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Ethoxyquin

Interim Registration Review Decision
Case Number 0003

September 2020

Approved by: _____

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Table of Contents

I. INTRODUCTION

This document is the Environmental Protection Agency's (EPA or the agency) Interim Registration Review Decision (ID) for ethoxyquin (PC Code 055501, case 0003), and is being issued pursuant to 40 CFR §155.56 and 155.58. A registration review decision is the agency's determination whether a pesticide continues to meet, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The agency may issue, when it determines it to be appropriate, an interim registration review decision before completing a registration review. Among other things, the interim registration review decision may require new risk mitigation measures, impose interim risk mitigation measures, identify data or information required to complete the review, and include schedules for submitting the required data, conducting the new risk assessment and completing the registration review. Additional information on ethoxyquin, can be found in EPA's public docket (EPA-HQ-OPP-2014-0780) at www.regulations.gov.

FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States must be registered by EPA based on scientific data showing that they will not cause unreasonable risks to human health or to the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the agency periodically re-evaluates pesticides to make sure that as these changes occur, products in the marketplace can continue to be used safely. Information on this program is provided at http://www.epa.gov/pesticide-reevaluation. In 2006, the agency implemented the registration review program pursuant to FIFRA § 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

EPA is issuing an ID for ethoxyquin so that it can (1) move forward with aspects of the registration review that are complete and (2) implement interim label amendments (see Appendix A). For the current use of ethoxyquin, EPA has made a "No Effect" determination for Federally listed Threatened/Endangered Species (referred to as "listed" species) and concluded that there will be "No Habitat Modification" for all designated critical habitats for listed species under the Endangered Species Act (ESA) § 7. The agency will complete endocrine screening for ethoxyquin, pursuant to the Federal Food, Drug, and Cosmetic Act (FFDCA) § 408(p), before completing registration review.

Ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) is a quinoline-based antioxidant. Currently, products containing ethoxyquin are registered for use to prevent scalding (browning) in pears, and it is applied through post-harvest indoor application via drench-in-line spraying, thermal fogging, and/or impregnated wraps. These processes all take place within a warehouse prior to packing. Furthermore, the Food and Drug Administration (FDA) has established food additive tolerances for residues of ethoxyquin in/on paprika, chili powder, ground chili spices, and several edible products of animals under 21 CFR §172.140. The FDA has also established food additive tolerances for residues of ethoxyquin in/on animal feed, fish food, pet food, and

several dehydrated forage crops under 21 CFR §573.380 and §573.400. Several color additives to chicken feed, including dried algae meal and Aztec marigold (*Tagetes erecta L.*) meal/extract which are regulated by FDA under 21 CFR §73.275 and §73.295, respectively, also contain ethoxyquin (0.3% maximum) and must meet the food additive tolerance limitations for ethoxyquin in animal feed prescribed in 21 CFR §573.380. In addition, fish meal and fish scrap, which are regulated under 46 CFR (Shipping) and under 49 CFR (Transportation), are required to contain at least 100 ppm or 400 ppm of anti-oxidant (ethoxyquin) at the time of shipment (46 CFR §148.265 and 49 CFR §173.218) or production (46 CFR §148.265), respectively. The first pesticide product containing ethoxyquin was registered in 1965; a Reregistration Eligibility Decision (RED) for ethoxyquin was completed in 2004. Since then, EPA has reviewed the risk assessment and supporting documents for ethoxyquin to determine if updates were necessary for ethoxyquin labels.

This document is organized in five sections: the *Introduction*, which includes this summary and a summary of public comments and EPA's responses; *Use and Usage*, which describes how and why ethoxyquin is used and summarizes data on its use; *Scientific Assessments*, which summarizes EPA's risk and benefits assessments; the *Interim Registration Review Decision*, which describes the mitigation measures required to address risks of concern and the regulatory rationale for EPA's ID; and, lastly, the *Next Steps and Timeline* for completion of this registration review.

A. Updates Since the Proposed Interim Decision was Issued

In May 2020, EPA published the PID for ethoxyquin. In this ID, there are no updates to what was proposed in the PID.

B. Summary of Ethoxyquin Registration Review

Pursuant to 40 CFR §155.50, EPA formally initiated registration review for ethoxyquin with the opening of the registration review docket for the case. The following summary highlights the docket opening and other significant milestones that have occurred thus far during the registration review of ethoxyquin.

- December 2014 - The *Ethoxyquin Preliminary Work Plan* (PWP*)*, *Ethoxyquin. Human Health Assessment Scoping Document to Support Registration Review*, and *Registration Review: Preliminary Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments for Ethoxyquin* were posted to the docket for a 60-day public comment period.

- September 2015 - The *Final Work Plan* (FWP) for ethoxyquin was issued. Public comments were received during the 60-day comment period for the ethoxyquin PWP. The public comments did not change the schedule, risk assessment needs, or data requirements in the FWP.

- December 2015 – A Generic Data Call-In (GDCI) for ethoxyquin, GDCI-055501-1542, was issued for data needed to conduct the registration review risk assessments. All human health data required by the GDCI have been submitted and evaluated by the agency. All environmental fate, ecological risk, endangered species, and human health drinking water exposure data required by the GDCI have been waived by the agency.

- November 2019 – The agency announced the availability of the following assessments to support the ethoxyquin registration review for a 60-day public comment period:
    - *Ethoxyquin: Draft Human Health Risk Assessment in Support of Registration Review*, September 20, 2019.
    - *Review of Data Submitted in Support of a Waiver Request for Studies Identified in the Generic Data Call-in (GDCI) for Ethoxyquin*, December 14, 2016.
    - *Federally Listed Species Determination for the Registration Review of Ethoxyquin*, September 20, 2019.

  During the 60-day public comment period, the agency received three comments, which did not change the risk assessments or registration review timeline for ethoxyquin.

- May 2020 – The agency announced the availability of the PID in the docket for a 60-day public comment period.

- September 2020 – The agency is now announcing the availability of the ID in the docket.

C. Summary of Public Comments on the Proposed Interim Decision and Agency Responses

During the 60-day public comment period for the ethoxyquin PID, which opened on May 5, 2020 and closed on July 6, 2020, the agency received public comments from two sources: the Northwest Horticultural Council (NHC) and the United States Department of Agriculture's Office of Pest Management Policy (USDA OPMP). These comments, and the agency's response to those comments are summarized below. The agency thanks both commenters for their feedback.

Comment Submitted by USDA OPMP in EPA-HQ-OPP-2014-0780-0024

Comment: USDA OPMP emphasized the importance of ethoxyquin as the primary antioxidant used to manage scald in postharvest pears. Also, given ethoxyquin's indoor-only use pattern, USDA OPMP supports the agency's *de minimis* ecological risk conclusion.

EPA Response: The agency thanks USDA OPMP for their support. The agency agrees that ethoxyquin is an important tool used to prevent decay and scald in pears. Furthermore, the agency has determined, based on ethoxyquin's limited, indoor-only use pattern, that the likelihood of exposure for non-target organisms from the use of ethoxyquin is low and represents *de minimis* exposure potential.

Comments Submitted Concerning the Updated Glove Statements

Comment: Both NHC and USDA OPMP (EPA-HQ-OPP-2014-0780-0025 and EPA-HQ-OPP-2014-0780-0024, respectively) support the agency's requirement to update the glove statements

on product labels. Both organizations agree that the required label changes will not negatively impact product usage.

EPA Response: The agency thanks NHC and USDA OPMP for their support. The agency is requiring updates to the glove statements to improve label clarity and consistency.

II. USE AND USAGE

Ethoxyquin is a quinolone-based antioxidant registered for use on pears to control scald (browning). Ethoxyquin is formulated as an emulsifiable concentrate, and as an impregnated paper wrap. Applications of ethoxyquin occur post-harvest via drench/in-line spray treatment, thermal fogging, and/or wrapping with impregnated paper. Additionally, applications can be made as a non-split application (*i.e.*, a one-time application), split application (*e.g.*, two applications at half the rate), or wrapped as noted above.

Based on a report from packinghouses in Washington and Oregon; where approximately 40% and 30% of the total U.S. pear production occurs, respectively. Ethoxyquin is important for the storage of non-organic D'Anjou pears (>85%) and Bosc pear varieties (~15%).[1] There are no reports on ethoxyquin usage rates, however, the agency estimates that ethoxyquin is used to treat approximately 33% of U.S. pear-tons produced annually. This estimate considers pear varieties and ethoxyquin use patterns, and state and federal use reports.[1,2,3]

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

A summary of the agency's human health risk assessment was presented in the PID. The agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of ethoxyquin. There were no dietary, residential, bystander, aggregate or occupational risks of concern. The human health risk conclusions for ethoxyquin have not changed since the PID, and no further human health data are expected to be needed for this registration review. For additional details on the human health assessment for ethoxyquin, see the *Ethoxyquin: Draft Human Health Risk Assessment in Support of Registration Review*, dated September 20, 2019, which is available in the docket.

[1] Kupferman E. 2014. *Ethoxyquin Use in the Commercial Pear Industry of Washington and Oregon*. A Report Commissioned by the Northwest Horticultural Council and Pear Bureau Northwest. Submitted by Dr. Eugene Kupferman, Professor Emeritus, Washington State University. October 10, 2014.
[2] California Department of Pesticide Registration (CDPR). 2012-2016. California Department of Pesticide Regulation – Pesticide Use Reporting. Summary of pesticide use data - Indexed by Chemicals. Available at: https://www.cdpr.ca.gov/docs/pur/purmain.htm
[3] USDA. 2003. Agricultural Chemical Usage Postharvest Applications – Apples and Pears. United States Department of Agriculture (USDA) National Agricultural Statistics Service. March 2003.

1. Human Incidents and Epidemiology

EPA completed a review of existing incident data for ethoxyquin in the Incident Data System (IDS) and the Centers for Disease Control and Prevention/National Institute of Occupational Safety and Health (CDC/NIOSH) Sentinel Event Notification System for Occupational-Risk Pesticides (SENSOR) databases. In the current IDS analysis from January 1, 2014 to May 22, 2019, no ethoxyquin incidents were reported to either Main or Aggregate IDS. A query of SENSOR-Pesticides 1998-2015 identified no cases involving ethoxyquin.

Based on the absence of incidents reported to both the IDS and SENSOR-Pesticides, there does not appear to be a concern at this time. The agency will continue to monitor the incident information. Additional analyses will be conducted if ongoing human incident monitoring indicates a concern.

2. Tolerances

Tolerances for ethoxyquin are established in 40 CFR §180.178. No change to the established tolerance definition (parent only) is recommended; however, the agency will propose the following revisions to the tolerance expression for ethoxyquin in 40 CFR §180.178:

(a) General. Tolerances are established for residues of ethoxyquin, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) in or on the commodity.

The only established tolerance is in/on pear, and the level (3 parts per million) does not require any revision and is harmonized with established Codex and Canadian maximum residue limits (MRLs).

3. Human Health Data Needs

No data deficiencies were identified for ethoxyquin, and the agency does not anticipate any further data needs for ethoxyquin.

B. Ecological Risks

The agency has determined, based on ethoxyquin's indoor-only use pattern, that the likelihood of exposure for non-target organisms from the use of ethoxyquin is low and represents *de minimis* exposure potential. Therefore, the agency determined that a risk assessment was not warranted. For additional details on this determination, see the *Review of Data Submitted in Support of a Waiver Request for Studies Identified in the Generic Data Call-in (GDCI) for Ethoxyquin*, which is available in the public docket.

Threatened/Endangered Species

Given the limited use pattern and the low probability of non-target organism exposure to ethoxyquin, the agency has issued a "No Effect" determination for listed species and concluded that there will be "No Habitat Modification" for all designated critical habitats for listed species from the current use of ethoxyquin. Therefore, the agency has concluded that consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service under ESA § 7(a)(2) is not required. For further details on the NE determination, see the *Federally Listed Species Determination for the Registration Review of Ethoxyquin*, which is available in the public docket.

1. Ecological Incidents

Reviews of the Incident Data System (IDS) and Aggregate IDS were conducted for the ethoxyquin registration review. As of February 4, 2020, there were no ecological incidents reported in either database for ethoxyquin.

The agency will continue to monitor ecological incident information as it is reported to the agency. Detailed analyses of these incidents are conducted if reported information indicates concerns for risk to non-target organisms.

2. Ecological and Environmental Fate Data Needs

Although multiple environmental fate and ecological effects studies were identified in the Generic Data Call-in for ethoxyquin, additional information provided by the registrant on the use of the compound provided sufficient evidence to support a determination of *de minimis* exposure. The agency waived the remaining fate and effects data and does not require any further data for ethoxyquin at this time.

C. Benefits Assessment

Ethoxyquin is a quinolone-based antioxidant used to control scald, which is a post-harvest physiological disorder that develops in cold-storage for some pear varieties. Scald discolors the skin of pears, turning them brown and unmarketable. Ethoxyquin is the primary method of controlling scald[4], and the only alternative, 1-MCP (1-methylcyclopropene), has limited success in pears.

[4] USDA. 2016. The Commercial Storage of Fruits, Vegetables, and Florist and Nursery Stocks. United States Department of Agriculture (USDA) Agricultural Research Service. Agriculture Handbook Number 66. Revised February 2016.

IV. INTERIM REGISTRATION REVIEW DECISION

A. Label Amendment and Regulatory Rationale

The agency has reviewed the risks and benefits associated with the registered uses of ethoxyquin. Given ethoxyquin's indoor-only use pattern, the agency has determined that the likelihood of ecological risk is low and represents *de minimis* ecological exposure potential for products containing ethoxyquin. Additionally, there are no human health risks of concern, however, the agency is requiring an updated glove statement to improve label clarity and consistency. For details on the updated glove statement language, please reference Appendix A.

1. Update Glove Statement

The agency is requiring an update to gloves statements to be consistent with Chapter 10 of the Label Review Manual. In particular, the agency is requiring the removal of reference to specific categories in EPA's chemical-resistance category selection chart and requiring that labels specify the appropriate glove types to use. For example, the chemical-resistant glove statements in the label should remove "such as" language and not state the solvent category, but rather add all acceptable glove types that provide high-level chemical resistance for the solvent category as mentioned in Table 3 of Chapter 10 of the Label Review Manual. This minor clarification does not fundamentally change the personal protective equipment that workers are currently required to use.

B. Tolerance Actions

There are no changes to the tolerance definition for ethoxyquin in 40 CFR §180.178, however, the human health risk assessment recommended changes to the tolerance expression. Refer to Section III. A. 2 for additional details. The agency will use its FFDCA rulemaking authority to make the needed changes to the tolerance.

C. Interim Registration Review Decision

In accordance with 40 CFR §155.56 and 155.58, the agency is issuing this ID. Except for the Endocrine Disruptor Screening Program (EDSP) component of this case, the agency has determined that no additional data are required at this time.

In this ID, the agency is making no human health or environmental safety findings associated with the EDSP screening of ethoxyquin. The agency's final registration review decision for ethoxyquin will be dependent upon the result of an EDSP FFDCA § 408(p) determination.

D. Data Requirements

The agency does not anticipate calling-in additional data for registration review of ethoxyquin at this time.

V. NEXT STEPS AND TIMELINE

A. Interim Registration Review Decision

A Federal Register Notice will announce the availability of this Interim Registration Review Decision for ethoxyquin. However, a final decision for ethoxyquin may be issued without the agency having previously issued an interim decision. A final decision on the ethoxyquin registration review case will occur after an EDSP FFDCA § 408(p) determination.

B. Implementation of Mitigation Measures

The ethoxyquin registrants must submit amended labels that include the label changes described in Appendix A. The revised labels and requests for amendment of registrations must be submitted to the agency for review within 60 days following issuance of the Interim Registration Review Decision in the docket.

Registrants must submit a cover letter, a completed Application for Registration (EPA form 8570-1) and electronic copies of the amended product labels. Two copies for each label must be submitted, a clean copy and an annotated copy with changes. In order for the application to be processed, registrants must include the following statement on the Application for Registration (EPA form 8570-1):

"I certify that this amendment satisfies the requirements of the Ethoxyquin Interim Registration Review Decision and EPA regulations at 40 CFR Section 152.44, and no other changes have been made to the labeling of this product. I understand that it is a violation of 18 U.S.C. Section 1001 to willfully make any false statement to EPA. I further understand that if this amendment is found not to satisfy the requirements of the Ethoxyquin Interim Registration Review Decision and 40 CFR Section 152.44, this product may be in violation of FIFRA and may be subject to regulatory and/or enforcement action and penalties under FIFRA."

Within the required timeframe, registrants must submit the required documents to the Re-evaluation section of EPA's Pesticide Submission Portal (PSP), which can be accessed through EPA's Central Data Exchange (CDX) using the following link: https://cdx.epa.gov/. Registrants may instead send paper copies of their amended product labels, with an application for a fast-track, agency-initiated non-PRIA label amendment to Matthew B. Khan at one of the following addresses, so long as the labels and application are submitted within the required timeframe:

VIA US Mail
USEPA Office of Pesticide Programs
Pesticide Re-evaluation Division
Mail Code 7508P
1200 Pennsylvania Ave NW
Washington, DC 20460-0001

VIA Courier
Pesticide Re-evaluation Division
c/o Front End Processing
Room S-4910, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Appendix A: Required Labeling Changes for Ethoxyquin Products

Description	Required Label Language for Ethoxyquin Products	Placement on Label
	End Use Products	
Updated Gloves Statement	Update the glove statements to be consistent with Chapter 10 of the Label Review Manual[5]. In particular, remove reference to specific categories in EPA's chemical-resistance category selection chart and list the appropriate chemical-resistant glove types to use.	In the Personal Protective Equipment (PPE) within the Precautionary Statements and Agricultural Use Requirements, if applicable

[5] https://www.epa.gov/sites/production/files/2018-04/documents/lrm-complete-mar-2018.pdf