

US EPA ARCHIVE DOCUMENT



United States
Environmental Protection
Agency

Prevention, Pesticides
and Toxic Substances
(7508C)

EPA 738-R-04-011
November 2004

Reregistration Eligibility Decision (RED)

Ethoxyquin

US EPA ARCHIVE DOCUMENT

**REREGISTRATION ELIGIBILITY DECISION (RED)
for
Ethoxyquin**

CASE 0003

Includes chemicals:

055501 1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline

Approved by:

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

Date:

Ethoxyquin Team

Office of Pesticide Programs:

Health Effects Division

David Hrdy
Abdallah Khasawinah
Dave Jaquith
Jerry Stokes

Biological and Economics Analysis Division

Jihad Alsadek

Registration Division

Cynthia Giles- Parker

Special Review and Reregistration Division

Tom Brennan

Executive Summary

The U.S. Environmental Protection Agency (EPA or the Agency) has completed the reregistration eligibility decision for the pesticidal uses of ethoxyquin for post-harvest/ indoor uses on pears. The decision includes a comprehensive assessment of the required data and the use patterns of currently registered products.

The Agency has conducted a risk assessment for the active ingredient ethoxyquin to support a reregistration eligibility and tolerance reassessment decision for this pesticide. The risk assessment team, using a streamlined process for lower risk pesticides, selected relevant toxicity endpoints and estimated doses for risk assessment of various exposure conditions. The acute and chronic dietary risks are both below the Agency's level of concern. Although ethoxyquin has not been determined to be a carcinogen and no cancer data are available, a bounding endpoint Q^*_1 of $0.04 \text{ (mg/kg/day)}^{-1}$ as a possible dietary endpoint for ethoxyquin was assessed as a conservative estimate considering the lack of data. The assessment produced an estimated cancer risk of less than 2×10^{-6} which does not exceed the Agency's level of concern.

No drinking water risk assessment scenarios were done because the waste water from the drench application onto the fruit is recycled and there is very low likelihood of water contamination from the registered indoor use of ethoxyquin. In addition, no products are registered that would result in residential exposure of ethoxyquin. Potential worker exposure occurs while mixing/loading the chemical during treatment, and while sorting/packing/culling after the application to pears. The Agency's assessment shows that mixers/loaders must wear gloves to obtain an acceptable margin of exposure above 100, the Agency's level of concern. The mixer/loader lifetime cancer risk is 2.1×10^{-6} and does not exceed the Agency's level of concern. The estimates of exposure for the sorting/packing/culling of pears were derived from residue chemistry data, surface area calculations, and a scientific literature study. The margin of exposure level is greater than 1800 and does not exceed the Agency's level of concern. Lifetime cancer risk for workers handling fruit is 1.8×10^{-7} , and also does not exceed the Agency's level of concern.

Based on the current uses, no aggregate exposure risk assessments were conducted. Because there are no outdoor uses and low likelihood of water exposures, risk to non-target species or endangered species is not anticipated, and no ecological risk assessment was conducted.

The Agency has found that sufficient data are available to create a safety finding for the current uses. The single current tolerance on pears for ethoxyquin is reassessed, and the products containing ethoxyquin are eligible for reregistration provided that a label change stating that mixers/loaders are required to wear gloves is added.

I. Determination of Reregistration Eligibility for Ethoxyquin

Section 4(g)(2)(A) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) calls for the Environmental Protection Agency (EPA or the Agency) to determine, after submission of relevant data concerning an active ingredient, whether products containing the active ingredient are eligible for reregistration. This is determined in the reregistration eligibility decision (RED). The EPA has reviewed all relevant data and assessed the potential risks posed by exposure to ethoxyquin. Based on this assessment, EPA has determined that ethoxyquin is eligible for reregistration and tolerance reassessment provided that the label change outlined in this document is adopted. Accordingly, should a registrant fail to implement the label change identified in this document, the Agency may take further regulatory action for ethoxyquin.

II. Chemical Overview

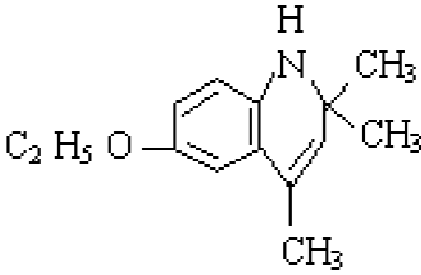
A. Regulatory History

Developed by Monsanto in the 1950's, Ethoxyquin is used primarily, under Food and Drug Administration regulation 21 CFR § 172.140, as a preservative in animal feed for stabilizing fat soluble vitamins (such as vitamins A and E) to maintain the quality of feed. Ethoxyquin has a feed-additive tolerance in certain dehydrated crops such as alfalfa, clover, grasses, and sorghum to retard the destruction of carotene and vitamin E (published by the FDA under 21 CFR § 573.400). It is also used as an antioxidant for the preservation of color in the production of chili powder, paprika, and ground chili (21 CFR § 172.140), and as a stabilizer and anti-degradation agent for rubber (21 CFR § 177.2600).

Ethoxyquin was initially registered as a pesticide in 1965 as an antioxidant used as a deterrent of scald in pears and apples through a pre-harvest spray and post-harvest dip or spray. Scald is a physiological disorder of fruit which results in the discoloration of large areas of the fruit. It is currently registered for use on pears through a post-harvest indoor application via a drench and/or impregnated wrap. Four products are registered; one emulsifiable concentrate and three impregnated materials. There are two companies, Decco, Ceraxagri, Inc. and Wrap Pack Inc., who are ethoxyquin registrants.

B. Chemical Identification

- Common Name: Ethoxyquin
- Case number: 0003
- Basic manufacturer: Ceraxagri, Inc.

Table 1. Ethoxyquin Structure and Nomenclature	
Chemical Structure	
Empirical Formula	C ₁₄ H ₁₉ NO
Molecular Weight	217.34
Common name	Ethoxyquin
IUPAC name	1,2-dihydro-2,2,4-trimethylquinolin-6-yl ethyl ether
CAS name	6-ethoxy-1,2-dihydro-2,2,4-trimethylquinoline
CAS Registry Number	91-53-2
PC Code	55501
End-use product/EP	Deccoquin, Pear Wrap I, Pear Wrap III
Chemical Class	Quinoline
Known Impurities of Concern	None

C. Use Profile and Estimated Use of Pesticide

Ethoxyquin is registered for use as an antioxidant to control scald (browning) in pears. It can be applied post-harvest by spraying/drenching, paper wrapping, or a combination thereof. Currently only two formulation types are registered for this chemical, which includes an emulsifiable concentrate (1 product) and an impregnated wrap (3 products). Additionally, applications can be made as a non-split application, split application, or wrapped as noted below:

<u>Application Method</u>	Rates (ppm)
Non-split application (Single Application)* - drenching; spray (brush bed or conveyor rolls); or - combined (w/ packout wax treatment)	2700 ppm
Split application (Double Application)* - drenching (applied within 2 days of harvest), and - line spray (stored pears washed & packed)	1000 ppm 1700 ppm
Impregnated Wrap (Wrap within 1 week post-harvest)	1000 ppm

* These two methods of application are not to be used in combination with one another. Additionally, the maximum application rate must not exceed 2700 ppm.

Production of ethoxyquin is estimated to be less than 25,000 lbs. active ingredient over the past five years (averaging less than 5,000 lbs. active ingredient per year); hence, ethoxyquin is being considered as a minor use chemical.

III. Summary of Human Health and Environmental Risk Assessments

The Health Effects Division (HED) Risk Assessment (29 July 2004, Hrdy) details the EPA's human health risk findings and conclusions for ethoxyquin. This technical support document is available on the Internet at <http://www.epa.gov/edocket> and in the Office of Pesticide Program's (OPP) public docket for viewing. The OPP docket is located in Room 119, Crystal Mall #2, 1801 South Bell Street, Arlington, VA, and is open Monday through Friday, excluding legal holidays, from 8:30 AM to 4:00 PM.

A. Human Health Risk Assessment

The ethoxyquin risk assessment was done using a streamlined process for lower risk/ exposure pesticide chemicals. The toxicology and risk assessment teams evaluated the entire toxicological database, the information on use patterns, and the exposures to ethoxyquin. Relevant toxicity endpoints and doses for the risk assessment of various exposure conditions were selected; no endpoint relevant to the general population was identified. Ethoxyquin has been the subject of numerous studies because of its wide use as an antioxidant. Although the ethoxyquin toxicology database is not complete, the toxicology database provides adequate information for evaluating and characterizing the risks under FIFRA and FQPA for the limited use of this chemical.

Ethoxyquin has low to moderate acute toxicity by the oral (Category III), dermal (Category III), and inhalation (Category III) exposure routes. It is not an eye irritant (Category IV), and it produces minimal irritation to the skin (Category IV). Tests in animals show it to have a weak sensitizing potential. Extensive human experience from the use of this chemical showed strong

association with contact dermatitis that ceased upon discontinuation of working in an ethoxyquin environment.

The primary target organs affected by ethoxyquin in experimental animals are the liver and the kidneys. Dogs are more susceptible to ethoxyquin toxicity than rats with elevated liver enzymes and microscopic findings in the liver occurring at doses as low as 4 mg/kg/day over a 90 day feeding period. Studies indicate that ethoxyquin is not a teratogen or a developmental toxicant in rats or rabbits; ethoxyquin did not cause developmental effects in rats tested at doses of 350 mg/kg/day during gestation, or in rats at doses as high as 500 mg/kg of a 67% ethoxyquin formulation, and no developmental effects were seen in rabbits where the maximum dose of 3 mg/kg/day was administered.

Ethoxyquin has not been tested for its carcinogenic potential. In a two-year study, the closely related chemical, 1,2-dihydro-2,2,4-trimethylquinoline, showed *some* evidence of carcinogenic activity in rats. The only suggestion of a potential carcinogenic effect for ethoxyquin came from a Manson *et al* (1987) study where feeding male Fisher 344 rats ethoxyquin at 0.5% formulation (5000 ppm, equivalent to 250 mg/kg/day) for 23 weeks caused severe damage to the kidneys and produced many hyperplastic and putative preneoplastic tubules. A number of authors, especially Gaylor and Krewski, have concluded that the association between maximum tolerated dose (MTD) and cancer potency is sufficiently robust and can be used to estimate boundaries on cancer potency (refer to Human Health Risk Assessment Document for further reference). The Gaylor and Krewski estimation method is applicable to ethoxyquin, as suggested by the Manson *et al* study that produced putative preneoplastic tubules in male rats.

Table 2. Summary of Toxicological Endpoints and Other Factors Used in the Risk Assessment of the Ethoxyquin			
Exposure Scenario	Dose (mg/kg/day)	*Special FQPA Safety Factor and Level of Concern for Risk Assessment	Endpoint for Risk Assessment
Dietary Risk Assessments			
Acute Dietary	NOAEL = >3 mg/kg/day UF = 100 Acute RfD = 0.03 mg/kg/day	FQPA SF = 1 aPAD = $\frac{\text{acute RfD}}{\text{FQPA SF}}$ = 0.03 mg/kg/day	Developmental study in rabbits (published) where the maximum dose tested of 3 mg/kg/day had no developmental effects
Chronic Dietary all populations	NOAEL = 2 mg/kg/day UF = 100 Chronic RfD = 0.02 mg/kg/day	FQPA SF = 1 cPAD = $\frac{\text{chronic RfD}}{\text{FQPA SF}}$ = 0.02 mg/kg/day	90-day subchronic study in dogs LOAEL = 4 mg/kg/day based on elevated liver enzymes and microscopic findings in the liver (cytoplasmic vacuolation and minimal hepatocellular necrosis).
Non-Dietary Risk Assessments			
Dermal . All durations	NOAEL = 2 mg/kg/day (Oral) 100% absorption is assumed	Residential : not required Occupational LOC for MOE = 100	90-day subchronic study in dogs LOAEL = 4 mg/kg/day based on elevated liver enzymes and microscopic findings in the liver (cytoplasmic vacuolation and minimal hepatocellular necrosis).
Cancer	There are no guideline studies assessing this effect in animals. It is structurally similar to 1,2-dihydro-2,2,4-trimethylquinoline which showed evidence of carcinogenicity (kidney tumors) in male rats. Ethoxyquin is also a nephrotoxin in male rats. A theoretical upper bound Q_1 for ethoxyquin was calculated to be 0.04 (mg/kg/day) ¹ .		

There is low concern (and no residual uncertainty) for pre- and/or postnatal toxicity resulting from exposure to ethoxyquin. The available data show no indication of increased susceptibility (quantitative or qualitative) to rats or rabbits to *in utero* exposure. A developmental neurotoxicity study is not required as there was no evidence of neurotoxicity or neuro pathology from the available studies. The special FQPA safety factor is reduced to **1X** in risk assessments for this chemical.

1. Dietary Risk From Food

Acute, chronic, and cancer dietary risk assessments were conducted using the Lifeline Model Version 2.0 and the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 2.03), which use food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The acute reference dose had a safety factor of 100 applied (10X for interspecies variation and 10X for intraspecies variation). The chronic reference dose had a safety factor of 100 applied (10x for interspecies variation and 10X for intraspecies variation). The ethoxyquin dietary assessment included food exposure from EPA registered pesticidal use in pears as well as ethoxyquin's FDA approved uses as an antioxidant in feeds (e.g., meat, poultry, eggs) and as a food preservative (e.g, spices).

The toxicity endpoints selected and risk results for relevant exposure scenarios are summarized in table 3 and 4 below. Exposure estimates are expressed in mg/kg body weight/day, and risk is expressed as a percent of the acute/chronic Population Adjusted Dose (a/cPAD). The aPAD is the dose at which a person could be exposed to on any given day and no adverse health effects would be expected. The cPAD is the dose at which an individual could be exposed over the course of a lifetime and no adverse health effects would be expected. A risk that is less than 100% of the acute or chronic PAD does not exceed EPA's risk concern.

Because of the highly conservative nature of the assessment, 95th percentile was deemed acceptable. Acute and chronic dietary exposure analyses was created using a Tier I, highly conservative assessment using tolerance level residues and 100% crop and feed treated.

Females 13- 49 years of age was the population of interest for the aPAD, as the endpoint is based on developmental effects. The overall acute dietary risk from residues in foods was 14 % of the aPAD at the 95th percentile of exposure for the females 13-49 years old sub-population.

Table 3. Ethoxyquin Acute Dietary Exposure Analysis			
Population Subgroup	aPAD (mg/kg/day)	95 th Percentile	
		Exposure (mg/kg/day)	% aPAD
Females 13-49 years old	0.03	0.004311	14

The overall chronic dietary risk from residues in foods was based on the General U.S. population, and young children, the population of interest because they are the most exposed. The average dietary exposure for the general U.S. Population was 5% of the cPAD, 15% of the cPAD for all infants (< 1 year old), and 14% of the cPAD for children 1 to 2 years of age.

Table 4. Ethoxyquin Chronic Dietary Exposure and Risk			
Population Subgroup*	cPAD (mg/kg/day)	Chronic Dietary	
		Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.02	0.001064	5
All Infants (< 1 year old)	0.02	0.003066	15
Children 1-2 years old	0.02	0.00287	14

Both the acute and chronic endpoint analyses were below the Agency's level of concern.

2. Hypothetical Cancer Dietary Exposure Results and Characterization

Cancer risks are calculated by multiplying the 70 year exposure estimate for the U.S. population by the Q^* , and are expressed as a probability of developing cancer. Ethoxyquin has been determined to not be a carcinogen and no adequate guideline studies for rats and mice have been submitted for carcinogenic potential of ethoxyquin. To ensure safety in the absence of ethoxyquin specific carcinogenicity studies, a bounding Q^* of $0.04 \text{ (mg/kg/day)}^{-1}$ was created using the Q^* bounding estimation procedure and the maximum tolerated dose (MTD) of ethoxyquin.

a. Residue Data Used for Cancer Assessment

The hypothetical cancer assessment included the FIFRA use on pears, the FDA regulated uses on spices as a food preservative and the antioxidant use in feeds from which secondary residues may result in meat, poultry, and eggs. The assessment was performed using field trial results of 1.31 ppm of ethoxyquin present on pears after 14 days, and was refined, to match the use pattern of ethoxyquin, by the fraction of fresh non- Bartlett pears. USDA Agricultural Statistics for 2003 were used to adjust for the 45% of pears that were cultivated in U.S. that are non-Bartlett pears. The assessment only included spices that were dried; ethoxyquin is not applied to fresh herbs and spices. The inclusion of all dried spices is considered conservative since ethoxyquin is registered for use on only chili and paprika.

b. Results

Using tolerances to represent ethoxyquin residues in foods including the food preservative use in spices and the antioxidant use in feeds from which secondary residues may result in meat and poultry, 100% of the non-Bartlett pear variety crop, the refined assessment produced a estimated cancer risk of less than 2×10^{-6} .

Population Subgroup	Q^* (mg/kg/day) ⁻¹	Exposure (mg/kg/day)	Estimated Lifetime Cancer Risk
US General Population (EPA and FDA regulated uses)	0.04	0.001065	1.9 E-6

Q^* is the estimated slope factor for ethoxyquin from the bounding estimation Q^* estimation method.

Because only a small percentage of livestock feeds are treated, further refinement of the assessment could be made through the use of field trial data, FDA monitoring data for pears and livestock feeds, or the percent of crop treated for the pears and livestock feeds. Factors that lead to the conclusion for refinement include:

- Upper bound estimate of potency (Q_1^*)
- Tolerance (upper bound) residues for spices, meat products, and eggs
- High- end residue value for pears
- Assumption that all pears that could be treated are treated
- Assumption that all dried spices are treated while only paprika and chili are actually treated
- Assumption of 100% crop treated for meat products and eggs

Given these high end inputs and assumptions, the EPA concludes that potential cancer risk is below the Agency's level of concern.

2. Dietary Risk from Water

No drinking water scenarios are presented because ethoxyquin is indoor use only and waste water from the drench application onto the fruit is commonly recycled. There is very low likelihood of water contamination from the registered indoor use of ethoxyquin.

3. Residential Risks

A residential exposure assessment was not performed because there are no registered products containing ethoxyquin that would result in residential exposure.

4. Aggregate Risk

Aggregate exposure risk assessments were considered under FQPA, but because residential and water exposures are not anticipated to result from any of the current uses of ethoxyquin, the results are the same as the dietary risks, and below the Agency's level of concern.

5. Occupational Handler and Post-Application Risks

Based on currently registered labels for ethoxyquin, EPA assessed potential occupational scenarios for the chemical. Application rates were obtained from representative label rates for pears or treated wrappers. Dermal absorption is assumed to be 100%. Occupational assessment was based on non-cancer and potential cancer risk for ethoxyquin handlers and post- application workers. Non-cancer risk for potentially exposed populations is measured by a Margin of Exposure (MOE), which determines how close the occupational exposures come to a No Observed Adverse Effect Level (NOAEL). Estimations of occupational cancer risk from ethoxyquin use were based on the following assumptions:

1. Workers are exposed for 35 years over a 70 year life span.
2. Workers are exposed for 30 days per year.
3. The Q^*_1 for ethoxyquin is 0.04 per mg/kg/day.

Potential occupational exposure scenarios include:

1. Mixing/loading for post-harvest treatments using drench/spray application methods.
2. Exposure during post-harvest sorting/packing/culling pears following ethoxyquin treatment.
3. Handling treated pears wrapped in impregnated paper.

a. Mixer/Loader

As a model for mixers and loaders, the throughput from a citrus operation was used. A large citrus operation processes up to 2000 boxes. These boxes weigh approximately 90 lbs. The maximum application rate, 1 gallon of 52.2% product in 1999 gallons of waxing/rinsing solution, results in an application rate of approximately 2700 ppm. The assumed rate for application of ethoxyquin is 1 gallon per 8000-10,000 lbs of fruit (using the citrus model).

The workers in the baseline assessment are assumed to be wearing long sleeved shirts and long pants. A $MOE \geq 100$ is sufficient to protect occupational pesticide handlers. The mixer/loader scenario requires gloves be worn in order to achieve a MOE above 100 with gloves. The MOE for the mixer/loader scenario is 1500 which does not exceed the Agency's LOC. The estimated lifetime cancer risk for a mixer/loader wearing gloves is 2.1×10^{-6} and does not exceed the Agency's LOC.

b. Sorting/Packing/Culling

The Agency does not have data addressing the sorting/packing/culling of products following ethoxyquin treatment. The estimates of exposure were derived from residue chemistry data, surface area calculations, and a study found in scientific literature. The estimated residues on the surfaces of treated commodities were estimated using the following assumptions:

1. A "standard" apple or pear has a diameter of 2-3/4 inches (~7 cm) and weighs 138 grams. It is assumed that pears have approximately the same characteristics as apples. A medium size pear weighs 166 grams. For the purposes of this calculation pears are assumed to be roughly spherical.
2. The treatment equipment for all post-harvest treatments with ethoxyquin is essentially the same for pears as it is for citrus.
3. The average residue level in pears treated by both spray and wrapping is 0.873 ppm ($\mu\text{g/g}$).
4. All of the ethoxyquin in a pear is located on the surface.
5. The surface area of the palmar surface of the hands is 410 cm^2 . This area is considered to be total area exposed in an 8 hour day.

6. A study from the scientific literature indicates that less than 2 percent of material from glass plates treated with a dust is transferred to the hands after repeated pressing (Refer to the Human Health Risk Assessment document for further reference). The same amount is assumed to be transferred from a pear, i.e., the hand pressed to glass plate study is translated to grasping a fruit.

Though commonly worn, gloves are not required by label for the sorting/packing/culling process. The scenario was assessed assuming no gloves. The MOE for the above scenario is greater than 1800, therefore the risks for sorting/packing/culling do not exceed the Agency's LOC. The estimated lifetime cancer risk for workers handling treated fruit is 1.8×10^{-7} ; this does not exceed the Agency's LOC.

c. Impregnated Paper Handler

Based on scenarios with true historical exposure data, exposure from impregnated paper would not exceed (i.e. negligible in comparison to drench/spray scenario) the exposure from handling treated pears after drenching/spraying (PHED Surrogate Exposure Guide, AUG-1998). An assessment of handling impregnated paper exposure is not presented in this document.

B. Environmental Risk Assessment

1. Risk to Non-Target Species

Because use patterns include only indoor uses, there is low likelihood of outdoor or water exposures, and risks to non- target species are not anticipated.

2. Endangered Species Assessment

Because the pesticidal use pattern includes only the indoor food processing of pears, EPA has concluded that outdoor environmental or water exposure is highly unlikely and any exposure to terrestrial wildlife or aquatic organisms would be negligible. Therefore, EPA has determined that the pesticidal uses of ethoxyquin discussed in the RED will have no effect on federally listed endangered and threatened species.

C. Cumulative Risk

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have at this time available data to determine whether ethoxyquin 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 to ethoxyquin and any other substances, and ethoxyquin does not appear to produce a toxic metabolite that is also produced by other substances. Therefore, for the purposes of this tolerance reassessment, the Agency has not assumed that ethoxyquin 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/>.

D. Endocrine Disrupter Effects

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA as authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). There is no indication from existing data that ethoxyquin is an endocrine disruptor. When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, ethoxyquin may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

E. Tolerance Summary

A summary of the ethoxyquin tolerance reassessment is presented in the table below. A full description of the tolerance reassessment can be found in the HED risk assessment document. In the assessment, the Agency concluded that the residue of concern remains the parent ethoxyquin (40 CFR § 180.178). The current tolerance for ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) is in pears for pre or post-harvest use. The Agency is proposing the tolerance expression be amended for post-harvest use only.

Table 6. Tolerance Reassessment Summary for Ethoxyquin			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/correct Commodity Definition
Tolerances Listed Under 40 CFR § 180.178			
Pear	3.0	3.0	Based on available residue data that indicate residues of ethoxyquin as high as 3.0 ppm in or on pears. <i>[pear, post-harvest]</i>

1. Codex Harmonization

The Codex Alimentarius Commission has established maximum residue limits (MRLs) for ethoxyquin residues in/on pears at 3.0 ppm. The Codex MRL residue definition and the U.S. tolerance definition will be compatible after amending the ethoxyquin tolerance expression.

IV. Confirmatory Generic Data Requirements

The generic database currently supports the use of ethoxyquin on pears, and no confirmatory studies are required in the reassessment of the chemical ethoxyquin for this use. Should a registrant petition for the use of ethoxyquin to be expanded, at a minimum, the following data will be required:

- A teratology study in rabbits
- A 2-generation reproduction study
- A chronic oncogenicity study in rats
- A carcinogenicity study in mice
- A 21/28 dermal toxicity study

V. Label Changes

In order to be eligible for reregistration, all product labels are to be amended to incorporate measures outlined in this RED document. Furthermore, many of the existing labels for ethoxyquin need to be revised to provide clear use directions. EPA has determined that all mixer/loaders of ethoxyquin post-harvest application use must wear chemical resistant gloves. Table 7 describes how language on the labels should be amended.

VI. Attachment: Health Effects Division (HED) Risk Assessment for the Reregistration Eligibility Decision for Ethoxyquin (7-29-04)

Table 7. Summary of Labeling Changes for Ethoxyquin	
Description	Amended Labeling Language

End Use Products Intended for Occupational Use		
<p>PPE Requirements for Pesticide Handlers Established by the RED¹ for Liquid Formulations</p>	<p>“Some materials that are chemical-resistant to this product are (<i>registrant inserts correct chemical-resistant material</i>). If you want more options, follow the instructions for category [<i>registrant inserts A,B,C,D,E,F,G,or H</i>] “on an EPA chemical-resistance category selection chart.”</p> <p>“Personal Protective Equipment (PPE)” "Mixers, loaders and applicators and other handlers* must wear: - long sleeved shirt and long pants and -socks and shoes. In addition, mixers and loaders must wear chemical resistant gloves [registrant: insert appropriate glove material].”</p> <p>*Persons sorting, packing, culling, or otherwise handling treated pears and persons handling impregnated paper wrap are considered handlers and must wear the required handler PPE.</p> <p>NOTE: Employers must provide mixers and loaders with the appropriate type of chemical-resistant gloves in clean and operating condition and replace or appropriately clean the gloves after any day of use.</p>	<p>Immediately following/below Precautionary Statements: Hazards to Humans and Domestic Animals</p>
<p>User Safety Requirements</p>	<p>“Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry.”</p>	<p>Precautionary Statements: Hazards to Humans and Domestic Animals immediately following the PPE requirements</p>

<p>User Safety Recommendations</p>	<p>“User Safety Recommendations</p> <p>Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.</p> <p>Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.</p> <p>Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.”</p>	<p>Precautionary Statements under: Hazards to Humans and Domestic Animals</p>
<p>General Application Restrictions</p>	<p>“Do not apply this product in a way that will contact workers or other persons. Only protected handlers may be in the area during application.”</p>	<p>Place in the Direction for Use</p>

¹ PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.