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4

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 15-APR-2003

SUBJECT: Occupational, Residential and Recreational Exposure Characterization/Risk Assessment for **Imazapyr** for Use at Aquatic Sites and on Pasture/Rangeland. PC Code: 128821; DP Barcode: D289502.

FROM: J. Troy Swackhammer, Chemist
Registration Action Branch 1 (RAB1)
Health Effects Division (HED; 7509C)

TO: Dana Vogel, Chemist (Risk Assessor)
RAB1/HED (7509C)

THRU: G. Jeffrey Herndon, Branch Senior Scientist
RAB1/HED (7509C)

INTRODUCTION

The Registration Division (RD) has requested that HED assess the potential occupational and recreational (swimmers) exposures resulting from the proposed use of imazapyr (2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-oxo-1H-imadazol-2-yl]-3-pyridinecarboxylic acid), the active ingredient in Arsenal® (EPA Reg. No. 241-346), for control of invasive floating and emersed weeds at aquatic and wetland sites and for spot treatment on pastures and rangelands. RD has also requested an update on the registered residential and recreational uses of imazapyr. The risk estimates in this assessment are based on toxicological endpoints identified by HIARC in a meeting held on February 6, 2003 (see document dated 25-MAR-2003, TXR No. 0051689). At this meeting, the HIARC selected the following endpoints relevant to this assessment (see Attachment A for summary of acute toxicity and toxicological endpoints):

- Short-term incidental oral endpoint: 250 mg/kg bw/day (from chronic dog study).
- Short-term dermal and inhalation endpoint: 250 mg/kg bw/day (from chronic dog study) with 100% dermal and inhalation absorption factors.

HIARC and RAB1 also concluded that no special FQPA safety factor is required for imazapyr. Additionally, since HIARC chose the same endpoint for dermal and inhalation routes of exposure, the margins of exposure (MOEs) for dermal and inhalation risks presented in this risk assessment are expressed as combined MOEs.

The durations used to distinguish between short-, intermediate-, and long-term exposures are based HED's exposure duration policy (see HED Hot Sheet #17, 04-JUN-2001):

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- Short-term incidental oral endpoint: 250 mg/kg bw/day (from chronic dog study).
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HIARC and RAB1 also concluded that no special FQPA safety factor is required for imazapyr. Additionally, since HIARC chose the same endpoint for dermal and inhalation routes of exposure, the margins of exposure (MOEs) for dermal and inhalation risks presented in this risk assessment are expressed as combined MOEs.

The durations used to distinguish between short-, intermediate-, and long-term exposures are based HED's exposure duration policy (see HED Hot Sheet #17, 04-JUN-2001):

- Short-term exposure duration, defined as lasting from 1 day to 1 month.
- Intermediate-term exposure duration, defined as lasting from 1 to 6 months.
- Long-term exposure duration, defined as lasting longer than 6 months.

Additionally, the HED Carcinogenicity Peer Review Committee classified imazapyr as a **Group E** carcinogen (no evidence of human carcinogenicity).

In summary, this ORE memo includes exposure and risk assessments for the following:

- Occupational handler and post-application worker exposures for proposed aquatic and pasture/rangeland uses.
- Residential exposures by adults and children for registered use on walkways, patios, driveways and bare ground.
- Recreational exposures by adults and children for registered uses at recreational sites (golf courses and fairgrounds) and proposed aquatic use (swimming in treated waters).

CONCLUSIONS

Occupational: Imazapyr is currently registered for use on noncropland sites such as utility rights-of-ways, utility plant sites, petroleum tank farms, forestry (conifer release), golf courses and ornamental turf (commercial and recreational sites). The registrant, BASF, is requesting registration of imazapyr to control invasive aquatic weeds on wetlands within forestry or non-crop sites and for floating and emersed weed control at aquatic sites, including ponds, lakes, reservoirs, rivers and estuarine areas. Ground, boat and aerial applications are permitted per the proposed label. Note that the proposed label specifies that pesticide handlers wear personal protective equipment (PPE) consisting of a long-sleeved shirt, long pants, and shoes with socks.

Commercial aquatic handlers are anticipated to have short-term dermal and inhalation exposures based on anticipated use pattern information from aquatic weed control professionals. Combined MOEs (dermal and inhalation exposures) for mixer/loaders supporting aerial, boat, and ground-based applications range from **10** to 890, when handlers wear PPE specified on the proposed label. The MOE for mixer/loaders supporting aerial applications (MOE = 10) is of concern to HED (MOE < 100, occupational); however, with the addition of waterproof gloves to mixers/loaders, all combined MOEs range from 130 to 48,000 and do not exceed HED's level of concern.

Workers entering treated sites could potentially have short-term dermal exposures. The MOE for workers entering treated wetland (aquatic) sites the day of application is 430 and does not exceed HED's level of concern. The restricted entry interval (REI) on the parent label is 12 hours, **however, imazapyr is Toxicity Category I for primary eye irritation.** Under the Worker Protection **Standard (WPS; 40 CFR Part 170), an interim 48-hour REI is required for an active ingredient that has an acute toxicity of Category I.** HED recommends that RD review the REI on the parent label.

Residential: RD has confirmed that there is one imazapyr formulation registered for residential use. The label for the product (EPA Reg. No. 239-2657) specifies that it is to be used on driveways, brick patios, walkways, and bare ground. Application is by sprinkler can. It is not be used on lawns. Residential handlers are anticipated to have short-term dermal and inhalation

exposures; the combined MOE for dermal and inhalation exposures is 85,000. Based on the labeled use pattern, HED anticipates that the post-application residential dermal exposures experienced by adults and children would not be more than those experienced at recreational sites discussed below. However, HED anticipates that the soil ingestion scenario (non-dietary) is possible due to toddler hand-to-mouth behavior and treated bare ground. The MOE for toddler soil ingestion is greater than 1×10^6. All residential exposures assessed (representing a Tier 1 screening level assessment) do not exceed HED's level of concern (MOEs <100, residential).

Recreational: Imazapyr formulations are registered for use at recreational sites, including golf courses and fairgrounds. Although the registered labels indicate that the imazapyr is not intended for intense wear areas, adults and children could potentially experience short-term, post-application dermal exposures, and toddlers could also experience non-dietary oral exposures (from hand-to-mouth behavior) at fairground sites. MOEs for dermal exposures by child and adult golfers were both greater than 1×10^6. MOEs for dermal exposures by adults and children (toddlers) at recreational are 260,000 and 160,000, respectively. The combined non-dietary MOE for incidental ingestion by toddlers (for all hand-to-mouth behaviors) at fairground sites is greater than 1×10^6. The combined MOE for dermal and non-dietary oral exposures by toddlers is 150,000.

Additionally, although the proposed aquatic use is most likely intended for remote or inaccessible aquatic sites, adults and children swimming in treated areas could potentially experience short-term post-application incidental ingestion and dermal exposures. MOEs for incidental ingestion by toddler and adult swimmers range from 68,000 to 320,000, respectively; MOEs for dermal exposures by swimmers are all greater than 1×10^6. All recreational exposures assessed (representing a Tier 1 screening level assessment) do not exceed HED's level of concern (MOEs <100, recreational).

SUMMARY OF REGISTERED AND PROPOSED USE PATTERNS AND FORMULATIONS

Imazapyr is a systemic herbicide used to control most annual and perennial grasses, broadleaf weeds, and many brush and vine species. Imazapyr is readily absorbed though the leaves, stems, and roots and is translocated rapidly throughout the plant. Noticeable herbicidal activity may take up to several weeks. Imazapyr is currently registered for use on rights-of-way, non-irrigation ditches, fence rows, storage areas, forestry sites, and recreational sites, including golf courses and fairgrounds. The parent Arsenal® label indicates that aerial (fixed-wing aircraft and helicopters) and ground applications (groundboom, backpack sprayer, and hydraulic handgun) are permitted. The proposed amended label, which includes the aquatic site use, implies that boat-based applications are also permitted.

The registrant, BASF is requesting registration of imazapyr, the active ingredient in Arsenal® (EPA Reg. No. 241-346) for control of invasive aquatic weeds at aquatic sites, including ponds, lakes, reservoirs and estuarine waterbodies and for spot treatment on pasture and rangeland. Arsenal® is an aqueous solution (liquid formulation) containing 28.7% imazapyr (equivalent to 22.6% imazapyr ae or 2 lb. acid equivalent [ae] per U.S. gallon). A summary of these uses is provided below in Table 1.

Table 1. Summary of Proposed and Registered Use Patterns for Imazapyr			
Exposure setting:	**Occupational (this action)**	**Registered Residential**	**Registered Recreational**
Formulation	Arsenal® (Parent label: EPA Reg. No. 241-346), 22.6% ae imazapyr, 2 lb ae/gal, aqueous solution	Ortho GroundClear Triox Complete Vegetation Killer (EPA Reg. No. 239-2657), 0.08% imazapyr, 0.0056 lb ae/gal	Event™ (EPA Reg. No. 241-317), 0.6% ae imazapyr, 0.052 lb ae/gal
Use sites	Registered uses: rights-of-way, non-irrigation ditches, utility sites, petroleum tank farms, forestry sites. **Proposed uses: aquatic sites and spot treatment on pasture/rangeland.**	Driveways, parking areas, brick walls, gravel pathways, patios, sidewalks, bare ground	Golf course roughs, fairgrounds, roadsides, airports, cemeteries
Application methods	Registered uses: aerial and ground-based equipment. **Proposed uses: aerial, ground-based, boat-based, and backpack applications.**	Sprinkling can	Ground-based equipment
Maximum application rate/frequency	Proposed uses: 1) aquatic use: up to 1.5 lb ae/A/yr 2) spot trmt on pasture/ rangeland: 0.075 lb ae/0.1A up to 0.15 lb ae/0.1A/yr	0.0056 lb ae/300 ft^2, one application required for year-long control.	0.0041 lb ae/A, no yearly maximum/frequency restrictions

OCCUPATIONAL EXPOSURE AND RISK ASSESSMENT

a. Overview of Proposed Uses

Aquatic Weed Control

The following information provides an overview of the proposed use patterns for imazapyr in aquatic weed control from the following sources:

- Informational meeting with U.S. Army Corps of Engineers (USACE), University of Florida, South Florida Water Management District (SFWMD), and USDA-Agricultural Research Service (CA) on Aquatic Weed Control, August 17, 2001.

The USACE, Univ. of Florida, South Florida Water Management District (SFWMD) are members of the Federal Aquatic Herbicide Working Group. Most weed control boat applications involve approximately 2 - 3 acres per day, where 10 acres per day is the upper range anticipated for boat applications for maintenance programs (see RAB1 memo for triclopyr use in aquatic weed control [22-JUL-2002, D269448] for more background on aquatic weed control discussed in this meeting).

- Informational meeting with BASF, USACE, University of Florida, South Florida Water Management District, and University of Washington on imazapyr proposed uses, January 29, 2003.

The SFWMD envisions imazapyr to be used in the Everglades Restoration, particularly in Lake Okeechobee for melaleuca and torpedograss control. (Please see the *Melaleuca Management Plan*, Florida Exotic Pest Plant Council, May 1999 for more details on melaleuca management in South Florida. Imazapyr use is discussed in this document.) Melaleuca control programs typically involve aerial applications via helicopter followed by frill and girdle treatments via machete and backpack sprayer. One-time aerial applications per treatment area are envisioned by SFWMD. Crews also use chain saws to fell trees followed by stump and cut end treatment via hand-gunner from airboats. Aerial applicators could potentially treat up to 400 acres per day. Torpedograss control typically involves prescribed burns followed by aerial applications. The USACE discussed the use of imazapyr for phragmites control along the Atlantic and Gulf coasts as well as the Great Lakes. Anticipated spray equipment includes all-terrain vehicles (ATV's) equipped with spraybooms applying up to 3 pints/A (0.75 lb ae/A) Arsenal® followed by a prescribed burn.

The University of Washington discussed the use of Arsenal® for spartina control in Willapa Bay, Puget Sound and San Francisco Bay using airboats, ATV's and backpack sprayers. Treatment via airboat is anticipated to reach upwards of 5 acres/day.

Summary: Based on the proposed use patterns for this action, commercial handlers are anticipated to have short-term dermal and inhalation exposures. Workers entering treated sites could potentially have short-term dermal exposures. Only short-term handler and worker exposures are anticipated, since the USACE and SFWMD anticipate that most applications to be one-time applications based on the January 29, 2003 meeting. In cases where multiple applications are planned, USACE and SFWMD envision two split treatments at the 0.75 lb ae/A for a total of 1.5 lb ae/A/yr maximum rate (electronic communication from K. Getsinger, USACE to RD, 29-MAR-2003).

Spot Treatment on Pasture and Rangeland

The registrant also proposes to use imazapyr for control of undesirable vegetation in grass pasture and rangeland. The proposed label language indicates that spot treatment would involve 1/10 of an acre, although the registrant also proposed an application rate range between 2 to 48 fl. oz. per acre. The resulting maximum single application rate equates to 0.075 lb ae/0.1 A. Note that the registrant indicated to RD that they do not intend to exceed the 1.5 lb ae/A-yr (or 0.15 lb ae/0.1A/yr) maximum application rate. As such, the proposed application rate for spot treatment on pasture and rangeland would allow for 2 applications on a given 0.1 acre plot. However, this application information is not clearly stated on the proposed label.

Note to RD: HED recommends that the registrant clarify the single-application rate maximum and the maximum annual application rate for spot treatment on pasture/rangeland in the proposed label.

b. Occupational Handler Exposure Assumptions and Risk Assessment

No chemical-specific data were available to assess potential exposures to handlers from the proposed uses. However, application-specific data was available from a study conducted by G.A. Wojeck et al. (1983) regarding worker exposure to diquat dibromide use for aquatic weed control. The exposure data from this study were used in the RED for diquat dibromide completed in July 1995. Although the boat-based applications application scenarios described in this study are very similar to the proposed uses of imazapyr, specific exposure data from the Wojeck study were not used in this assessment, because no inhalation exposure data were available from this study. However, qualitative exposure comparisons in this study are useful for characterizations as discussed below. In summary, this exposure assessment was conducted using dermal and inhalation unit exposure data available in the Pesticide Handler's Exposure Database (PHED) Surrogate Table (v1.1., 1998).

Based on the above background information, the following exposure scenarios are anticipated:

- Mixer/loader supporting aerial (helicopter), boat, and ground applications at aquatic sites.
- Aerial, boat or ground applicator.
- Boat driver.
- Backpack sprayer, mixer/loader/applicator (MLAP; see discussion below).

Flagger scenarios are not anticipated since it appears to be impractical to use flaggers in an aquatic setting and the widespread use of GPS devices per discussions with aquatic herbicide specialists. Specific acreages treated daily by aquatic field crews are based on discussions with USACE and SFWMD presented above, except for the backpack sprayer assessment, where default assumptions from HED's Science Advisory Council for Exposure (ExpoSAC) Policy No. 9 (July 5, 2000) were used. Additionally, according to the Wojeck et al. study, applicators conducting surface weed control received approximately 9 times the estimated total body exposure as compared to boat drivers. Thus, for this assessment, only the boat-based applicator was included. The occupational handler scenarios included in this assessment are further characterized below:

- Mixer/loader supporting aerial applications.
  Explanation: Aerial applications are anticipated to treat higher acreages than ground or boat applications, based on discussions with the USACE and SFWMD. For this assessment, it is assumed that 400 acres could be treated per day, based on anticipated restoration treatments for melaleuca control.

- Mixer/loader and applicator supporting boat-based applications.
  Explanation: The proposed label specifies a maximum label rate of 1.5 lb ae/A for floating and emersed weed control. It is assumed that a boat applicator could treat up to approximately 10 acres/day based on discussions with the USACE and SFWMD. Acres treated via ATV are anticipated to be on-par or just below boat-based application.

- Boat- and truck-based handgun applicators conducting surface and wetland weed control.
  Explanation: Open boat applicators are expected to have to a higher exposure than aerial

applicators in open cockpits. HED assumed that a handgun applicator could treat up to approximately 10 acres/day based on discussions with the USACE and SFWMD.

- MLAP, backpack sprayer conducting frill or girdle treatments for melaleuca control using concentrated solutions.
  Explanation: Note that applicators using backpack sprayers conducting frill or girdle treatments are anticipated to have higher exposures than applicators conducting spot treatment at pasture/rangeland sites, since the maximum application rate using concentrated solutions is higher than the rate proposed for pasture/rangeland sites.

  Note on HED's MLAP Policy: HED's policy concerning MLAPs performing ground applications (ExpoSAC Draft Policy, March 29, 2000) directs that exposure and risk estimates for mixer/loaders and applicators for tractor-drawn equipment remain separate due to the conservative nature of the data in PHED, while the exposure and risk estimates for handheld equipment (e.g., backpack sprayers) be combined.

Table 2 presents the assumptions used in the handler assessments and corresponding risk estimates for proposed uses of imazapyr.

Table 2. Handler Exposure Assumptions and Risk Assessment for Proposed Uses of Imazapyr

Exposure Scenario	Unit Exposure[1] (mg/lb ae handled)	AR[2] (lbs ae/A, unless specified)	Acres/d[3] (unless specified)	Potential Daily Dose[4] (PDD; mg/kg bw/d)	Combined Short-term MOE[5]
Mixer/loader: liquid, open pour, supporting aerial application (by helicopter),	dermal: S/L w/o gloves[6]: 2.9 (HC) S/L w/gloves[6]: 0.023 (HC)	1.5	400	dermal: w/o gloves: 24.9 w/gloves: 0.197	w/o gloves: **10** w/gloves: 1,200
	inhalation: 0.0012 (HC)			inhalation: 0.0103	
Mixer/loader: liquid, open pour, supporting boat application	dermal: S/L w/o gloves: 2.9 (HC) S/L w/gloves[6]: 0.023 (HC)		10	dermal: w/o gloves: 0.621 w/gloves: 0.00493	w/o gloves: 400 w/gloves: 48,000
	inhalation: 0.0012 (HC)			inhalation: 2.57×10^{-4}	
Applicator: handwand from boat, truck or ATV	dermal: S/L w/o gloves: 1.3 (LC) S/L w/o gloves: 0.39 (LC)		10	dermal: w/o gloves: 0.279 w/gloves: 0.0836	w/o gloves: 890 w/gloves: 3,000
	inhalation: 0.0039 (HC)			inhalation: 8.36×10^{-4}	

Table 2. Handler Exposure Assumptions and Risk Assessment for Proposed Uses of Imazapyr

Exposure Scenario	Unit Exposure[1] (mg/lb ae handled)	AR[2] (lbs ae/A, unless specified)	Acres/d[3] (unless specified)	Potential Daily Dose[4] (PDD; mg/kg bw/d)	Combined Short-term MOE[5]
MLAP: backpack sprayer, girdle treatments, concentrated solution	dermal: S/L w/ gloves: 2.5 (LC); no w/o gloves data available	1.33 lb ae/gal conc. soln.	40 gal/d	dermal, w/gloves: 1.89	w/gloves: 130
	inhalation: 0.030 (LC)			inhalation: 0.0227	

Notes:

1. Source: Pesticide Handlers Exposure Database (PHED) Surrogate Exposure Table (v1.1., 1998). SL = single layer of clothing, without or with waterproof gloves. (HC) = high confidence data; (LC) = low confidence data; unit exposures for boat-based handwand applicators adopted from high-pressure handwand scenario in PHED for use in this assessment.
2. AR = Maximum application rate. Note: For MLAP backpack sprayer, application rate was based on: 40 gal/d x 2 qt Arsenal/3 qt solution x 2 lb ae/gal Arsenal = 53.3 lb ae/d.
3. Daily acres treated based on discussions with USACE and SFWMD for aerial and boat-based applications. Daily amount handled for backpack sprayer from Exposure SAC Policy No. 9, July 5, 2000.
4. Potential Daily Dose (PDD) = Unit exposure(mg/lb ai) x AR x Acres/Day x 1/BW (70 kg) x %Absorption (100% dermal absorption and 100% inhalation absorption rate to convert to oral equivalents per HIARC). Combined PDD = PDD_{dermal} + $PDD_{inhalation}$.
5. MOE = NOAEL/ADD; short-term dermal and inhalation NOAELs based on Oral NOAEL = 250 mg/kg/day. HED`s level of concern is for MOEs < 100 (occupational), so MOE is expressed as combination of dermal and inhalation risk.
6. S/L w/o gloves: single layer of clothing without gloves; S/L w/ gloves: single layer of clothing with gloves.

As shown in Table 2, all MOEs are above 100 and do not exceed HED's level of concern when handlers wear gloves. (Note that HED does not have "no glove" unit exposure data in PHED for backpack sprayers, so the "with gloves scenario was assessed.) However, it should be noted that the dermal exposure estimates are based on a 100% dermal absorption rate, so this assessment is considered conservative.

Note to PM: HED recommends that handlers wear waterproof gloves.

c. Post-Application Occupational Exposures and Assumptions

As discussed previously, personnel entering wetland sites and pasture/rangeland following applications could potentially have short-term dermal exposures. No post-application exposure is anticipated from floating or emersed weed control treatments. Post-application inhalation exposures are anticipated to be negligible given that the vapor pressure of imazapyr technical is $< 2 \times 10^{-7}$ mmHg.

No chemical-specific, post-application worker studies have been submitted by the registrant to support this registration action. As such, standard HED post-application assumptions were used to provide an estimate of post-application exposure risks to workers. Specifically, the residue transfer coefficient (TC) used in this assessment are from an interim TC policy developed by HED's ExpoSAC using proprietary data from the Agricultural Re-entry Task Force (ARTF) database (ExpoSAC Policy No. 3.1). It is the intention of HED's Science Advisory Council for Exposure that this policy will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature. The assumptions for this assessment are as follows:

- Maximum application rate: 1.5 lb a.e./A.
- 20% of the maximum application rate are available as dislodgeable foliar residues (DFR) available on Day 0 of treatment.
- Re-entry into treated wetland sites is anticipated to result in higher post-application dermal exposure than re-entry into treated pasture/rangeland. A TC of 1,500 cm^2/hour based on scouting in rice fields (Central value from ARF021) with full foliage development is used for this exposure assessment.
  Explanation: Note that there is no post-application data for post-application entry into treated wetland sites in ExpoSAC Policy No. 3.1, therefore, a surrogate scenario was selected from available data and adapted for this scenario (re-entry into treated wetland sites).
- Work day of 8 hours.

Table 3 presents the results of the post-application assessment for re-entry into treated wetland sites.

Table 3. Post-Application Worker Exposure and Risk Assessment for Proposed Use of Imazapyr in Wetlands					
Exposure Scenario	**AR (lb ae/A)**	**DFR[1] (ug/cm²)**	**TC (cm²/hr)**	**PDD[2] (mg/kg/day)**	**Short-term Dermal MOE[3]**
Re-entry into treated areas	1.5 lb ae/A	3.36	1,500	0.576	430

Notes
1. Surrogate DFR on Day 0 (no dissipation) = application rate (lb a.e./A) x 20% available as dislodgeable residue x 4.54E8 ug/lb x 2.47E-8 A/cm^2. Ex. calc = 1.5 lb ae/A x 0.20 x 4.54E8 ug/lb x 2.47E-8 A/cm^2 = 3.36 µg/cm^2.
2. ADD =DFR (3.36 ug/cm^2) x TC (1,500 cm^2/hr) x 8 hrs/day x 0.001 mg/ug x 1/ BW x %dermal absorption; BW= 70kg for adults; dermal absorption = 100%.
3. MOE = NOAEL/ ADD; short-term dermal NOAEL = 250 mg/kg bw/day. The level of concern is for MOEs < 100 (occupational).

The MOE for workers entering treated sites is 430 and does not exceed HED's level of concern for occupational exposures (MOEs <100).

d. REI

The REI on the parent label is 12 hours, however, imazapyr is Toxicity Category I for primary eye irritation. However, imazapyr is Category III for acute dermal toxicity and Category IV for primary skin irritation; imazapyr is not a dermal sensitizer. Under the WPS (40 CFR Part 170), a 48-hour interim REI is required for an active ingredient that has an acute toxicity of Category I. It should be noted that HED's post-application assessment does not include a post-application eye exposure assessment.

Note to RD: HED recommends that RD re-evaluate the REI of 12 hours on the parent label vs. an interim REI of 48 hours based on WPS requirements.

RESIDENTIAL EXPOSURE AND RISK ASSESSMENT/CHARACTERIZATION

This section discusses the residential exposure scenarios associated with the registered uses of imazapyr. The representative registered product is Ortho GroundClear Triox Complete Vegetation Killer (EPA Reg. No. 239-2657). Label instructions state that the product is intended for use on driveways, parking areas, brick walls, gravel pathways, patios, along sidewalks and bare ground. Mixing instructions are provided for up to 600 ft^2 (use 1 gal. product/300 ft^2 = 0.0056 lb ae/300 ft^2, so for 2 gal. product would be used for up to 600 ft^2). Application is via sprinkling can. The product is not intended for use on lawns per the registered label. Residential handlers are instructed to wear safety glasses. The anticipated exposure scenarios are:

- Residential handler: Short-term dermal and inhalation exposures from mixing/loading and application via sprinkling can (per label instructions). Note that the registered label states that the product offers long-term weed control and prevents re-growth for up to one year with a single application, so only short-term handler exposures are anticipated.
- Post-application: Adults and children are anticipated to have short-term dermal exposures; however, given that the product is not intended for lawn use, dermal exposures by adults

and children are considered to be negligible as compared to recreational post-application exposures (from treated turf) given that the application rate is higher for the golf course/fairground use pattern. However, toddlers could potentially ingest soil from treated bare ground (short-term soil ingestion from hand-to-mouth behavior) in the residential use scenario, so this exposure scenario *is* assessed below.

The following HED polices were used to estimate residential exposure for this assessment:

- Residential handler: Summary of HED's Reviews of Outdoor Residential Exposure Task Force (ORETF) Chemical Handler Exposure Studies; MRID 449722-0. ORETF Study Number OMA004 (hose-end sprayer, [as surrogate for sprinkling can]), April 30, 2001.
- Post-application exposures: *Standard Operating Procedures (SOPs) For Residential Exposure Assessment*s, Draft, 17-DEC-1997 and ExpoSAC Policy No. 11, 22-FEB-2001: *Recommended Revisions to the SOPs for Residential Exposure*.

a. Residential Handler Exposure Assumptions and Risk Estimates

Table 4 presents the exposure and risk assessment for homeowners performing spot treatments around the home.

Table 4. Residential Handler Exposure and Risk Assessment for Homeowner Use of Imazapyr

Exposure Scenario	Unit Exposure[1] (mg/lb ae handled)	AR[2]	Area treated per day[3]	Potential Dose Rate[4] (mg/kg bw/d)	Combined Short-term MOE[5]
MLAP, spot treatment, hose-end sprayer (as surrogate for sprinkling can, "mix your own"	dermal, short pants, short sleeves: 11 (HC)	0.0056 lb.ae/ 300 ft^2	1,000 ft^2	dermal: 0.00293	85,000
	inhalation: 0.016 (HC)			inhalation: 4.27×10^{-6}	

Notes:
1. Source: Summary of HED's Reviews of Outdoor Residential Exposure Task Force (ORETF) Chemical Handler Exposure Studies; MRID 449722-0. ORETF Study Number OMA004 (hose-end sprayer), April 30, 2001. HC = high confidence data.
2. AR = Maximum application rate; Source: Ortho GroundClear label (EPA Reg. No. 239-2657).
3. Daily acres treated Exposure SAC Policy No. 11, Feb. 22, 2001: Recommended Revisions to the SOPs for Residential Exposure.
4. Potential Dose Rate (PDR) = Unit exposure(mg/lb ai) x AR x Area treated/Day x 1/BW (70 kg) x %Absorption (100% dermal absorption and 100% inhalation absorption rate to convert to an equivalent oral equivalents per HIARC). Combined PDR = PDR_{dermal} + $PDR_{inhalation}$.
5. MOE = NOAEL/PDR; short-term dermal and inhalation NOAELs based on Oral NOAEL = 250 mg/kg/day. HED's level of concern is for MOEs < 100 (residential).

The MOE for residential handler use of imazapyr for spot treatments around the home is greater than 100 and does not exceed HED's level of concern.

b. Post-Application Toddler Exposure Assumptions and Risk Estimate

As discussed above, only the treated soil ingestion scenario is the anticipated residential, non-dietary exposure pathway for toddlers, since available residues for dermal transfer from bare ground or rough, hard surfaces, such as driveways, gravel walkways, etc. are anticipated to be lower than the available residues for the recreational use pattern. However, HED believes that toddlers would not routinely ingest soil, particularly on a daily basis, so any exposures via this pathway will most likely be short-term. The following assumptions were used to assess the soil ingestion scenario:

- DAT 0 residues are assumed to be available for short-term exposure.
- Toddler body weight: 15 kg.
- 100% of application rate is available in the top 1 cm of soil for soil ingestion exposures.
- A toddler can possibly ingest 100 mg soil/d.

Table 5 presents the assumptions for incidental soil ingestion by toddlers.

Table 5. Exposure and Risk Assessment for Incidental Soil Ingestion (Non-Dietary) by Toddlers Following Application of Imazapyr to Bare Ground Around Homes[1]

Activity	AR[2]	Soil Residue Estimate[3]	PDR (mg/kg bw/d)[4]	Short-term Non-Dietary MOE[5]
Soil Ingestion	0.0056 lb ae/300 ft^2	6.11 µg/g soil	4.07×10^{-5}	$> 1 \times 10^{o}$

Notes:
1. Sources: Standard Operating Procedures for Residential Exposure Assessments, Draft, December 17, 1997 and Exposure SAC Policy No. 11, Feb. 22, 2001: Recommended Revisions to the SOPs for Residential Exposure.
2. AR = maximum application rate on Ortho GroundClear label (EPA Reg. No. 239-2657).
3. Soil residue estimates based on the following protocol from the Residential SOPs: Soil Residue = 0.0056 lb ae/gal x 1 gal/300 ft^2 x 43,560 ft^2/A x fraction of residue in soil (100%)/cm x (4.54×10^8 µg/lb ai) x (2.47×10^{-8} A/cm^2) x 0.67 cm^3/g = 6.11 µg/g soil.
4. Potential Dose Rate (PDR; normalized to body weight of toddler) = (6.11µg/g soil x 100 mg soil/d x 10^{-6} g/µg)/15 kg = 4.07×10^{-5}.
5. MOE = NOAEL/PDR, where the short-term incidental oral NOAEL = 250 mg/kg/d; HED's level of concern is for MOEs < 100 (residential).

The MOEs calculated for incidental soil ingestion exposure by a toddler is greater than 100 and does not exceed HED's level of concern.

RECREATIONAL EXPOSURE AND RISK ASSESSMENT/CHARACTERIZATION

This section discusses the recreational exposure scenarios associated with the registered and proposed uses of imazapyr. These scenarios comprise:

- Registered uses: adult and child golfers, post-application dermal exposures at golf courses and fairgrounds.
- Proposed use: adult and child swimmers, post-application exposures following application to a lake or pond, incidental ingestion and dermal exposures.

Based on the proposed use pattern, it is possible, although unlikely (since swimmers are unlikely to use a waterbody where floating weeds are present), that the public may swim in a treated waterbody immediately following an application of Arsenal®. Based on discussions with USACE and SFWMD, the majority of treatments may occur at remote sites. However, since there are no specific prohibitions on the proposed label restricting public access to treated sites, a post-application assessment is included for adults, toddlers, and children swimming in treated waters immediately after application. This is considered a conservative assessment.

a. Post-application Golfer Exposure Assumptions and Risk Estimates

Golfer exposure assumptions are based on HED's ExpoSAC draft policy for Golfer Exposure for Adults and Children (July 2000). The exposure assumptions are:

- Round of golf (18 holes) takes 4 hours and average golfer plays 18 times per year, so short-term dermal exposures are anticipated. Inhalation exposures are considered to be negligible since the vapor pressure of imazapyr was reported by the registrant to be $< 2 \times 10^{-7}$ mmHg (vs. HED ExpoSAC vapor pressure threshold of 1×10^{-5} mmHg).
- 5% of the maximum application rate are available as turf transferrable residues (TTR) available on Day 0 (assumes no dissipation).
- TC for dermal exposure: 500 cm^2/hr based on golfers wearing short pants and short-sleeved shirts.
- The exposure estimate for child golfers is 1.7 times the adult exposure estimate to account for differences in body weight and surface area.
- Maximum labeled application rate: 0.0041 lb ae/A broadcast liquid formulation applications.

There are no chemical-specific, post-application exposure data available for imazapyr use on golf courses. In order to assess the potential post-application exposures, an estimate of TTR on Day 0 was used, and this TTR estimate is anticipated to represent the highest potential short-term post-application exposures for the registered use of imazapyr on golf courses (see Table 6 below).

Table 6. Post-Application Golfer Exposure and Risk Assessment for Registered Uses of Imazapyr at Golf Courses

Exposure Scenario	AR[1] (lb ae/A)	TC (cm^2/hr)	TTR[2] (ug/cm^2)	Potential Dermal Exposure (PDE; mg/kg/day)[3]	Short-term Dermal MOE[4]
Adult golfer	0.0041	500	0.00230	6.57×10^{-5}	$>1 \times 10^6$
Child golfer				1.12×10^{-4}	$>1 \times 10^6$

Notes

1. Maximum AR from Event™ (EPA Reg. No. 241-317) containing 16.3% imazethapyr and 0.6% imazapyr; total acid equivalent = 1.46 lb ae/gal. Imazapyr content = 10 fl. oz. product/A x gal/128 oz. x 1.46 lb ae/gal x 0.6/16.9 = 0.0041 lb ae/A.
2. TTR = application rate (lb a.i./A) x 5% available as dislodgeable residue x 4.54E+8 ug/lb x 2.47E-8 A/cm^2.
3. PDE = TTR (ug/cm^2) x TC (cm^2/hr) x 4 hrs/day x 0.001 mg/ug x 1/ BW x %dermal absorption; BW= 70kg for adult golfers; dermal absorption = 100%. DE for child golfers = Adult DE x 1.7 per ExpoSAC's Draft Golfer Policy.

4. MOE = NOAEL/ ADD; short-term dermal NOAEL = 250 mg/kg bw/day. HED's level of concern for recreational dermal exposures is for MOEs < 100.

The MOEs presented for golfer post-application exposures are greater than the 100, and therefore, do not exceed HED's level of concern.

b. Adult and Toddler Post-Application Exposure Assumptions and Risk Estimates at Fairground Sites

This section presents the post-application exposures to adults and toddlers to use of imazapyr at recreational sites, namely fairgrounds (see registered label: Event™, EPA Reg. No. 241-317). For this scenario, HED assumed that a lawn care operator (LCO) performed a liquid broadcast application to turf at a fairground site at the maximum label rate of 0.0041 lb ae/A to provide an estimate of the highest potential DFR. The following paragraphs further summarize the assumptions used in the residential post-application assessment.

Dermal Exposures (Adults and Toddlers)

The following assumptions were used to assess dermal exposures to adults and toddlers after contact with treated lawns:

- Adult and toddler body weights are 70 kg and 15 kg, respectively.
- 5% of the maximum application rate represents fraction of imazapyr available as dislodgeable residue on the day of treatment.
- Dermal TC for adults is 14,500 cm^2/hr and for toddlers, 5,200 cm^2/hr.
- Exposure duration is 2 hours.

Table 7 presents the post-application dermal exposure assumptions and risk estimates for adults and toddlers in the residential setting.

Table 7. Post-Application Dermal Exposure and Risk Assessment for Fairground Sites Treated with Imazapyr[1]

Exposure Scenario	AR (lbs a.e./A)[2]	DFR on Day 0 (µg/cm^2)[3]	PDR (mg/kg bw/d)[4]	Short-term Dermal MOE[5]
Adult	0.0041	0.00230	9.53×10^{-4}	260,000
Toddler			1.60×10^{-3}	160,000

Notes:

1. Sources: Standard Operating Procedures for Residential Exposure Assessments, Draft, December 17, 1997 and Exposure SAC Policy No. 11, Feb. 22, 2001: Recommended Revisions to the SOPs for Residential Exposure.
2. AR = Maximum AR from Event™ (EPA Reg. No. 241-317) containing 16.3% imazethapyr and 0.6% imazapyr; total acid equivalent = 1.46 lb ae/gal. Imazapyr content = 10 fl. oz. product/A x gal/128 oz. x 1.46 lb ae/gal x 0.6/16.9 = 0.0041 lb ae/A.
3. DFR = 0.0041lb ai/A x 0.05 x (4.54×10^8 µg/lb ai) x (2.47×10^{-8} A/cm^2) = 0.00230 µg/cm^2.
4. PDR = (0.00230 µg/cm^2 x 0.001 mg/µg x TC (cm^2/hr) x 2 hrs/d x % dermal absorption (100%)/BW (70

kg for adults and 15 kg for toddlers). Note: TC for adults, short-term = 14,500 cm^2/hr and TC for toddlers, short-term = 5,200 cm^2/hr.
5. MOE = NOAEL/PDR, where the short-term dermal NOAEL = 250 mg/kg/day. HED's level of concern is for MOEs <100.

All MOEs calculated for post-application dermal exposures are greater than 100 and do not exceed the HED's levels of concern for the respective exposure scenarios.

Hand-to-Mouth Exposure Assessment Assumptions (Toddlers)

Short-term incidental oral exposures by toddlers are anticipated to encompass hand-to-mouth behavior, object-to-mouth behavior (turf mouthing) and ingestion of treated soil. It should be noted that HED believes that incidental "ingestion" of residues on treated turf might occur on a repeated basis as a result of "normal" hand-to-mouth behavior, and thus, a toddler may possibly ingest herbicide that has been applied to the turf, including residues on soil. Therefore, the toxicological endpoint used to evaluate incidental ingestion by toddlers are the incidental oral endpoints. It should be noted that HED anticipates that toddler will only experience short-term exposures, since the registered use is for fairgrounds, so infrequent contact is expected.

The following assumptions were used to assess exposures to toddlers after contact with treated turf:

- DAT 0 residues are assumed to be available for the short-term and intermediate-term exposure durations.
- Toddler body weight: 15 kg.
- Toddler hand surface area is 20 cm^2, and a toddler performs 20 hand-to-mouth events per hour for short-term exposures.
- 5% of application rate represents fraction of imazapyr available for transfer to hands on the day of treatment with a 50% saliva extraction factor for hand-to-mouth exposures.
- For object-to-mouth exposures, 20% of application rate available as dislodgeable residues on the day of treatment, and the "object" area is approximately 25 cm^2.
- 100% of application rate is available in the top 1 cm of soil for soil ingestion exposures. Also, it is assumed that a toddler can ingest 100 mg soil/d.
- Exposure duration: 2 hours per day.

Table 8 presents the assumptions for incidental ingestion exposures by toddlers. Additionally, HED's ExpoSAC policy directs assessors to aggregate the risk estimates for incidental oral exposures ingestion and dermal exposures by a toddler, as it may be possible for a toddler to perform all of activities in a single day. Thus, Table 8 includes the combined exposure and risk estimates for incidental oral exposures by toddlers.

Table 8. Exposure and Risk Assessment for Incidental Ingestion (Non-Dietary) by Toddlers Following Application of Imazapyr at Fairground Sites[1]

Activity	AR (lba.e./A)[2]	Residue Estimate[3]	PDR (mg/kg bw/d)[4]	Short-term, Non-Dietary MOE[5]
Hand-to-mouth	0.0041	DFR: 0.00230 µg/cm^2	6.13 x 10^{-5}	>1 x 10^6
Object-to-mouth		DFR: 0.00920 µg/cm^2	1.53 x 10^{-5}	>1 x 10^7
Soil Ingestion		Soil residue: 0.0308 µg/g soil	2.05 x 10^{-7}	>1 x 10^9
Combined incidental ingestion exposure	---	---	7.68 x 10^{-5}	>1 x 10^6

Notes:

1. Sources: Standard Operating Procedures for Residential Exposure Assessments, Draft, December 17, 1997 and Exposure SAC Policy No. 11, Feb. 22, 2001: Recommended Revisions to the SOPs for Residential Exposure.
2. AR = Maximum AR from Event™ (EPA Reg. No. 241-317) containing 16.3% imazethapyr and 0.6% imazapyr; total acid equivalent = 1.46 lb ae/gal. Imazapyr content = 10 fl. oz. product/A x gal/128 oz. x 1.46 lb ae/gal x 0.6/16.9 = 0.0041 lb ae/A.
3. Residue estimates based on the following protocol from the Residential SOPs:
   a. Hand-to-mouth DFR = 0.0041 lb ai/A x 0.05 x (4.54 x 10^8 µg/lb ai) x (2.47 x 10^{-8} A/cm^2) = 0.00230µg/cm^2.
   b. Object-to-mouth DFR = 0.0041lb ai/A x 0.20 x (4.54 x 10^8 µg/lb ai) x (2.47 x 10^{-8} A/cm^2) = 0.00920 µg/cm^2.
   c. Soil Residue = 0.0041lb ai/A x fraction of residue in soil (100%)/cm x (4.54 x 10^8 µg/lb ai) x (2.47 x 10^{-8} A/cm^2) x 0.67 cm^3/g= 0.0308 µg/g soil.
4. Potential Dose Rate (PDR; normalized to body weight of toddler):
   a. Short-term Hand-to-mouth PDR = (0.00230 µg/cm^2 x 0.50 x 20 cm^2/event x 20 events/hr x 10^{-3} mg/µg x 2 hrs/d)/15 kg = 6.13 x 10^{-5} mg/kg bw/d .
   b. Object-to-mouth PDR = (0.00920 µg/cm^2 x 25 cm^2/d x 10^{-3} mg/µg)/15 kg = 1.53 x 10^{-5} mg/kg bw/d.
   c. Soil Ingestion PDR = (0.0308µg/g soil x 100 mg soil/d x 10^{-6} g/µg)/15 kg = 2.05 x 10^{-7} mg/kg bw/d.
7. MOE = NOAEL/PDR, where the short-term incidental oral NOAEL = 250 mg/kg/d; HED's level of concern is for MOEs < 100 (residential).

The MOEs calculated for incidental ingestion exposures by a toddler are negligible and do not exceed HED's level of concern. The MOE for the combination of incidental ingestion exposures by toddlers is > 1 x 10^6 and does not exceed HED's level of concern.

Aggregate Recreational Toddler Exposure

HED's ExpoSAC policy directs assessors to aggregate the risk estimates for the hand-to-mouth ingestion, object-to-mouth ingestion, soil ingestion and dermal exposures by a toddler, since it may be possible for a toddler to perform all of these incidental ingestion activities and receive dermal exposure from a treated lawn in a single day. Since the short-term incidental oral and dermal endpoints are based on the same toxicological study and effects, these exposures can be combined

per HIARC. As such, Table 9 presents the aggregate risk of the combination of the short-term incidental ingestion and dermal exposures for toddlers at fairground sites.

Table 9. Aggregate Risk Estimate for Short-term Incidental Ingestion and Dermal Exposures by Toddlers following Application of Imazapyr at Recreational Sites

Exposure	PDR (mg/kg bw/d)	Short-term MOE
hand-to-mouth ingestion	6.13×10^{-5}	$>1 \times 10^{6}$
object-to-mouth ingestion	1.53×10^{-5}	$>1 \times 10^{7}$
soil ingestion	2.05×10^{-7}	$>1 \times 10^{9}$
dermal	1.60×10^{-3}	160,000
Combined short-term incidental oral and dermal exposures[1]	1.68×10^{-3}	150,000

Notes:

1. MOE for combined short-term incidental oral and dermal exposures = $1/(1/MOE^{hand\text{-}to\text{-}mouth} + 1/MOE^{object\ to\ mouth} + 1/MOE^{soil\ ingestion} + 1/MOE^{dermal})$.
2. HED's level of concern is for MOEs < 100 (residential).

The aggregate MOE for short-term post-application incidental ingestion and dermal exposures by toddlers is 150,000 and does not exceed the HED's levels of concern (for MOEs <100).

c. Post-application Swimmer Exposure Assumptions and Risk Estimates

As discussed earlier, a post-application 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 for this 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 waterbody; 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 Standard Operating Procedures 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 10.

Table 10. Comparison of Assumptions for Post-Application Swimmer Exposure Assessments for Imazapyr		
Assumption	**Residential SOP for Swimmers in Pools**	**Arsenal® Application: Post-Application at Aquatic Sites**
Post-application concentration	100% available concentration post-application	Maximum imazapyr concentration in top one-foot of water column is approx. 550 ppb. Assuming 100% available is considered conservative.
Subsequent post-application	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.

Based on the above qualifiers, the assumptions used in the swimmer assessment are summarized below:

Incidental Ingestion by Swimmers

- The worst-case estimate of imazapyr in the top one-foot of the water column in a treated waterbody is 550 ppb. Assume that 100% of this concentration is available for ingestion.
- Ingestion rate: 0.05 L/hr.
- Exposure duration: 2 hrs/day for non-competitive adult and child swimmers.
- Body weight: 70 kg for adults, 29 kg for children (mean figure from SWIMODEL) and 15 kg for toddlers.

Dermal Exposure by Swimmers

- Same assumption on water concentration as above: 550 ppb.
- Body surface area: 20,670 cm^2 for adults and 14,580 cm^2 for toddler/child swimmers (mean figures from SWIMODEL).
- Exposure duration: 2 hrs/day for non-competitive adult and toddler/child swimmers.
- Permeability coefficient (K_p): 5.85 x 10^{-5} cm/hr (where K_{ow} = 1.3 {MRID 45119707}, molecular weight of imazapyr acid = 261.3).
- Body weight: 70 kg for adults, 29 kg for child swimmers (mean from SWIMODEL), 15 kg for toddlers.

Table 11 presents the assumptions and risk estimates for post-application exposures by swimmers.

Table 11. Post-Application Swimmer Exposure and Risk Assessments for Proposed Use of Imazapyr at Aquatic Sites

Exposure Scenario	AR (lb a.e./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}	$> 1 \times 10^{6}$

Notes

1. PDR, incidental oral exposure = concentration, C_w (mg/L) x ingestion rate, IgR (L/hr) x exposure time, ET (hrs/d) 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 1/1000 cm^3 x %Dermal Absorption (correct to oral equivalent) x 1/BW, where K_p is estimated as follows: $\log K_p = -2.72 + 0.71 \log K_{ow} - 0.0061 MW$; 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 = 100 short-term dermal NOAEL =250 mg/kg bw/d. The level of concern for short-term recreational exposures is for MOEs < 100.

The MOEs presented in Table 10 representing post-application exposure to imazapyr in aquatic weed control applications are greater than 100, and therefore, do not exceed HED's level of concern for short-term recreational exposures.

Incidents

A review of all incident data available in REFS (13-MAR-2003) revealed approximately 3 records (for a total of 8 incidents) involving humans. Seven of the incidents (from Record Nos. I011766 and I013322) were related to imazapyr, but it was not clear if the symptoms were directly related to imazapyr exposure. The eighth incident (from Record No. I011801) related to alleged spray drift exposure; however, the product referenced was a multiple, active-ingredient product, so it is not apparent if the symptoms were related to imazapyr exposure *per se*. It should be noted that a search of the incident data under the "definite, probable, or possible" certainty categories in REFS did not reveal any incident records for imazapyr.

cc: Chemical file, T. Swackhammer (RAB1), D. Vogel (RAB1)
RDI: ORE Team (03/20/03), ExpoSAC (03/27/03)

Attachment A

Acute Toxicity of Imazapyr

Guideline No.	Study Type	MRID #(s)	Results	Toxicity Category
81-1	Acute Oral	415510-02	LD_{50} = > 5000 mg/kg	IV
81-2	Acute Dermal	415510-03	LD_{50} = >2000 mg/kg	III
81-3	Acute Inhalation	252004	LC_{50} = >1.3 mg/L (gravimetric) > 5.1 mg/L (nominal)	III
81-4	Primary Eye Irritation	415510-01	Corneal Opacity; Conjuctivae: redness, Chemosis & Discharge; Vascularization of Cornea; Corrosive: Irreversible Eye Damage	I
81-5	Primary Skin Irritation	415510-05	non-irritating to slight erythema and edema	IV
81-6	Dermal Sensitization	252004	Negative	-

Summary of Toxicology Endpoint Selection

The doses and toxicological endpoints selected for imazapyr for various exposure scenarios are summarized below.

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13-50 years of age and General population including infants and children)	none	none	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); HIARC assumed this dose as an endpoint for RA for Imazapyr, based on skeletal muscle effects seen in dogs with structural analog, Imazapic.

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Short and Intermediate Term Incidental Oral (1-30 days and 1-6 months)	NOAEL= **250** mg/kg/day	**Occupational** LOC for MOE = **N/A** (**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); 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); 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); HIARC assumed this dose as an endpoint for RA for Imazapyr, based on skeletal muscle effects seen in dogs with structural analog Imazapic.
Cancer (oral, dermal, inhalation)	CPRC classified Imazapyr as Group E on April 26, 1995	N/A	**2-Year Chronic** [feeding] **Toxicity/Carcinogenicity Study in Rats**: HIARC recommended that Imazapyr be brought back to CARC (with all structural analogs). Issue: adequacy of dosing in the rat study (in which there was an increase in brain tumors.)

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, NA = Not Applicable, RA = Risk Assessment, CPRC = Carcinogenicity Peer Review Committee. CARC =Cancer Assessment Review Committee.