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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

June 21, 2001

MEMORANDUM

SUBJECT: *IMAZAPIC* - Report of the FQPA Safety Factor Committee

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

Handwritten signature of Brenda Tarplee in black ink.

THROUGH: Ed Zager, Chairman
FQPA Safety Factor Committee
Health Effects Division (7509C)

Handwritten signature of Ed Zager in black ink.

TO: William Donovan, Risk Assessor
Registration Action Branch 1
Health Effects Division (7509C)

PC Code: 129041

The FQPA Safety Factor Committee evaluated the available hazard and exposure data for imazapic on June 11, 2001 and recommended the FQPA safety factor to be used in human health risk assessments (as required by Food Quality Protection Act of August 3, 1996). The committee concluded that the FQPA safety factor could be removed (1x) in assessing the risk posed by this chemical.

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I. HAZARD ASSESSMENT

(Correspondence: W. Donovan to B. Tarplee dated 06/01/01; Responses prepared by W. Dykstra)

A. Adequacy of the Toxicology Database

The toxicology database is adequate for an FQPA assessment. There are rat and rabbit developmental toxicity studies and a 2-generation rat reproduction toxicity study with imazapic. A developmental neurotoxicity study with imazapic was not required by the HIARC.

B. Determination of Susceptibility

There is no indication of increased susceptibility to young exposed to imazapic in the available studies. In the developmental toxicity study in rats, there were no developmental or maternal effects seen up to the limit dose. In the developmental toxicity study in rabbits, no developmental effects were observed at the maternally toxic dose level. Additionally, there were no offspring, reproductive or parental effects in the 2-generation rat reproduction study up to the limit dose.

II. EXPOSURE ASSESSMENTS

A. Dietary Food Exposure Considerations

(Correspondence: W. Donovan to B. Tarplee dated 06/01/01)

Imazapic was approved for early postemergence use on peanuts to control broadleaf and grass weeds. The tolerance expression for peanut nutmeat includes parent imazapic and the hydroxymethyl metabolite (both free and conjugated). Imazapic is now proposed for use on pasture and rangeland grasses. There are currently no Codex MRLs for imazapic.

The HED Metabolism Assessment Review Committee (MARC) concluded that the residues of concern for grass consists of parent imazapic, metabolite CL 263284, and metabolite CL 189215; and the residues of concern in livestock commodities include parent imazapic and metabolite CL 263284 (*Memorandum: Results of the Health Effects Division (HED) Metabolism Assessment Review Committee Meeting Held on 22-MAY-2001. Chemical#s 128943 & 129041. Barcode D275136. Case 291904. Submission S581930. Dated June 7, 2001*).

Since this is a new chemical, there are no monitoring data or percent crop treated (%CT) information available for imazapic. The current residue database consists exclusively of crop field trial data.

The HED Dietary Exposure Evaluation Model (DEEM™) will be used to assess the risk from chronic dietary exposure to residues in food resulting from the use of imazapic (no acute endpoint was identified). This analysis is expected to use Tier 1 assumptions (tolerance level residues, 100% crop treated, default concentration factors) for all commodities.

The Committee recognizes that further refinement to the dietary food exposure analyses may be required as the risk assessment is developed. Therefore, provided the final dietary food exposure assessment does not underestimate the potential risk for infants and children, the safety factor recommendations of this Committee stand.

B. Dietary Drinking Water Exposure Considerations

(Correspondence: to B. Tarplee dated 06/01/01)

The environmental fate database is adequate to characterize drinking water exposure for the parent compound. These data indicate that parent imazapic is extremely persistent, highly mobile, stable to hydrolysis, and highly soluble. The major route of dissipation appears to be transport with water and therefore contamination of ground water and surface water appears possible. Once in ground water or surface water where light can not penetrate, imazapic will be very persistent. This assessment is consistent with other imidazolinone chemicals. EFED has requested that the registrant conduct a number of ground water monitoring studies.

At least five degradates were identified in the aqueous photolysis study and the maximum percent of applied radioactivity in the aqueous photolysis study reported. However, the HED MARC concluded that for risk assessment purposes, the residue of concern in drinking water is imazapic *per se*. Any photolysis products are expected to be no more toxic than the parent compound and are expected to occur in low levels; thus inclusion of parent only in the drinking water risk assessment should adequately account for risks posed by this chemical (*Memorandum: Results of the Health Effects Division (HED) Metabolism Assessment Review Committee Meeting Held on 22-MAY-2001. Chemical#s 128943 & 129041. Barcode D275136. Case 291904. Submission S581930. Dated June 7, 2001.*).

No monitoring data are currently available for imazapic. Surface Water drinking water concentrations were estimated with EFED's FIRST screening model which includes the index reservoir (IR) and percent crop area (PCA) concepts. The SCI-GROW model was used to estimate the concentration of imazapic in drinking water from shallow ground water sources.

The Committee recognizes that further refinement to the dietary drinking water exposure analyses may be required as the risk assessment is developed. Therefore, *provided the final dietary drinking water exposure assessment includes all environmental*

degradates of toxicological concern and does not underestimate the potential risk for infants and children, the safety factor recommendations of this Committee stand.

C. Residential Exposure Considerations

(Correspondence: M. Dow to B. Tarplee dated 05/29/01)

There are no current or proposed residential uses of Imazapic.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

A. Recommendation of the Factor

The Committee recommended that the FQPA safety factor be removed (1x).

B. Rationale for Removing the FQPA Safety Factor

The Committee concluded that the safety factor could be removed for imazapic because:

1. There is no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure;
2. A developmental neurotoxicity study (DNT) with imazapic is not required; and
3. The dietary (food and drinking water) and non-dietary (residential) exposure assessments will not underestimate the potential exposures for infants and children.

FQPA SAFETY FACTOR COMMITTEE MEETING

June 11, 2001

~~Imazapic~~

Name	Division/Branch
Jess Rowland	SIMB / HED
WJBM	HED
Debbie McCull	RD
Connie Welch	AD
Will DONOVAN	RABI / HED
Mark Dow	RABI / HED
Jeff Herndon	RABI / HED
Bill Dykstra	RABI / HED
Kathy Davis	BEAD
Ray West	HED
Susan Markovitz	HED / TOK
Edward Gayer	HED
Bill [Signature]	HED / SIMB