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Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Cyhexatin

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

This is the Environmental Protection Agency's (hereafter referred to as EPA or the Agency) "Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision for Cyhexatin," which was approved on June 13, 2005. This document is also known as a Tolerance Reassessment Decision, or TRED. A Notice of Availability of this tolerance reassessment decision and an announcement of a 30-day public comment period will be published in the *Federal Register*.

Introduction

The Federal Food, Drug and Cosmetic Act (FFDCA), as amended by FQPA, requires EPA to reassess all the tolerances for registered chemicals in effect on or before the enactment of the FQPA on August 3, 1996. 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. Once a safety finding has been made, the tolerances are considered reassessed. Existing tolerances associated with cyhexatin must be reassessed in accordance with FFDCA, as amended by FQPA.

EPA has completed its review of the public comments on the risk assessment and is issuing its risk management decision for cyhexatin. The last U.S. product registration was canceled in 1989, so human exposure to this pesticide is strictly through the consumption of treated imported foods. Residential and occupational exposures as well as dietary exposure through drinking water are not expected because there is no domestic use of cyhexatin. Therefore, aggregate acute and chronic risk are attributable only to the food sources from dietary exposure to imported food treated with cyhexatin.

There are currently 41 tolerances for cyhexatin. However, the manufacturers had indicated that they were supporting only the tolerances for apple (fresh, juice, sauce, and dried) and citrus (orange juice). The estimated acute dietary risks from use of cyhexatin on these commodities exceed the Agency's level of concern. Because of this acute dietary concern, the manufacturers have withdrawn support for all tolerances with the one exception of the orange juice tolerance.

Safety Finding

EPA has evaluated the dietary risks from the importation of oranges to be processed into orange juice and has determined that there is reasonable certainty that no harm to any population subgroup will result from exposure to cyhexatin treated oranges. The acute dietary exposure estimate for orange juice is below the Agency's level of concern. The most highly exposed sub-population was children 1 - 2 years of age, at 35% of the aPAD. Since the manufacturers have now indicated support for only orange juice, all existing cyhexatin tolerances will be revoked and a tolerance will be established for orange, juice. This tolerance will be time-limited pending submission and review of the necessary generic data .

Regulatory History

Cyhexatin (Case number 0237, active ingredient number 101601) is an organotin compound used as an insecticide/acaricide to control mites on a variety of crops. There are 41 tolerances established, under 40 CFR 180.144, for combined residues of cyhexatin and its organotin metabolites for use on almonds, apples, citrus, hops, macadamia nuts, stone fruits, pears, strawberries, walnuts, and animal commodities.

Cyhexatin was first registered in the U.S. in 1972 by the Dow Chemical Company for the control of plant-feeding mites infesting fruit crops and ornamentals. The Cyhexatin Registration Standard was issued in 1985. The last U.S. product registration was canceled in 1989. The current registrants for cyhexatin outside the U.S. are Cerexagri Inc., and Oxon-Italia SpA.

In the Federal Register of January 21, 1998 (63 FR 3057) (FRL-5743- 8), EPA issued a proposed rule for cyhexatin announcing the proposed revocation of all of the cyhexatin tolerances for canceled active ingredients and inviting public comment for consideration and for support of tolerance retention under FFDCA standards.

In response to the January 21, 1998 FR Notice four comments were received by the Agency to support the tolerances and request the Agency not to proceed with revocation.

A comment was received by the Agency from Elf Atochem requesting that the tolerances for cyhexatin not be revoked. Elf Atochem claimed it had pending applications for new registration. The Agency received these applications for new product registrations in 1996 from Elf Atochem (now Cerexagri Inc.), but they have since been withdrawn (4581-GIE, 4581-GIG, and 4581-GIU).

A comment was received by the Agency from Oxon-Italia requesting that the tolerance for cyhexatin on citrus not be revoked. Oxon-Italia stated it is developing residue data for submission to the Agency. In follow-up correspondence to the Agency, Oxon-Italia, through its agent, further committed to provide the data required to maintain the tolerances of cyhexatin on imported citrus crops. The data have been evaluated and the results are presented in this TRED document.

A comment was received by the Agency from the California Citrus Quality Council (CCQC) requesting that the tolerance for cyhexatin on citrus not be revoked. CCQC cited Elf Atochem's submission that indicated data were being developed and concerns about imports into the United States. As noted before, the data have been evaluated and the results are presented in this TRED.

A comment was received by the Agency from the U.S. Hop Industry Plant Protection Committee requesting that the tolerance for cyhexatin on hops not be revoked, claiming that a section 18 request was submitted for the 1998 growing season in Washington, Oregon, and Idaho. The last Section 18 for use of cyhexatin on hops was issued in 1999 for the states of Washington and Idaho. In the year 2000 a request for use of cyhexatin on hops was denied due to worker risks. No further requests for the use of cyhexatin on hops have been submitted.

In summary, because of Cerexagri's and Oxon-Italia's interests in developing the data necessary to maintain the existing tolerances EPA did not revoke the cyhexatin tolerances. This decision was published in the Federal Register on October 26, 1998 (63 FR 57062) (FRL-6035-8).

In 1999 a tolerance petition (9E6053) was received from Cerexagri, Inc., to support tolerances with no U.S. registrations (import tolerances) on apples and grapes.

In the fall of 2004, at the cyhexatin SMART meeting, the manufacturers Cerexagri Inc., and Oxon-Italia, indicated their intention to support only the apple and citrus tolerances for import purposes. The estimated acute dietary risks from use of cyhexatin on oranges to be processed into juice, and on apples (fresh, juice, sauce, and dried), at the registered rates in Argentina, Brazil, and Chile exceed the Agency's level of concern. However, the estimated dietary risks from use of cyhexatin only on oranges to be processed into orange juice does not exceed the Agency's level of concern.

The cyhexatin preliminary dietary risk assessment with the supporting documents was released to the public on November 10, 2004 (69 FR 65178) (FRL-7684-6) with a 60 day commenting period. In addition to the comments submitted by the manufacturers, there were 29 comments submitted by Brazilian government officials, academia, growers and businessmen in support of the continued use of cyhexatin on citrus in Brazil. There were no comments submitted, other than by the manufacturers, for the support of the use of cyhexatin on apples.

In light of this information both Cerexagri Inc., and Oxon-Italia have withdrawn support for all tolerances with the one exception of the citrus tolerance. Since the manufacturers have now indicated support for only orange juice, all existing cyhexatin tolerances will be revoked and a tolerance will be established for orange, juice. This tolerance will be time-limited pending submission and review of necessary generic data requirements listed in this document.

Cumulative Risk Assessment

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 Agency considers other substances because 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 does not have, at this time, available data to determine whether cyhexatin has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to cyhexatin and any other substances and cyhexatin does not appear to produce a toxic metabolite produced by other substances which have tolerances in the U. S. For the purposes of this tolerance reassessment action, therefore, EPA has not assumed that cyhexatin has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's OPP concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at: http://www.epa.gov/fedrgstr/EPA-PEST/2002/January/Day-16/.

Health Effects

Cyhexatin has moderate acute toxicity by the oral route (Category II), and is highly irritating to the skin and eyes. Dermal toxicity studies demonstrated dermal histopathology at the lowest doses administered (0.1 mg/kg/day).

Available data in rats indicate that the liver is the major target organ (effects include changes in organ weight and histopathological findings, especially in the bile duct, at 1 mg/kg/day in the chronic rat study - the lowest dose tested). Body weight loss was also seen consistently in the rat studies, and nervous system pathology was seen in a chronic study. The main target organs in dogs appear to be heart, kidney and liver.

In accordance with EPA's Guidelines for Carcinogen Risk Assessment, cyhexatin is classified as "data are inadequate for an assessment of human carcinogenic potential," based on consideration of both mouse and rat cancer studies. Liver tumors in female rats provide, at most, suggestive evidence of carcinogenicity. Tumors were adenomas only, were seen in only one sex and at one dose level, which may be excessive. No pre-neoplastic lesions were noted in the rat study.

In the mouse carcinogenicity study, no treatment-related tumors were seen in males or females, however, dosing may not have been high enough in both sexes to assess the carcinogenic potential of cyhexatin. A sub-chronic toxicity study in mice is necessary and will address uncertainty related to the

adequacy of the dosing in the mouse cancer study. There is no concern for mutagenicity associated with cyhexatin. For a complete discussion of the cyhexatin cancer assessment see, "CYHEXATIN: Report of the Cancer Assessment Review Committee," dated April 7, 2005.

The cyhexatin data base for prenatal developmental toxicity consist of one rat and eight rabbit studies. The reproductive toxicity data base consists of a two multi-generation reproduction studies and a 1-generation reproduction study. The NOAELs (No observed adverse effect level) and LOAELs (lowest observed adverse effect level) used in the cyhexatin risk assessment were determined based on a weight-of-evidence evaluation of all available developmental and reproduction studies.

Cyhexatin is a developmental toxicant producing effects in some cases at doses lower than maternally toxic doses. The specific effect was hydrocephaly with a developmental toxicity NOAEL of 0.5 mg/kg/day (based on a synthesis of results of 4 of the developmental toxicity studies in rabbits) and a LOAEL of 0.75 mg/kg/day, the lowest dose of the 3 rabbit studies in which hydrocephaly was noted. Studies were conducted by both oral and dermal routes of administration. Maternal toxicity was seen at the same or higher doses. Maternal toxicity was noted as mortality, abortions, increased post-implantation loss, and decreased body weight gain.

In the rat developmental study no developmental toxicity was noted at the dose levels tested. Maternal toxicity was noted as decreased body weight and food consumption and increased liver weight.

In reproduction studies in rats, pup toxicity consisting of decreased pup weight was seen at doses that also caused decreased body weight and food consumption in parental animals. Decreased litter size was noted at a higher dose level in one reproduction study. There was no evidence of increased susceptibility in any of the multi-generation reproduction studies in rats.

For a complete discussion of the results of the all the cyhexatin developmental and reproduction studies see, "Cyhexatin: Toxicology Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED)", dated April 20, 2005 or the Cyhexatin: HED Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED), dated April 21, 2005.

With respect to the Food Quality Protection Act, the special FQPA factor was reduced to 1x for acute dietary exposure scenarios because of the robust developmental and reproductive data base indicating no residual uncertainties for pre- or post-natal toxicity. The Agency has determined that dietary exposure estimates are conservative and unlikely to underestimate the potential risk for infants and children.

However, for cyhexatin there are data gaps for a developmental neurotoxicity study and a rat oral subchronic study. An assessment of the appropriate data base uncertainty factor (DB_{UF}) for the DNT requirement, for the aRfD, both for females 13-49 and for the general population was conducted.

The dose analysis for determining the DB_{UF} for the DNT requirement was based on the 13-week neurotoxicity study in the rat and on a rat reproduction study and on the distribution of NOAELs and LOAELs and dose levels in these studies. Based on these comparisons, a 1x DB_{UF} safety factor for aRfD for females 13-49 was selected. Similarly, based on the dose analysis, the acute dietary RfD for general population required a 3x DB_{UF} safety factor.

Table 1. Studies Used in Dose Analysis Procedure

Study	Doses (mg/kg/day)	NOAEL	LOAEL
Rat - 13-week neurotoxicity study	0, 0.5, 2, 11	2.0 mg/kg/day	11 mg/kg/day
Rat - 2-Generation reproduction study	0, 0.1, 0.5, 6	0.5 mg/kg/day	6 mg/kg/day (both for offspring and adults)

The Dose Analysis procedure is based, in this instance, on the NOAELs of 0.5 mg/kg/day in the rat 2-generation study and the NOAEL of 0.5 mg/kg/day (below the higher NOAEL of 2 mg/kg/day) in the 13-week neurotoxicity study in the rat.

For endpoint selection, the aRfD for females 13-49 is based on the NOAEL of 0.5 mg/kg/day in a rabbit developmental study. This aRfD has the same value as the NOAELs (0.5 mg/kg/day) from the two above studies, so no data base uncertainty factors are needed.

For the aRfD for the general population, the selected NOAEL of 2 from the 13-week neurotoxicity needs to be divided by a 3x DB_{UF}, resulting in a value of 0.6 mg/kg/day, which is comparable to the 0.5 mg/kg/day NOAELs from the above 2 studies.

For the chronic RfD, an assessment of the appropriate DB_{UF} safety factor for the DNT requirement was also conducted. The cRfD is based on the NOAEL of 0.25 mg/kg/day from the 1-year dog study. The cRfD of 0.25 mg/kg/day based on the 1-year dog study is already less than 0.5 mg/kg/day in the rat 13-week neurotoxicity study and the rat reproduction study and, therefore, no DB_{UF} is needed.

A summary of the toxicological dose and endpoints for cyhexatin that were used in the dietary risk assessment is shown below in Table 2.

Table 2. Toxicological Dose and Endpoints used in the Dietary Risk Assessment

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF[a] and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13-49 years of age)	NOAEL = 0.5 mg/kg/day UF = 100 Acute RfD = 0.005 mg/kg/day	FQPA SF = 1 aPAD = acute RfD / FQPA SF = 0.005 mg/kg/day	Rabbit Developmental Studies LOAEL = 0.75 mg/kg/day based on hydrocephalus. (based on synthesis of results from 4 rabbit developmental studies)
Acute Dietary[b] (general population)	NOAEL = 1.99 mg/kg/day UF = 300 Acute RfD = 0.0067 mg/kg/day	FQPA SF = 1 aPAD = acute RfD / FQPA SF = 0.0067 mg/kg/day	13-week neurotoxicity study LOAEL = 10.94 mg/kg/day based on decreased body weight and food consumption, clinical signs, and functional observational battery findings.
Chronic Dietary (All populations)	NOAEL= 0.25 mg/kg/day UF = 100 Chronic RfD = 0.0025 mg/kg/day	FQPA SF = 1 cPAD = chronic RfD / FQPA SF = 0.0025 mg/kg/day	One-Year Dog Study LOAEL = 0.5 mg/kg/day based on increased kidney weight

[a] FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose.
UF = uncertainty factor, 10x for interspecies extrapolation, 10x for intraspecies variability, and 3x for lack of a developmental neurotoxicity study and a rat oral subchronic study (for Acute Dietary, general population, and subpopulations other than females 13-49).
[b]An acute reference dose for the general population was based on the 13 week neurotoxicity study because an acute neurotoxicity study was not available.

Acute and Chronic Dietary (food only) Exposure and Risk Assessment

An acute and chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03), which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998.

Residues used in both the acute and chronic dietary exposure analyses were the highest average field trial (HAFT) residues. For apples, field trials were conducted in France and Italy and for oranges field trials were conducted in Brazil. Since these studies were conducted at lower than maximum labeled application rates, the residues were adjusted to the maximum application rate for apples by using a factor of 5x, and adjusted to account for the missing metabolite, monocyclohexylstannoic acid by using a factor of 1.3x. Processing factors from the available processing studies were also adjusted for the missing metabolite. The processing studies were included with the submission of the residue field trials on apples and oranges. All apple and orange juice samples from the processing studies had non-

detectable residues. An average of the reported processing factors was used (0.3x). A distribution of the available field trial data was` not used because of residue chemistry data deficiencies.

A relatively conservative acute dietary exposure assessment was conducted for all supported cyhexatin food uses (imported apples and orange juice). Because of residue chemistry database deficiencies, high end field trial residues were used, modified by processing factors from cyhexatin processing studies. The acute dietary exposure assessment was refined using percent imports and percent of crop treated in the exporting countries. This assessment concludes that for all supported commodities, the acute dietary exposure estimate is above the Agency's level of concern for children 1 - 2 years of age at 223 % of the aPAD at the 99.9th percentile; for all infants < 1 year of age at 187% of the aPAD, and for children 3 - 5 years of age at 151% of the aPAD. Apple juice and apple sauces were the risk drivers.

An additional acute dietary exposure analysis was performed for orange juice alone. The acute dietary exposure estimates for this analysis were below the Agency's level of concern. The most highly exposed sub-population was children 1 - 2 years of age, at 35% of the aPAD.

Similarly, a relatively conservative chronic dietary exposure assessment was conducted for all supported cyhexatin food uses (imported apples and orange juice). The same residues were used as in the acute dietary exposure assessment because of residue chemistry database deficiencies. Dietary risk estimates are provided for the general U.S. population and various population subgroups. This assessment concludes that for all supported commodities, the chronic dietary exposure estimates are below the Agency's level of concern for all population subgroups. The chronic dietary exposure estimate for the highest exposed population subgroup, children 1-2 years of age, is 6% of the cPAD.

Table 3. Summary of Dietary Exposure and Risk for Cyhexatin based on uses on apples and oranges (for orange juice).

Population Subgroup [a]	Acute Dietary (99.9th Percentile)[b]			Chronic Dietary		
	aPAD, mg/kg	Exposure, mg/kg/day	% aPAD	cPAD, mg/kg/day	Exposure, mg/kg/day	% cPAD
General U.S. Population	0.007	0.004132	59	0.0025	0.000020	1
All Infants (< 1 yr)	0.007	0.013101	187		0.000087	4
Children 1-2 yrs	**0.007**	**0.015600**	**223**		**0.000139**	**6**
Children 3-5 yrs	0.007	0.010587	151		0.000085	3
Children 6-12 yrs	0.007	0.005361	77		0.000031	1
Youth 13-19 yrs	0.007	0.002537	36		0.000014	1
Adults 20-49 yrs	0.007	0.001752	25		0.000009	<1
Females 13-49 yrs	0.005	0.002035	41		0.000010	<1

[a] The values for the population with the highest risk for each type of risk assessment are bolded.

[b] The 99.9th percentile is used because field trial residues, % imports, and % crop treated were used as the residue inputs.

Table 4 Summary of Dietary Exposure and Risk for Cyhexatin based on current tolerance for citrus only.			
Population Subgroup [a]	Acute Dietary (99.9th Percentile)[b]		
	aPAD, mg/kg	Exposure, mg/kg/day [c]	% aPAD
General U.S. Population	0.007	0.000877	13
All Infants (< 1 yr)		0.000907	13
Children 1-2 yrs		**0.002434**	**35**
Children 3-5 yrs		0.001809	26
Children 6-12 yrs		0.001199	17
Youth 13-19 yrs		0.000862	12
Adults 20-49 yrs		0.000604	9
Females 13-49 yrs	0.0005	0.000645	13

[a] The values for the population with the highest risk for each type of risk assessment are bolded.

[b] The 99.9th percentile is used because anticipated residues, % crop treated, and % imports were used as the residue inputs.

Aggregate Risk and Risk Characterization

In accordance with the FQPA, EPA must consider pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD). When aggregating exposures and risks from various sources, EPA considers both the route and duration of exposure.

An aggregate risk assessment is not required for cyhexatin. Dietary exposure from imported food is the only pathway being assessed. There are no U.S. registrations, and therefore no residential or drinking water exposure is anticipated.

Tolerance Reassessment Summary

Tolerances for the combined residues of cyhexatin and its organotin metabolites (calculated as cyhexatin) are established under 40 CFR §180.144. There are currently no registered uses of cyhexatin in the United States. Since the manufacturers have indicated support for only orange juice all existing cyhexatin tolerances will be revoked and a tolerance will be established for orange, juice. This tolerance will be time-limited pending submission and review of necessary generic data requirements listed in this TRED document. A summary of cyhexatin tolerance reassessment is presented in Table 5.

Table 5. Tolerance Reassessment Summary for Cyhexatin.			
Commodity	Current Tolerance Listed in 40 CFR §180.144 (ppm)	Reassessed Tolerance (ppm)	Comments [*Correct Commodity Definition*]
Almond	0.5	Revoke	No registered or proposed uses
Almond, hulls	60	Revoke	No registered or proposed uses
Apple	2	Revoke	No registered or proposed uses
Cattle, fat	0.2	Revoke	Tolerances are not needed for use of cyhexatin on citrus in Brazil
Cattle, kidney	0.5	Revoke	
Cattle, liver	0.5	Revoke	
Cattle, meat byproducts, except kidney and liver	0.2	Revoke	
Cattle, meat	0.2	Revoke	
Citrus pulp, dried	8	Revoke	Commodity not expected to be imported into the U. S.
Citrus, fruits	2	Revoke	Commodity not expected to be imported into the U. S.
Goat, fat	0.2	Revoke	Tolerances are not needed for use of cyhexatin on citrus in Brazil
Goat, kidney	0.5	Revoke	
Goat, liver	0.5	Revoke	
Goat, meat byproducts, except kidney and liver	0.2	Revoke	
Goat, meat	0.2	Revoke	
Hog, fat	0.2	Revoke	
Hog, kidney	0.5	Revoke	
Hog, liver	0.5	Revoke	
Hog, meat byproducts, except kidney and liver	0.2	Revoke	
Hog, meat	0.2	Revoke	
Hop	30	Revoke	No registered or proposed uses
Hop, dried	90		
Horse, fat	0.2	Revoke	Tolerances are not needed for use of cyhexatin on citrus in Brazil
Horse, kidney	0.5	Revoke	
Horse, liver	0.5	Revoke	
Horse, meat byproducts, except kidney and liver	0.2	Revoke	
Horse, meat	0.2	Revoke	

Table 5. Tolerance Reassessment Summary for Cyhexatin.			
Commodity	Current Tolerance Listed in 40 CFR §180.144 (ppm)	Reassessed Tolerance (ppm)	Comments [*Correct Commodity Definition*]
Milk, fat (=N in whole milk)	0.05	Revoke	
Nectarine	4	Revoke	No registered or proposed uses.
Nut, macadamia	0.5	Revoke	No registered or proposed uses.
Peach	4	Revoke	No registered or proposed uses.
Pear	2	Revoke	No registered or proposed uses.
Plum, prune, dried	4	Revoke	No registered or proposed uses
Plum, fresh prune	1	Revoke	No registered or proposed uses
Sheep, fat	0.2	Revoke	Tolerances are not needed for use of cyhexatin on citrus in Brazil
Sheep, kidney	0.5	Revoke	
Sheep, liver	0.5	Revoke	
Sheep, meat byproducts, except kidney and liver	0.2	Revoke	
Sheep, meat	0.2	Revoke	
Strawberry	3	Revoke	No registered or proposed uses.
Walnut	0.5	Revoke	No registered or proposed uses.
Cyhexatin Tolerances Proposed to be Published in 40 CFR §180.144			
Apple, wet pomace	6	do not publish	6H5463; commodity will not be imported
Citrus, oil	44	do not publish	6H5463; commodity will not be imported
Orange, juice		0.1	Orange juice is the only citrus commodity to be imported

Additional Generic Data Requirements

The toxicology data gaps for cyhexatin are:
1) Subchronic mouse - this study will be used to reevaluate the dose levels in the mouse carcinogenicity study.
2) Acute Neurotoxicity.
3) A Developmental Neurotoxicity study is not required at this time. This study will be required if the use is to be expanded beyond the orange juice tolerance.

The residue chemistry data gaps for cyhexatin are:
1) Analytical method for all residues of concern. The current analytical method detects cyhexatin, *per se*, and dicyclohexyloxostannane (DCTO). The method does not include

monocyclohexylstannoic acid (MCTA). The analytical method needs to be rewritten to include MCTA, and validation data must be provided.

2) Multiresidue method data.

3) Processing studies reflecting analysis for all residues of concern. The processing studies do not include analysis for monocyclohexylstannoic acid (MCTA). The samples must be reanalyzed for MCTA, and storage stability data must be provided.

4) Livestock feeding studies may be required if the use is to be expanded.

This document summarizes the Agency's decision on the tolerance reassessment for cyhexatin. Please contact Tom Myers of my staff with any questions regarding this decision. He may be reached by phone at (703) 308-8589 or by e-mail at myers.tom@epa.gov.

Sincerely,

Debra Edwards, Ph.D.
Director Special Review and Reregistration Division

Technical Support Documents
for the Cyhexatin TRED

1. Susan V. Hummel (USEPA/OPPTS/OPP/HED). Cyhexatin: HED Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED). PC Code: 101601. Reregistration Case No. 0237. April 21, 2005.

2. Susan V. Hummel (USEPA/OPPTS/OPP/HED). Cyhexatin: Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision Document (TRED) and a Proposal for the Establishment of Import Tolerances for Citrus Juice and Concentrate, and Apples. April 15, 2005.

3. Jessica Kidwell, (USEPA/OPPTS/OPP/HED). Cyhexatin: Report of the Cancer Assessment Review Committee, PC Code: 101601, April 7, 2005.

4. Thurston G. Morton (USEPA/OPPTS/OPP/HED). Cyhexatin Revised Acute and Chronic Dietary Exposure Assessment for the Tolerance Reassessment Eligibility Decision. May 5, 2005.

5. William Dykstra (USEPA/OPPTS/OPP/HED). Cyhexatin: Toxicology Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED). PC Code: 101601. Reregistration Case No. 0237. April 20, 2005.