Imazapyr:
Review for Use in Lakes & Ponds
in Massachusetts

January, 2012

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1. Introduction

The purpose of this review is the evaluation of the active ingredient imazapyr when formulated for the use as an aquatic herbicide for weed control in lakes and ponds in Massachusetts. The regulatory process for registration and approval for use of new aquatic herbicides in Massachusetts' lakes and ponds requires a special review of new aquatic herbicide active ingredients.

The initial review of imazapyr was prepared with the objective to provide information for the Massachusetts Pesticide Board Subcommittee's evaluation for registration of the aquatic herbicide. Following the registration by the Subcommittee, the new aquatic herbicide active ingredient is subject to a review for addition to the Eutrophication and Aquatic Plant Management in Massachusetts Final Generic Environmental Impact Report (GEIR) (Mattson et al., 2004). The GEIR is intended to provide guidance to lake and pond managers, conservation commissions, and citizens concerned with lake management issues. It was also developed to provide a basis for a more consistent and effective lake management in the Commonwealth. The GEIR describes technical approaches and management options for control of aquatic vegetation and for the protection and enhancement of lakes and ponds in Massachusetts. It was written to allow for more efficient navigation through the regulatory process and satisfy the requirements of the Massachusetts Environmental Policy Act (MEPA). Use of a herbicide that is included in the GEIR implicitly confers compliance with MEPA requirements for the application of herbicides to aquatic habitats in the Commonwealth (301 CMR 11.00).

The technical guidance in the GEIR includes information on the herbicides that are approved for use in lakes and ponds to control aquatic vegetation (Appendix III of GEIR). These herbicide profiles include information on chemical and physical properties of the herbicide, its uses and application, mode of action, toxicity, and environmental fate. Potential for risks to human health and the environment are also addressed and, if applicable, regulatory restrictions that go beyond those on the product label may be included.

In order to have new active ingredients and products added to the GEIR, a critical technical review is conducted by staff of MassDEP-ORS and MDAR[1]. The review is conducted with an emphasis on non-target aquatic toxicity. The recommendations may include additional restrictions on use of the herbicide. The review presented here is intended to provide the basis for the update to the GEIR with the new active ingredient imazapyr.

The general use profile for imazapyr is for control of weeds, brush and undesirable vegetation on terrestrial and aquatic sites. Relative to the use in rights-of-way (ROW), it is worthwhile to point out that imazapyr is included on the Sensitive Areas Materials List for Rights-of-Way (ROW) vegetation management in MA. Herbicide products on this list have gone through a special review and approval process that is conducted collaboratively by MDAR and MassDEP for herbicide use in sensitive areas in ROW, such as water bodies and inhabited areas. The increased level of control is sought for ROW herbicides to ensure that these sensitive areas are sufficiently protected from potential risks associated with herbicide use.

[1] MassDEP-ORS – Massachusetts Department of Environmental Protection – Office of Research and Standards; MDAR – Massachusetts Department of Agricultural Resources

At the time of this review, there were ten products registered in Massachusetts for use on sites other than lakes and ponds. The following products were requested for addition to the GEIR, such that these products would be allowed for use in lakes and ponds in Massachusetts:

- Habitat® Herbicide; EPA. Reg. No. 241-426; Application date: 2/12/2004
- Imazapyr E Pro 2 VM & Aquatic herbicide; (EPA. Reg. No. 81959-8; Application date: 5/27/2004

These products are very similar in composition, both having the same active ingredient content of 28.7% isopropyl amine salt of imazapyr. Habitat® herbicide is labeled for aquatic and wetland use only, while Imazapyr E Pro 2 herbicide labeled uses include both terrestrial and aquatic sites. At the time of the preparation of this review, Imazapyr E Pro 2 was registered in MA for terrestrial use only.

As a result of the reregistration review of imazapyr that was completed by USEPA in 2006, a number of review and risk assessment documents were available as information sources for the review presented here. Documents and links to e-docket are available at the EPA website: Imazapyr | Pesticides | US EPA (www.epa.gov/oppsrrd1/reregistration/imazapyr). The e-docket provides access to information, including risk assessments and decision documents related to the reregistration review of imazapyr. The special review for aquatic use in MA draws primarily from the information available in the e-docket. Additional information was retrieved from the various sources, including published scientific studies and government documents. A guide to the various information sources that were used with the preparation of this special review is included in Appendix 1.

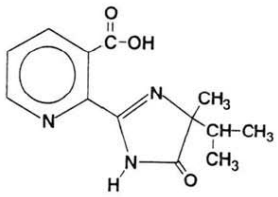
2. Chemical Overview

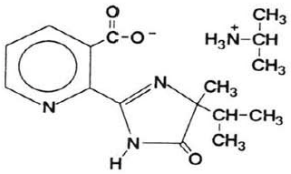
2.1. Chemical Identity

Imazapyr is part of the imidazolinone chemical class. Imazapyr is a systemic, non-selective, pre- and post-emergent herbicide used for the control of a broad range of terrestrial and aquatic weeds, and controls plant growth by preventing the synthesis of branched-chain amino acids. Imazapyr is applied either as an acid or as the isopropylamine salt (US EPA, 2006).

The nomenclature is summarized in the Table 2.1 below:

Table 2.1. Imazapyr Acid and Salt Nomenclature

Imazapyr, acid	
Structure	
Molecular Formula	$C_{13}H_{15}N_3O_3$
IUPAC Name	[2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-nicotinic acid]
CAS Number	81334-34-1
PC Code	128821

Imazapyr, salt	
	
Molecular Formula	$C_{13}H_{15}N_3O_3C_3H_9N$
IUPAC Name	2-Propanamine, 2-(4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3-pyridinecarboxylate
CAS Number	81334-34-1
PC Code	128821

Source: RED for Imazapyr (USEPA, 2006)

2.2. Registration and Reregistration History

Imazapyr technical was first registered in 1985; however, a non-crop end use product had been previously registered in July 1984. The first food use on corn was registered in April 1997. In 2003, the aquatic and grassland uses were registered which resulted in the establishment of additional tolerances. Currently there are 24 tolerances listed in 40 CFR § 180.500 for residues of the herbicide imazapyr, applied as the acid or isopropylamine salt, which were reassessed in 2003. The reregistration review of imazapyr by U.S. EPA determined that the registered uses continued to meet the regulatory standards and the reregistration decision was issued in 2006 (USEPA, 2006).

2.3 Pesticide Type, Class, and Mode of Action

Imazapyr is an imidazolinone herbicide that is used for control of most annual and perennial broadleaf weeds and grasses, woody species, and riparian and emergent aquatic weed species. This family of herbicides was discovered by American Cyanamid Company in the 1970's. Imazapyr is formulated both as an acid and as an isopropylamine salt. Uptake of imidazolinone herbicides is primarily through the foliage and roots. The herbicide is then translocated to meristematic tissue (buds or areas of growth) by the xylem and phloem where it inhibits acetohydroxyacid synthase [AHAS; also known as acetolactate synthase (ALS)], an enzyme involved in the synthesis of three essential amino acids (valine, leucine, isoleucine). These amino acids are required for protein synthesis and cell growth. Imazapyr disrupts protein synthesis and interferes with cell growth and DNA synthesis, causing the plant to slowly die. AHAS is not present in mammals, birds, fish, or insects, making it specifically toxic to plants (US EPA, 2005A).

2.4 Physical and Chemical and Environmental Fate Properties

Important characteristics relative to the application of imazapyr in and near aquatic systems include the compound being an anionic, organic acid that is non-volatile and degrades through photolysis in clear shallow waters (US EPA Level I, 2005A). A summary of selected physical/chemical and fate properties for imazapyr and imazapyr isopropylamine salt is presented in Table 2.2.

The herbicide imazapyr is a water soluble, weak acid with a pK_a of about 3.8. Based on this pK_a imazapyr is mainly in anionic form at typical environmental pHs (61% ionized at pH 4, 94% ionized at pH 5, greater than 99% ionized at pH 6 and higher). The behaviors of the acid and salt forms are expected to be similar. Commercial formulations contain imazapyr acid or the imazapyr isopropylamine salt, both of which are generally dissolved in a water solution.

The environmental fate characteristics of imazapyr are that it is an anionic, organic acid (pK_a = 3.8) that is non-volatile, and is both persistent and mobile in soil. Laboratory studies show that

imazapyr is essentially stable to hydrolysis, aerobic and anaerobic soil degradation as well as aerobic and anaerobic aquatic metabolism. Imazapyr is not expected to bioaccumulate in aquatic organisms because it exists as an anion at typical environmental pH values

Upon direct application, or indirect release into surface water, photolysis is the only identified mechanism for imazapyr degradation in the environment. The half-life of imazapyr is approximately 3 to 5 days in surface water. The major identified metabolites were pyridine hydroxy-dicarboxylic acid, pyridine dicarboxylic acid, and nicotinic acid. Under laboratory aerobic aquatic conditions, the aerobic aquatic metabolism half-lives for hydroxy-dicarboxylic acid and pyridine dicarboxylic acid were in the range of 3 to 8 days in two different sediment/water systems.

Based on a low vapor pressure of $<10^{-7}$ mm Hg at 60°C, volatilization is an unlikely route of dissipation from soil. Present as an anion at typical environmental pH values, imazapyr tends to be weakly sorbed to most soils and sediments. For anionic compounds, sorption would tend to diminish with increasing environmental pH. In several studies involving a total of 11 different soils and sediments, adsorption coefficients were low, as demonstrated by batch/bulk equilibrium sorption coefficients (K_D) that range from 0.04 to 3.4 mL/g, with a median of 0.6 mL/g. There was no apparent correlation with soil organic matter.

Table 2.2. Some Physical, Chemical and Environmental Fate Properties of Imazapyr and the Isopropylamine Salt of Imazapyr.[1]

Chemical name Acid 2-[4,5-Dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3pyridinecarboxylic acid Salt 2-Propanamine, 2-(4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3-pyridinecarboxylate	
Empirical Formula Acid Salt	 $C_{13}H_{15}N_2O_3$ $C_{13}H_{15}N_2O_3 \cdot C_3H_9N$
Molecular Weight Acid Salt	 261.28 320.39
Aqueous Solubility at 25°C (acid)	11.1 g/L
pK_a (acid)	3.8
Vapor Pressure at 60°C (acid)	$<10^{-7}$ mm Hg
Henry's Law Constant at 25°C (acid)	$<7 \times 10^{-17}$ atm x m3/mol
Log P_{ow} at pH 7 and 20°C (acid)	0.22
Environmental Fate Properties	
Hydrolysis half life (pH 7)	stable
Aqueous photolysis half lives	$t_{½}$ = 2.5 - 5.3 days
Aerobic metabolism half-lives	stable
Anaerobic metabolism half-lives	stable
Soil-water distribution coefficients (K_d)	0.04 - 3.4

[1] Source: Table IIS-2 (p. 12) in Level I Screening Risk Assessment (US EPA, 2005A)

An environmental fate summary table is included in Appendix 2. Detailed descriptions of information on the environmental fate summaries and degradates can be found in Appendix A of Level I Screening Ecological Risk Assessment for Reregistration of Imazapyr (US EPA 2005A).

Laboratory bioconcentration studies with bluegill sunfish, eastern oyster, and grass shrimp indicate that parent imazapyr, even though long-lived in the environment, is not subject to bioconcentration (bioconcentration factor <1). Imazapyr's relatively high solubility in water and low n-octanol-to-water partitioning ratio is also consistent with little likelihood of bioconcentration.

2.5 Product Formulation

The product labels indicate that the Habitat and Imazapyr E Pro herbicide products are liquid formulations of isopropylamine salt of imazapyr at a concentration of 28.7% by mass, which corresponds to 2 lbs of acid equivalent per gallon of product (BASF, 2008; Etigra, 2007).

According to information available in a review document on the use of imazapyr herbicide to control invasive cordgrass in the San Francisco Estuary (Pless, 2005), the inert ingredients in the Habitat herbicide are most likely similar to the composition of the Arsenal herbicide formulation and most likely include water and a small amount of acidifier. Information on the Habitat formulation obtained from the registrant confirms this. The formulation does not contain surfactants. No additional information was available on the Imazapyr E Pro formulation, but it can be expected to be very similar to the Habitat herbicide.

The product labels indicate that treatment of post-emergent vegetation requires the addition of spray adjuvants to the tank mix. As directed on the label, only adjuvants labeled for aquatic use should be utilized. Specific recommendations for adjuvants include those that contain non-ionic surfactants, methylated seed oils, and silicone-based surfactants.

3 Use Characterization

3.1. Use Sites

Imazapyr is used for pre- and post-emergence control of a broad range of weeds, including terrestrial annual and perennial grasses, broad-leaved herbs, woody species, and riparian and emergent aquatic species.

The focus of this special review is on the use as an herbicide for direct application to lakes and ponds. Aquatic uses of imazapyr are for control of undesirable emergent and floating aquatic vegetation in and around standing and flowing water including estuarine and marine sites. These include control of undesirable wetland, riparian and terrestrial vegetation growing in and around standing and flowing water.

Imazapyr is also applied terrestrially on field corn and grass, a variety of commercial and residential use sites, including forestry sites, rights-of-way, fence rows, hedge rows, drainage systems, outdoor industrial areas, outdoor buildings and structures, domestic dwellings, paved areas, driveways, patios, parking areas and walkways. Imazapyr may also be used as a spot treatment in recreation areas, athletic fields, and golf course roughs (US EPA, 2006).

The product labels provide language related to the use sites where the product can be applied including the following:

- Aquatic use applications can only be made by federal or state agencies, such as Water Management District personnel, municipal officials and the U.S. Army Corps of Engineers, or those applicators who are licensed or certified as aquatic pest control applicators and are authorized by the state or local government.

- Treatment to other than non-native invasive species is limited to only those plants that have been determined to be a nuisance by a federal or state government entity.

- Applications may be made to private waters that are still, such as ponds, lakes and drainage ditches where there is minimal or no outflow to public waters.

- Applications may be made to public waters such as ponds, lakes, reservoirs, marshes, bayous, drainage ditches, canals, streams, rivers, and other slow-moving or quiescent bodies of water for control of aquatic weeds or for control of riparian and wetland weed species.

- There are no restrictions on the use of water in the treatment area for recreational purposes, including swimming and fishing. There are no restrictions on livestock consumption of water from the treatment area.

3.2. Application Methods

Aquatic applications of these imazapyr herbicide products are made as a liquid. Application methods include aerial application and application via boat. Aqueous imazapyr formulations may be mixed with surfactants or oils for application. Applications to smaller areas may be made with handheld equipment, including backpack sprayers, sprinkling cans, and handgun sprayers.

Habitat and Imazapyr E Pro maybe be selectively applied by using low-volume directed application techniques or may be broadcast applied by using ground equipment, water craft or by helicopter. In addition, the products may also be used for cut stump, cut stem and frill and girdle treatments within aquatic sites. Applications should be made in such a way as to maximize spray interception by the target vegetation (moisten but not drench) while minimizing spray drift and the amount of overspray that enters the water (US EPA, RED, 2006).

The products must be applied to the emergent foliage of the target vegetation and have little to no activity on submerged aquatic vegetation. The product concentrations resulting from direct application to water are not expected to be of sufficient concentration or duration to provide control of target vegetation. Application should be made in such a way as to maximize spray interception by the target vegetation while minimizing the amount of overspray that enters the water.

3.3. Use Rates

Labeled application rates of imazapyr for aquatic sites range from 0.5 to 1.5 acid equivalent per acre (lbs a.e./acre).

3.4. Target Species

Imazapyr-based herbicides will control various floating, emerged and terrestrial/marginal weed species. It is effective against aquatic problem species such as alligator weed, *Arundo donax*, cattail, parrot feather, *Phragmites*, purple loosestrife, saltcedar, *Spartina*, water hyacinth, and water primrose. A complete list of weeds controlled can be found on the product label (BASF, 2008; Etigra, 2007).

4. Human Health Risk Assessment

4.1. Summary of USEPA Assessment

As part the registration review, USEPA has conducted human health risk assessments for imazapyr. The risk conclusions of these assessments are summarized below. Appendix 3 provides the summary of the USEPA's revised human health effects and ecological risk assessments for imazapyr, as presented fully in the documents, *Imazapyr: HED Chapter of the Reregistration Eligibility Decision Document,* dated December 8, *2005* and *Reregistration Eligibility Decision for Imazapyr* (RED), US EPA (2006).

The HED abstract states that imazapyr is of low toxicity via the oral, dermal, and inhalation routes of exposure. Toxicity studies reveal no effects to minimal effects, even at the highest dose tested in toxicological studies. Imazapyr is a Toxicity Category 1 primary eye irritant. Chronic dietary exposure to residues of imazapyr, including residues in drinking water, is not of concern for any population subgroup, including the US general population, females 13-49 years of age, children, and infants. There is the potential for exposure to occupational and residential handlers of imazapyr, although dermal and inhalation risks are below HED's level of concern for all scenarios. Post-application exposures (including incidental oral exposure to toddlers, and oral and dermal exposure from swimming activities in treated lake water) are also below HED's level of concern. Short- and long-term aggregate risks are not of concern.

The chronic oral reference dose (cRfD) for imazapyr of 2.5 mg/kg/day was established based on a No-Observed-Adverse-Effect-Level (NOAEL) of 250 mg/kg/day, the highest dose level tested in the 1-year dog feeding and an Uncertainty Factor (UF) of 100 to account for both the interspecies extrapolation and intraspecies variability. An acute RfD could not be established because no appropriate endpoint attributable to a single dose was available (USEPA, 2005B).

Summaries of the human health risk assessments as presented in the HED document (USEPA, 2005B) and the RED document (USEPA, 2006) referred to above are available in Appendix 3.

Relative to the aquatic use pattern, the risk related to recreational uses of treated water bodies and the risk associated with drinking water exposure are addressed and summarized below.

4.2 Recreational Uses

Imazapyr may be applied by broadcast application to aquatic freshwater sites to control floating or emergent aquatic vegetation. Adults and children may be exposed when swimming in treated water bodies following application of imazapyr. The potential for post-application incidental ingestion and dermal exposure to adults, children, and toddlers as a result of swimming in treated waters immediately following application has also been assessed. Post-application risks to adults, children, and toddlers swimming in imazapyr-treated waters are below the Agency's level of concern (i.e., MOEs greater than 100) with MOEs ranging from 68,000 to greater than 1,000,000. More information on the risk assessment for recreational use on aquatic sites can be found in Appendix 4.

4.3 Drinking Water Assessment

USEPA considered the exposure to imazapyr from drinking water resulting from aquatic applications. The estimated drinking water concentrations (EDWC's) for both surface and ground water from direct application to surface water are both 61 µg/L (USEPA, 2005B). This estimate does not take into account the current imazapyr label requirement of a one-half mile setback from drinking water intakes because the Agency does not currently have an approved methodology for calculating EDWCs in water bodies where pesticides are applied with a setback distance from drinking water intakes. As a result, the EDWC is more conservative than had setback distances been considered. Direct applications to water were modeled assuming uniform application over an entire reservoir at the maximum labeled rate.

The exposure from drinking water was considered with the aggregate risk assessment based on the combined exposures from food, drinking water, and, if applicable, residential exposure. The chronic risk from food plus drinking water was assessed by exposure estimates from chronic dietary (food) and chronic drinking water assessment (USEPA, 2006). The combined chronic exposure for the general U.S. population and all population subgroups was less than 0.1 % of chronic Population-Adjusted Dose (cPAD). The cPAD for imazapyr is 2.5 mg/kg/day (see also Appendix 3).

For imazapyr, the aggregate risk assessments were conducted for the short-term (food + drinking water + short-term residential) and for the long-term (food + drinking water only). Based on the current use patterns of imazapyr, USEPA does not expect exposure durations that would result in intermediate- or long-term residential exposures; therefore long-term aggregate risk assessment consisted of exposure from food and drinking water only.

For adult short-term aggregate exposure, the Agency aggregated chronic food and drinking water exposures with residential handler and post-application exposures. The adult residential exposure scenarios resulting from application and post-application activities on turf were used. For short-term aggregate exposure to children, the Agency aggregated chronic food and drinking water exposures for toddlers (1-2 years of age) and combined these with post-application dermal and incidental oral exposures (combined hand-to-mouth, object-to-mouth, and soil ingestion) from activity on turf. The estimated MOEs are above 100, with values of 410 for children and 720 for adults. Therefore, short-term aggregate risks are below the Agency's level of concern. Because the Agency does not expect chronic residential exposure, long-term aggregate risks are equal to chronic dietary risks (food plus water) as described above. For a complete discussion, see also Section 7 of the *Imazapyr: HED Chapter of the Reregistration Eligibility Decision Document* (USEPA, 2005B).

For the review presented here, an additional drinking water risk assessment was done by considering the health-based screening level for imazapyr. Health-Based Screening Levels (HBSLs)[2] are benchmark concentrations of contaminants in water that may be of potential concern for human health, if exceeded. HBSLs are non-enforceable benchmarks that were developed by the USGS in collaboration with USEPA and others using USEPA methodologies

[2] For more information on HBSLs see: USGS Health-Based Screening Levels

for establishing drinking-water guidelines and the most current, USEPA peer-reviewed, publicly available human-health toxicity information (Toccalino et al., 2008).

For noncarcinogens, the HBSL represents the contaminant concentration in drinking water that is not expected to cause any adverse effects over a lifetime of exposure. HBSL calculations adopt USEPA assumptions for establishing drinking-water guidelines, namely, lifetime ingestion of 2 liters of water per day by a 70-kilogram adult. For non-carcinogens, it also is assumed that 20 percent of the total contaminant exposure comes from drinking water sources and that 80 percent comes from other sources (for example, food and air). If data are available to quantify the percentage of contaminant exposure that comes from water, then a data-derived percentage is used instead of the default of 20 percent. More information on the calculation of HBLSs can be found on the USGS website (USGS Health-Based Screening Levels).

Comparisons of measured or estimated contaminant concentrations in water to HBSLs can indicate when measured concentrations may be of potential human-health concern and can provide an early indication of when contaminant concentrations in ambient water resources may warrant further study or monitoring.

The HBSL that has been established for imazapyr is 20,000 ug/L. The estimated drinking water concentration considered in the risk assessment by USEPA was 61 µg/L (USEPA, 2005B). This value is well below the HBSL of 20,000 µg/L and therefore is not of concern.

Associated with the application of imazapyr to surface water, is a concern for the imazapyr to travel with surface water recharging groundwater that may subsequently be used as drinking water. A conservative screening-level risk assessment can be made by considering the recharge of groundwater with surface water with no attenuation of imazapyr concentrations. Estimated surface water concentrations of imazapyr one month after application can be used as a surrogate for worst case drinking water concentrations over an intermediate duration. The values in Table 5.1 in Section 5.2.1 show a predicted range of 25 to 40 µg imazapyr/L. These values are well below the HBSL of 20,000 µg/L indicating that this exposure route is not of concern. Even the short-term peak concentrations (84 to 552 µg/L) would be below the HBSL. Degradation would also take place in the surface and ground further reducing the imazapyr concentrations.

5.0 Ecological Risk Assessment

USEPA conducted an ecological risk assessment as part of the evaluation associated with the reregistration of imazapyr. This risk assessment is described in *Level I Screening Ecological Risk Assessment for the Registration of Imazapyr* (USEPA, 2005A), which is a technical support document for the RED for imazapyr. For the purpose of the special review presented here, the information most relevant to the evaluation of the aquatic use pattern is included below.

The imazapyr analysis consisted of evaluating environmental fate data, modeling exposure concentrations, and evaluating toxicity information to characterize potential risks to the defined endpoints. The analysis is based on screening-level modeling of estimated exposure concentrations combined with information from imazapyr toxicity studies.

5.1 Ecological Hazard Characterization

5.1.1 Active Ingredient Imazapyr

The Level I Screening Risk Assessment document (USEPA, 2005A) summarizes the effects characterization as described below. The acid and salt moieties for imazapyr are expected to behave similarly; therefore, they are used interchangeably. In order to communicate whether the acid or salt form of imazapyr was tested, the results of the ecotoxicity studies were expressed in terms of either active ingredient (a.i.) or acid equivalents (a.e.).

Aquatic animals: Available acute toxicity data for aquatic species indicate that imazapyr acid is practically non-toxic to fish and invertebrates with LC_{50} and EC_{50} values for fish and invertebrates >100 mg a.i./L. Following chronic exposure, a decrease in larval survival was observed in freshwater fish (NOAEC/LOAEC = 43.1/92.4 mg a.i./L). There were no other observed adverse effects to freshwater fish or invertebrates following chronic exposure to imazapyr acid. Estimated chronic effects for estuarine/marine fish and invertebrates are uncertain because no chronic data were submitted by the registrant. The NOAEC values for marine/estuarine fish and invertebrates were derived based on the assumption that freshwater and estuarine/marine fish and freshwater and marine/estuarine invertebrates are of equal sensitivity. Available studies on aquatic animals with the isopropylamine salt indicate that the salt is no more toxic than the acid.

The only sublethal effect observed in the acute aquatic animal studies is a decrease in shell deposition in the eastern oyster. The NOAEC/LOAEC for this effect was 109/173 mg/L. No other sublethal effects were observed in the aquatic animal studies.

Laboratory bioconcentration studies with bluegill sunfish, eastern oyster, and grass shrimp indicate that parent imazapyr, even though long-lived in the [terrestrial] environment, is not subject to bioconcentration (bioconcentration factor <1). Therefore, food-chain exposures are not expected to be significant in aquatic systems.

Aquatic Plants: Studies indicate that imazapyr acid is highly toxic and expected to exert detrimental effects to aquatic vascular plants at the maximum application rate up to 1.5 lbs ae/acre. The EC_{50} for the aquatic vascular plant (duckweed) is 0.024 mg a.e./L (NOAEC 0.01 mg/L), based on inhibition of plant growth and reduction of frond count. The toxicity of the isopropylamine salt to duckweed was similar to the acid, with a 14-day EC_{50} of 0.018 mg ae/L (NOAEC = 0.011 mg ae/L).

Avian and Mammalian Toxicity: Available acute and chronic toxicity data indicate that imazapyr acid is practically non-toxic to upland game birds and waterfowl (acute LD_{50}>2,150 mg ae/kg bw for both bobwhite quail and mallard ducks and the acute dietary LC_{50} >5000 mg a.i./kg diet for both bobwhite quail and mallard ducks). Chronic NOAECs for bobwhite quail/mallard duck = 1,670/>2000 mg a.i./kg diet, highest concentrations tested). Acute and chronic toxicity data also indicate that imazapyr acid is practically non-toxic to mammals. (Acute LD_{50} value of >5,000 mg a.i./kg bw; rat reproduction study NOAEL = 738 mg a.i./kg bw/day: 10,000 ppm, highest concentration tested). Acute and subacute exposures did not cause sublethal effects in mammals. Acute contact studies indicate that imazapyr acid is practically non-toxic to honey bees (LD_{50} > 100 µg a.i./bee). Available studies on terrestrial animals with the isopropylamine salt indicate that the salt is no more toxic than the acid.

Terrestrial Plants: Terrestrial plant toxicity studies with monocots and dicots indicate that seedling emergence and vegetative vigor are severely impacted by exposure to imazapyr acid and to the isopropylamine salt of imazapyr. Seedling emergence, based on "fresh weight", was adversely impacted in monocots (wheat) at an EC_{25} of 0.0046 lb ae/acre (0.52 mg ae/m^2) and in dicots (sugar beet) with an EC_{25} of 0.0024 lb ae/acre (0.27 mg ae/m^2). In the wheat, severe stunting, interveinal chlorosis, and cessation of growth occurred at doses >0.0078 lb ae/acre (0.88 mg ae/m^2). After 28 days, imazapyr acid resulted in >60% crop injury in sugar beets at all doses >0.031 lb ae/acre (3.48 mg ae/m^2). Vegetative vigor in monocots, based on "fresh weight", was adversely impacted by both imazapyr acid and the isopropylamine salt of imazapyr at an EC_{25} of 0.012 lb ae/acre (1.35 mg ae/m^2) in wheat and 0.010 lb ae/acre (1.12 mg ae/m^2) in onion, respectively. In vegetative vigor studies with dicots, imazapyr acid was more toxic than the isopropylamine salt of imazapyr with EC_{25} of 0.0009 lbs ae/acre (0.10 mg ae/m^2) (cucumber) and 0.0016 lbs ae/acre (0.18 mg ae/m^2) (sugar beet), respectively. Non-lethal effects included stunting, chlorosis, and necrosis.

Metabolites: Metabolites hydroxy-dicarboxylic acid and pyridine dicarboxylic acid are expected to be more polar, thus more rapidly excreted than imazapyr, and no more toxic than the parent compound. Additionally, pyridine hydroxy-dicarboxylic acid is considered to be less stable than the parent compound. Nicotinic acid is a possible neurotoxin at high dose levels, but there is no concern for these effects at low exposures. Nicotinic acid (also called niacin and referred to as Vitamin B3) is considered an essential nutrient.

A summary of ecological effects data from Level I Screening Level Risk Assessment can be found in Appendix 6.

EPA typically uses fish as a surrogate for aquatic-phase amphibians when amphibian toxicity data are not available. In the case of imazapyr, no acute or chronic toxicity data are available for

aquatic-phase amphibians. EPA conducted a comprehensive assessment of the risks of imazapyr use to federally-listed California Red Legged Frog (CRLF), *Rana aurora draytonii* (Hurley and Shanaman, 2007). Fish were used as a surrogate to estimate direct acute and chronic risk to aquatic-phase CRLF. The risk assessment indicated that no direct effects are expected on either the aquatic or terrestrial phase CRLF. There are also no indirect effects expected for the CRLF through direct effect to either its terrestrial or aquatic food sources. The CRLF may be adversely affected through direct effects on habitat and ecosystem structure.

Trumbo (unpublished) exposed bull frog tadpoles to imazapyr solutions for 96 hours. The reported 96-h LC_{50} concentration for imazapyr acid was 799.6 mg ae./L, indicating that imazapyr is not very toxic to bull frog tadpoles.

5.1.2 Adjuvants

The toxicity of adjuvants was considered in risk assessments of imazapyr herbicide applications in estuaries in Washington State (Entrix, 2003) and San Francisco (Pless, 2005). Commonly used adjuvants included non-ionic alkylphenol ethoxylates and/or fatty acids (e.g., R-11®, X-77®), and crop-oil based concentrates (e.g., Agri-Dex®, Hasten®). On the basis of EPA toxicity criteria, the non-ionic alkylphenol ethoxylates (e.g., R-11®, X-77®) are moderately acutely toxic to aquatic species. The crop-oil based surfactants would be considered practically non-toxic. Smith et al. (2004) characterized the toxicity of four surfactants to juvenile rainbow trout and implications for their use over water. The 96-h LC_{50} values were 6.0 mg/L for R-11®, 17 mg/L for LI 700®, 74 mg/L for Hasten, and 271 mg/L for Agri-Dex®. The 96-h EC_{50}s (on-bottom gilling behavior) were 4.4 mg/L for R-11® and 17 mg/L for LI 700®.

Curran (2003) determined the toxicity of formulated herbicide product Arsenal Herbicide (a.i., imazapyr) with and without the adjuvants Agri-Dex® and Hasten® using juvenile rainbow trout. The 96-h LC_{50} value for Arsenal Herbicide without adjuvant was 77,716 mg/L. In systems containing Arsenal plus adjuvant, the 96-h LC_{50} was expressed as mg/L surfactant and were reported to be 113 mg/L for Hasten® and 479 mg/L for Agri-Dex®. These values were compared with the LC_{50} values for the surfactants alone which were 74 mg/L for Hasten® and 271 mg/L for Agri-Dex®. Since this source of information was a meeting abstract, no further evaluation of data was possible for the review presented here. The authors concluded that the data suggest that the Arsenal Herbicide formulation has low toxicity to juvenile rainbow trout, the toxicity the tank mixes is driven by the surfactants, and depending on the type of surfactant and its percentage in the tank mix, surfactants may pose greater hazard to non-target species than Arsenal Herbicide. Adjuvants and surfactants were also considered in human health and ecological effects risk assessments of imazapyr use for controlling vegetation in riparian corridors (AMEC, 2009). The most frequently used adjuvants were identified to be Agri-Dex®, Dyne-Amic®, Class-Act® and R-11®. It should be noted that the assessment did not consider direct applications to water. Reference was made to a study by Smith et al. (2004), which was cited above. While toxicity data were reviewed, the document did not include a formal exposure and risk assessment for the adjuvants.

5.2 Aquatic Exposure Assessment for Direct Applications to Water

5.2.1 Active ingredient Imazapyr

The Level I screening level risk assessment document (USEPA, 2005A) describes a procedure for estimating the environmental concentration following an application of imazapyr directly to the entire surface of the standard pond following uniform mixing throughout its volume. The maximum concentration of imazapyr was calculated, as described below, by simply dividing the total mass of pesticide applied to the pond by its volume. The "standard pond" has a surface area of 1.00 hectare and is 2.00 meters (6.56 feet) deep, and therefore it has a volume of 20,000 cubic meters or 2.00×10^7 liters (L). The maximum imazapyr application rate derived from the label is 1.50 lb/acre, and since 1.00 lb/acre is equivalent to 1.121 kg/ha, the application rate is equivalent to 1.682 kg/ha or 1.682×10^9 μg/ha or 168.2 mg/m^2 Thus, the peak concentration for imazapyr applied to water 2 meters deep is:

$(1.682 \times 10^9$ μg/ha x 1.00 ha)/$(2.00 \times 10^7$ L) = 84.1 μg/L

By simple proportional dilution calculations for theoretical lakes with shallower water depths (0.3 m [1 ft], and 0.9 m [3.0 ft]) , and assuming no attenuating factors such as foliar interception, direct application at the maximum rate of 1.50 pounds a.i./acre to the entire surface area of these lakes would produce acute, peak concentrations of 552 and 184 μg/L, respectively.

In order to estimate imazapyr concentrations in the pond as a function of time, the Environmental Fate and Effect Division (EFED) of US EPA used the Generic Estimated Environmental Concentration (GENEEC) model as described in the Level I screening risk assessment (US EPA, 2005A). The GENEEC2 model is designed to simulate the ecological exposure to aquatic organisms from runoff and spray drift of chemicals applied *terrestrially* on an adjacent field. To assess the exposure for direct application of imazapyr to a water body, EFED had to adjust the GENEEC2 modeling routine and use proportionality factors to yield simulated concentrations that matched the directly calculated peak concentration values. The model predicted essential the same concentration levels with time; for example, in a 1-ft deep water body, the concentration was predicted to decrease from the peak concentration of 552 μg/L to 549 μg/L at 21 days and 542 μg/L at 60 days.

For the purpose of the review presented here, the change in concentration with time was modeled with the AQUATOX model, an alternative water model that is available from USEPA. AQUATOX is an ecosystem simulation model that predicts the fate of various pollutants, such as excess nutrients and organic chemicals, and their effects on aquatic ecosystems. It has the capability to estimate the concentration in a water body from *direct application* of pesticides to a water body. An overview of the model is given in Appendix 5. The fate portion of the model was used here to characterize the dissipation of imazapyr following an application to a standard pond. EECs[3] for aquatic uses were calculated for the direct application to the surface of standing water bodies of 1.0 ft (0.30 m), 3.0 ft (0.91 m), 3.94 ft (1.2 m) and 6.6 ft (2.0 m depths (Appendix 5). The 6.6 ft (2.0 m) depth is representative of the water depth in the standard pond scenario used by EFED for most ecological effects assessments. The 1 and 3 foot water depths are typical of use conditions in irrigation and drainage ditches, and for edge of pond depths, where problematic

[3] EEC – estimated environmental concentration

aquatic weeds are typically found. The 3.94 ft depth was included since it is the depth in the model scenario used in AQUATOX (a Missouri farm pond).

Detailed information on the model input and results can be found in Appendix 5. Figure 5.1 shows the modeled imazapyr concentration and dissipation in a 3-ft deep pond. Similar trends in concentration and dissipation were found with the other pond depths (Appendix 5, Fig. A5-1 through Fig. A5-4). The model results indicate that dissolved imazapyr dissipates in large part within a month following the application and that dissipation of imazapyr is primarily the result of photolysis (Fig. 5.1). The modeling was done with the longest photolysis half-life value of 5.3 d.

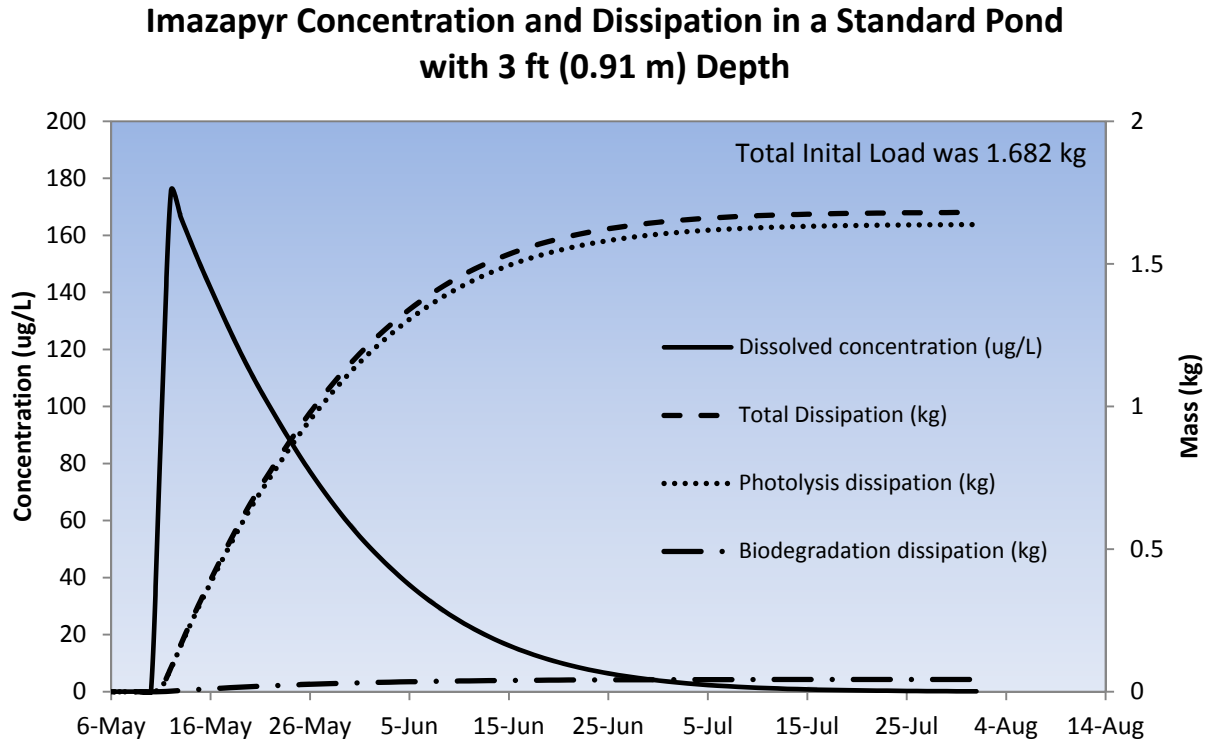


Figure 5.1. AQUATOX model-predicted imazapyr concentration and dissipation in standard pond with 3 ft depth. Application of 1.68 kg imazapyr (1.5 lbs/acre) was on May 10th. See Appendix 5 for modeling details and additional modeling results.

Table 5.1. Summary of the AQUATOX model estimated concentrations of imazapyr concentration in the standard pond with the depths as described above and in Appendix 5.

Depth		Concentration (μg/L)		
ft	m	Peak	1 Month	2 Months
6.6	2.0	81.6	25	4.4
3.9	1.2	134	28	2.8
3.0	0.91	174	25	1.4
1.0	0.30	516	40	0.9

The depth of the pond appears to be an important factor in the dissipation rate of imazapyr in the pond water. Application of the herbicide in a shallow pond results in a higher peak concentration. On the other hand, more intense light penetration in a shallow pond will result in a higher photolysis rate (Appendix 5, Fig. A5-6). The initial trend of higher peak concentrations with lower depth is reversed after 2 months when deeper ponds show slightly higher residual concentrations. This may be attributed to the lower photolysis rate in deeper ponds (Fig. A5-6). The concentration trend after 1 month is intermediate to the trends observed in initial peak concentration levels and the residue levels after 2 months of dissipation. This may be the result of variation in dissipation due to differences in peak concentration and photolysis rate with pond depth.

EFED also considered the exposure in a tidal open water bodies. In addition to applying imazapyr directly to the entire surface of the standard pond and the concentrations based on water depths, EFED also considered the potential of imazapyr to reach plants inhabiting semi-aquatic sites adjacent to or on the edge of the water body. In shallow-water communities, if imazapyr is applied to 1 foot depth of water (1 acre area), then some water moves onto land (i.e., berm washes out, boat wake sloshes water over bank, wind pushed water over berm, etc.). It was assumed that six inches of that water moves to a terrestrial site (1 acre area) where it dries up and deposits imazapyr on the ground. If 1.5 pounds were applied to 1 acre of the 1 foot of water, and half of that water moves (1 acre site) and dries, then 1.5, 2, or 0.75 pounds (lbs/acre) would have been deposited upon the 1-acre terrestrial site where the water moved. If the entire amount of water is moved from the aquatic site to the terrestrial site, where it dried, then the entire 1.5 pounds would have been deposited to that acre. In open water bodies, if imazapyr is applied (1.5 lbs/acre) to one acre of a tidal area at low tide, and the incoming tide pushes the entire amount of water to an acre of intertidal zone, then 1.5 lbs/acre would have been deposited. If a 6.6-feet depth of tide comes in on that one acre and 6 inches of that water would overflow to flood an intertidal zone terrestrial site, then 6 inches (0.5 feet) of the 6.6 feet of water would move. The amount of imazapyr deposited upon the terrestrial site would be 1.5 lbs/acre × (0.5/6.6) = 0.11 lbs/acre. If one foot of that 6.6-feet depth of tide moves, then there would be twice the amount of deposition, or 1.5 lbs/acre × (1.0/6.6) = 0.23 lbs/acre (US EPA, 2005A).

5.2.2 Adjuvants

The application of Habitat and Imazapyr E Pro to post-emergent vegetation requires the addition of an adjuvant to the tank mix. As pointed out in the review for imazapyr use in the San Francisco Estuary (Pless, 2005), adjuvants may greatly increase the toxicity of the herbicide tank mix solution. Pless (2005) considered several adjuvants as used in tank mixes in the ecological risk assessment. The environmental properties and toxicity of adjuvants were also considered with the assessment of imazapyr herbicide use in estuaries in Washington State (Entrix, 2003). Both reviews considered estimated adjuvant concentration in water in an estuary scenario. For the purpose of this special review presented here, the environmental concentration of two adjuvants Agri-Dex® and Hasten® was estimated in a pond scenario as described below.

It was assumed that the adjuvant was used in a 1% v/v concentration in the tank mix (the label requires >0.25%). It was further assumed that the application volume was 50 gallons per acre (label requirement is >5 gal for ground applications). A 1% v/v adjuvant concentration in the 50

gal spray volume would correspond to a 1.89 L adjuvant volume per acre. Based on the density of Agri-Dex (0.879 kg/L, Agri-Dex MSDS), this volume corresponds to 1.66 kg Agri-Dex adjuvant per acre. The peak concentration of Agri-Dex® in a 1-acre water body with a 1-foot depth can be calculated as follows: 1.66×10^6 mg / ($4047\ m^2 \times 0.3048\ m \times 1000\ L/m^3$) = 1.35 mg/L. For the 6.56-feet (2-meter) and 3-feet depths the concentrations are 0.21 mg/L(mg/L) and 0.45 mg/L(mg/L), respectively. The values for another commonly used adjuvant Hasten® are very similar for the same adjuvant concentration given that the density of Hasten® is very similar compared to Agri-Dex (0.9 kg/L, Hasten® MSDS). It should be noted that these calculations assumed no interception by target vegetation and no sorption to sediment. The adjuvant concentrations calculated above are slightly lower than the values for adjuvant concentrations that were reported in Entrix (2003). Those calculations assumed a density of 1 kg/L, whereas the actual density of the adjuvant products Agri-Dex® and Hasten® is less than 1 kg/L.

5.3. Field Studies on Environmental Fate and Exposure of Imazapyr

Studies that were conducted by the registrant to support the product registration indicated shallow pond dissipation half-lives in the range of 5 to 15 days (cited in Mangels and Ritter, 2000). Mangels and Ritter (2000) characterized the dissipation of imazapyr in flowing water bodies (canal, river) and lake settings by model simulations using a range of environment variables to represent a variety of conditions that could occur in different water bodies. The application scenario considered an application of imazapyr at the maximum rate of 1.5 lbs ae per acre to emerged, established vegetation on, in, or near water, based on which it was assumed that 75% of the applied product was intercepted by the vegetation. The simulations were performed using the Exposure Analysis Modeling System (EXAMS II) and modeling scenarios representative of applications in a flowing water body and a lake environment. The results for the flowing water body with the lowest velocity scenario (worst-case) indicated maximum concentrations at the edge of the treated area to be below 10 μg/L (ppb) within 8 hrs, below 5 μg/L within 2 d, and below 2 μg/L within 7 d. Under the highest velocity conditions, the imazapyr concentrations were below 5 μg/L within 1 hr. For the lake setting with the lowest dispersion rate (i.e., worst-case) scenario the maximum concentrations at the edge of the treated area were below 10 μg/L within 2 d, below 5 μg/L within 4 d, and below 2 μg/L within 8 d. In the scenario with the highest dispersion rate, the concentrations were below 2 μg/L within 12 hrs.

It appears that the registrant conducted studies in Florida and Missouri pond systems on the occurrence of imazapyr and its degradation products in tissues of bluegill, tilapia, catfish and crayfish. These data were described in the review by Entrix (2003) with reference to Mangels and Ritter (2000). However, this reference to Mangels and Ritter (2000) appears to be incorrect as is indicated by the description of that study above; the studies described in the Entrix (2003) review were most likely obtained from the registrant. Below is a summary of the information presented in the Entrix (2003) review. The ponds contained 75, 28, 213 or 261 μg/L imazapyr following treatments of Arsenal® herbicide to the banks and outer edges of the ponds at a rate of 1.5 lb ae/acre in spray solutions of 21 to 23 gal. Ultimate concentrations in the ponds varied due to dilutional profiles inherent to the ponds (e.g., volumes). The initial pond water concentrations

were in the range of 28 to 261 μg/L, the initial pond sediment concentrations were in the range of 1.5 to 10.2 μg/L. The half-life of imazapyr in the pond water ranged from 3.9 days in the Florida pond to 14.5 days in the Missouri pond. Imazapyr residues were detected in fish samples in only one of the Missouri ponds taken at 3 hours post-treatment (0.636 ppm in bluegill, 0.233 ppm in catfish, 0.068 ppm in tilapia, and 0.059 ppm in crayfish). No residues were detected in fish samples taken at later times.

As noted earlier, photodegradation is the dominant degradation process for imazapyr in surface water and it occurs relatively rapidly. Field dissipation experiments were conducted by the product registrant in shallow Florida and Louisiana freshwater pond systems. These studies were summarized in the document on the ecological risk assessment of the use of imazapyr to control cordgrass in estuarine habitat of Washington State (Entrix, 2003). Imazapyr (formulated as Arsenal) was applied to the surface of the water at 1.5 lb ae/acre. Dissipation (field degradation) was followed in water and sediment over 180 days. Figure 5.2 reflects study results from water and sediment analyses from the Louisiana pond study through the first 30 days of study, over which period the vast majority of dissipation had occurred. Similar results were obtained with the Florida pond system (not shown) although degradation was slightly faster and there did not appear to be the initial spike in the sediment concentration that was observed in the Louisiana pond system. The first-order half-lives in the water and sediment were 1.9 and 12.8 days, respectively. No detectable residues of imazapyr were found in the water and sediment after 14 and 59 days, respectively.

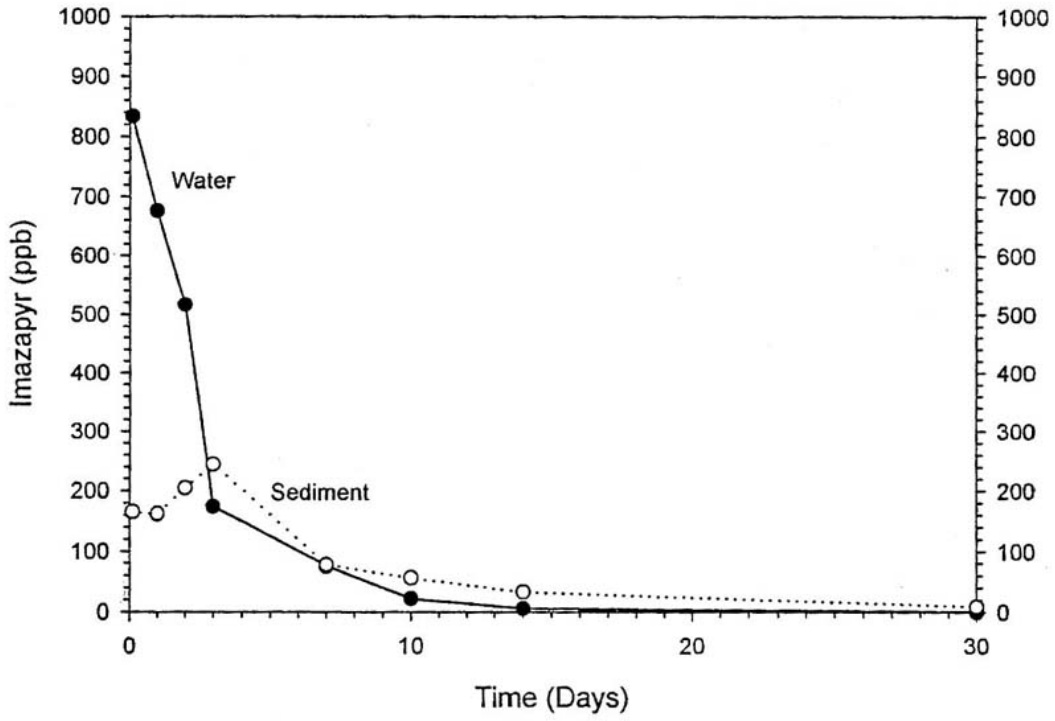


Figure 5.2. Residues of imazapyr in water and sediment from a Louisiana pond treated with 1.5 lb ae/acre. *(Source: Entrix, 2003)*

It should be noted that the results from the model simulations for environmental concentrations in Table 5.1 (Section 5.2.1) show a similar trend compared to the observations in field studies as described above. The somewhat longer dissipation time indicated by the AQUATOX model data depicted in Fig. 5.1 may be attributed to the modeling with the longest photolysis half-life of 5.3 d. The reported range in photolysis half-life is from 2.5 to 5.3 d. Shorter photolysis half-life would result in faster dissipation.

Patten (2003) studied the persistence of imazapyr when used to control cordgrass in an estuary. Imazapyr was applied at 1.68 kg ae/acre (1.5 lbs ae/acre) with 1% v/v Agri-Dex adjuvant. The persistence of imazapyr in water and sediment followed an exponential decay. The geometric mean of imazapyr concentration over 76 hours in the 0.6 to 20 m zone outside the spray area was 0.1 mg/L (or 100 μg/L) in water and 3.2 μg/g in fresh weight sediment. It was stated that these concentrations were 5 to 6 orders of magnitude lower than levels needed to affect aquatic invertebrates and fish. The imazapyr levels in water and sediment approached non-detect levels at 40 and 400 hrs, respectively, and the corresponding half-lives were reported in the range of <0.5 and 1.6 days, respectively.

The fate of imazapyr in mesocosm systems representing the situation in cypress domes in Southeastern United States was characterized in a study by Fowlkes et al. (2003). The half-life of imazapyr in these systems was in the range of 3.2 to 3.4 days.

5.4 Risk Characterization

5.4.1 Active Ingredient Imazapyr

Ecological risk characterization integrates the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. Level I Screening Risk Assessment (US EPA, 2005A) was based on a deterministic approach to evaluate the likelihood of adverse ecological effects to non-target species. In this approach, risk quotients (RQs) are calculated by dividing EECs by ecotoxicity values for non-target species, both acute and chronic. RQs are then compared to established levels of concern (LOCs). These LOCs are criteria used by US EPA to indicate potential risk to non-target organisms and the need to consider regulatory action.

Aquatic Organisms

Available acute toxicity data for aquatic species indicate that imazapyr acid is practically non-toxic to fish and invertebrates with LC_{50} and EC_{50} values >100 mg/L. The only sublethal effect observed in the acute aquatic animal studies was a decrease in shell deposition in the eastern oyster. The NOAEC/LOAEC for this effect was 109/173 mg/L. In order to compare these values with an exposure value, the highest peak EEC in surface water was selected from the aquatic uses, which utilize direct application to water. The EEC estimation assumes a 1-foot water depth. A comparison of the ecotoxicity values of 100,000 – 173,000 μg/L with the peak EEC in surface water (552 μg/L) (Section 5.2.1), indicates a 181 to 313-fold difference between the highest estimated EEC and the concentrations which produced either no effects (100,000 – 109,000 μg/L) or a decreased shell deposition in oysters (173,000 μg/L). The estimated peak

EEC in surface water from the granular uses is less than 552 μg/L. Therefore, it is concluded that the acute risk to fish and aquatic invertebrates is expected to be very low.

Following chronic exposure, the NOAEC/LOAEC for freshwater fish is 43.1/92.4 mg/L and the NOAEC for freshwater invertebrates is 97.1 mg/L, the highest concentration tested. For aquatic uses (direct application to water, assuming 1 foot water depth), the highest chronic EECs as determined by USEPA-EFED are 549 μg/L (21 day) and 542 μg/L (60 day). Using the NOAEC of 43.1 mg/L (43,100 μg/L) for freshwater fish and the 60-day EEC of 542 μg/L, the RQ is 0.013. For invertebrates the RQ is 0.006. These RQ values are below the lowest LOC of 0.05 for acute risk to endangered aquatic animals. Note that the AQUATOX model estimated concentrations reported in Section 5.2.1 are much lower than the concentrations used by EFED. Consequently, the associated RQ values would also be lower.

The risk estimation described above indicates that there is minimal risk of direct acute effects to fish and aquatic invertebrates. In addition, there are no chronic risks to fish and invertebrates. Consequently, fish and invertebrates inhabiting surface waters adjacent to an imazapyr treated field would not be at risk for adverse acute and/or chronic effects on reproduction, growth and survival when exposed to imazapyr directly or through residues from imazapyr applications.

Regarding chronic risk, it was stated that there is an uncertainty for estuarine/marine fish and invertebrates, since no toxicity data were available to observe the prolonged effects of imazapyr to estuarine/marine fish and invertebrates. This area of uncertainty was addressed to some extent by an estuarine field study conducted by Patten (2003) which showed an exponential dissipation pattern (see Section 5.3). Patten (2003) also studied the osmoregulatory capacity of Chinook salmon (*Oncorhynchus tshawytscha*) smolts based on plasma sodium level and gill ATP-ase. The results indicated that it was not affected by imazapyr at concentrations up to 1600 μg/L.

The RED[4] document (USEPA, 2006) further includes the assessment that concludes that the imazapyr direct application to water scenario for aquatic uses indicated exceedances of the non-endangered LOCs for vascular plants inhabiting various water depths (see Table 5.2). Likewise, endangered vascular plant LOCs were exceeded for the direct application to waters at all three depths considered. There were no LOC exceedances for non-vascular aquatic plants.

Table 5.2. Aquatic Plant Risk Quotient Summary for Aquatic Use

Scenario	Water Depth	Non-endangered		Endangered
		Non-Vascular	Vascular	Vascular
Direct Application to Water (1.5 lbs a.e./acre)	1 foot	0.048	31**	50*
	3 feet (0.91 m)	0.016	10**	17*
	6.6 feet (2 m)	<0.01	4.7**	7.6*

* indicates an exceedance of Endangered Species LOC (LOC=1).
** indicates an exceedance of Acute Risk LOC (LOC=1).

[4] RED – Reregistration Eligibility Decision

Terrestrial Organisms

For birds as well as mammals, acute risk quotients were not estimated because there was no mortality or any other signs of toxicity in either the acute oral studies or the acute dietary studies. For terrestrial non-crop uses with spray applications of 1.5 lb ae/acre, the highest EEC concentration for birds is 410 mg/kg bw for short grass consumed by a 20 g bird. The adjusted LD_{50} for 20 g birds would be > 1,549 mg/kg bw. There is an approximately four-fold difference between these two values. Since there were neither mortalities nor clinical signs of toxicity at 1,549 mg/kg bw, the acute risk to birds following spray applications is likely to be low. The chronic LOC for birds is not exceeded for any of the registered uses.

For terrestrial non-crop uses with spray applications, the highest EEC concentration for mammals is 343 mg/kg bw for short grass consumed by a 15 g mammal. The adjusted LD_{50} for 15 g mammals would be >10,989 mg/kg bw. There is an approximately 32-fold difference between these two values. Since there were neither mortalities nor clinical signs of toxicity at 10,989 mg/kg bw, the acute risk to mammals following spray applications is likely to be low. The chronic LOC for mammals is not exceeded for any of the registered uses.

US EPA currently does not quantify risks to terrestrial non-target insects; however, available data on honey bees indicate that the risk to terrestrial non-target insects is likely to be low. Imazapyr acid and its isopropylamine salt have shown no indication of inducing endocrine-related effects following exposure.

The US EPA (2006) document summarized the ecological risk as follows: “There are no risks of concern to terrestrial birds, mammals, and bees, or to aquatic invertebrates and fish. However, there are ecological risks of concern associated with the use of imazapyr for non-target terrestrial plants and aquatic vascular plants, and potential risks to federally listed threatened and endangered species (“listed species”) which include aquatic vascular plants, terrestrial and semi-aquatic monocots and dicots that cannot be precluded at this time.”

For a complete discussion, see the *Screening Level I Ecological Risk Assessment for the Reregistration Eligibility Decision Document for Imazapyr* (US EPA, 2005A). Summary tables of the environmental risk conclusions and risk descriptions is included in Appendix 7.

5.4.2 Risk Assessment of Adjuvants

Adjuvants

As pointed out in the review by Pless (2005), the toxicity of the herbicide/adjuvant mixture is driven by the surfactant. The risk quotients presented by Pless (2005), based on environmental concentrations in an estuary scenario, were in the range of 0.13-0.051. The higher value was determined in association with the adjuvant Hasten®. That value marginally exceeded the level of concern (LOC) of 0.05 for endangered fish. It was pointed out that the highest measured exposure was extremely conservative in that the pesticide was applied directly to the estuary sediment (mud flat) without interception by vegetation and measured in the 3 hours later in the first overflow.

For the consideration of the application in a pond, the estimated environmental concentrations (EECs) of the Agri-Dex® and Hasten® adjuvants were presented in Section 5.2.2. These two adjuvants were selected based on the availability of toxicity data for product with adjuvant (Curran et al., 2003). The highest estimated concentration in a water body with 1-foot depth was 1.35 mg/L. Based on the 96-hr LC_{50} of 479 mg/L expressed as adjuvant (Curran et al., 2003) for the product plus adjuvant mixture, the risk quotient is 0.0028. For the Hasten® adjuvant, the risk quotient would be 0.012. These values are below levels of concern for aquatic species as established by USEPA (2011), the most sensitive for endangered species acute risk being 0.05.

Entrix (2003) conducted a risk assessment of four adjuvants that have uses with glyphosate- and imazapyr-based aquatic herbicides. In addition to Hasten® and Agri-Dex®, the LI 700® and R-11® were included in the exposure and risk assessment. Since the spray-volume requirements for glyphosate-based herbicide are higher compared to imazapyr-based herbicides, the risk quotients were evaluated as a function of spray volume. The risk quotients were based on the LC_{50} values for juvenile rainbow trout as reported by Smith et al. (2004). The same procedure was used here for the concentrations developed for a pond scenario as described in Section 5.2.2. Figure 5.3 shows that the R-11 adjuvant exceeds the most sensitive Level of Concern (LOC) over the entire application volume range considered, while the Hasten® and Agri-Dex® adjuvants do not exceed the most sensitive LOC even at the highest application volume. In the review by Entrix (2003), it is pointed out that glyphosate-based herbicides require large application volumes (up to 100 gal/acre for efficacy), while 5 to 20 gal/acre can be used for imazapyr-based herbicides to yield equivalent results. Consequently, imazapyr-based herbicide applications are associated with lower adjuvant exposures compared to glyphosate-based herbicides.

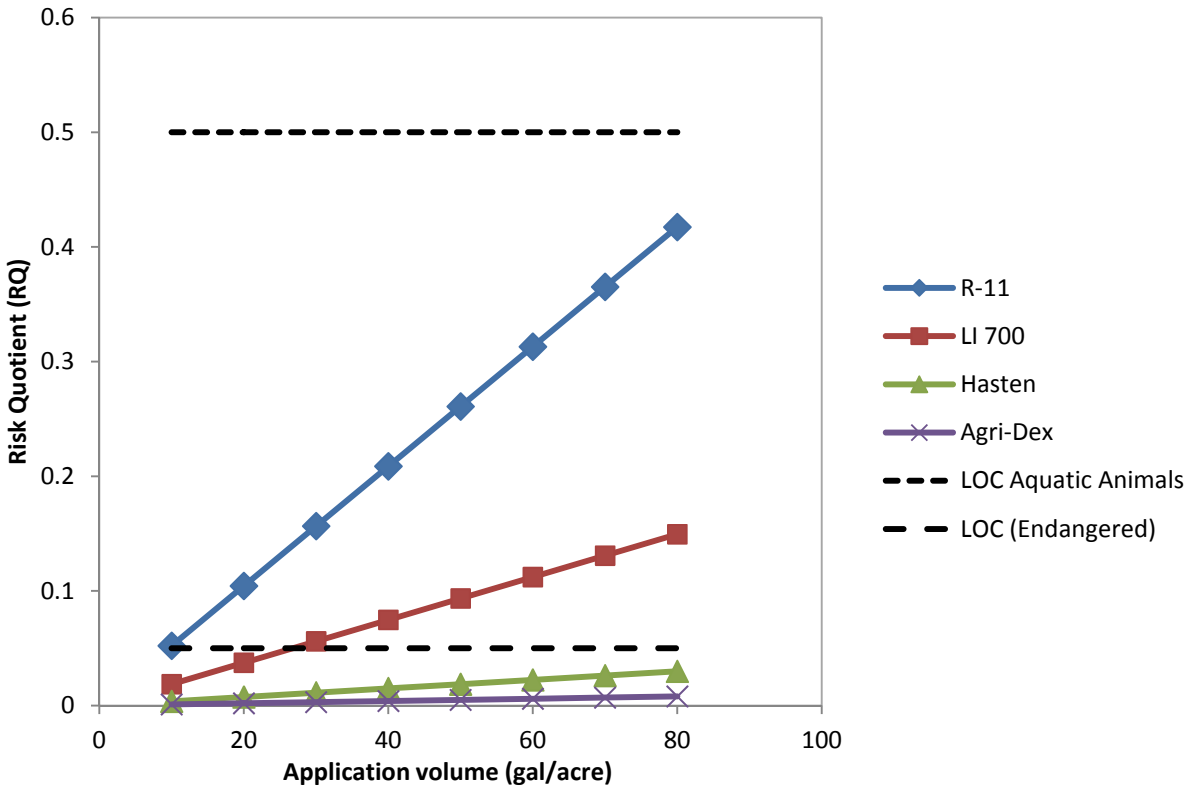


Figure 5.3. Risk quotient (RQ) of four spray adjuvants based on adjuvant concentrations associated with applications to a 1-foot deep water body. The adjuvant concentration was 1% v/v. The risk quotient was calculated based on the 96-h LC50 values for rainbow trout as reported by Smith et al. (2004). The RQ values are compared with the Levels of Concern (LOC) for acute risk as developed by US EPA (2011).

Smith et al. (2004) estimated water depth at which the 96-h LC_{50} value for juvenile trout would be reached with an application volume of 20 gal/acre and labeled tank mix concentration (0.5 – 5%). The authors determined the water depths at which LC_{50} for the exposed trout would be reached. When used at the minimum recommended percentage of adjuvant in the tank mix the LC_{50} depth was <16 mm for R-11 and < 5 mm for the Agri-Dex®, Hasten® and LI 700®. At the maximum label recommended percentages of adjuvant in the tank mix, the LC_{50} depth for Agri-Dex would remain <5 mm, for Hasten it would be 10 mm and for LI 700 it would be 43 mm. It was concluded that Agri-Dex posed the lowest hazards to fish among the surfactants evaluated.

Acidifier

The potential risk of the small amount of acidifier in the product formulation was evaluated in the reviews by Entrix (2003) and Pless (2005). It was stated that the toxicity of the acidifier to aquatic organisms can be classified as slightly toxic. It was concluded that the risk from the small amounts of acidifier in the product formulation and the even lower levels in the tank mix would not pose significant risks to aquatic organisms.

5.4.3 Uncertainties, Assumptions, Limitations and Data Gaps

Every risk assessment has inherent uncertainties. The ecological risk assessment overview by US EPA (2011) states that in interpreting the risk, the risk assessor evaluates the lines of evidence supporting or refuting risk estimates in terms of the following factors: adequacy and quality of data, degree and type of uncertainty, and relationship of evidence to risk assessment questions. For a risk characterization to be useful to risk managers, it must be transparent, clear, consistent, and reasonable (the TCCR principles).

Uncertainties, assumptions, strengths, limitations, and data gaps related to the ecological risk assessment of imazapyr herbicides is considered in the Level I screening risk assessment (US EPA, 2005A) and in the review for Washington State (Entrix, 2003). Summarized below are some of the aspects considered to be most relevant to the special review present here.

The exposure assessment was conducted assuming a worst-case scenario in which all of the applied spray solution was deposited on the water surface and subsequently mixed in the water column below. This assessment is most likely very conservative given that typical application of the spray solution toward the emerged target vegetation will result in interception of a large fraction of the spray solution. The estimated environmental concentrations, and consequently the associated risks, are therefore likely to be lower than the values outlined or described in the risk assessment reviewed here.

The review for use of imazapyr in Washington State (Entrix, 2003) describes uncertainties and data gaps relative to the risk assessment of imazapyr use in estuaries for control of cordgrass (*Spartina*). Even though the main data gaps were presented in the context of the risk assessment in an estuarine environment, they could be considered to have relevance to risk assessment for use of imazapyr in fresh water environments. Therefore, they are included and summarized below:

- Studies pertaining to the effect of imazapyr on aquatic or water-dependent species other than fish, e.g., amphibians, are limited

- Specific data on the toxicity of imazapyr to sediment-associated organisms typical of north temperate (marine) environments is generally lacking and represents a significant data gap

- Residues of imazapyr in treated plant material and the degradation of the herbicide over time in plant tissue were not identified in the literature. Exposure calculations in this assessment therefore relied on estimated concentrations in the plant tissue. Empirical residues from plants would increase confidence in the exposure and risk estimates

- Effects on the microrhizosphere and microflora in a treated water bodies (estuary) have not been explored. Long term implications of herbicide use on nutrient dynamics could affect microflora.

- Effects on non-target aquatic environment (salt-marsh) plants native to areas where invasive species, such as *Spartina*, has colonized are poorly understood. Limited data on only a few species have been reported.

- Persistence and stability of imazapyr in dead and decaying vegetation is not known. Can leachate from decaying vegetation retain herbicidal activity thereby potentially delaying the recovery of native aquatic environment (salt marsh) plants?

- Drift concentrations of imazapyr off-site by treatment method (e.g., backpack, boom sprayer, etc.,) have not been quantified. However, worst-case scenario exposure conditions in direct application sites did not indicate significant risk.

- Effects on (marine) phytoplankton: could herbicide treatments affect nutrient transfer to higher trophic levels if phytoplankton are inhibited?

- Effects on water-surface microlayer associated organisms and microflora in this surface water film are not known.

The Entrix (2003) review states that while the above data gaps represent uncertainty, the existing information on the toxicity and fate of the compound is substantial and suggests that it would be unlikely that significant negative impacts would be found in studies addressing the above data gaps—with the possible exceptions of effects on other non-target plants and phytoplankton.

6. Risk Mitigation

The potential movement from the application area and risk to non-target organisms is addressed by product label statements, including the following:

Environmental Hazards
Treatment of aquatic weeds may result in oxygen depletion or loss due to decomposition of dead plants. This oxygen loss may cause the suffocation of some aquatic organisms. Do not treat more than one half of the surface area of the water in a single operation and wait at least 10 to 14 days between treatments. Begin treatment along the shore and proceed outward in bands to allow aquatic organisms to move into untreated areas. Do not contaminate water when disposing of equipment washwaters or rinsate. This pesticide is toxic to vascular plants and should be used strictly in accordance with the drift precautions on the label.

Precautions for Potable Water Intakes
Do not apply these products directly to water within one-half mile upstream of an active potable water intake in flowing water (i.e., river, stream, etc.) or within one-half mile of an active potable water intake in a standing body of water such as lake, pond or reservoir. To make aquatic applications around and within one-half mile of active potable water intakes, the water intake must be turned off during application and for a minimum of 48 hours after the application. These aquatic applications may be made only in the cases where there are alternative water sources or holding ponds, which would permit the turning off of an active potable water intake for a minimum period of 48 hours after the applications.

Application to Waters used for Irrigation
Water treated with these products may not be used for irrigation purposes for 120 days after application or until product residue levels are determined by laboratory analysis, or other appropriate means of analysis, to be 1.0 ppb or less.

Information Related to Application Methods
Applications made to moving bodies of water should be made while traveling upstream to prevent concentration of this herbicide, in water. Do not apply to bodies of water or portions of bodies of water where emergent and/or floating weeds do not exist.
When application is to be made to target vegetation that covers a large percentage of the surface area of impounded water, treating the area in strips may avoid oxygen depletion due to decaying vegetation. Oxygen depletion may result in the suffocation of some sensitive aquatic organisms. Do not treat more than one half of the surface area of the water in a single operation and wait at least 10 to 14 days between treatments. Begin treatment along the shore and proceed outward in bands to allow aquatic organisms to move into untreated areas.
Avoid wash-off of sprayed foliage by spray boat or recreational boat backwash for one hour after application.

Avoiding Injury to Non-Target Plants
When making applications along shorelines where desirable plants may be present, caution should be exercised to avoid spray contact with their foliage or spray application to the soil in which they are rooted. Shoreline plants that have roots that extend into the water in an area where the

herbicide has been applied generally will not be adversely affected by uptake of the herbicide from the water.

Managing Off-Target Movement

To minimize spray drift, the label contains drift reduction advisory information address various equipment- and weather-related factors that determine the potential for spray drift. The factors addressed on the label include control of droplet size, application height, swath adjustment, wind, temperature and humidity, and temperature inversions.

Additional restrictions may be imposed with the permitting of the use of these products in Massachusetts lakes and ponds.

References

AMEC, 2009. Human Health and Ecological Effects Risk Assessment, Imazapyr Risk Assessment Washington State. Prepared by AMEC Geomatrix, Inc., Lynwood, WA for Washington State Department of Agriculture, Olympia, WA. Available at: http://www.ecy.wa.gov/programs/wq/pesticides/seis/HHRA&ERA_063009.pdf

BASF, 2008. Product label for Habitat®. BASF Corporation, Research Triangle Park, North Carolina.

Curran, C. et al., 2003. Toxicity of Rodeo® and Arsenal® tank mixes to juvenile rainbow trout. University of Washington, Seattle, WA, USA. Meeting Abstract for SETAC 24th Annual Meeting.

Curran, C. A., J. M. Grassley, et al. (2004). "Toxicity of R-11® Surfactant to Juvenile Rainbow Trout: Does Size Matter?" Bulletin of Environmental Contamination and Toxicology **72**(2): 401-408.

Etigra, 2007. Product label for Imazapyr E-Pro 2 VM & Aquatic Herbicide. Etigra, Iverness, FL.

Entrix, Inc. 2003. Ecological Risk Assessment of the Proposed Use of the Herbicide Imazapyr to Control Invasive Cordgrass (Spartina spp.) in Estuarine Habitat of Washington State. Prepared for Washington State Department of Agriculture, Project No. 3000901.

Fowlkes, M.D. et al., 2003. Effects of the herbicide imazapyr on benthic macroinvertebrates in a logged pond cypress dome. Environ. Toxicol. Chem. 22:900-907.

Hurley, P. and Shanaman, L., 2007. Risks of Imazapyr Use to the Federally Listed California Red Legged Frog. Pesticides Effects Determination. Environmental Fate and Effects Division, Office of Pesticide Programs, USEPA. Accessed on April 28, 2011 at: http://www.epa.gov/espp/litstatus/effects/redleg-frog/index.html#imazapyr

Mangels, G. and A.M. Ritter, 2000. Estimated environmental concentrations of imazapyr resulting from aquatic uses of Arsenal herbicide. American Cyanamid Co., Princeton, NJ.

Mattson, M.D., P.J. Godfrey, R.A. Barletta and A. Aiello, 2004. Eutrophication and Aquatic Plant Management in Massachusetts. Final Generic Environmental Impact Report. Edited by Kenneth J. Wagner. Department of Environmental Protection and Department of Conservation and recreation, Executive Office of Environmental Affairs, Commonwealth of Massachusetts. Available at: http://www.mass.gov/dcr/watersupply/lakepond/techassist.htm

Patten, K., 2003. Persistence and non-target impact of imazapyr associated with smooth cordgrass control in an estuary. J. Aquatic Plant Management 41:1-6.

Pless, P. 2005. Use of Imazapyr Herbicide to Control Invasive Cordgrass (Spartina spp.) in the San Francisco Estuary: Water Quality, Biological Resources, and Human Health and Safety. Prepared for San Francisco Estuary Invasive Spartina Project. Prepared by Petra Pless, D.Env. Leson & Associates, Berkeley, CA.

Smith, B.C. et al., 2004. Toxicity of four surfactants to juvenile rainbow trout: Implications for use over water. Bull. Environ. Contam. Toxicol. 72:647-654.

Toccalino, P.L., Norman, J.E., Booth, N.L, and Zogorski, J.S., 2008, Health-based screening levels: A tool for evaluating what water-quality data may mean to human health: U.S. Geological Survey, National Water-Quality Assessment Program, accessed *July 28, 2011*, at http://water.usgs.gov/nawqa/HBSL/.

Trumbo, J. (unpublished). The impact of imazapyr and triclopyr on bull frog tadpoles. Accessed on April 28 at: http://www.cal-ipc.org/symposia/archive/pdf/2008/7Trumbo.pdf

USEPA, 2005A. Level I Screening Ecological Risk Assessment for the Reregistration of Imazapyr December 9, 2005 B Stephen Carey, Pamela Hurley, and Lucy Shanaman

USEPA, 2005B. Revised HED Chapter of the Reregistration Eligibility Document (RED). USEPA, Office of Prevention, Pesticides and Toxic Substances. December 8, 2005.

USEPA, 2006. Reregistration Eligibility Decision (RED) Document for Imazapyr

USEPA, 2011. Technical Overview of Ecological Risk Assessment. Accessed at: http://www.epa.gov/oppefed1/ecorisk_ders/toera_risk.htm

Appendix 1

Guide to Sources of Information Used for the Special Review of Imazapyr as a New Active Ingredient in Aquatic Herbicides for Use in Lakes and Ponds in Massachusetts.

Documents related to EPA's reregistration review of imazapyr are available in the e-docket OPP-2005-0495 at the regulation.gov website: search "all document types" for "OPP-2005-0495"

The following documents were included as information sources for the special review of imazapyr for use in lakes and ponds in Massachusetts:

1. Reregistration Eligibility Decision (RED) Document for Imazapyr (2006)
2. *Imazapyr: HED Chapter of the Reregistration Eligibility Decision Document*, dated December 8, 2005.
3. Level 1 Screening Ecological Risk Assessment for the Reregistration of Imazapyr December 9, 2005 B Stephen Carey, Pamela Hurley, and Lucy Shanaman
    - APPENDIX A Environmental Fate Summaries and Structures of Imazapyr Transformation Products- Level 1 Screening Ecological Risk Assessment for the Reregistration of Imazapyr
    - APPENDIX B Aquatic Exposure Modeling for Terrestrial Applications (GENEEC2) - Level 1 Screening Ecological Risk Assessment for the Reregistration of Imazapyr
    - APPENDIX C Calculation Methods and GENEEC2 Model Input/Output Tables Showing Estimated Environmental Concentrations (EECs) for Direct Application to Water- Level 1 Screening Ecological Risk Assessment for the Reregistration of Imazapyr
    - APPENDIX E Ecological Effects Data - Level 1 Screening Ecological Risk Assessment for the Reregistration of Imazapyr
4. Tier I Drinking water concentrations (surface and ground water) for the herbicide imazapyr/Arsenal applied to terrestrial and aquatic environments. Kincade, S. et al., Office of Prevention, Pesticides, and Toxic Substances, Memo dated May 11, 2005.

5. **EPA Risk Assessment for California Red-legged Frog**

    Documents available at: Effects Determinations for the California Red-legged Frog and other California Listed Species | Endangered Species Protection Program: Pesticides | US EPA

    - Risks of Imazapyr Use to the Federally Listed California Red Legged Frog (2007)

- Appendix A: Environmental Fate
- Appendix B: Ecological Effects Characterization

6. US Forest Service Reviews

Imazapyr: Human Health and Ecological Risk Assessment, 2004; Available at: http://www.fs.fed.us/foresthealth/pesticide/pdfs/121804_Imazapyr.pdf

7. Washington State Reviews and Risk Assessments

Ecological Risk Assessment of the Proposed Use of the Herbicide Imazapyr to Control Invasive Cordgrass (Spartina spp.) in Estuarine Habitat of Washington State. 2003.

Available at:
http://www.ecy.wa.gov/programs/wq/pesticides/final_pesticide_permits/noxious/risk_assessment_Imazapyr.pdf

This document is also available at regulations.gov

Appendix 2

Environmental Fate Summary Table from Level I Screening Risk Assessment (US EPA, 2005A).

Appendix 2. Degradation and Metabolism of Imazapyr (source: Level I, US EPA, 2005)

Study MRID	Study Type	System	Imazapyr half-life	Maximum transformation products (% of applied radiation)					
				CL 288247 [1]	CL 252974	CL 119060	CL 9140	CL 252974 5	CO[2]
00132359	Hydrolysis (161-1)	pH 5 at 25°C	Stable	ND[2]	ND	ND	ND	ND	ND
		pH 7 at 25°C	Stable	ND	ND	ND	ND	ND	ND
		pH 9 at 25°C	Stable	ND	6.9	ND	ND	ND	ND
00131617	Photolysis in water (161-2)	pH 5 and 9 at 25°C (12 hour exposure cycle)	2.5 - 5.3 days	ND	ND	9.7	22.7	ND	NA[3]
40003713	Photolysis in soil (161-3)	Loamy sand soil	Stable (~149 days)	ND	ND	ND	ND	ND	NA
41023201	Aerobic Soil Metabolism (162-1)	Loamy sand soil	Stable	ND	ND	ND	ND	ND	7
45119701	Aerobic Soil Metabolism (162-1) (Supplemental)	Loamy sand soil	(~5.9 years) >296 days	ND	3	ND	ND	ND	6
00131619	Anaerobic Soil Metabolism (162-2)	Loamy sand soil	Stable (>60 days)	ND	ND	ND	ND	ND	ND
40003712	Anaerobic Aquatic Metabolism (162-3)	Total system	>120 days	ND	ND	ND	ND	ND	ND
41002301	Aerobic Aquatic Metabolism (162-4)	Total system	>120 days	ND	ND	ND	ND	ND	1.1
45119702	Aerobic Aquatic Metabolism (162-4) - Degradate metabolism	Total system (CL 119060 metabolism) (CL 9140 metabolism)	4.9 days 3.6 days	NA NA	NA NA	NA NA	20.4 NA	ND ND	44.9 53
42192101	Terrestrial field dissipation (164-1)	Bare ground / Silt loam soil Hillsboro, Oregon	143 days	NA	NA	NA	NA	NA	NA
42192102	Terrestrial field dissipation (164-1)	Bare ground / Sandy loam soil Janesville, North Carolina	64 days	NA	NA	NA	NA	NA	NA
40003714	Forestry Dissipation (164-3)	Aerial application, residues measured	12-40 days (vegetation) 37-44 days (litter)	NA	NA	NA	NA	NA	NA

Appendix 3

Summaries of Human Health Risk Assessments from EPA documents:

From RED (USEPA, 2006)

III. Summary of Risk Assessment

The following is a summary of the Agency's revised human health effects and ecological risk assessment for imazapyr, as presented fully in the documents, *Imazapyr: HED Chapter of the Reregistration Eligibility Decision Document*, dated December 8, *2005*, and *Screening Level Ecological Risk Assessment for the Reregistration Eligibility Decision Document for Imazapyr*, dated December 8, 2005. The purpose of this summary is to assist the reader by identifying key features and findings of these risks assessments, and to help the reader better understand the conclusions reached in the assessments.

The human health and ecological risk assessment documents and supporting information listed in Appendix C were used to reach the regulatory decisions for imazapyr. While the risk assessments and related addenda are not included in this document, they are available in the Public Docket, under docket number OPP-2005-0495 and on the internet at http://www.regulations.gov. Hard copies of these documents may be found in the OPP public docket under this same docket number.

A. Human Health Risk Assessment

The Agency has conducted a human health assessment for imazapyr for the purposes of making a reregistration decision. The Agency evaluated toxicological and chemistry studies submitted for imazapyr and determined that the data are adequate to support a reregistration decision. In addition, the Agency has conducted dietary, drinking water, residential, aggregate, and worker assessments to determine the potential risks associated with the use of imazapyr. More in-depth details of the health effects of imazapyr are provided in the human health risk assessment.

For a complete discussion, see Section 6.0 of *Imazapyr: HED Chapter of the Reregistration Eligibility Decision Document*, dated December 8, 2005.

1. Hazard Profile

The toxicological database for imazapyr is complete. Imazapyr has low acute toxicity via the oral (Toxicity Category IV) and dermal (Toxicity Category III) routes of exposure. Imazapyr has been placed in acute Toxicity Category II for the inhalation route of exposure. It is not irritating to the skin, and is negative for dermal sensitization; however, imazapyr results in irreversible eye damage (Toxicity Category I) as seen in Table 1. Normally, an acute hazard value is chosen from acute (non-lethal), subchronic, or developmental toxicity studies from which there is reasonable evidence that a single exposure can lead to a potential effect. The available data suggest that a single exposure to imazapyr does not result in an effect of concern for risk assessment purposes.

Table 1. Acute Toxicity Data for Imazapyr

Guideline Number Study Type	Toxicity Category
870.1100 Acute Oral Toxicity	IV
870.1200 Acute Dermal Toxicity	III
870.1300 Acute Inhalation Toxicity	II
870.2400 Acute Eye Irritation	I Tested with 99.3% technical fine powder
870.2500 Acute Dermal Irritation	IV
870.2600 Skin Sensitization	Negative

Most of the toxicity studies with imazapyr showed no effects to minimal effects, even at the HDT (highest dose tested). There is no evidence of acute or chronic neurotoxicity resulting from exposure to imazapyr. No developmental toxicity was observed in rabbits or rats up to the HDT; however, maternal toxicity, based on salivation, was observed in rats at the mid-dose (300 mg/kg/day). Neither the rat nor the rabbit study showed an increased susceptibility of the fetus to imazapyr administered pre-natally or post-natally. In addition, a 2-generation reproduction rat study did not show increased susceptibility to offspring at doses up to the HDT. There were no compound-related effects in a one-year dietary toxicity study in beagle dogs up to the HDT. Imazapyr was classified by the Agency in October 1995 as a "Group E" chemical, with no evidence of carcinogenicity in at least 2 adequate studies in the rat and mouse. This decision was reaffirmed on May 22, 2003 by a subcommittee of the Cancer Assessment Review Committee (CARC). Imazapyr is negative for mutagenic potential and a quantitative cancer risk assessment is not required.

The Agency selected NOAELs and endpoints for risk assessment purposes in February 2003. A 1-year dog feeding study with a NOAEL of 250 mg/kg/day was selected for calculating the chronic RfD because it was the lowest NOAEL in the imazapyr database. Actually, the 250 mg/kg/day dose in the dog study was both the NOAEL and the highest dose tested for that study. Because there were no adverse effects seen in the dog study or in any of the imazapyr toxicity studies, EPA relied on a structural analog, the pesticide imazapic (Cadre®), to choose an endpoint. Imazapic causes skeletal muscle effects in dogs at 5000 ppm (137 mg/kg/day in males and 180 mg/kg/day in females). Despite imazapyr's structural similarity to imazapic, as well as its similarity to the pesticides, imazethapyr and imazamethabenz-methyl (Assert®), the available data do not support the conclusion that these pesticides share a common mechanism of toxicity such that combined exposure to them would result in cumulative effects. First, as noted, the toxicity data for imazapyr show no adverse effects, including no skeletal muscle effects. Second, the toxic endpoints for the three structurally similar pesticides are quite varied: imazapic (skeletal muscle effects); imazethapyr (an increased incidence of clinical signs during gestation, ulcerations in the mucosal layer of the stomach and gall bladder, increased abortions, maternal deaths, decrements in body weight gain) and imazamethabenz-methyl (transient decreased body weight, mild liver effects, slight increase in a common kidney lesion). Accordingly, for the purposes of this RED, EPA has not assumed that imazapyr has a common mechanism of toxicity.

Non-cancer risk estimates are expressed as a margin of exposure (MOE) that is a ratio of the dose from a toxicological study selected for risk assessment, typically a NOAEL, to the predicted exposure. Estimated MOEs are compared to a level of concern that reflects the dose selected for risk assessment and uncertainty factors (UFs) applied to that dose. The standard UF is 100X and includes a 10X for interspecies extrapolation (to account for differences between laboratory animals and humans) and a 10X for intraspecies variation (to account for differences between humans). Additional uncertainty or safety factors may also be applied. In the case of imazapyr, the Agency's level of concern is an MOE of 100 which includes a factor of 10X for interspecies extrapolation and 10X for intraspecies variation. The Special FQPA Safety Factor has been reduced to 1X because there are no residual exposure uncertainties, no increased sensitivity to infants and children, and the toxicity database is essentially complete. Table 2 shows the endpoints selected to assess risks for imazapyr.

Table 2. Summary of Toxicological Doses and Endpoints for Imazapyr Used in the Human Health Risk Assessment

Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF and Level of Concern (LOC) for Risk Assessment**	**Study and Toxicological Effects and MRID No.**
Acute Dietary (Females 13-50 years of age and General population including infants and children)	An acute dietary endpoint was not selected based on the absence of an appropriate endpoint attributable to a single dose.		
Chronic Dietary (All populations)	NOAEL= **250** mg/kg/day UF = **100** **Chronic RfD** = **2.5** mg/kg/day	FQPA SF = **1x** **cPAD** = chronic RfD / FQPA SF = **2.5** mg/kg/day	**1-Year Dog** [feeding] **Study** No LOAEL was demonstrated with imazapyr at doses up to 250 mg/kg/day (HDT; MRID 41039502). [HIARC assumed this dose as an endpoint for RA for imazapyr, based on skeletal muscle effects seen in dogs with structural analog imazapic.]
Short and Intermediate Term Incidental Oral (1-30 days and 1-6 months)	NOAEL= **250** mg/kg/day	**Residential** LOC for MOE =100)	**1-Year Dog** [feeding] **Study** No LOAEL was demonstrated with imazapyr at doses up to 250 mg/kg/day (HDT; MRID 41039502). [HIARC assumed this dose as an endpoint for RA for imazapyr, based on skeletal muscle effects seen in dogs with structural analog imazapic.]

Short and Intermediate and Long-Term Dermal (1 to 30 days, 1 to 6 months, >6 months)	Oral study NOAEL= **250** mg/kg/day (dermal absorption rate = **100 %**)	**Occupational** LOC for MOE = **100** (**Residential** LOC for MOE = **100**)	**1-Year Dog** [feeding] **Study** No LOAEL was demonstrated with imazapyr at doses up to 250 mg/kg/day (HDT; MRID 41039502). [HIARC assumed this dose as an endpoint for RA for imazapyr, based on skeletal muscle effects seen in dogs with structural analog imazapic.]
Short- and Intermediate and Long-Term Inhalation (1 to 30 days, 1 to 6 months, >6 months)	Oral study NOAEL= **250** mg/kg/day (inhalation absorption rate **= 100%)**	**Occupational** LOC for MOE = **100** (**Residential** LOC for MOE = **100**)	**1-Year Dog** [feeding] **Study** No LOAEL was demonstrated with imazapyr at doses up to 250 mg/kg/day (HDT; MRID 41039502). [HIARC assumed this dose as an endpoint for RA for imazapyr, based on skeletal muscle effects seen in dogs with structural analog imazapic.]
Cancer	Classified as Group E. No evidence of carcinogenicity; risk assessment not required.		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic),RfD = reference dose, MOE = margin of exposure, LOC = level of concern.

Appendix 4

Selected section on Human Health Risk Assessment related to Aquatic Applications of Imazapyr

From RED (USEPA, 2006):

Recreational Uses

Imazapyr may be applied by broadcast application to aquatic freshwater sites to control floating or emergent aquatic vegetation. Adults and children may be exposed when swimming in treated water bodies following application of imazapyr. The potential for postapplication incidental ingestion and dermal exposure to adults, children, and toddlers as a result of swimming in treated waters immediately following application has also been assessed. Post-application risks to adults, children, and toddlers swimming in treated waters following application of imazapyr are below the Agency's level of concern with MOEs ranging from 68,000 to >1,000,000.

Chronic Risk from Food and Drinking Water

To assess chronic risk from food plus drinking water, exposure estimates from chronic dietary (food) and chronic drinking water assessments were combined in the DEEM™ modeling program. The modeled EDWC of imazapyr in surface water of 79µg/L was used in the chronic dietary (food plus water) assessment. This value was established by modeling imazapyr non-crop uses at the highest maximum application. The combined chronic exposure for the general U.S. population and all population subgroups is <0.1% of the cPAD. The most highly exposed population subgroup is infants <1 year old. The exposure values are below the Agency's level of concern.

Aggregate Risk

Aggregate risk combines exposure from food, drinking water, and, if applicable, residential exposure. For imazapyr, the following aggregate risk assessments were conducted: short-term aggregate (food + drinking water + short-term residential) and long-term aggregate risk assessment (food + drinking water only). Based on the current use patterns of imazapyr, the Agency does not expect exposure durations that would result in intermediate- or long-term residential exposures; therefore long-term aggregate risk assessment consists of exposure from food and drinking water only. A cancer aggregate risk assessment is not required because imazapyr is classified as a Group E chemical, "not likely to be carcinogenic".

For adult short-term aggregate exposure, the Agency aggregated chronic food and drinking water exposures with residential handler and post-application exposures. The adult residential exposure scenarios resulting from application and post-application activities on turf were used. For short-term aggregate exposure to children, the Agency aggregated chronic food and drinking water exposures for toddlers (1-2 years of age) and combined these with post-application dermal

and incidental oral exposures (combined hand-to-mouth, object-to-mouth, and soil ingestion) from activity on turf. The estimated MOEs are above 100, with values of 410 for children and 720 for adults. Therefore, short-term aggregate risks are below the Agency's level of concern.

Because the Agency does not expect chronic residential exposure, long-term aggregate risks are equal to chronic dietary risks (food plus water). As described above in Section 5, these risks are below the Agency's level of concern.

For a complete discussion, see Section 7.0 of the *Imazapyr: HED Chapter of the Reregistration Eligibility Decision Document,* dated December 8, 2005.

6.3.2 Recreational Uses (from HED, USEPA, 2005B)

Imazapyr may be applied by broadcast application to aquatic freshwater sites to control floating or emergent aquatic vegetation. Adults and children may be exposed should they swim in treated water bodies following application of imazapyr. HED has assessed for potentialpostapplication incidental ingestion and dermal exposure to adults and children as a result of swimming in treated waters immediately following application.
The following is excerpted from: *Imazapyr in/on Rangeland and Aquatic Sites. Health Effects Division (HED) Risk Assessment. Dana Vogel. DP Barcode DP291393. July 17, 2003.*

A postapplication assessment is included for adults, toddlers, and children swimming in treated waters immediately after an application, since the proposed label does not prohibit swimming in treated waters. The registrant submitted a field dissipation study using Arsenal® (MRID:45119707) applied at a rate of 1.6 lb ae/A. At four test sites (Florida and Missouri), the highest imazapyr concentration observed was approximately 196 ppb in Missouri; however, at the Florida sites, the Environmental Fate and Effects Division (EFED) noted that the initial concentrations of imazapyr were only about one-third of the amount applied. Accounting forthis observation, the highest imazapyr concentration could have approached 500 ppb. Therefore, HED estimated a worst-case concentration for imazapyr in the top one-foot of the water column in a treated water body; this peak estimate is 550 ppb and is anticipated to be conservative.
The exposure assumptions used in the swimmer assessment are based on HED's SOP for Residential Exposure Assessments, Draft, December 17, 1997 and HED's SWIMODEL V 1.0 (W. Dang and Versar, 27-MAR-1999) for swimming pools adapted for this assessment. It should be noted that the Residential SOP/SWIMODEL assumptions are considered to be conservative for use in assessing the lake/pond swimmer scenario as explained in Table 6.3e.

Table 6.3e: Comparison of Assumptions for Postapplication Swimmer Exposure Assessments for Imazapyr

Assumption	Residential SOP for Swimmers in Pools	Arsenal® Application:Postapplication at Aquatic Sites
Postapplication concentration	100% available concentration postapplication	Maximum imazapyr concentration in top one-foot of water column is approx. 550 ppb. Assuming 100% available isconsidered conservative.

Subsequent postapplication	Assumed not to dissipate	Exposed foliage is the intended target of treatments. Any spray entering water column is anticipated to dissipate.
Duration of exposure	5 hours for competitive adult 2 hours for non-competitive child	2 hours assumed, since floating or emerged weeds will be present making competitive swimming (training) very difficult
Inhalation exposure	Assumed for pool swimmers	No significant inhalation exposure is anticipated.An inhalation assessment is not included.

Table 6.3f presents the risk estimates for postapplication exposures by swimmers. Short-term MOEs from dermal and incidental oral exposures to treated lake water (from swimming activities) are below HED's level of concern (i.e., the MOEs are greater than 100).

Table 6.3f: Postapplication Swimmer Exposure and Risk Assessments for Proposed Use of Imazapyr at Aquatic Sites

Exposure Scenario	AR (lb ae/A)	Concentration in water (ppb)	Potential Dose Rate (PDR; oral)[1] or Absorbed Dose Rate (ADR;dermal) [2] (mg/kg/day)	Short-term MOE[3]
Incidental Ingestion, adult	1.5	550 (0.55 mg/L)	7.86×10^{-4}	320,000
Incidental Ingestion, child			1.90×10^{-3}	130,000
Incidental Ingestion, toddler			3.67×10^{-3}	68,000
Dermal, adult			1.90×10^{-5}	$> 1 \times 10^{7}$
Dermal, child			3.24×10^{-5}	$> 1 \times 10^{6}$
Dermal, toddler			6.26×10^{-5}	$> 1 \times 10^{6}$

1. PDR, incidental oral ingestion = concentration, C_w (mg/L) x ingestion rate, IgR (L/hr) x exposure time, ET (hrs/day) x 1/BW (adult=70 kg; child = 29 kg; toddler = 15 kg)

2. ADR= concentration, C_w (mg/L) x dermal surface area exposed, SA (cm^2) x ET x K_p (cm/hr) x 1/l000 cm^3 x %Dermal Absorption (correct to oral equivalent) x 1/BW, where K_p is estimated as follows: log K_p = -2.72 +0.71log $_{ow}$ - 0.0061MW; K_{ow} =1.3, MW = 261.3, so $K_p = 5.85 \times 10^{-5}$ cm/hr.

3. MOE = NOAEL/PDR; short-term incidental oral NOAEL = 250 mg/kg/day short-term dermal NOAEL =250 mg/kg bw/day. The level of concern for short-term recreational exposures is for MOEs < 100.

APPENDIX 5

Estimated Environmental Concentrations (EECs) and Dissipation Behavior of Imazapyr following Direct Application to Water

As part of the ecological risk assessment described in *Level I Screening Ecological Risk Assessment for the Registration of Imazapyr* (USEPA, 2005), the Environmental Fate and Effects Division (EFED) of USEPA conducted an exposure assessment to estimate environmental concentrations of imazapyr associated with the direct application of imazapyr to surface water. The assessment consisted of direct calculation of peak environmental concentrations and screening level modeling of estimated exposure concentrations.

Direct Calculation of Peak Concentrations

EFED developed a "standard pond" for aquatic exposure assessments. The "standard pond" has a surface area of 1.00 hectares and is 2.00 meters deep and therefore it has a volume of 20,000 cubic meters or 2.00×10^7 liters (L). Assuming imazapyr application directly to the entire surface of the standard pond, no attenuation by foliar interception and uniform mixing throughout its volume, the maximum pond concentration of imazapyr is calculated by dividing the total mass of pesticide applied to the pond by its volume at three water depths.

The maximum imazapyr application rate is 1.50 lb/acre, and since 1.00 lb/acre is equivalent to 1.121 kg/ha, the application rate is equivalent to 1.682 kg/ha or 1.682×10^9 μg/ha. Thus, the peak concentration for imazapyr is:

$$(1.682 \times 10^9 \text{ μg/ha} \times 1.00 \text{ ha})/(2.00 \times 10^7 \text{ L}) = 84.1 \text{ μg /L (ppb)}$$

Direct application of 1.5 pounds of imazapyr to the surface of water bodies 1.0 feet, 3.0 feet and 3.94 feet deep would produce ***acute, peak concentrations of 552, 184 and 140 μg/L (ppb),*** respectively.

The 2 meter (6.56 feet) depth is representative of the water depth in the standard pond scenario used by EFED for most ecological effects assessments. The 1 and 3 foot water depths are typical of use conditions in irrigation and drainage ditches, and for edge of pond depths, where problematic aquatic weeds are typically found. The 3.94 ft depth was included since it is the default depth used in the Missouri farm pond model scenario in AQUATOX.

Modeling of Concentration and Dissipation of Imazapyr in Standard Pond

In order to estimate imazapyr concentrations in the pond as a function of time, used the Generic Estimated Environmental Concentration (GENEEC) model as described in Level I screening risk assessment (US EPA, 2005). The GENEEC2 model is designed to simulate the ecological exposure to aquatic organisms from runoff and spray drift of chemicals applied *terrestrially* on an adjacent field. To assess the exposure for direct application of imazapyr to a water body,

EFED had to adjust the GENEEC2 modeling routine and use proportionality factors to yield simulated concentrations that matched the directly calculated peak concentration values.

AQUATOX is an alternative model that is available from USEPA and has the capability to estimate the concentration in a water body from *direct application* of pesticides to a water body. AQUATOX is an ecosystem simulation model that predicts the fate of various pollutants, such as excess nutrients and organic chemicals, and their effects on aquatic ecosystems. An overview of the model is given in Appendix 5. For the purpose of the aquatic exposure assessment for the review presented here, the AQUATOX model was used to estimate the concentration and dissipation characteristics of imazapyr in a standard pond. The fate portion of the model was used to here to characterize the dissipation of imazapyr following an application to a standard pond.

Brief overview of the AQUATOX Model

AQUATOX is an ecosystem simulation model that predicts the fate of various pollutants, such as excess nutrients and organic chemicals, and their effects on aquatic ecosystems, including fish, invertebrates, and aquatic plants. AQUATOX is a valuable tool for ecologists, biologists, water quality modelers, and anyone who performs ecological risk assessments for aquatic ecosystems.

AQUATOX simulates the transfer of biomass, energy and chemicals from one compartment of the ecosystem to another. It does this by simultaneously computing each of the most important chemical or biological processes for each day of the simulation period; therefore it is known as a process-based or mechanistic model. AQUATOX can predict not only the environmental fate of chemicals in aquatic ecosystems, but also their direct and indirect effects on the resident organisms. Therefore it has the potential to establish causal links between chemical water quality and biological response and aquatic life uses.

AQUATOX is the only general ecological risk model that represents the combined environmental fate and effects of conventional pollutants, such as nutrients and sediments, and toxic chemicals in aquatic ecosystems. It considers several trophic levels, including attached and planktonic algae and submerged aquatic vegetation, invertebrates, and forage, bottom-feeding, and game fish; it also represents associated organic toxicants. It has been implemented for streams, ponds, lakes, estuaries, reservoirs, and experimental enclosures.

The fate portion of the model, which is applicable especially to organic toxicants, includes: partitioning among organisms, suspended and sedimented detritus, suspended and sedimented inorganic sediments, and water; volatilization; hydrolysis; photolysis; ionization; and microbial degradation. The effects portion of the model includes: acute toxicity to the various organisms modeled; and indirect effects such as release of grazing and predation pressure, increase in detritus and recycling of nutrients from killed organisms, dissolved oxygen sag due to increased decomposition, and loss of food base for animals.

AQUATOX is the latest in a long series of models, starting with the aquatic ecosystem model CLEAN (Park et al., 1974) and subsequently improved in consultation with numerous

researchers at various European hydrobiological laboratories, resulting in the CLEANER series (Park et al., 1975, 1979, 1980; Park, 1978; Scavia and Park, 1976) and LAKETRACE (Collins and Park, 1989). The MACROPHYTE model, developed for the U.S. Army Corps of Engineers (Collins et al., 1985), provided additional capability for representing submersed aquatic vegetation. Another series started with the toxic fate model PEST, developed to complement CLEANER (Park et al., 1980, 1982), and continued with the TOXTRACE model (Park, 1984) and the spreadsheet equilibrium fugacity PART model. AQUATOX combined algorithms from these models with an ecotoxicological construct borrowed from the FGETS model (Suárez and Barber, 1992); and additional code was written as required for a truly integrative fate and effects model (Park, 1990, 1993). In the late 1990s, AQUATOX was restructured and linked to Microsoft Windows interfaces to provide even greater flexibility, capacity for additional compartments, and user friendliness.

- AQUATOX Release 1 was produced in 2002 and was the first EPA release to run under Windows.
- AQUATOX Release 2 was completed in 2003 and included more state variables and multi-age-class fish along with a refined user-interface.
- AQUATOX Release 2.1 was completed in 2005 and included additional chemical modeling options and variable stoichiometry among numerous other refinements.
- AQUATOX Release 2.2 was completed in 2006 and included updated simulations and parameter databases along with minor interface enhancements.
- AQUATOX Release 3 was completed in 2009 and includes linked segments, simulations of estuaries, dramatically improved output capabilities, and many other model improvements.

In 2009, EPA released an enhanced version of AQUATOX, Release 3, which includes the capability to represent estuaries and to more realistically model nutrients. More information on the model and its applications, including references to peer-reviewed publications, is available at http://www.epa.gov/waterscience/models/aquatox/.

Model Input

The model package contains a number of scenarios. The model guidance suggests to select a scenario from the model package, and modify it as needed to make it more representative for a specific situation and conditions. The model results are suggested to be used for screening-level assessments. For the purpose of the review presented here, the model was used to simulate the fate of imazapyr in the default Missouri farm pond. The study on esfenvalerate in a Missouri Farm Pond was selected as a starting scenario. The state variable defined for this model scenario and their initial values are listed in Table A5.1. The site characteristics and chemical parameters are shown in attached Table A5-1 and Table A5-2.

The site characteristic for the latitude was adjusted to 42 in order to make it more representative for the light situation in MA. The dimensions of the pond were modified to represent the dimensions of the EPA standard pond: Surface area of 1 ha (10000 m^2), a depth of 2 m (6.56 ft),

and a resulting volume of 20,000 m^3. Subsequently, depths of 1.2 m (3.94 ft), 0.91 m (3 ft) and 0.304 m (1ft) (with associated volumes) of this pond were also simulated.

Chemical Properties and Fate Data were adjusted to be representative of imazapyr (see Appendix 2). The following parameter values were used (see also Section 2.4):

Molecular weight: 261; dissociation constant: 3.8; Henry's Law constant: 7.1E-17; Octanol-water partitioning constant (log): 0.22; Water partitioning coefficient: 50; rate of anaerobic microbial degradation: 0.00198 (calculated using the half life value of 120 d and k = ln(20/half life); Maximum rate of aerobic microbial degradation: 0.00198 (see above); and photolysis rate: 0.1308 (based on half life of 5.3 d).

The herbicide application was programmed to occur on May 10th at an amount of 1682 g per day (1.5 lbs a.i./acre = 1.682 kg/ha). The model simulation was run from May 1st through August 31st.

Results

From the output, the following parameters were selected: dissolved imazapyr concentration, imazapyr photolysis, imazapyr biodegradation and total loss of imazapyr. The results are presented in graphs that are shown below.

Note the differences in the concentration scale in the graphs of ponds with different depths. The data indicate that photolysis has the largest contribution to the total dissipation of imazapyr. It should also be noted that a conservative value for photolysis (longest half life of 5.3 d was used in the modeling). Field data may show faster dissipation rates.

The depth of the pond appears to be an important factor in the dissipation of imazapyr in pond water. Application in a shallow pond results in a higher peak concentration (Fig. A5-5). On the other hand, more intense light penetration in a shallow pond will result in a higher photolysis rate as is indicated in the graph showing the photolysis as a function of pond depth (Fig. A5-6). The initial trend of the higher peak concentrations with lower depth is reversed after 2 months when the deeper ponds show slightly higher residual concentrations. This may be attributed to the lower photolysis rate in deeper ponds. The concentration trend after 1 month is intermediate to the trends observed in initial peak concentration levels and the relatively low levels after 2-months of dissipation. This may be the result of variation in dissipation due to differences in peak concentration and photolysis rate with pond depth.

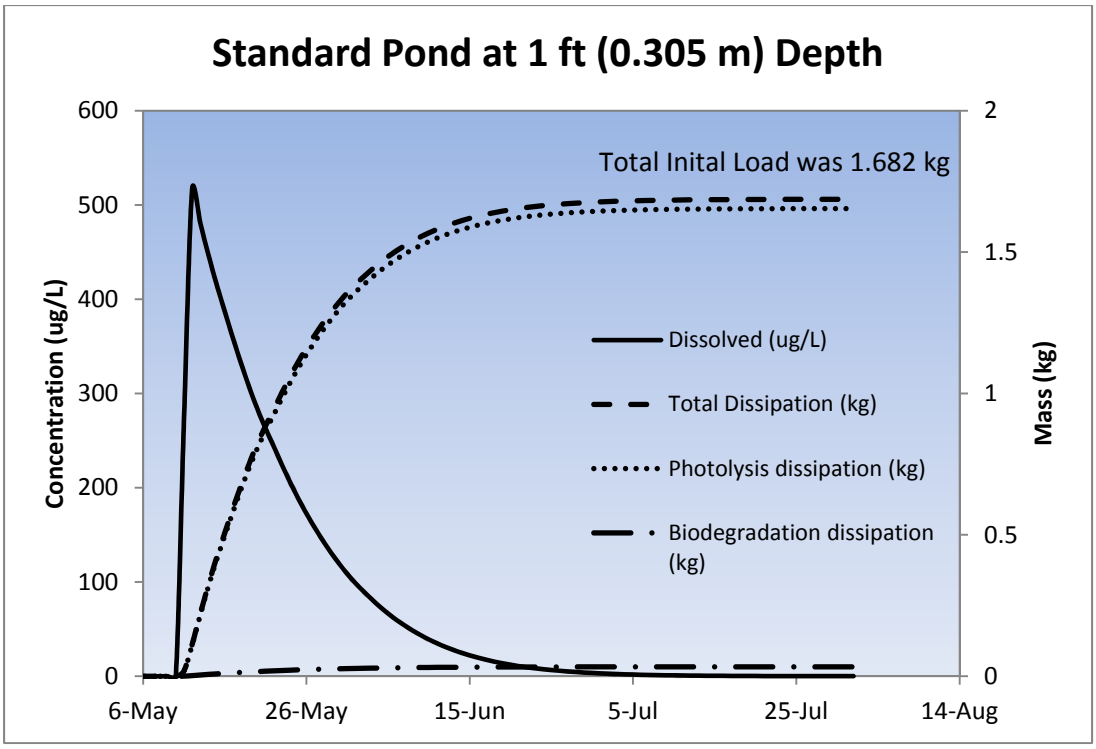


Figure A5-1 AQUATOX mode-predicted imazapyr concentration and dissipation in standard pond with 1 ft depth.

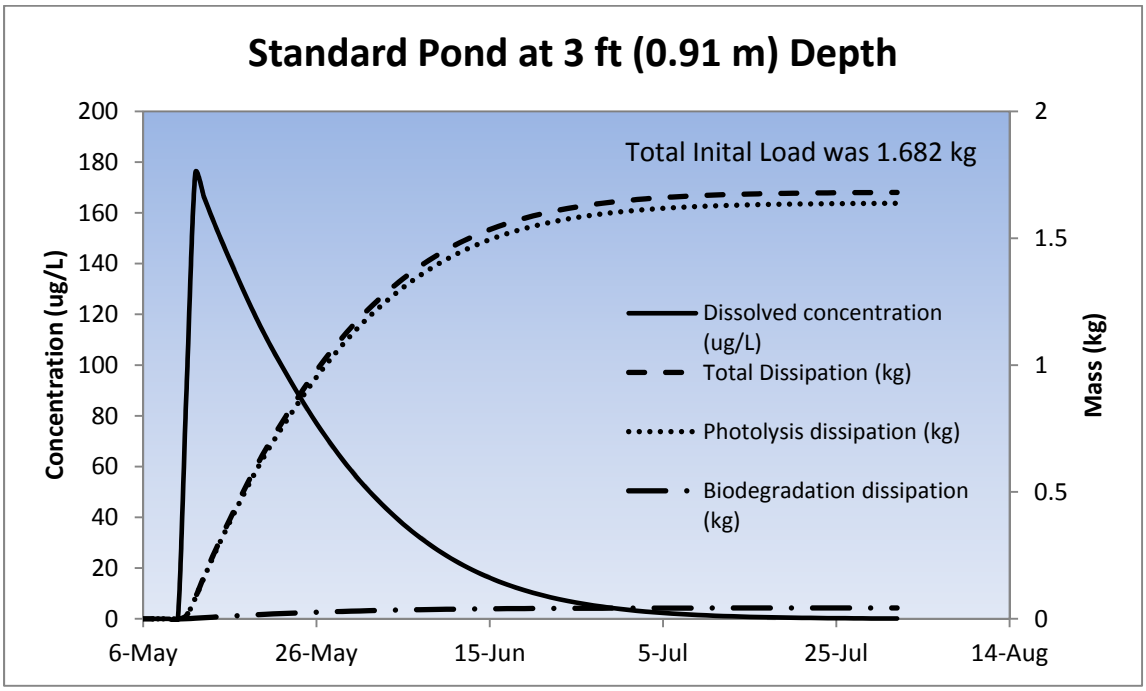


Figure A5-2 AQUATOX model-predicted imazapyr concentration and dissipation in standard pond with 3 ft depth.

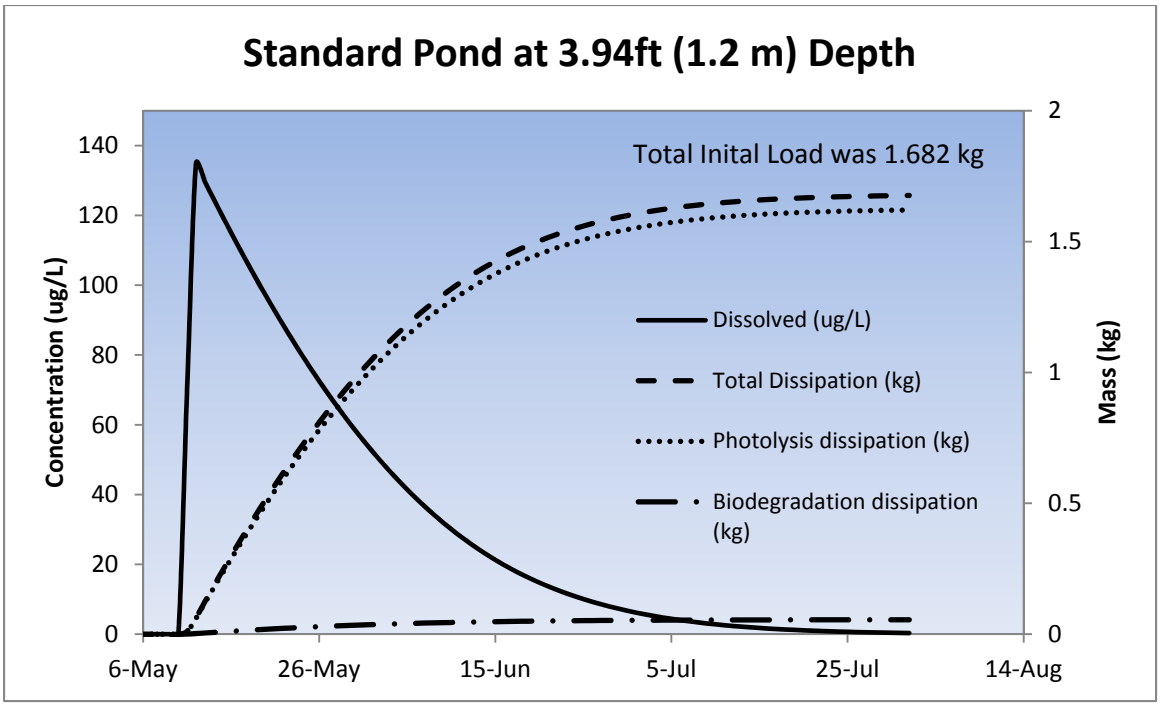


Figure A5-3 AQUATOX model-predicted imazapyr concentration and dissipation in standard pond with 3.94 ft depth.

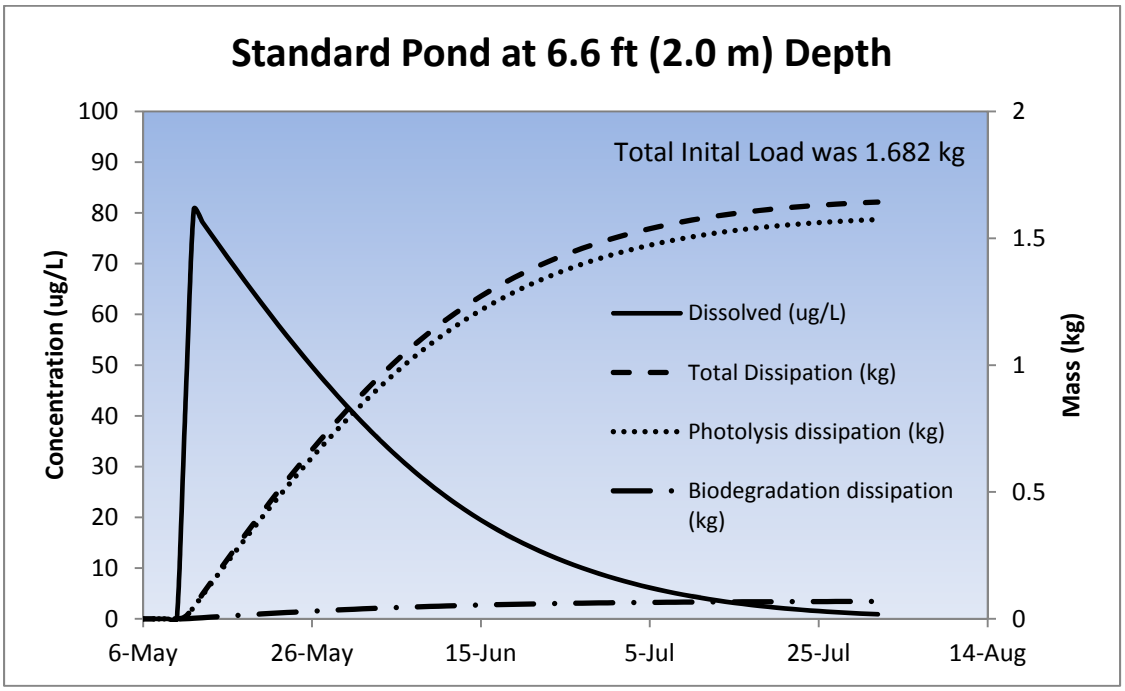


Figure A5-4 AQUATOX model-predicted imazapyr concentration and dissipation in standard pond with 6.6 ft depth.

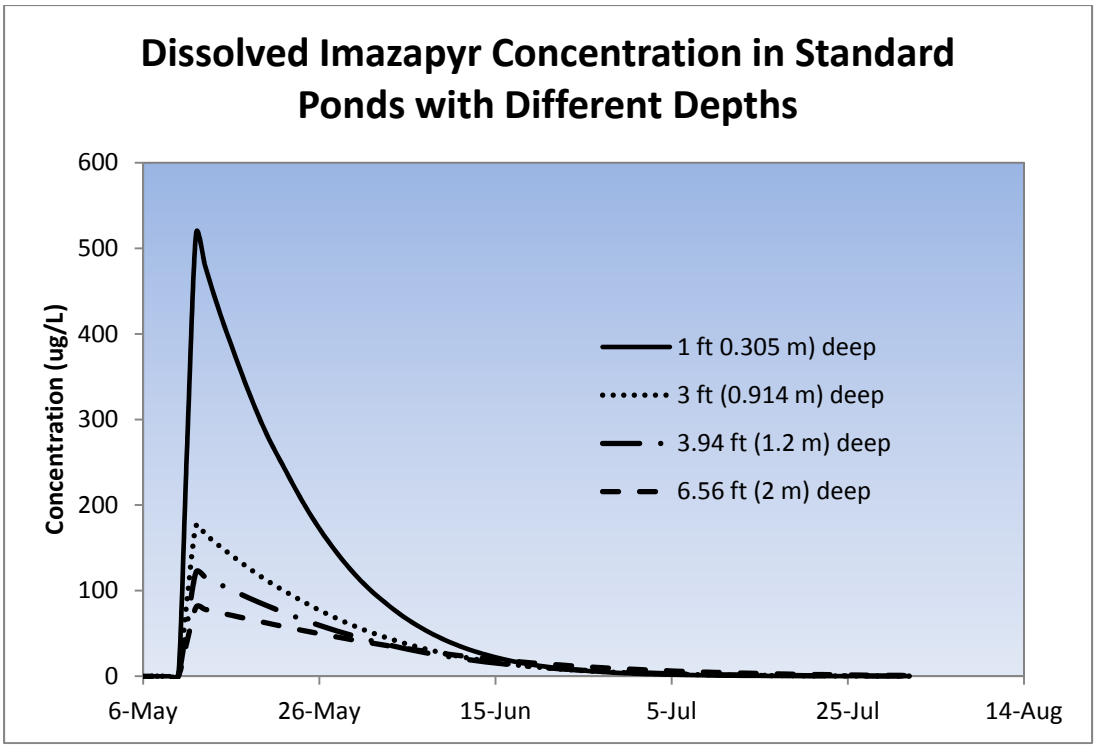


Figure A5-5 AQUATOX model-predicted imazapyr concentration in standard ponds with different depths.

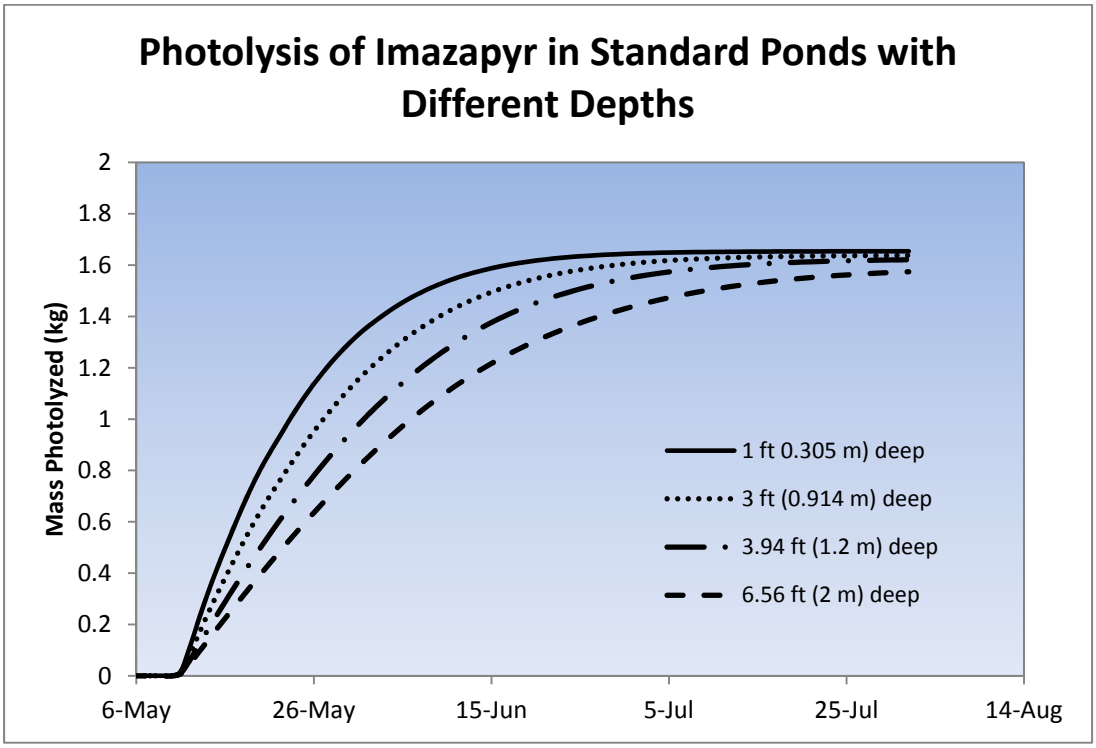
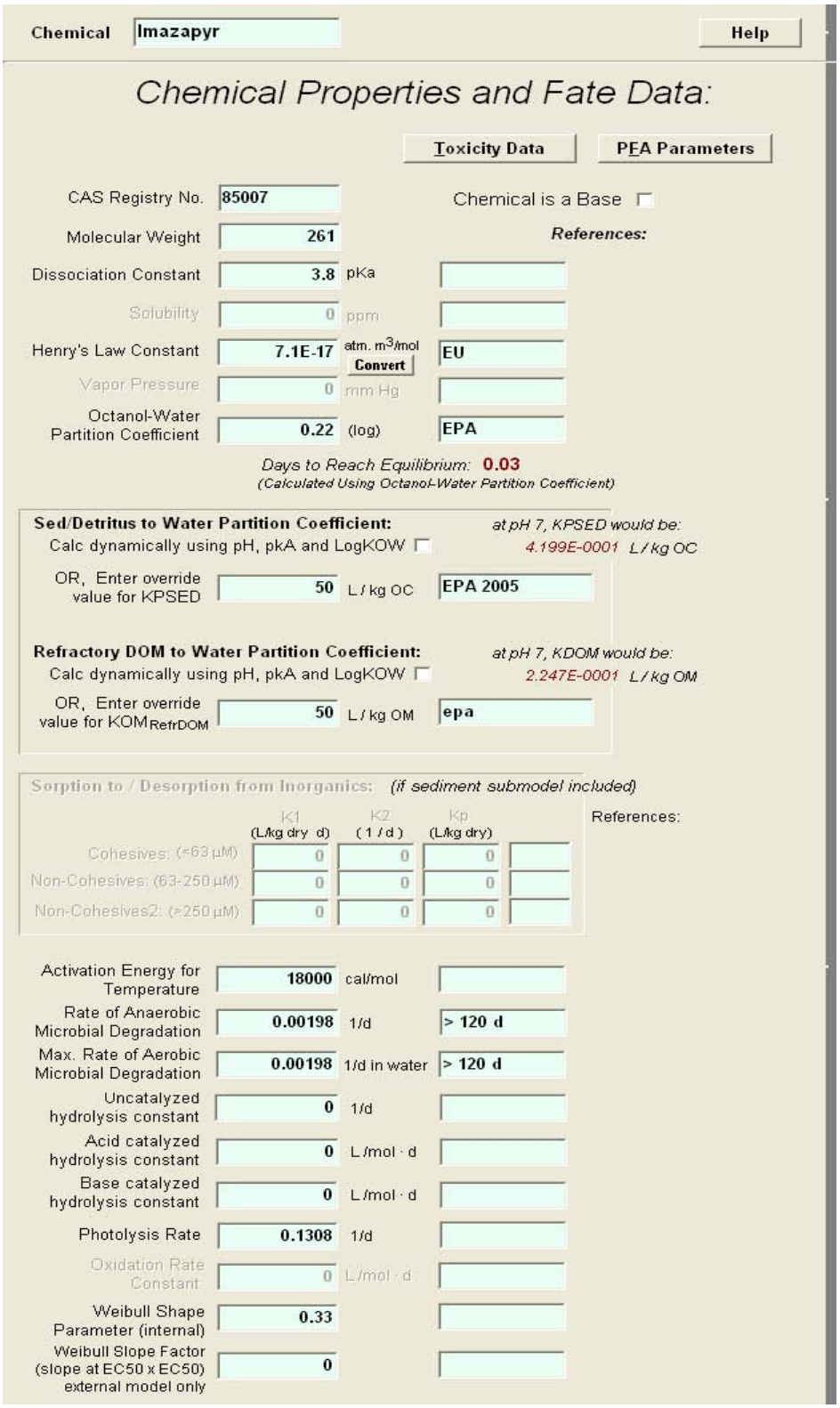


Figure A5-6 AQUATOX model-predicted imazapyr dissipation in standard ponds with different depths.

Table A5.1 AQUATOX State Variables for Missouri Farm Pond and their initial values

State Variable Name	Init. Cond.	Units
NH3 & NH4+	0.08	mg/L
NO3	0.05	mg/L
Tot. Sol. P	0.05	mg/L
CO2	1.5	mg/L
Oxygen	12	mg/L
R detr sed	3	g/m2 dry
L detr sed	3	g/m2 dry
R detr diss	0.72	mg/L dry
L detr diss	0.18	mg/L dry
R detr part	0.08	mg/L dry
L detr part	0.02	mg/L dry
BuryRDetr	2	g/m2
BuryLDetr	2	g/m2
Peri High-Nut Diatom	36.86	g/m2 dry
Phyt High-Nut Diatom	0.00	mg/L dry
Peri, Green	0.01	g/m2 dry
Phyto, Green	0.00	mg/L dry
Phyt, Blue-Greens	0.00	mg/L dry
Cryptomonas	0.07	mg/L dry
Myriophyllum	36.67	g/m2 dry
Chironomid	2.29	g/m2 dry
Daphnia	0.05	mg/L dry
Copepod	0.32	mg/L dry
Sphaerid	2.46	g/m2 dry
Mayfly (Baetis)	0.24	g/m2 dry
Rotifer, Keratella	0.07	mg/L dry
Gastropod	3.68	g/m2 dry
Shiner	4.02	g/m2 dry
Largemouth Bass, YOY	0.21	g/m2 dry
Largemouth Bass, Lg	4.43	g/m2 dry
Water Vol	2004	cu.m
Temp	16	deg. C
Wind	0	m/s
Light	333	Ly/d
pH	6.8	pH

Table A5-2 AQUATOX input values for imazapyr chemical properties and fate data



Chemical: Imazapyr — Help

Chemical Properties and Fate Data:

Toxicity Data | PEA Parameters

CAS Registry No.	85007	Chemical is a Base ☐	
Molecular Weight	261	References:	
Dissociation Constant	3.8	pKa	
Solubility	0	ppm	
Henry's Law Constant	7.1E-17	atm. m^3/mol (Convert)	EU
Vapor Pressure	0	mm Hg	
Octanol-Water Partition Coefficient	0.22	(log)	EPA

Days to Reach Equilibrium: **0.03**
(Calculated Using Octanol-Water Partition Coefficient)

Sed/Detritus to Water Partition Coefficient: *at pH 7, KPSED would be:* *4.199E-0001 L / kg OC*
Calc dynamically using pH, pkA and LogKOW ☐

OR, Enter override value for KPSED	50	L / kg OC	EPA 2005

Refractory DOM to Water Partition Coefficient: *at pH 7, KDOM would be:* *2.247E-0001 L / kg OM*
Calc dynamically using pH, pkA and LogKOW ☐

OR, Enter override value for $KOM_{RefrDOM}$	50	L / kg OM	epa

Sorption to / Desorption from Inorganics: *(if sediment submodel included)*

	K1 (L/kg dry d)	K2 (1 / d)	Kp (L/kg dry)	References:
Cohesives: (<63 µM)	0	0	0	
Non-Cohesives: (63-250 µM)	0	0	0	
Non-Cohesives2: (>250 µM)	0	0	0	

Activation Energy for Temperature	18000	cal/mol	
Rate of Anaerobic Microbial Degradation	0.00198	1/d	> 120 d
Max. Rate of Aerobic Microbial Degradation	0.00198	1/d in water	> 120 d
Uncatalyzed hydrolysis constant	0	1/d	
Acid catalyzed hydrolysis constant	0	L/mol · d	
Base catalyzed hydrolysis constant	0	L/mol · d	
Photolysis Rate	0.1308	1/d	
Oxidation Rate Constant	0	L/mol · d	
Weibull Shape Parameter (internal)	0.33		
Weibull Slope Factor (slope at EC50 x EC50) external model only	0		

Appendix 6

Ecological Effects (Appendix E from Level I, USEPA, 2005A)

APPENDIX 6. Ecological Effects Data

Studies are with imazapyr acid, unless otherwise noted

71-1 Avian Acute Oral

Bobwhite Quail. MRID 00131633 (Acceptable). In a 14-day oral gavage study, imazapyr acid was determined to be practically non-toxic to bobwhite quail with an LD_{50} of >2,150 mg ae/kg. The study is scientifically sound and follows the guideline protocols.

Mallard Duck. MRID 00131634 (Acceptable). In a 14-day oral gavage study, imazapyr acid was determined to be practically non-toxic to mallard ducks with an LD_{50} of >2,150 mg ae/kg. The study is scientifically sound and follows the guideline protocols.

71-2 Avian Subacute Dietary

Imazapyr acid

Bobwhite Quail. MRID 00131635 (Acceptable). In an 8-day dietary study, imazapyr acid was determined to be practically non-toxic to upland game birds (bobwhite quail) with an LC_{50} >5000 ppm. The study is scientifically sound and generally followed guideline protocols; however, there was some unexplainable low weight gains and mortality at the 625 ppm test concentration.

Mallard. MRID 00131636 (Acceptable). In an 8-day dietary study, imazapyr acid was determined to be practically non-toxic to mallard ducklings with an LC_{50} >5000 ppm.. The study is scientifically sound and generally followed guideline protocols.

Imazapyr isopropylamine salt

Bobwhite Quail. MRID 00147115 (Acceptable). In an 8-day dietary study, the isopropylamine salt of imazapyr was determined to be practically non-toxic to upland game birds (bobwhite quail) with an LC_{50} >5000 ppm. The study is scientifically sound and generally followed guideline protocols. This study was conducted with the formulated product to ensure that isopropylamine did not affect the toxicity of the active ingredient.

71-4 Avian Reproduction

Bobwhite Quail. MRID 45119714a (Acceptable). In a one-generation reproductive toxicity study, imazapyr acid produced no evidence of treatment-related adverse effects on adult or reproductive parameters with an NOAEC of 1670 ppm. The study is scientifically sound and generally followed guideline protocols.

Mallard. MRID 45119714b (Invalid). In a one-generation reproductive toxicity study, imazapyr acid resulted in a significant reduction in the ratio of viable embryos/eggs at the 1,670 ppm

treatment level. However, the study was determined to be invalid due to bacterial contamination and high embryonic mortality in the controls. EFED recommended that another study be conducted to determine the reproductive toxicity of imazapyr to waterfowl.

Bobwhite Quail. MRID 43831401 (Originally Supplemental; Reclassified Core). In a one-generation reproductive toxicity study, imazapyr acid resulted in reduced hatchlings/live embryo at 2000 ppm (LOEC; NOEC = 1000 ppm); however, the study was originally determined to be supplemental due to guideline deficiencies (primarily, EECs would be higher than highest dose tested and control egg shell cracking was 13%). EFED reevaluated the studies and determined that the dosing did reflect the maximum EEC and that the handling and measurement deficiencies did not reflect a dose-response relationship; consequently, the study was reclassified as core and the NOEC was changed to 2000 ppm.

Mallard. MRID 43831402 (Originally Supplemental; Reclassified Core). In a one-generation reproductive toxicity study, imazapyr acid produced no evidence of treatment-related adverse effects on adult or reproductive parameters with an NOAEC of 1890 ppm (measured concentration; 2000 ppm nominal concentration). However, the study was originally determined to be supplemental due to guideline deficiencies (primarily, EECs would be higher than highest dose tested, inaccurate measurement of egg shell thickness, and insufficient pre-egg laying period. EFED reevaluated the studies and determined that the dosing did reflect the maximum EEC and that the measurement deficiencies did not reflect a dose-response relationship; consequently, the study was reclassified as core and the NOAEC was established at 2000 ppm.

72-1 Freshwater Fish Acute

Imazapyr acid

Rainbow Trout. MRID 00131629 (Acceptable). In a 96-hour acute test, imazapyr acid was determined to be practically non-toxic to rainbow trout with an LC_{50} of >100 mg/L. The NOEC was determined to be 100 mg/L. The study is scientifically sound and meets guideline protocols.

Bluegill Sunfish. MRID 00131630 (Acceptable). In a 96-hour acute test, imazapyr acid was determined to be practically non-toxic to bluegill sunfish with an LC_{50} of >100 mg/L. The NOEC was determined to be 100 mg/L. The study is scientifically sound and meets guideline protocols.

Channel Catfish. MRID 00131631(Acceptable). In a 96-hour acute test, imazapyr acid was determined to be practically non-toxic to channel catfish with an LC_{50} of >100 mg/L. The NOEC was determined to be 100 mg/L. The study is scientifically sound and meets guideline protocols.

Imazapyr isopropylamine salt

Rainbow Trout. MRID 45119713 (Acceptable). In a 96-hour flow-through test, imazapyr isopropylamine salt was determined to be practically non-toxic to rainbow trout with an LC_{50} of >110 mg ae/L (mean measured concentration; nominal concentration 120 mg ae/L). The NOEC was determined to be 110 mg ae/L. The study is scientifically sound and meets guideline

protocols.

Bluegill Sunfish. MRID 00147116 (Acceptable). In a 96-hour test, imazapyr isopropylamine salt was determined to be practically non-toxic to bluegill sunfish with an LC_{50} of >818 mg ae/L (1000 mg ai/L). The study is scientifically sound and meets guideline protocols.

72-2 Freshwater Invertebrate Acute

Imazapyr acid
Daphnia. MRID 00131632 (Core). In a 48-hour acute test, imazapyr acid was determined to be practically non-toxic to daphnids with an EC_{50} of >100 mg/L. The study is scientifically sound and meets guideline protocols.

Imazapyr isopropylamine salt
Daphnia. MRID 00147117 (Core). In a 48-hour static test, imazapyr isopropylamine salt was determined to be practically non-toxic to daphnids with an EC_{50} of 614 mg ae/L (750 mg ai/L). The study is scientifically sound and meets guideline protocols.

72-3a Estuarine/Marine Fish Acute

Silverside Minnow. MRID 41315801(Acceptable). In a 96-hour flow-through test, imazapyr acid was determined to be practically non-toxic to silverside minnow with an LC_{50} of >184 mg ai/L (mean measured concentration; nominal concentration 200 mg ai/L). The NOEC was determined to be 184 mg ai/L. The study is scientifically sound and meets guideline protocols.

72-3b Estuarine/Marine Invertebrate Acute

Eastern Oyster. MRID 45119710 (Acceptable). In a 96-hour flow-through test, imazapyr acid was determined to be practically non-toxic to the eastern oyster with an EC_{50} of >132 mg ai/L (mean measured concentration; nominal concentration 120 mg ai/L). No mortalities were observed in either the treated or control groups. The control shell deposition during the study was 2.46 mm. The NOAEC was determined to be 132 mg ai/L, the highest concentration tested. No significant adverse effects were observed on shell deposition for any treated group. The study is scientifically sound and meets guideline protocols.

Eastern Oyster. MRID 41315802 (Supplemental). In a 96-hour flow-through test, imazapyr acid was determined to be practically non-toxic to the eastern oyster with an EC_{50} of >173 mg ai/L (mean measured concentration; nominal concentration 200 mg ai/L; the highest concentration tested). No mortalities were observed in either the treated or control groups. There was a statistically significant decrease in mean shell deposition at 173 mg/L when compared to the control group ($p \leq 0.05$). The NOAEC was determined to be 109 mg ai/L. Originally, this study was classified as invalid because the control oyster growth (1.35 mm new shell deposition) did not meet the guideline requirement of 2 mm (amendment to SEP, dated 9/1990). In addition, the

flow rate of the test solution was 1.05 L/oyster/hour. The protocols recommended by the SEP (APHA, 1981 and EPA, 1976) state that each oyster should receive a minimum of 5 L/oyster/hour. This study was later upgraded to supplemental. The memorandum stated that shell growth in the control group may be used as an indicator of stress for the oysters. Less than 2 mm shell growth in the control group indicates that the oysters may be undergoing stress. The low flow-through rate with no supplemental food added in this study may have contributed to stress on the oysters. For this study, it appears that the seawater was trucked in from the ocean to Gainesville, Florida. During such time, the food organisms (such as algae) may have been inhibited during the transport and storage. The oysters in the study may not have fed well because of the combination of the lower amount of available food organisms in the shipped sea water, the low flow rate and the lack of supplemental food added; thereby, contributing to inadequate shell deposition. However, since there was some dose-response, the study was upgraded to supplemental.

Pink Shrimp. MRID 41315803 (Acceptable). In a 96-hour flow-through test, imazapyr acid was determined to be practically non-toxic to pink shrimp with an LC_{50} of >189 mg ai/L (mean measured concentration; nominal concentration 200 mg ai/L). There was one mortality at the second highest concentration level (111 mg/L), which does not appear to be related to treatment. No other signs of toxicity were observed. Therefore, the NOAEC was determined to be 189 mg ai/L, the highest concentration tested. The study is scientifically sound and meets guideline protocols.

72-4a Freshwater Fish Early Life Stage

Fathead Minnow. MRID 45119711 (Acceptable). In an early life-stage flow-through test, imazapyr acid produced no treatment-related effects on embryonic survival, time to hatch, alevin survival, terminal length, or wet and dry weight. The NOEC was determined to be 118 mg ai/L (mean measured concentration; nominal concentration 120 mg ai/L). The study is scientifically sound and meets guideline protocols.

Rainbow Trout. MRID 41315804 (Supplemental). In an early life-stage flow-through test, imazapyr acid resulted in significantly reduced percent hatch and an observed reduction on survival at 92.4 mg/L (mean measured concentration; nominal concentration 100 mg/L). No abnormalities in embryonic or juvenile development were observed. The MATC was >43.1 and <92.4 mg/L; thus the geometric mean MATC was 63.1 mg/L. The study did not meet all guideline requirements (feeding limited the growth of replicates with higher fish densities).

72-4b Freshwater Invertebrate Life Cycle

Daphnia. MRID 41315805 (Acceptable). In a life cycle flow-through test, imazapyr acid produced no treatment-related effects on survival, growth and reproduction of first generation daphnids. No physical or behavioral abnormalities were observed. The MATC and NOEL were determined to be ≥97.1 mg/L. The study is scientifically sound and meets guideline protocols.

72-5 Freshwater Fish Life Cycle

Fathead Minnow. MRID 45119712 (Supplemental). In a full life cycle flow-through test, imazapyr acid produced no treatment-related effects on growth, embryo survival, time to hatch, or larval and juvenile survival of the F_0 and F_1 generations. No treatment-related effects were observed on percent spawning frequency, mean number of eggs produced per female or mean percent fertilization success. The NOEC was reported at the nominal concentration of 120 mg ai/L (mean measured concentration 118 mg ai/L). The study is scientifically valid but did not meet all guideline requirements (F_1 generation was maintained for 4 weeks instead of 8 weeks).

81-1 Acute Mammalian Oral

Imazapyr acid

Rat. MRID 132030 (Acceptable). In an acute oral study, imazapyr acid was determined to have a low toxicity (Toxicity Category III) to rats with an LD_{50} >5000 mg/kg. The study is scientifically sound and meets guideline protocols.

Imazapyr isopropylamine salt

Rat. MRID 00147049 (Acceptable). In an acute oral study, imazapyr isopropylamine salt was determined to exhibit no toxicity (Toxicity Category IV) to rats with an LD_{50} of >5000 mg/kg (>4090 mg ae/kg). The study is scientifically sound and meets guideline protocols.

Rat. MRID 44735301 (Acceptable). In an acute oral study, imazapyr isopropylamine salt was determined to exhibit no toxicity (Toxicity Category IV) to rats with an LD_{50} of >5000 mg/kg (>4090 mg ae/kg). The study is scientifically sound and meets guideline protocols.

83-3 Mammalian Developmental

Rat. MRID 00131611 (Acceptable). In a 2-generation developmental study, imazapyr acid produced maternal toxicity in Sprague Dawley rats at 1000 mg ai/kg/day (LOAEL), based on salivation in the gravid dams between gestation days 8-15. The findings were determined to be treatment-related. The NOAEL was 300 mg /kg bw/day. No treatment-related effects were reported for developmental parameters. The study is scientifically sound and meets guideline protocols.

Rabbit. MRID 00131613 (Acceptable). In a 2-generation teratology study, imazapyr acid produced no treatment-related effects for maternal or developmental parameters; consequently, the NOAEL for both endpoints was $\geq$400 mg/kg bw/day in New Zealand white rabbits. The study is scientifically sound and meets guideline protocols.

83-4 Mammalian Reproduction

Rat. MRID 41039505 (Acceptable). In a 2-generation reproduction study, imazapyr acid produced no treatment-related effects for maternal or developmental parameters; consequently, the parental systemic, reproductive, and offspring NOAEL was ≥738 mg/kg bw/day in males and 933.3 mg/kg bw/day in females. The study is scientifically sound and meets guideline protocols.

122-2 Aquatic Plant Nonvascular

Imazapyr acid

Green algae. MRID 40811802 (Acceptable). In a Tier II toxicity test with *Selenastrum capricornutum*, the 7 day EC_{50} for cell density was 71 mg ai/L (NOEC = 50.9 mg ai/L). The study is scientifically sound and meets the guideline protocols.

Blue-green algae. MRID 40811802 (Acceptable). In a Tier II toxicity test with *Anabaena flos-aquae*, the7-day EC_{50} for cell density was 12.2 mg ai/L (NOEC = 9.6 mg ai/L). The study is scientifically sound and meets the guideline protocols.

Marine diatom. MRID 40811802 (Acceptable). In a Tier II toxicity test with *Skeletonema costatum*, the7-day EC_{50} for cell density was 92 mg ai/L (NOEC = 15.9 mg ai/L). The study is scientifically sound and meets the guideline protocols.

Diatom. MRID 40811802 (Acceptable). In a Tier II toxicity test with *Navicula pelliculosa*, the 7-day EC_{50} for cell density was >41 mg ai/L (NOEC = 41 mg ai/L). The study is scientifically sound and meets the guideline protocols.

Imazapyr isopropylamine salt

Green algae. MRID 43889102 (Acceptable). In a Tier II toxicity test with green algae, the 7-day EC_{50}, based on slight changes in cell shape was 11.5 mg ae/L (NOEC = 7.16 mg ae/L). The study is scientifically sound and meets the guideline protocols.

123-1(a) Seedling Emergence - Tier II

Imazapyr Acid

Monocots (4 species) and Dicots (4 species). MRID 40811801 (Supplemental). In a Tier II seedling emergence study, the most sensitive monocot tested was wheat (EC_{25} 0.0046 lb ae/acre, EC_{05} 0.00099 lb ae/acre; shoot weight). The most sensitive dicot tested was sugarbeet (EC_{25} 0.0024 lb ae/acre, EC_{05} 0.00017 lb ae/acre; shoot weight). Due to deficiencies in the study, the guideline requirements are only partially fulfilled; acceptable data endpoints were used in the risk assessment.

Nontarget Terrestrial Plant Seedling Emergence Toxicity (Tier II)

Species	% ai	EC25 (lbs ai/A)	NOEC / [EC05]	Endpoint Affected	MRID No.	Study Classification
	22.6%				408118-01	
Monocot- Corn		0.025	0.0156	height		invalid[2]

Nontarget Terrestrial Plant Seedling Emergence Toxicity (Tier II)

Species	% ai	EC25 (lbs ai/A)	NOEC / [EC05]	Endpoint Affected	MRID No.	Study ClassificationA
Monocot- Oat		0.054	0.0156	"		supplemental[3]
Monocot- Onion		0.034	[0.01][A]	weight[4]		supplemental[3]
Monocot- Wheat		0.0046	[0.00099][A]	"		supplemental[3]
Dicot- Sunflower		0.0027	[0.000021][A]	height		invalid[2]
Dicot- Soybean		0.012	0.0078	"		invalid[2]
Dicot- Pea		0.093	0.0624	weight[4]		invalid[2]
Dicot-Cucumber		0.0043	[0.000005][A]	"		invalid[2]
Dicot- Sugarbeet		0.0024	[0.00017][A]	"		supplemental[3]
Dicot- Tomato		0.008	0.0003	"		supplemental[3]

[1]Determination of the most sensitive species is based on EC_{25} values; results are based on the non-linear regression analysis.
[2] Large seedlings were subjected to overcrowding, 10 seeds were planted in a 4-in dixie cup.
[3] Small seedlings could be subjected to overcrowding, 10 seeds were planted in a 4-in dixie cup.
[4] Fresh weight was recorded instead of dry weight.
[A] The NOEC value is above the EC25, equal to the EC25, or below the lowest concentration, an EC05 value is used instead. .

123-1(b) Vegetative Vigor - Tier II

Imazapyr acid

Monocots (4 species) and Dicots (4 species). MRID 40811801 (Supplemental). In a Tier II vegetative vigor study, the most sensitive monocot tested was wheat (EC_{25} 0.012 lb ae/acre, NOEC 0.0039 lb ae/acre; shoot weight). The most sensitive dicot tested was cucumber (EC_{25} 0.0009 lb ae/acre, EC_{05} 0.000064 lb ae/acre; shoot height). Due to deficiencies in the study, the guideline requirements are partially fulfilled; acceptable data endpoints were used in the risk assessment.

Species	% a.i.	EC_{25} (lbs ae/A)	NOEC [EC05] (lbs ae/A)	Endpoint affected	MRID No.	Study classification
	22.6%				408118-01	
Monocot-Corn		>0.0156[A]	0.0078	weight[2]		supplemental[3]
Monocot-Oats		0.013	0.0039	height		supplemental[3]
Monocot-Onion		--	--	n/a[C]		invalid
Monocot-Wheat		0.012	0.0039	weight[2]		supplemental[3]
Dicot-Soybean		--	--	n/a[C]		invalid
Dicot-Pea		--	--	n/a[C]		invalid
Dicot-Sugarbeet		0.00097	[0.00039][B]	weight[2]		supplemental[3]

Species	% a.i.	EC_{25} (lbs ae/A)	NOEC [EC05] (lbs ae/A)	Endpoint affected	MRID No.	Study classificationA
Dicot-Sunflower		0.0054	0.0039	weight[2]		supplemental[3]
Dicot-Cucumber		0.0009	[0.000064][B]	height		supplemental[3]
Dicot-Tomato		>0.0156[A]	0.00097	weight[2]		supplemental[3]

[1]Determination of the most sensitive species is based on EC_{25} values.
[2] Fresh weight was recorded instead of dry weight.
[3] the toxicity values could be underestimated since the study was tested with older plants (28D) at a less sensitive stage of growth (timing of application).
[A] The EC25 value is above the highest concentration tested.
[B] The NOEC value is above the EC25, equal to the EC25, or below the lowest concentration, an EC05 value is used instead.
[C] No data

Imazapyr isopropylamine salt

Monocots (3 species) and Dicots (2 species). MRID 43889101 (Core). In a Tier II vegetative vigor study, chlorosis, stunting, and plant death. The most sensitive monocot tested was onion (EC_{25} 0.010 lb ae/acre, NOEC 0.004 lb ae/acre; shoot weight). The most sensitive dicot tested was sugar beet (EC_{25} 0.0016 lb ae/acre, NOEC 0.0008 lb ae/acre; shoot weight). The study is scientifically sound and meets guideline protocols.

Monocots (4 species) and Dicots (4 species). MRID 40003711 (Supplemental). This study was a modified Tier II vegetative vigor study that did not meet guideline requirements. Only descriptive summary data was presented; consequently effect levels were not determined. Observed effects included chlorosis, stunting, leaf tip burning, necrosis, and plant death.

123-2 Aquatic Plant Vascular

Imazapyr acid

Duckweed. MRID 40811802 (Acceptable). In a 14-day toxicity test with duckweed, the EC_{50} for frond production was 0.024 mg ai/L and the NOEC was 0.01 mg ai/L. Imazapyr is considered highly toxic and expected to exert a detrimental effect on vascular aquatic plants. The study is scientifically sound and meets guideline protocols.

Imazapyr isopropylamine salt

Duckweed. MRID 43889102 (Acceptable). In a 14-day toxicity test with duckweed, the EC_{50} for frond production was 0.018 mg ai/L and the NOEC was 0.011 mg ai/L. The study is scientifically sound and meets guideline protocols.

Appendix 7

Selected Information on Ecological Risk Characterization (From Level I, USEPA, 2005A):

A. **Summary Tables**

Table A7-1. Summary of Environmental Risk Conclusions for Aquatic Animals and Plants.

Assessment Endpoint	Use Patterns with LOC Exceedances	Summarized Risk Characterization[1]
Acute Risk to Freshwater Fish and Amphibians [1]	None	LC_{50} values all greater than highest concentration tested. RQs not estimated; however, if highest concentration tested were used to calculate RQs, acute LOCs would not be exceeded for any uses.
Chronic Risk to Freshwater Fish and Amphibians [1]	None	Chronic LOC not exceeded for any uses.
Acute Risk to Freshwater Invertebrates	None	LC_{50} values all greater than highest concentration tested. RQs not estimated; however, if highest concentration tested were used to calculate RQs, acute LOCs would not be exceeded for any uses.
Chronic Risk to Freshwater Invertebrates	None	Chronic LOC not exceeded for any uses.
Acute Risk to Estuarine/Marine Fish	None	LC_{50} values all greater than highest concentration tested. RQs not estimated; however, if highest concentration tested were used to calculate RQs, acute LOCs would not be exceeded for any uses.

[1] Fresh water fish are surrogate for aquatic-phase amphibians

Table A7-2. Summary of Environmental Risk Conclusions for Aquatic Animals and Plants.		
Assessment Endpoint	**Use Patterns with LOC Exceedances**	**Summarized Risk Characterization[1]**
Chronic Risk to Estuarine/Marine Fish	No data available	Estimated chronic effects for estuarine/marine fish uncertain because no chronic data were submitted by the registrant; in estimating risk, an assumption was made that marine/estuarine fish would be of similar sensitivity as the freshwater fish.
Acute Risk to Estuarine/Marine Invertebrates	None	LC_{50} values all greater than highest concentration tested. RQs not estimated; however, if highest concentration tested were used to calculate RQs, acute LOCs would not be exceeded for any uses.
Chronic Risk to Estuarine/Marine Invertebrates	No data available	Estimated chronic effects for estuarine/marine invertebrates uncertain because no chronic data were submitted by the registrant; in estimating risk, an assumption was made that marine/estuarine invertebrates would be of similar sensitivity as the freshwater invertebrates.
Risk to Aquatic Plants	Terrestrial Noncrop Uses (1.5 lb ae/acre) Terrestrial Noncrop Uses (0.9 lb ae/acre) Terrestrial Noncrop Granular Uses (0.5 lb ae/acre) Aquatic Noncrop Uses (1.5 lb ae/acre)	Endangered and non-endangered LOCs are exceeded for aquatic vascular plants from high application rate. No LOCs were exceeded for aquatic non-vascular plants. Endangered and non-endangered LOCs are exceeded for aquatic vascular plants from low application rate. No LOCs were exceeded for aquatic non-vascular plants. Endangered and non-endangered LOCs are exceeded for aquatic vascular plants from low application rate. No LOCs were exceeded for aquatic non-vascular plants. Endangered and non-endangered LOCs are exceeded for aquatic vascular plants from high application rate. No LOCs were exceeded for aquatic non-vascular plants.

[1] includes granular, ground and aerial applications unless specified.

Table A7-3. Summary of Environmental Risk Conclusions for Terrestrial Animals and Plants.		
Risk Conclusion	**Use Patterns with LOC Exceedances**	**Summarized Risk Characterization**
Acute Risk to Birds (and reptiles)	None	LC_{50}/LD_{50} values all greater than highest concentration tested. RQs not estimated. Acute risk to birds is low because highest estimated EECs are one quarter (broadcast spray) to one-half (granular application) of highest concentration tested in acute studies which produced no mortalities and no clinical signs of toxicity.

Chronic Risk to Birds (and reptiles)	None	Chronic LOC not exceeded for any uses.
Acute Risk to Mammals	None	LC_{50} values all greater than highest concentration tested. RQs not estimated. Acute risk to mammals is low because highest estimated EECs are 1/32 (broadcast spray) to less than 1/10 (granular application) of highest concentration tested in acute studies which produced no mortalities and no clinical signs of toxicity.
Chronic Risk to Mammals	None	Chronic LOC not exceeded for any uses.
Risk to Non-target Invertebrates	None likely	Low toxicity to bees. Qualitative assessment indicates probable low risk.

Table IB-2. Summary of Environmental Risk Conclusions for Terrestrial Animals and Plants.

Risk Conclusion	**Use Patterns with LOC Exceedances**	**Summarized Risk Characterization**

Risk to Terrestrial Plants	Terrestrial Noncrop Uses (1.5 lb ae/acre)	Endangered and non-endangered LOCs are exceeded for terrestrial monocots and dicots in dry and semi-aquatic areas receiving a combination of runoff and drift and from spray drift alone from high application rate via ground and aerial applications and exceeded for plants in areas receiving runoff via granular application.
	Terrestrial Noncrop Uses (0.9 lb ae/acre)	Endangered and non-endangered LOCs are exceeded for terrestrial monocots and dicots in dry and semi-aquatic areas receiving a combination of runoff and drift and from spray drift alone from low application rate via ground and aerial applications. However, the non-endangered LOC is not exceeded for monocots receiving spray drift alone via ground applications. Endangered and non-endangered LOCs are exceeded for terrestrial monocots and dicots in dry and semi-aquatic areas receiving runoff from low application rate via granular broadcast application.
	Terrestrial Noncrop Granular Uses (0.5 lb ae/acre)	Endangered and non-endangered LOCs are exceeded for terrestrial monocots and dicots in semi-aquatic areas receiving a combination of runoff and drift via ground and aerial applications for corn use. The endangered LOC is exceeded for dicots in dry areas receiving a combination of runoff and drift and from spray drift alone via ground and aerial applications, and exceeded for monocots in dry areas receiving a combination of runoff and drift via aerial application.
	Clearfield corn (0.014 lbs ae/acre)	Endangered LOCs were not exceeded for monocots in dry areas receiving a combination of runoff and drift via ground application and from spray drift alone via ground and aerial applications. The non-endangered LOC was not exceeded for monocots and dicots in dry areas receiving a combination of runoff and drift and from spray drift alone via ground and aerial applications.
	Aquatic Noncrop Uses (1.5 lb ae/acre)	Endangered and non-endangered LOCs are exceeded for terrestrial monocots and dicots adjacent to or on the edge of a water body receiving a combination of runoff and drift and from spray drift alone via ground and aerial applications.

B. Risk Description

1. Risks to Aquatic Organisms

In the conceptual model, direct application, spray drift and surface runoff/leaching to adjacent bodies of water were predicted as the most likely sources of exposure of imazapyr and the isopropylamine salt of imazapyr to nontarget aquatic organisms. Risks to aquatic organisms (i.e. fish, invertebrates, and plants) were assessed based on modeled estimated environmental concentrations (EECs) and available toxicity data. Aquatic EECs for the ecological exposure to imazapyr were estimated using GENEEC2 employing the standard field pond scenario (Table IIIB-2).

The risk hypothesis stated that the use of imazapyr has the potential to cause adverse effects to both terrestrial and aquatic animals and plants. The assessment refutes this hypothesis regarding animals in that direct effects to terrestrial and aquatic animals are unlikely. The hypothesis is confirmed for terrestrial and aquatic plants, and, through possible indirect effects, for adverse effects to nontarget terrestrial and aquatic animals.

a. Animals

Fish and Invertebrates

Available acute toxicity data for aquatic species indicate that imazapyr acid is practically non-toxic to fish and invertebrates with LC_{50} and EC_{50} values >100 mg/L. The only sublethal effect observed in the acute aquatic animal studies is a decrease in shell deposition in the eastern oyster. The NOAEC/LOAEC for this effect was 109/173 mg/L. In order to compare these values with an exposure value, the highest peak EEC in surface water was selected from the aquatic uses, which utilize direct application to water. The EEC estimation assumes a 1-foot water depth. A comparison of the ecotoxicity values listed above (between 100000 - 173000 ppb) with the peak EEC in surface water (552 ppb), indicates a 181 to 313-fold difference between the highest estimated EEC and the concentrations which produced either no effects (100000 - 109000 ppb) or a decreased shell deposition in oysters (173000 ppb). The estimated peak EEC in surface water from the granular uses is less than 552 ppb. Therefore, it is concluded that the acute risk to fish and aquatic invertebrates is expected to be very low.

Following chronic exposure, the NOAEC/LOAEC for freshwater fish is 43.1/92.4 mg/L and the NOAEC for freshwater invertebrates is 97.1 mg/L, the highest concentration tested. Chronic risk quotients are all < 0.002 for all scenarios except for the aquatic uses. For aquatic uses (direct application to water, assuming 1 foot water depth), the highest chronic EECs are 549 ppb (21 day) and 542 ppb (60 day). Using the NOAEC of 43.1 mg/L (43100 ppb) for freshwater fish and the 60-day EEC, the estimated RQ would be 0.013. All other scenarios (Table III B-3) would have RQs <0.013 because the EECs are significantly lower than 549 ppb and 542 ppb.

Consequently, the risks for acute and chronic adverse effects related to reproduction, growth, and survival are low for fish and invertebrates inhabiting surface waters adjacent to an imazapyr treated field. The assumption of minimal risk for marine/estuarine fish and invertebrates

following chronic exposure is based on an assumption of equal sensitivity to their freshwater counterparts. However, if estuarine/marine fish and invertebrates studies are submitted and are more sensitive to potential adverse chronic effects of imazapyr, then risks may be underestimated for these taxonomic groups.

An *in situ* microcosm study found no effects following a single application of imazapyr up to a concentration of 19.8 mg/L on the macroinvertebrate community of a logged pond cypress dome. Comparing this NOAEC (19800 ppb) with the peak EEC in surface water (552 ppb) indicates a 36-fold difference. Although the data from this study are limited because examinations were conducted at the family/genus level and effects on individual species were not examined , it does support the laboratory studies on aquatic invertebrates. When taken together, all the studies combined indicate that the risk to benthic organisms is not likely.

b. Aquatic Plants

Toxicity studies indicate that imazapyr acid is highly toxic and expected to exert detrimental effects to aquatic vascular plants. The imazapyr acid EC_{50} for the freshwater vascular plant (duckweed) is 0.024 mg/L (NOAEC 0.01 mg/L), based on inhibition of plant growth and reduction of frond count. The toxicity of the isopropylamine salt of imazapyr to duckweed is similar to the acid, with a 14-day EC_{50} of 0.018 mg ae/L (NOAEC = 0.011 mg ae/L). Studies with non-vascular aquatic plants (algae and diatoms) indicate that imazapyr acid and its salt are not expected to exert detrimental effects to non-vascular plants, at the maximum application rate when compared to the LOCs for non-listed and listed species. Risk to non-vascular plants is then compared to the listed species LOC for any potential indirect effects to listed plant and animal species.

For the use scenarios modeled (Table II.e.) for imazapyr, there were no LOC exceedances for listed and non-listed aquatic non-vascular plants (Tables IVA-5 and IVA-6) from direct effects. However, the LOCs for non-endangered and endangered aquatic vascular plants were exceeded for the terrestrial non-cropped spray and granular uses (at high and low application rates) and for the aquatic non-cropped uses, at application rates of 1.5 lb ae/acre. For the Clearfield corn use, LOCs were not exceeded for non-endangered and endangered aquatic vascular plants. Consequently, aquatic vascular plants inhabiting surface waters adjacent to a treated field, and those exposed via direct application to water, would be at risk for adverse effects to growth and development as a result of the labeled uses of the pesticide. The potential risk to endangered aquatic vascular plants will be discussed in greater detail in Section IV.B.4.

2. Risks to Terrestrial Organisms

In the conceptual model, direct application, ground deposition, spray drift, root uptake, and wind erosion of soil particles with resulting residues on foliage and on flowers and seeds are the most likely sources of imazapyr exposure to nontarget terrestrial organisms, including listed species. Risks to terrestrial organisms (i.e. birds, mammals, and plants) were assessed based on modeled EECs and available toxicity data.

a. Animals

Birds

Acute risk quotients were not estimated for birds because there was no mortality nor any other signs of toxicity in either the acute oral studies or the acute dietary studies. For terrestrial non-crop uses with spray applications of 1.5 lb ae/acre, the highest EEC concentration for birds is 410 mg/kg bw for short grass consumed by a 20 g bird. The adjusted LD_{50} for 20 g birds would be > 1549 mg/kg bw. There is an approximately four-fold difference between these two values. Since there were neither mortalities nor clinical signs of toxicity at 1549 mg/kg bw, the acute risk to birds following spray applications is likely to be low.

Following granular applications, the highest LD_{50}/square foot is > 0.5 for 20 g birds. This means that the estimated EEC is approximately one-half of the highest concentration tested in the acute study which produced no mortalities and no clinical signs of toxicity. Therefore, again, the acute risk to birds following a broadcast granular application is also likely to be low.

The chronic LOC for birds is not exceeded for any of the registered uses.

Mammals

As with birds, risk quotients were not estimated for mammals because there was no mortality or clinical signs of toxicity observed in the acute oral study. For terrestrial noncrop uses with spray applications, the highest EEC concentration for mammals is 343 mg/kg bw for short grass consumed by a 15 g mammal. The adjusted LD_{50} for 15 g mammals would be >10989 mg/kg bw. There is an approximately 32-fold difference between these two values. Since there were neither mortalities nor clinical signs of toxicity at 10989 mg/kg bw, the acute risk to mammals following spray applications is likely to be low.

Following granular applications, the highest LD_{50}/square foot is 0.09 for 15 g mammals. Therefore, the estimated EEC is less than one-tenth of the highest concentration tested in the acute study, which produced no mortalities and no clinical signs of toxicity. The acute risk to mammals following a broadcast granular application is also likely to be low.
The chronic LOC for mammals is not exceeded for any of the registered uses.

Terrestrial Non-target Insects

The available terrestrial insect toxicity data, based on tests with honey bees, suggests that imazapyr is practically non-toxic to bees. Tests with honey bees provide an acute LD_{50} > 100 µg/bee. Risk to terrestrial insects in the direct treatment area is expected to be low.

b. Terrestrial Plants

Based on the toxicity data presented in Ecological Effects Section , the results indicate that for the non-crop terrestrial uses at both the high and low application rates by ground and aerial spray, the Non-Endangered Species LOC (with the exception of monocots at the low rate as a

result of spray drift alone from ground application) and the Endangered Species LOC were exceeded for monocots and dicots located adjacent to treated areas, inhabiting semi-aquatic areas, and as a result of a combination of runoff and spray drift and spray drift alone.

4. Endocrine Effects

Imazapyr and its isopropylamine salt have shown no indication of inducing endocrine-related effects following exposure.