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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

July 12, 2002

CERTIFIED MAIL

Dear Registrant:

This is the Environmental Protection Agency's (hereafter referred to as EPA or the Agency) "Report of FQPA Tolerance Reassessment Progress and Interim Risk Management Decision" (TRED) for Imazalil that was completed on July 12, 2002. A Notice of Availability, soliciting public comment for a 30 day period, will be published in the *Federal Register* (FR) shortly.

The Federal Food Drug and Cosmetic Act (FFDCA), as amended, requires EPA to reassess all the tolerances for registered chemicals in effect on or before the date of the enactment of the Food Quality Protection Act (FQPA) in August of 1996 against the new safety standard adopted in the FQPA. In reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. The tolerances are considered reassessed once the safety finding has been made or a modification or revocation occurs.

The Agency has evaluated the dietary risk associated with imazalil and has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to imazalil when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, the tolerances established for residues of imazalil in/on raw agricultural commodities are now considered reassessed as safe under section 408(q) of the FFDCA.

FQPA requires that EPA consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect, as would a higher level of exposure to any of the other substances individually.

EPA did not perform a cumulative risk assessment as part of this tolerance reassessment review of imazalil, because the Agency has not determined if there are any other chemical substances that have a mechanism of toxicity common with that of imazalil. If EPA identifies other substances that share a common mechanism of toxicity with imazalil, then a cumulative risk assessment will be conducted that includes imazalil once the final framework EPA will use for conducting cumulative risk assessments is available. Further, EPA is in the process of developing criteria for characterizing and testing endocrine disrupting chemicals and plans to implement an Endocrine Disruptor Screening Program. Imazalil will be reevaluated at that time and additional studies may be required.

The Agency's human health findings for the pesticide imazalil, were discussed in a closure conference call held on July 11, 2002, and are summarized in the attached chemical overview of the risk assessments. These risk assessments and other documents pertaining to the imazalil tolerance reassessment decision are listed at the end of this document and are available on the Internet at http://www.epa.gov/pesticides/reregistration/status.htm and in the public docket for viewing.

This document addresses 34 tolerances, 32 of which were in existence in August 1996 and are considered reassesssed. Tolerances for residues in/on *plant commodities* are established under 40 CFR §180.413(a). They are currently expressed in terms of the combined residues of imazalil [1-(2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl)-1*H*-imidazole] and its metabolite R014821 [1-(2,4-dichlorophenyl)-2-(1*H*-imidazole-1-yl)-1-ethanol]. The Agency has determined that the current tolerance expression for plant commodities is appropriate.

Tolerances for residues in *animal commodities* are established under 40 CFR §180.413(b). They are currently expressed in terms of the combined residues of imazalil and its metabolites R014821 and R042243 [3-[1-(2,4-dichlorophenyl)-2-(1*H*-imidazole-1-yl)ethoxyl]-1,2-propanediol]. The tolerance expression for animal commodities listed under 40 CFR §180.413(b) should be amended to regulate imazalil and any metabolite containing the 2,4-dichlorophenyl moiety. Because of issues related to residue analytical methods, EPA hereby defines a list of marker metabolites representing the 2,4-dichlorophenyl group moiety. The total toxic residues will then be adjusted using the ratios of imazalil and the marker metabolites that were found in the animal metabolism studies. The marker compounds in milk and ruminant tissues are imazalil, FK772, and FK284; these marker compounds collectively represent the following percentages of the total toxic residues, as determined by the ruminant metabolism studies: 21% in milk, 72% in muscle, 71% in kidney, 44% in liver, and 33% in fat. The marker compounds in eggs and poultry tissues are imazalil, FK858, and FK326 or FK259; these marker compounds collectively represents the following percentages of the total toxic residues, as determined by the poultry metabolism studies: 69% in eggs, 45% in liver, 52% in fat, and 100% in muscle.

The Table below summarizes EPA's tolerance reassessment decision for imazalil, which accounts for 32 tolerance reassessments.

TOLERANCE REASSESSMENT SUMMARY FOR IMAZALIL

Commodity	Current Tolerance, ppm	Reassessed Tolerance, ppm	Comment *[Correct Commodity Definition]*
Tolerances Established Under 40 CFR §180.413(a)			
Bananas (Whole)	3.00	3.0	The tolerance for banana pulp should be revoked because it is the Agency policy to establish a tolerance on the whole commodity (including peel after removing and discarding crown tissue and stalk). The available data on banana pulp may be used for the purpose of dietary risk assessment. / *Banana*
Bananas (Pulp)	0.20	Revoke	
Barley, forage	0.5	Revoke	This RAC has been deleted from Table 1 of OPPTS GLN 860.1000.
Barley, grain	0.05	0.1	A higher tolerance is needed to reflect the sensitivity of the data-collection method and to account for apparent residues in/on control grain samples.
Barley, straw	0.5	0.5	
Citrus fruit (POST-H)	10.0	10.0	*Fruit, citrus, postharvest*
Citrus oil	25.0	200	*Citrus, oil*
Citrus pulp (dried)	25.0	25	*Citrus, dried pulp*
Cottonseed	0.05	Revoke	The tolerance should be revoked because there are no registered uses of imazalil on cottonseed, and no registrants have committed to support imazalil use on cottonseed.
Wheat, forage	0.5	0.5	
Wheat, grain	0.05	0.1	A higher tolerance is needed to reflect the sensitivity of the data-collection method and to account for apparent residues in/on control grain samples.
Wheat, straw	0.5	0.5	
Tolerances To Be Proposed Under 40 CFR §180.413(a)			
Barley, hay	None established	0.5	The available data for barley forage and straw will be translated to barley hay.
Wheat, hay	None established	0.5	The available data for wheat forage and straw will be translated to wheat hay.
Tolerances Established Under 40 CFR §180.413(b)			
Cattle, fat	0.01	0.01	
Cattle, liver	0.50	0.20	
Cattle, meat	0.01	0.02	
Cattle, mbyp	0.01	0.20	*Cattle, meat byproducts*
Goats, fat	0.01	0.01	*Goat, fat*
Goats, liver	0.50	0.2	*Goat, liver*
Goats, meat	0.01	0.02	*Goat, meat*
Goats, mbyp	0.01	0.20	*Goat, meat byproducts*
Hogs, fat	0.01	Revoke	§180.6(a)3

Commodity	Current Tolerance, ppm	Reassessed Tolerance, ppm	Comment *[Correct Commodity Definition]*
Hogs, liver	0.50	Revoke	§180.6(a)3
Hogs, meat	0.01	Revoke	§180.6(a)3
Hogs, mbyp	0.01	Revoke	§180.6(a)3
Horses, fat	0.01	Revoke	§180.6(a)3
Horses, liver	0.50	0.20	*Horse, liver*
Horses, meat	0.01	0.02	*Horse, meat*
Horses, mbyp	0.01	0.20	*Horse, meat byproducts*
Milk	0.01	0.02	
Sheep, fat	0.01	0.01	
Sheep, liver	0.50	0.20	
Sheep, meat	0.01	0.02	
Sheep, mbyp	0.01	0.20	*Sheep, meat byproducts*

The Codex Alimentarius Commission has established several maximum residue limits (MRLs) for imazalil in/on various raw agricultural commodities. The Codex MRLs are expressed in terms of imazalil *per se*. The Codex MRLs and the U.S. tolerances are incompatible with respect to the tolerance expression. The U.S. tolerances for plant commodities are in expressed terms of the combined residues of imazalil and its metabolite R014821. The expression of U.S. tolerances for animal commodities will be amended to include imazalil and any metabolite containing the 2,4-dichlorophenyl moiety. Both Codex and U.S. have established MRLs/tolerances for bananas, citrus fruits, and wheat grain, forage, hay, and straw. However, the residue levels are not in harmony presumably because of differences in agricultural practices.

This document also contains a generic Data Call-In (DCI) that outlines further data requirements for this chemical. Note that registrants of imazalil must respond to DCIs issued by the Agency within 90 days of receipt of this letter.

The following confirmatory data requirements have been initially identified by the Agency:

Toxicology Data for OPPTS Guidelines:

- 870.6300 Developmental Neurotoxicity in Rats
- 870.6200 Acute Neurotoxicity Study in Rats
- 870.6200 Subchronic Neurotoxicity Study in rats

Product and Residue Chemistry Data for OPPTS Guidelines:

- 860.1340 Residue analytical Method - Animal Commodities
- 860.1360 Multiresidue Method
- 860.1480 Egg and poultry fumigation Study

Occupational Exposure Data for OPPTS Guidelines

- Exposure study of citrus treatment applicators (wax application and foamers)
- Post application inhalation and dermal exposure following smoke generator or spraying applications in chicken hatcheries

If you have questions on this document, please contact the Chemical Review Manager, Dayton Eckerson at *(703) 308-8038*.

Sincerely,

Lois A. Rossi, Director
Special Review and
Reregistration Division

Attachments: List of Supporting Documents
Overview of Imazalil Risk Assessment
Generic Data Call-In (DCI)