 mg/L)
Glyphosate	Fathead minnows	97 mg/L.
AMPA	Rainbow trout	520 mg/L
POEA	Fathead minnows	1.0

(Giesy et al. 2000)

~~The smaller the amount of the chemical required to kill 50% of the test organisms in the toxicity bioassay (LC_{50}), the more toxic the chemical is.~~ Clearly the concentrated surfactant POEA, and the concentrated Roundup formulation ~~of Rodeo®~~ *WHY IS THIS REFERRED TO AS "RODEO WITH SURFACTANT ADDED"?* with surfactant added, are more toxic than the active ingredient (glyphosate) its self.

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In acute toxicity studies with amphibians, glyphosate was found to be is practically nontoxic to slightly toxic, while Roundup® (glyphosate with POEA) was slightly to moderately toxic (Geisy et al. 2000). *WHY THE DISCUSSION ON ROUNDUP? IS THIS A "WORST-CASE" SURFACTANT SCENARIO?*

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Human Health Toxicological Data

~~Thus far in this summary, we have discussed available toxicological data for wildlife. The U.S. EPA has also amassed a large body of information on the toxicity of glyphosate to humans.~~ WHAT DOES THIS REFER TO? I AM NOT AWARE OF A LARGE BODY OF INFO ON THE TOXICITY OF GLYPHOSATE TO HUMANS? The calculations of risk performed for human health risk assessments are different from those performed for wildlife exposure. TRUE Human health assessments focus on an increased risk of cancer. CAN BE TRUE DEPENDING ON THE PESTICIDE BUT SINCE GLYPHOSATE IS A CATEGORY E THIS IS IRRELEVANT ~~Cancer slope factors, which are a measure of risk, are calculated by comparing the average daily dose (ADD) of the chemical of concern (COC) to a reference dose (RfD).~~

AGAIN THE IRIS DATABASE IS COMPLETELY OUTDATED AND THIS SECTION APPEARS TO WRITTEN BASED ON THE SAME SECTION IN THE SERA 2002 DOCUMENT PAGES 3 & 4. THE AUTHOR OF THE SERA SECTION IS ABSOLUTELY INCORRECT AND CLEARLY DOES NOT UNDERSTAND THAT THERE ARE **NOT TWO RFDS** JUST ONE AND AN OUTDATED IRIS.

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THE U S. EPA BASES ITS RISK ASSESSMENT FOR HUMANS ON THE LOWEST NOAFL RECORDFD IN THF VARIOUS STUDIES. FOR GLYPHOSATE IT IS FROM THE RABBIT TERATOLOGY STUDY AND IT WAS 175 MG/KG/DAY.

For glyphosate, RfD has been set at 1.75 mg/kg/dev (175 mg/kg/day NOAEL divided by the uncertainty factor of 100X = 1.75 mg/kg/day.

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In 1996, Congress unanimously passed landmark pesticide food safety legislation called the Food Quality Protection Act (FQPA). The FQPA mandated that allowable exposure levels more closely consider infants and children. The FQPA required the U.S. EPA to apply an additional 10-fold uncertainty factor to account for exposure to children, who have higher relative exposure because of their lower body weight. However, EPA was given the option of applying a lesser uncertainty factor "only if, on the basis of reliable data, such margin will be safe for infants and children" (FQPA 1996). The additional uncertainty factor, when applied to the RfD, yields an exposure level called the chronic Population Adjusted Dose (cPAD).

EPA reviewed the toxicological database for glyphosate, determined that it was complete and concluded there was no indication of increased sensitivity to glyphosate among infants and children. Therefore, EPA used an FQPA uncertainty factor of 1, resulting in a cPAD for glyphosate of 1.75 mg/kg/day, the same as the RfD.

~~The U.S. EPA has derived two human health toxicity reference doses (RfD's) for glyphosate: one derived by the U.S. EPA Office of Pesticides in the Registration~~

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~~Eligibility Decision (RED) for glyphosate (USEPA, 1993a), the other derived by the Agency RfD workgroup and summarized on the Integrated Risk Information System – IRIS (USEPA 1993b). The key study concerning these RfDs as well as the potential reproductive effects of glyphosate is a three-generation study on rats conducted by Monsanto (Monsanto, 1981). This study was used as the basis for the U.S. EPA RfD for human health, as described on IRIS. The U.S. EPA Agency wide RfD for glyphosate is 0.1 mg/kg/day based on the NOAEL of 10 mg/kg/day for reproductive effects (Monsanto, 1981). In the RED, the U.S. EPA Office of Pesticides recommends a substantially higher RfD of 2.0 mg/kg/day for glyphosate (U.S. EPA 1993a).~~

~~Both the RED and IRIS use 30 mg/kg/day as a NOAEL for systemic toxic effects. Because focal tubular dilation was noted in the kidneys of high-dose third generation male pups, 30 mg/kg/day is used as the LOAEL (lowest observable adverse effects level) for reproductive effects based on a teratogenicity study in rabbits (detailed in the U.S. EPA RED 1993a p. 15), a second NOAEL of 175 mg/kg/day was derived for glyphosate based on a study of rabbits. The EPA did not discuss this value when it selected 30 mg/kg/day as the basis for the RfD. The World Health Organization (WHO) recognizes a NOEL of 175 mg/kg body weight per day (WHO 1994).~~

Neurotoxicity, Immunotoxicity and Endocrine Disruption.

The U.S. EPA has conducted risk assessments for glyphosate (U.S. EPA 1993) as part of its periodic registration review process and has determined that glyphosate's registration should be maintained because it can be used "without significant risk to humans or wildlife" (SERA 2002). Similarly the Unites States Forest Service (USFS) has commissioned risk assessments on glyphosate (SERA 1996) to assess the risk of using these herbicides in applications that are specific to USFS programs. These reports formed the basis of work upon which recent refined risk assessments for the toxicological endpoints of neurotoxicity, immunotoxicity and endocrine disruption have been performed.

In a recent risk report commissioned by the USFS on three commonly used herbicides, the potential for glyphosate to cause neurotoxicity, immunotoxicity and endocrine disruption was evaluated. No evidence was found to support glyphosate as a neurotoxicant, immunotoxicant or endocrine disruptor (SERA 2002). SERA found no evidence that glyphosate is a direct neurotoxicant in humans or other species. Several long-term experimental studies of dogs, mice and rats did not find evidence of neurotoxicity to the brain. Nor was evidence of neurological effects found among forest workers who mixed and sprayed Roundup® in a small clinical investigation of worker exposure.

Glyphosate does not appear to be an immunotoxicant in humans or other animals, based on results from the available studies in humans and experimental studies in rodents. "This conclusion is supported not only by an extensive set of standard mammalian bioassays on toxicity, but also by an *in vivo* assay specifically designed to detect humoral immune response, and an *in vitro* assay specifically designed to detect cell mediated immune response" (SERA 2002).

Three specific tests on the potential effects of glyphosate on the endocrine system were conducted. No effects were reported in any of the tests. "The conclusion that glyphosate

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is not an endocrine disruptor is reinforced by epidemiological studies that have examined relationships between occupational farm exposures to glyphosate formulations and risk of spontaneous miscarriage, fecundity, sperm quality and serum reproductive hormone concentrations" (SERA 2002). None of these studies have found positive associations between exposure to glyphosate formulations and any reproductive or endocrine outcomes.

Other Studies

Results of in situ bioassays of wetlands treated with Rodeo® suggest that the herbicide did not pose a hazard to aquatic invertebrates (Gardner & Grue 1996). Growth of duckweed was reduced 48 hours after exposure to Rodeo® however. This indicates that Rodeo® may pose a greater hazard to non-target aquatic vegetation than to other aquatic organisms.

In the "Ecotoxicological Risk Assessment for Roundup Herbicide" (Giesy et al. 2000) ~~the active ingredient in~~ Roundup® ~~(RU)~~, glyphosate, and the surfactant ~~polyethoxylated tallowamine (~~POEA~~), and the major glyphosate metabolite AMPA,~~ where subjected to current ecological risk assessment methodology to provide a measure of environmental safety ~~for use of Roundup® and Rodeo® herbicidal product.~~ "Worst-case" assumptions, and no observable effects levels (NOELs) from the most sensitive test species were used to calculate very conservative hazard quotients. (A hazard quotient gives an estimate of relative risk).

The results of the acute risk assessment for ~~Rodeo~~Roundup® ~~formulated with POEA surfactant~~Geisy never used the phrase Rodeo formulated with POEA surfactant. !, showed minimal risk (HQ's < 1.0) for all aquatic taxa (microorganisms, aquatic macrophytes, fresh-water invertebrates, fish, and amphibians) in environments 2-m-deep ~~or less~~. In shallow water (0.15 m), acute hazard values approached, or in some instances exceeded, minimal risk levels (HQ's > 1.0) warranting further investigation. An examination of risk assessment assumptions revealed that herbicide degradation, sorption, and interception by target vegetation of greater than 50% would mitigate the potential for effects in shallow waters (i.e.: bringing the HQ values back below 1.0). Evaluations of chronic risk looked at the components and metabolites of Rodeo® independently. Chronic risk evaluations indicated minimal risk for all components and metabolites, even in shallow waters.

Geisy et al. (2000) concluded that the use of Rodeo® it was not Rodeo that this statement was used for it was Roundup for aquatic habitat restoration can be safely carried out, but requires consideration of items such as application rate, depth of water and percent vegetation converge.

Surfactants

The formulation of Rodeo® is: isopropylamine (IPA) salt of glyphosate (53.5%), and water (46.5%). A surfactant must be added before application to effectively control weeds. This allows the user to select a surfactant that meets the specific needs of the weed control program. Efficacy and potential toxicity to non-target aquatic organisms are the two factors that most often guide surfactant selection.

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There are many different surfactants on the market. Polyethoxylated tallowamine (POEA) is a commonly used surfactant and is part of the formulation of Roundup®. Another surfactant, nonylphenol ethoxylate surfactant or R-11, is specifically identified for use in aquatic environments.

Polyethoxylated tallowamine (POEA), the surfactant used in Roundup®, is more toxic to aquatic animals than is the active herbicidal ingredient glyphosate. The lowest LC_{50} value for POEA for aquatic animals is 0.65 mg/L (Folmar et al. 1979), which is at the upper end of the toxicity range for surfactants. A toxicity assessment of POEA for aquatic organisms could therefore be used as a conservative estimate for other surfactants. Use of POEA toxicity data as a baseline for aquatic risk, would provide protective estimates for the use of other less toxic surfactants.

Acute toxicity values LC_{50} for POEA to fish range between 1.0 mg/l for Bluegill sunfish and fathead minnows, to 7.4 mg/l for Rainbow trout. Chronic NOEL of POEA for mammals ranged from 15 mg/kg/d in a 21-day rat study, to 52 mg/kg/d in a 1-month rat study. The toxicity value for the R-11 metabolite NP, based on 96-h LC_{50} tests, is 0.13 mg/L, which also puts this compound in the highly toxic category (Staples et al 1998). Further review of surfactant toxicities should be made to assist Invasive Plant Program directors in the selection of a surfactant most protective of the environment.

Secondary effects

The creation of open water habitat in wetlands through the use of herbicides such as Rodeo, create trade-offs between wildlife populations. Studies have noted an increase in populations of some aquatic invertebrates, and species of birds following treatment of cattail choked wetlands with Rodeo® (Linz et al. 1999; Baltezore, Leitch & Linz 1994). Rails, shorebirds and waterfowl will increase when vegetation is thinned, while numbers of red-winged blackbirds, wrens, upland game, furbearers and deer may decline (Baltezore, Leitch & Linz 1994). In some cases, short-term declines in populations may be anticipated because of changes in habitat (i.e.: temporary diminishment of food sources, and nesting or shelter sites). Therefore, ecological assessment endpoints of any habitat rehabilitation program, needs to reflect the long-term goals of the program.

Summary

A review of key documents and studies assessing the acute and chronic toxicity, neurotoxicity, immunotoxicity, and endocrine disruption risks of glyphosate-based herbicides, indicates that non-target organisms are exposed to minimal risk through the use of these herbicides. The surfactants used in the formulation of glyphosate-based herbicides, or mixed with the aquatic herbicides Aquamaster® and Rodeo® before application, are far more toxic than the active ingredient itself. A well-administered management program for the control of noxious weeds can minimize potential exposure and toxicity to non-target organisms through use of Best Management Practices. Application rate, depth of water and percent vegetation converge are key factors in minimizing unwanted aquatic exposures. The surfactants can be selected to minimize toxicity to aquatic organisms for herbicides such as Rodeo. Further investigation into toxicity values for a variety of surfactants would enable Weed Control Program

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Managers to make surfactant decisions that would be most protective of human health and the environment.

At CDFA, the goal of our noxious weed management programs is to protect and restore social, economic and wildlife land values, in the most efficient and environmentally protective ways possible. We advocate the use of herbicides as a tool in the eradication of smaller noxious weeds invasions, and the containment of large-scale infestations. The economic and environmental cost of herbicide use for intensive short-term eradication efforts, pales in comparison to the cost of ongoing containment efforts for noxious weeds that have permanently established themselves on our landscapes. Stopping aggressive noxious weed species like purple loosestrife from invading new wetland and aquatic areas in California is a high priority. The use of relatively non-toxic aquatic herbicides such as Aquamaster® and Rodeo® is our best tool.

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