imazapic

Review Date: 7/6/2009

Type	Systemic herbicide
Controls	Grasses, broad leaf plants and vines. It can also used to suppress grass height in non-cropland areas.
Mode of Action	Inhibits the function of enzyme required for the synthesis of branched chain amino acids (Reference 1).

Thurston County Review Summary:

Even though imazapic is considered low in toxicity to all tested organisms, and the risk of toxicity from an herbicidal exposure is low in hazard, it also caused developmental toxicity without maternal toxicity. Imazapic is also considered high in hazard for mobility and persistence, and is therefore is given a conditional rating.

MOBILITY

Property	Value	Reference	Rating
Solubility (mg/L)	2,150 - 36,000	1	High
Soil Sorption (Kd=mL/g)	0.13 - 4	1	High
Organic Sorption (Koc=mL/g)	112	1	High

Mobility Summary:

Imazapic is very soluble in water and can be expected to bind poorly to organic and inorganic soil. The mobility hazard of imazapic is considered high.

PERSISTENCE

Property	Value	Reference	Rating
Vapor Pressure (mm Hg)	0.00000064	1	Moderate
Biotic or Aerobic Half-life (days)	113	1	High
Abiotic Half-life (days)	106	1	High
Terrestrial Field Test Half-life (days)	31 - 410	1	High
Hydrolysis Half-life (days)	Not found		
Anaerobic Half-life (days)	2,440	1	High
Aquatic Field Test Half-life (days)	30	1	Moderate

Persistence Summary:

The vapor pressure of imazapic is high enough to have some of it evaporate from plants and surface soil. Soil bacteria does not seem to significantly degrade imazapic and it is likely to take over 100 days for it to break down to half of the applied concentration. In anaerobic settings (aquatic sediments or deep soil) the compound may persist for many years. Imazapic is considered moderately persistent in water (likely to break down to half of the original concentration in one month). The overall persistence hazard of imazapic is considered high.

BIOACCUMULATION

Property	Value	Reference	Rating
Bioaccumulation Factor	"no evidence"	3	Low
Bioconcentration Factor	0.11	1	Low
Octanol/Water Partition Coefficient	Kow = 295	1	Low

Bioaccumulation Summary:

Imazapic has a moderate affinity to organics material (Kow = 295) which gives it a potential to bioaccumulate. In bioaccumulation studies, imazapic was fed to rats and up to 75% was excreted within 24 hours of ingestion resulting in a low bioconcentration factor (Reference 1). The bioaccumulation hazard of imazapic is rated as low.

ACUTE TOXICITY

Test Subject	Value	Reference	Rating
Mammalian (LD50)	>5,000 mg/kg	1	Low
Avian (LD50)	> 2,150 mg/kg	1	Low
Honey bee or insect (LD50)	>100 ug/bee	1	Low
Annelida -worms (LC50)	Not found		
Fish (LC50)	>100 mg/L	1	Low
Crustacean (LC50)	> 97.7 mg/L	1	Low
Mollusk (LC50)	> 99.2 mg/L	1	Low
Amphibian (LD50 or LC50)	Not found		

Acute Toxicity Summary:

Single dose testing of imazapic indicates that it is low in toxicity to all organisms tested (mammals, birds, bees, fish, crustaceans and oysters).

ACUTE TOXICITY - Risk Assessment

Subject and Scenario	Dose of Concern	Exposure	Margin of Safety	Route	Reference	Rating
Adult mixing and applying with backpack sprayer	0.5 mg/kg/day	0.015 mg/kg/day	33	Skin absorption + inhalation	3	Low
Adult mixing and applying with groundboom sprayer	0.5 mg/kg/day	0.03 mg/kg/day	17	Skin absorption + inhalation	3	Low
Women 13+ drinking treated surface water	0.175 mg/kg/day	0.015 mg/kg/day	11.6	Ingestion	2	Low
Exposures from combined sources were not evaluated						

Acute Toxicity Risk Assessment Summary

For oral exposures, the EPA added a safety factor of x10 to the standard x100 due to the potential for pre- and post-natal toxicity (since maternal toxicity was elicited at higher concentrations than developmental toxicity to offspring was observed). The dose of concern is calculated to be the No Observeable Adverse Effect Level (NOAEL = 175 mg/L) divided by 1000, which is 0.175 mg/L.

Since imazapic is a mobile chemical, there is a potential for it to get into surface or ground water and so the EPA conducted a drinking water risk assessment. The worst-case scenario is for contaminated surface water to be used for drinking water. The calculated exposure is more than eleven times less than the calculated dose of concern and is rated as low in hazard.

For dermal (skin absorption) and inhalation exposures a safety of 300 was required by EPA (additional x3 safety factor added due to lack of NOAEL in a critical study). The USDA evaluated applicator exposure scenarios using EPA safety factors although they did not use the EPA's dose of concern (they created their own, more conservative value, because the EPA waived dermal toxicity assessments for lack of a toxicological endpoint). The worst-case scenario was to workers mixing and applying imazapic with groundboom sprayers. The potential exposures were calculated to be 17 times less than the USDA's dose of concern.

The risk for toxicity from short-term exposures to imazapic from herbicidal use is considered low in hazard.

CHRONIC TOXICITY

Property	Value	Adverse Effect	Reference	Rating
Carcinogenicity	E	Evidence of non-carcinogenicity for humans	1	Low
Mutagenicity	Negative	- -	1	Low
Neurotoxicity - (NOAEL)	Waived	- -	3	Low
Endocrine Disruption	Not listed	- -	4	Low
Developmental Toxicity (NOAEL)	175 mg/kg/day	Increased rudimentary ribs	2	Check risk
Reproductive Toxicity (NOAEL)	1,474 mg/kg/day	None	2	Check risk
Chronic Toxicity (NOAEL)	137 mg/kg/day	Muscle degeneration	2	Check risk

Chronic Toxicity Summary:

Developmental toxicity to offspring was noted at 350 mg/kg/day, which was below the concentration that toxicity was seen in the parent, indicating that imazapic causes reproductive toxicity. In a different long-term study, toxicity was noted at lower doses, 137 mg/kg/day, and so this lower concentration was used to evaluate toxicity from long term exposures. Worst-case scenarios for long-term imazapic exposures were from eating food with residual herbicide on it, all of these scenarios were considered low in hazard for toxicity. No herbicidal uses of imazapic would be expected to have a long-term potential exposure greater than those from food sources so, all long-term exposures are considered low in hazard for toxicity.

So, even though long-term exposures are considered low in hazard the rating for long-term exposure toxicity is considered moderate because developmental toxicity was seen before maternal toxicity.

CHRONIC TOXICITY - Risk Assessment

Subject and Scenario	Dose of Concern	Exposure	Margin of Safety	Route	Reference	Rating
Long-term contact to treated weeds is not expected						
Combined exposures were not evaluated						
Drinking water exposure could not be evaluated	0.5 mg/kg/day	Value provided not normalized to	Unknown	Ingestion	2	Assumed low
Dietary exposres were not evaluated						

Chronic Toxicity Risk Assessment Summary:

The EPA concluded that there were no long-term exposures to imazapic expected from non-dietary or non-occupational sources. Thurston County reviews do not evaluate exposures from herbicide use on crops. The potential long-term exposures to contaminated drinking water was reviewed by the EPA and was considered not of concern although the calculations were not provided. When the drinking water exposures were added to the dietary exposures the combined exposure was not of concern to the EPA and the dietary exposure consisted of 1.4% of the dose of concern (low risk).

The risk of toxicity from long-term exposures to imazapic through herbicidal use is considered low in hazard.

DegradationProducts:

The toxicity of imazapic metabolites were considered adequately assessed in the qualitative in vivo studies of imazapic (Reference 1).

Comments:

Imazapic is not considered a skin sensitizer (Category IV) but is a moderate eye irritant (Category III).

References

1. Durkin, P. and Follansbee, M., Syracuse Environmental Associates, Inc. Prepared for USDA, Forest Service. Imazapic - Human Health and Ecological Risk Assessment - Final Report. December 4, 2004.
2. USEPA. Imazapic - Ammonium; Pesticide Tolerances for Emergency Exemptions. [Federal Register: October 6, 1999 (Volume 64, Number 193)].
3. USDA Forest Service -Pacific Northwest Region-Invasive Plant EIS. Appendix Q Human Health Risk Assessment. May 2005.
4. Scorecard - The Pollution Information site. Health Effects: Endocrine Toxicants (Accessed 7/6/2009). http://www.scorecard.org/health-effects/