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Pyrasulfotole

Proposed Interim Registration Review Decision
Case Number 7272

March 2021

Approved by: _____

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I. INTRODUCTION

This document is the Environmental Protection Agency's (EPA or the Agency) Proposed Interim Registration Review Decision (PID) for pyrasulfotole (PC Code 000692, case 7272). In a registration review decision under the Federal Insecticide, Fungicide, Rodenticide Act (FIFRA), the Agency determines whether a pesticide continues to meet FIFRA's registration standard.[1] Where appropriate, the Agency may issue an interim registration review decision before completing a registration review.[2] Among other things, the interim registration review decision may determine that new risk mitigation measures are necessary, lay out 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.[3] For more information on pyrasulfotole, see EPA's public docket (EPA-HQ-OPP-2016-0391) at www.regulations.gov.

FIFRA[4] 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. In 2006, the Agency began implementing the registration review program. EPA will review each registered pesticide every 15 years. Through the registration review program, the Agency intends to verify that all registered pesticides continue to meet the registration standard as the ability to assess and reduce risk evolves and as policies and practices change. By periodically re-evaluating pesticides as science, public policy, and pesticide-use practices change, the Agency ensures that the public can continue to use products in the marketplace that do not present unreasonable adverse effects. For more information on the registration review program, see http://www.epa.gov/pesticide-reevaluation.

The Agency is issuing a PID for pyrasulfotole so that it can (1) move forward with aspects of the registration review that are complete and (2) implement interim risk mitigation (see Appendices A and B). EPA is currently working with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (the Services) to improve the consultation process for national threatened and endangered (listed) species for pesticides under the Endangered Species Act (ESA).[5] The Agency has not yet fully evaluated pyrasulfotole's risks to federally listed species. However, EPA will complete its listed-species assessment and any necessary consultation with the Services before completing the pyrasulfotole registration review. Before completing registration review, EPA will also complete endocrine screening for pyrasulfotole under the Federal Food, Drug, and Cosmetic Act (FFDCA).[6] For more information on the listed-species assessment and the endocrine screening for the pyrasulfotole registration review, see Appendices C and D.

[1] Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) § 3(g), 7 U.S.C. § 136a(g); 40 C.F.R. § 155.57.
[2] 40 C.F.R. §§ 155.56, 155.58.
[3] 40 C.F.R. § 155.56.
[4] As amended by the Food Quality Protection Act (FQPA) of 1996, Pub. L. No. 104-170, 110 Stat. 1489.
[5] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.
[6] Federal Food, Drug, and Cosmetic Act (FFDCA) § 408(p), 21 U.S.C. § 346a(p).

Pyrasulfotole is an HPPD (4-hydroxyphenylpyruvate dioxygenase) inhibitor in Group 27, according to the Weed Science Society of America's (WSSA) mode of action classification for herbicides. The compound works by blocking enzymatic activity of HPPD, which functions to catabolize tyrosine; tyrosine breakdown products in turn are necessary for the synthesis of chlorophyll. End-use pyrasulfotole products are formulated as emulsifiable or soluble concentrates that can be applied aerially or via ground as a post-emergent spray to control an array of annual broadleaf weeds. Products containing pyrasulfotole are registered for use on barley, oats, sorghum, wheat, rye, triticale, grass grown for seed, and Conservation Reserve Program (CRP) land. There are no registered residential uses for products containing pyrasulfotole.

Pyrasulfotole was first registered in 2007, and no Reregistration Eligibility Decision was issued. Currently, there are six FIFRA Section 3 registrations and one Special Local Need (SLN) registration.

This document is organized in five sections: *Introduction*, which includes this summary and a summary of public comments and EPA's responses; *Use and Usage*, which describes how and why pyrasulfotole is used and summarizes data on its use; *Scientific Assessments*, which summarizes EPA's risk and benefits assessments, updates or revisions to previous risk assessments, and provides broader context with a discussion of risk characterization; *Proposed Interim Registration Review Decision*, which describes the mitigation measures proposed to address risks of concern and the regulatory rationale for EPA's PID; and, lastly, *Next Steps and Timeline* for completion of this registration review.

A. Summary of Pyrasulfotole Registration Review

Pursuant to 40 CFR § 155.50, EPA formally initiated registration review for pyrasulfotole 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 pyrasulfotole.

- November 2016 - The *Pyrasulfotole Preliminary Work Plan* (PWP*)*, dated September 17, 2016, the *Registration Review - Preliminary Problem Formulation for the Human Health Drinking Water and Ecological Risk Assessments in Support of Registration Review of Pyrasulfotole*, dated July 28, 2016, and the *Pyrasulfotole Human Health Assessment Scoping Document in Support of Registration Review*, dated August 4, 2016 and other supporting documents were posted to the docket for a 60-day public comment period.

- August 2017 - The *Pyrasulfotole Final Work Plan* (FWP), dated March 22, 2017, was issued. Comments were received from the Center for Biological Diversity, the FIFRA Endangered Species Task Force, and Bayer CropScience. The comments did not alter the registration review timeline or planned risk assessments for pyrasulfotole, but comments from Bayer resulted in the following changes to the anticipated data requirements: 1) a data need that was already satisfied was removed from the list of planned data requirements (acute oral toxicity test with adult honeybees), and 2) a data need that was

inadvertently omitted in the PWP was added (chronic oral toxicity test with adult honeybees).

- February 2019 - A Generic Data Call-In (GDCI-000692-1678) for pyrasulfotole was issued for data needed to conduct the registration review risk assessments. The guideline 835.4100 aerobic soil metabolism study remains outstanding. See Section III for details.

- November 2020 - The Agency announced the availability of the *Pyrasulfotole Human Health Draft Risk Assessment for Registration Review*, dated September 18, 2020, and the *Pyrasulfotole: Draft Risk Assessment for Registration Review*, dated September 24, 2020 and other supporting documents for a 60-day public comment period. The Agency received public comments from four organizations. These comments and the Agency's responses are summarized below. The comments did not change the risk assessments or registration review timeline for pyrasulfotole.

- March 2021 - The Agency has completed the PID for pyrasulfotole. The PID will be posted to the docket for for a 60-day public comment period. The following documents will also be posted at the same time:

    - *Pyrasulfotole: Addendum to the Draft Risk Assessment for Registration Review*, dated February 22, 2021
    - *Pyrasulfotole: Response to Public Comments on the Draft Ecological Risk Assessment and Drinking Water Assessment for Registration Review*, dated March 18, 2021.
    - *Pyrasulfotole: Response to Comments on the Draft Human Health Risk Assessment for Registration Review*, dated March 1, 2021

B. Summary of Public Comments on the Draft Risk Assessments and Agency Responses

During the 60-day public comment period for the pyrasulfotole Draft Risk Assessments, which opened on November 5, 2020 and closed on January 4, 2021, the Agency received public comments from four sources. Comments were submitted by the National Agricultural Aviation Association (NAAA), the United States Department of Agriculture (USDA), the Center for Biological Diversity, and Bayer CropScience (a pyrasulfotole technical registrant). Substantive comments, comments of a broader regulatory nature, and the Agency's responses to those comments are summarized below. The Agency thanks all commenters for their comments and has considered them in developing this PID.

Comments Submitted by National Agricultural Aviation Association (Docket ID: EPA-HQ-OPP-2016-0391-0023)

Comment: The NAAA provided comments regarding the spray drift analysis conducted in the draft risk assessment, particularly concerning the spray drift model, AgDRIFT, and the inputs used in the model (*e.g.*, aircraft type, swath width and displacement, number of passes, wind speed, height for wind speed measurement, boom length and boom drop, droplet size,

atmospheric stability, and surface roughness). NAAA believes that the tier-1 component of the AgDRIFT model is inadequate because some of the assumptions it uses are unrealistic. NAAA recommended the use of the Multiple Application Assessment Method (MAAM) to model drift potential for products that can be applied multiple times annually on a crop. NAAA also recommended a refined assessment with a higher tiered model.

EPA Response: The Agency acknowledges and thanks NAAA for their comments. AgDRIFT is the currently approved model for evaluating potential spray drift from a pesticide application. The Agency appreciates the additional suggestions provided by NAAA for revising the AgDRIFT modeling inputs and continues to work with industry to update and improve modeling methods to better reflect typical application practices. At the recent December 2020 Center of Excellence in Regulatory Science in Agriculture (CERSA) workshop, EPA, NAAA, and other stakeholders discussed these potential refinements for AgDRIFT modeling. EPA is currently reviewing these suggestions and will consider them for future risk assessment. However, modeling for a national-level assessment is first conducted using maximum application rates, limitations, and instructions listed on the pesticide pyrasulfotole labels. In the absence of specific use directions and application restrictions implemented across all product labels, default assumptions (based on empirical data) are used.

Comments Submitted by USDA (Docket ID: EPA-HQ-OPP-2016-0391-0024)

Comment: USDA noted the benefits of pyrasulfotole for use as an herbicide for cereals grains, where it serves as a tank-mix partner for pyridine and triazine herbicides. Pyrasulfotole also provides reliable control of weeds that are resistant to glyphosate and group 2 herbicides such as chlorsulfuron, diclofop-methyl, imazamox, and mesosulfuron-methyl. USDA concurred with the Agency's ecological risk assessment, which concluded that pyrasulfotole is unlikely to pose any risks of concern to aquatic organisms, birds, or bees, and is unlikely to pose acute risks to mammals. USDA also reiterated that chronic risk quotients (RQs) for mammals do not exceed the level of concern (LOC) when the Lowest Observed Adverse Effects Levels (LOAELs) and a default foliar dissipation half-life are considered. As an herbicide, pyrasulfotole poses potential risk to non-target plants; however, USDA requested that EPA consider practical measures that minimize ecological exposure and that account for existing mitigations, since all active labels for formulated pyrasulfotole products include spray drift management language as well as surface water and ground water advisory statements.

EPA Response: EPA appreciates the information provided by USDA on the benefits of pyrasulfotole. In developing risk mitigation for pyrasulfotole, the Agency considered current spray drift labeling as well as practical measures to minimize ecological exposure. See Section IV of this document for proposed risk mitigation.

Comments Submitted by Center for Biological Diversity (CBD) (Docket ID: EPA-HQ-OPP-2016-0391-0025)

Comment: CBD's comments focus on the EPA's duty to consult with the Services on the registration review of pyrasulfotole in accordance with the Endangered Species Act (ESA). The CBD comments mention various aspects of the risk assessment process, specifically use of the best available data, including all necessary data and studies, particularly to develop listed species risk assessments, and evaluation of effects on listed species and their designated critical habitat. In addition, CBD expressed concern about effects on pollinators and other beneficial insects, effects on human health or environmental safety concerning endocrine disruption, and any additive, cumulative or synergistic effects of the use of pyrasulfotole.

EPA Response: EPA has reviewed CBD's comments and is addressing many of the concerns regarding listed species as part of its ongoing collaborative work with the Services and USDA to improve the consultation process for listed species for pesticides in accordance with the Endangered Species Act (ESA) § 7. See the Endangered Species Assessment in Appendix C of this document for more information. The EPA will address concerns specific to pyrasulfotole, particularly with regard to pollinators, ESA, and endocrine disruption, in connection with the development of its final registration review decision for this pesticide. See Endocrine Disruptor Screening Program in Appendix D of this document for more information regarding endocrine disruption. The EPA is currently developing an Agency policy on how to consider claims of synergy being made by registrants in their patents. On September 9, 2019, the EPA released an interim process for public comment, available at regulations.gov in docket EPA-HQ-OPP-2017-0433. After the Agency has considered public comment on the proposed policy, and once that policy has been finalized, the EPA will consider its implications on the EPA's final decision for pyrasulfotole.

Comments Submitted by Bayer CropScience (Docket ID: EPA-HQ-OPP-2016-0391-0026)

Comment: Bayer CropScience provided comments on both the human health and ecological risk assessments. Comments on the human health risk assessment focused on the model organism used by the Agency; Bayer noted that EPA should use the mouse model for assessing cancer risk and for deriving the chronic dietary reference dose.

Comments on the ecological risk assessment focused on conservatism in the assessment of risk to mammals and plants and noted a typo listed for the soil half-life for aquatic modeling. Bayer submitted a benchmark dose analysis and suggested that EPA use the lower limit of a benchmark dose for mammalian risk assessment. Bayer argued that the exposure assumptions for the semi-aquatic plant assessment are too conservative, the modeling assumes that 50% or more of the application rate would runoff into the receiving environment. Bayer suggests that the nontarget terrestrial plant assessment should use endpoints from pyrasulfotole only studies instead of studies with pyrasulfotole co-formulated with another pesticide active ingredient. Bayer also noted that it submitted additional pollinator studies in September 2020 which would allow for a tier I pollinator risk assessment.

EPA Response: EPA acknowledges that the rat is no longer an appropriate species for human health risk assessment, as noted in the recent 2020 white paper, *HPPD Inhibiting Herbicides: State of the Science*. The cancer classification of "Suggestive Evidence of Carcinogenic

Potential" was determined prior to the 2020 white paper and was based on the 2005 Cancer Guidelines. The current chronic dietary endpoint is protective of all the observed tumor types. Under current practices, the cancer descriptors are not updated unless the registrant submits new data and requests a formal cancer reclassification. EPA agrees that the current chronic dietary endpoint is now based on the mouse, the revised chronic dietary reference dose is 0.0136 mg/kg/day, which is similar to the previous rat value. When appropriate, EPA will update the characterization associated with the cancer quantification.

In response to comments on the ecological risk assessment, the Agency agrees that the correct soil half-life input for aquatic modeling should be 480 days instead of 317 days and will use the corrected value in future risk assessments. The Agency has not verified the benchmark dose analysis submitted by Bayer, but the proposed mammalian endpoint would still result in chronic risks of concern for small and medium mammals consuming short grass and would not change the overall risk conclusion for mammals.

Bayer is correct that the plant modeling assumes that 50% of the pyrasulfotole application rate will be present in runoff entering into semi-aquatic areas. The screening level estimates for runoff do not account for chemical and field-specific properties that could impact the concentration of pyrasulfotole in runoff; however, the risk characterization presented in the risk assessment are adequate to inform risk management and the Agency does not intend to revise the semi-aquatic plant assessment.

The Agency acknowledges that terrestrial plant data for pyrasulfotole alone exhibited lower toxicity to terrestrial plants compared to studies where pyrasulfotole was co-formulated with another pesticide. However, there are risks of concern for terrestrial plants in both types of studies and the Agency selects the most sensitive toxicity endpoints from the available database to ensure that risk estimates are adequately protective.

EPA has reviewed the new pollinator studies and has revised the pollinator risk assessment; see the *Pyrasulfotole: Addendum to the Draft Risk Assessment for Registration Review*, available in the public docket, for updated risk estimates.

II. USE AND USAGE

Pyrasulfotole provides post-emergence weed control of broadleaf weeds and is registered for use on cereal grains (*i.e.*, barley, oats, rye, sorghum, triticale and wheat), grasses grown for seed, forage, and hay, as well as on conservation reserve program (CRP) land. Pyrasulfotole can be applied aerially or via groundboom equipment. Some registrations allow application via handheld/backpack sprayers or irrigation systems.

Based on available agricultural market research data for 2015-2019, the approximate usage of pyrasulfotole was about 160,000 pounds of active ingredient (a.i.) on about 5.2 million total acres treated (TAT) per year across all crops and states surveyed.[7] The majority of pyrasulfotole

[7] Kynetec USA, Inc. 2020. "The AgroTrak® Study from Kynetec USA, Inc." Database Subset: 2015-2019.

usage was on spring wheat, with about 94,000 pounds of a.i. applied on about 3.3 million total acres.[7] In winter wheat, 29,000 pounds of a.i. were applied on 930,000 total acres and 24,000 pounds of a.i. were applied to 710,000 total acres of sorghum.[7] All of these crops were treated on average once per season.[7] Average per-application rates vary between 0.027 pounds a.i./A in fallow land up to 0.034 pounds a.i./A in sorghum.[7]

In terms of the percentage of total crop acreage treated with pyrasulfotole, 22% of spring wheat was treated with pyrasulfotole; other major use sites for pyrasulfotole include barley (11% of the crop treated) and sorghum (11% of the crop treated).[7] Usage of pyrasulfotole was also observed on winter wheat (3% of the crop treated) and in fallow land (<1% of the crop treated).[7] The only non-crop use of pyrasulfotole is on conservation reserve program (CRP) land. The Agency does not have any pesticide usage data from CRP land.

All reported pyrasulfotole agricultural usage was applied as a premix with bromoxynil between 2015-2019.[7] All U.S. registered products containing pyrasulfotole also contain bromoxynil, except for one registration (EPA Registration # 264-1024), which had no reported usage during that period. Current formulations for pyrasulfotole include emulsifiable concentrate and soluble concentrate.

Pyrasulfotole is applied to actively growing crops between 1-leaf and flag-leaf (for wheat, barley, rye, and triticale). Pyrasulfotole may be applied to grain and forage sorghum at the 3-leaf stage up to 30 inches or until flag-leaf emergence, whichever is first. Pyrasulfotole may be applied to CRP acres and grasses grown for seed anytime from pre-emergence to established grass. Pyrasulfotole/bromoxynil provides control of annual cocklebur, lambsquarters, nightshade, pigweed, ragweed, velvetleaf, wild mustard, and chickweed.[8,9]

For more information on pyrasulfotole use, usage, and benefits, please refer to the *Pyrasulfotole (000692) Screening Level Usage Analysis (SLUA)*, dated June 16, 2020 and the *BEAD Chemical Profile (BCP) for Registration Review: Pyrasulfotole (000692)*, dated June 15, 2016, which are available in the public docket.

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

A summary of the Agency's human health risk assessment is presented below. The Agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of pyrasulfotole. For additional details on the human health assessment for this case, see the *Pyrasulfotole Human Health Draft Risk Assessment for Registration Review*, the *Pyrasulfotole Occupational and Residential Exposure Assessment for*

[8] MSU. 2013. Weed response to herbicides in small grains. Michigan State University (MSU) Extension. http://www msuweeds.com/assets/2013WeedGuide/2013WGsmallgrain.pdf.
[9] Reddy SS, Stahlman PW, Geier PW, Peterson DE. 2012. Broadleaf weed control and crop safety with premixed pyrasulfotole and bromoxynil in winter wheat. American Journal of Plant Sciences 3:1613-1618.

Registration Review, and the *Pyrasulfotole Chronic Dietary (Food and Drinking Water) Exposure and Risk Assessment to Support the Human Health Risk Assessment for Registration Review*, which are available in the public docket. The Agency also recently evaluated the toxicology profile and mode of action/adverse outcome pathway for the HPPD inhibiting herbicides; this evaluation is detailed in the document entitled *HPPD Inhibiting Herbicides: State of the Science*, which is also available in the docket.

1. Risk Summary and Characterization

Dietary Risks

No toxic effects attributable to a single exposure to pyrasulfotole have been identified; therefore, an acute dietary risk assessment was not conducted. The chronic dietary risk estimates for pyrasulfotole for the general U.S. population and all population subgroups were below the Agency's level of concern (LOC) of 100% of the chronic population-adjusted dose (cPAD). For chronic dietary exposure, the most highly exposed population subgroup was children (1-2 years old), with risk estimates equal to 14% of the cPAD, where risk estimates exceeding 100% of the cPAD are of concern.

Pyrasulfotole was classified as having "Suggestive Evidence of Carcinogenic Potential" based on increased incidences of corneal tumors in male rats (oral carcinogenicity study, MRID 46801910) and urinary bladder tumors in male and female mice (oral carcinogenicity study, MRID 46801909). The revised chronic dietary reference dose (cRfD) of 0.0136 mg/kg/day, derived from the LOAEL of 13.6 mg/kg/day in mice (from the mouse dietary carcinogenicity study, MRID 46801909) along with a 1,000-fold uncertainty factor, is protective of both non-cancer and cancer effects. Therefore, a separate cancer dietary risk assessment was not conducted for pyrasulfotole.

Residential and Aggregate Risks

There are no registered residential uses and/or commercial uses at residential sites for pyrasulfotole at this time. Therefore, a quantitative residential exposure assessment was not conducted. Since there are no residential exposures for pyrasulfotole, all aggregate exposures are equivalent to dietary exposure estimates, which are not of concern.

Non-Occupational Spray Drift Risks

Spray drift risks from lawn deposition in areas adjacent to treated fields were assessed. A dermal endpoint was not selected for pyrasulfotole due to the lack of effects attributable to a single dose; therefore, only children's (1 to <2 years old) incidental oral risk estimates were quantitatively assessed. Children's incidental oral risk estimates were not of concern at the field edge for groundboom or aerial applications, with margins of exposures (MOEs) ranging from 280,000 for aerial application to 3,200,000 for ground application (where MOEs below the LOC of 100 are of concern).

Cumulative Risks

The Agency has determined that the HPPD inhibitors, including pyrasulfotole, share a common mechanism of action (MOA)/adverse outcome pathway (AOP). As a result, a cumulative assessment will be performed for the HPPD inhibitors once all individual chemical risk assessments to support registration review have been completed.

Occupational Handler Risks

An occupational handler assessment was conducted to assess risk to individuals involved in the pesticide application process. Since a dermal endpoint was not selected for pyrasulfotole, only inhalation exposures were quantitatively assessed. There are no inhalation risks of concern for registered uses of pyrasulfotole using label-directed personal protective equipment (PPE), which comprises of long-sleeved shirt and long pants, shoes, socks and chemical-resistant gloves. MOEs for occupational handler inhalation exposure scenarios ranged from 480,000 to 22,000,000 (where MOEs below the LOC of 100 are of concern).

Occupational Post-Application Risks

A quantitative dermal post-application exposure assessment was not conducted, since a dermal endpoint was not selected for pyrasulfotole. The restricted entry intervals (REIs) listed on the registered labels (12 hours for the standalone pyrasulfotole product and 24 hours on labels for pyrasulfotole products which are co-formulated with other active ingredients) are considered protective of post-application exposure.

Although a quantitative occupational post-application inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for occupational/commercial handlers. Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than post-application exposure. Therefore, it is expected that the occupational handler inhalation exposure estimates would be protective of occupational post-application inhalation exposure scenarios. Since occupational handler inhalation risk estimates were not of concern, occupational post-application inhalation risks are not of concern.

2. Human Incidents and Epidemiology

Pyrasulfotole human incidents were previously reviewed in 2016. At that time, based on the low frequency and severity of pyrasulfotole incident cases reported to the Incident Data System (IDS) and the National Institute of Occupational Safety and Health (NIOSH) Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides, further investigation was not warranted.

In the current IDS analysis from January 1, 2015 to June 30, 2020, no pyrasulfotole incidents were reported to Main IDS and 10 pyrasulfotole incidents (all classified as minor severity) were reported to Aggregate IDS. A query of SENSOR-Pesticides 2013-2015 identified three cases involving pyrasulfotole. All three cases occurred from the same occupational exposure event. One case was moderate in severity and two cases were low in severity. All three individual cases

were farmworkers. A migrant farmworker reported over the phone that a group of workers were exposed to a pyrasulfotole-containing herbicide product (EPA Reg. No. 264-1023), and possibly another product which was not reported. The three farmworkers were weeding in a grain field when an applicator started spraying the field without giving them notice or allowing them to safely clear the field. No enforcement findings were reported. Two cases went to the emergency room and the third declined to seek medical treatment. The moderate severity case was treated for lower respiratory pain, nausea, confusion, strong headache, muscle and joint weakness, memory loss, and fatigue. Other symptoms reported among the low severity cases included cough, upper respiratory pain, lower respiratory pain, eye pain/irritation, diarrhea and vomiting.

The Agricultural Health Study (AHS) is a federally-funded study that evaluates associations between pesticide exposures and cancer and other health outcomes and represents a collaborative effort between the US National Cancer Institute (NCI), National Institute of Environmental Health Sciences (NIEHS), Centers for Disease Control and Prevention's (CDC's) NIOSH, and the US EPA. Pyrasulfotole is not included in the AHS, and therefore this study does not provide information for this report.

Based on the continued low frequency and severity of pyrasulfotole incidents reported to both 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.

3. Tolerances

The tolerances for pyrasulfotole can be found in 40 CFR § 180.631. Anticipated tolerance actions include commodity definition revisions and the correction of values to be consistent with the Organization for Economic Cooperation and Development (OECD) Rounding Class Practice. The Agency anticipates the following changes to the tolerances for pyrasulfotole, which are summarized in Table 1. The Agency intends to undertake these tolerance actions pursuant to its Federal Food, Drug Cosmetic Act (FFDCA) authority.

Table 1: Summary of Anticipated Tolerance Actions

Pyrasulfotole 40 CFR § 180.631]: Summary of Anticipated Tolerance Actions			
Commodity	Established Tolerance (ppm)	Anticipated Tolerance (ppm)	Comments
(a) General			
Grain, aspirated fractions	-	0.4	Commodity definition revisions. Corrected value to be consistent with OECD Rounding Class Practice
Aspirated grain fractions	0.40	remove	
Barley, hay	0.30	0.3	Corrected values to be consistent with OECD Rounding Class Practice
Barley, straw	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice
Cattle, liver	3.0	3	Corrected values to be consistent with OECD Rounding Class Practice
Cattle, meat byproducts, except liver	0.70	0.7	Corrected values to be consistent with OECD Rounding Class Practice

Pyrasulfotole 40 CFR § 180.631]: Summary of Anticipated Tolerance Actions			
Commodity	Established Tolerance (ppm)	Anticipated Tolerance (ppm)	Comments
Goat, liver	3.0	3	Corrected values to be consistent with OECD Rounding Class Practice
Goat, meat byproducts, except liver	0.70	0.7	Corrected values to be consistent with OECD Rounding Class Practice
Grass, forage, fodder and hay, group 17, forage	-	25	Commodity definition revision
Grass, forage	25	remove	
Grass, forage, fodder and hay, group 17, hay	-	3.5	Commodity definition revision
Grass, hay"	3.5	remove	
Hog, liver	0.30	0.3	Corrected values to be consistent with OECD Rounding Class Practice
Horse, liver	3.0	3	Corrected values to be consistent with OECD Rounding Class Practice
Horse, meat byproducts, except liver	0.70	0.7	Corrected values to be consistent with OECD Rounding Class Practice
Oat, forage	0.10	0.1	Corrected values to be consistent with OECD Rounding Class Practice
Oat, hay	0.50	0.5	Corrected values to be consistent with OECD Rounding Class Practice
Oat, straw	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice
Poultry, meat byproducts	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice
Rye, forage	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice
Rye, straw	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice
Sheep, liver	3.0	3	Corrected values to be consistent with OECD Rounding Class Practice
Sheep, meat byproducts, except liver	0.70	0.7	Corrected values to be consistent with OECD Rounding Class Practice
Sorghum, grain, grain	0.70	0.7	Corrected values to be consistent with OECD Rounding Class Practice
Sorghum, grain, stover	0.80	0.8	Corrected values to be consistent with OECD Rounding Class Practice
Wheat, forage	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice
Wheat, hay	0.80	0.8	Corrected values to be consistent with OECD Rounding Class Practice
Wheat, straw	0.20	0.2	Corrected values to be consistent with OECD Rounding Class Practice

There are no established Mexican or Codex maximum residue limits (MRLs) for pyrasulfotole. The U.S. and Canadian tolerance/MRL expressions are harmonized and the numerical values are harmonized for all commodities except for livestock commodities, for which U.S. tolerance values are higher than the corresponding MRLs (due to higher dietary burdens in the U.S.).

4. Human Health Data Needs

No additional human health data are required to support registration review.

B. Ecological Risks

A summary of the Agency's ecological risk assessment is presented below. The Agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of pyrasulfotole. For additional details on the ecological assessment for pyrasulfotole, see the *Pyrasulfotole: Draft Risk Assessment for Registration Review* and the *Pyrasulfotole: Addendum to the Draft Risk Assessment for Registration Review*, which are available in the public docket.

EPA is currently working with its federal partners and other stakeholders to implement a Revised Method[10] for assessing potential risk to listed species and their designated critical habitats. Once the scientific methods necessary to complete risk assessments for listed species and their designated critical habitats have been fully implemented, the Agency will complete its endangered species assessment for pyrasulfotole. See Appendix C for more details. As such, potential risks for non-listed species only are described below.

1. Risk Summary and Characterization

Terrestrial Risks

Mammals

No acute risks of concern were identified for mammals; risk quotients (RQs) were not calculated due to a non-definitive endpoint (no mortality occurred in the rat acute oral toxicity study, MRID 46801836). The Agency therefore concludes that pyrasulfotole use is unlikely to result in acute risks to mammals.

Chronic RQs for mammals ranged from 0.02 to 2.9 assuming upper-bound estimates of dietary consumption and exceed the level of concern (LOC) of 1 for use on sorghum, grass, and CRP land. A default foliar dissipation half-life value of 35-days was used to calculate these risk estimates because only two reliable half-life values were available from empirical data. In order to characterize risk, risk estimates were generated using a refined foliar dissipation half-life of 2.85 days, and the resulting chronic RQs range from 0.01 to 1.7. Since mammals are not expected to consume only pyrasulfotole-treated foods as 100% of their diet, risk estimates were also generated using mean estimates of dietary consumption. Chronic RQs generated from mean estimates of dietary consumption range from 0.01 to 1.04 using the default foliar dissipation half-life (35-days).

[10] https://www.regulations.gov/document?D=EPA-HQ-OPP-2019-0185-0084

Given the assumptions used in risk assessment (maximum application parameters, default foliar dissipation half-life, and upper bound estimates of dietary consumption of pyrasulfotole-treated foods), chronic risk estimates for mammals are likely to be lower than estimated.

Birds, Reptiles, and Terrestrial-Phase Amphibians

No risks of concern were identified for birds or for reptiles and terrestrial-phase amphibians, for which birds serves as surrogates. Acute RQs were not calculated due to a non-definitive endpoint (no mortality in the northern bobwhite acute oral toxicity [MRID 46801729] and subacute dietary [MRID 46801730] studies). Chronic RQs ranged from 0.01 to 0.1 and were not of concern (where RQs less than the LOC of 1 are not of concern). Risk estimates were based on a no observed adverse effect concentration (NOAEC) above which there was reduced body weight gain (↓115%) at the lowest observable adverse effect concentration (LOAEC) and did not indicate risks of concern.

Terrestrial Invertebrates (honey bees)

Most pyrasulfotole uses are on crops that are wind-pollinated and are not considered attractive to bees; however, bees (both *Apis* and non-*Apis*) may be exposed from treated sorghum and forage grass when flowering. Furthermore, bee exposure to pyrasulfotole is possible from flowering weeds on-site and weeds off-site due to spray drift.

Only non-definitive acute endpoints are available for adult honey bees; therefore, acute RQs were not calculated. However, low mortality (0-10%) was observed at the highest treatment level in the acute adult oral and contact toxicity studies which were 80 to 625 times above the adult bee oral and contact estimated environmental concentrations (EECs) for the highest single application rate (0.045 lb ai/A for cereal grains). This indicates a low likelihood of adverse acute effects on adult bees from registered pyrasulfotole uses. The larval acute oral RQ was not of concern (acute RQ=0.07, acute LOC=0.4). The adult and larval chronic dietary-based RQ was also not of concern (chronic RQ=0.07, chronic LOC=1). Given the lack of LOC exceedances, there are no acute or chronic risks of concern for adult and larval *Apis* or non-*Apis* bees for currently registered pyrasulfotole uses. Although pyrasulfotole use does not present direct risks to bees, it does pose risks of concern for terrestrial plants both on-and off-site which could indirectly affect pollinators that rely on these plants for forage and shelter.

No incidents involving bees are reported in the Incident Data System (IDS) for registered uses of pyrasulfotole as of December 2020; however, the lack of incidents is not an indication that exposure and incidents involving bees or other taxa do not occur from pyrasulfotole use. Due to the low risk for individual bees posed by currently registered uses of pyrasulfotole, the Agency is not recommending submission of additional Tier 2 and Tier 3 bee data, including the non-guideline honey bee semi-field test, the non-guideline residues in pollen and nectar, or guideline 850.3040 field testing for pollinators at this time.

Terrestrial Plants

As expected for an herbicide, risks exceed the level of concern for non-target terrestrial plants. Risks of concern were observed in dicotyledonous plants (dicots) only and the most sensitive effect was reduced dry weight. RQs range from 0.11-80 for exposure to runoff and spray drift combined and exceed the Agency's LOC of 1 for terrestrial and semi-aquatic (*i.e.*, wetlands) plants.

To characterize risk from spray drift, the distance from the edge of the field to below toxicity threshold was estimated for both ground and aerial application using the AgDRIFT model and assuming labeled application parameters. Potential risks of concern for terrestrial plants occur up to 33 feet from the edge of treated fields for ground applications (assuming 4 ft release height, medium droplets, and a maximum application rate of 0.045 lb ai/A). Potential risks of concern occur up to 256 feet from the edge of treated fields for aerial applications (assuming a medium to coarse droplet size, and a 0.045 lb ai/A maximum application rate).

Pyrasulfotole is highly soluble in water and moderately mobile in the environment; it is stable to hydrolysis, photolysis, and biotic metabolism in aquatic systems. There is potential for transport to surface and groundwater. Based on these fate properties, the Agency assessed risks to non-target terrestrial plants from residues in irrigation water and determined that RQs for dicot terrestrial plants (RQs ranged from 5 to 35) exceed the level of concern from exposure in groundwater-derived irrigation water. The most sensitive endpoint for non-listed monocots is 2.9 times higher than the estimated exposure level from ground-water derived irrigation water; therefore, there is low risk to monocots for this exposure scenario.

Fish

No risks of concern were identified for fish. Acute RQs for fish were not calculated due to non-definitive endpoints resulting from the lack of adverse effects attributable to a single dose. Chronic RQs for freshwater fish ranged from 0.009 to 0.03 and were not of concern (where the LOC is 1). Chronic RQs were not calculated for estuarine/marine fish due to the lack of data; however, estuarine/marine fish would have to be at least 33 times more sensitive than freshwater fish to exceed the Agency's chronic LOC.

Aquatic Invertebrates

No risks of concern were identified for aquatic invertebrates. Acute RQs for freshwater invertebrates were not calculated due to a non-definitive endpoint (no mortality was observed). Acute RQs for estuarine/marine invertebrates ranged from 0.009 to 0.02 and were not of concern (where the LOC is 0.5). Chronic RQs for freshwater inverts range from <0.001 to 0.002 and were not of concern (where the LOC is 1). Chronic RQs for estuarine/marine inverts were not calculated due to the lack of data; however, estuarine/marine invertebrates would have to be 674 times more sensitive than freshwater invertebrates on a chronic basis to exceed the Agency's LOC.

Aquatic plants

There are no risks of concern identified for either vascular or non-vascular aquatic plants (RQs for aquatic plants range from <0.01-0.69, LOC is 1). Vascular plants were 300 times more sensitive compared to non-vascular plants. The most sensitive effect observed was decreased frond dry weight. Effects in non-vascular plants include reduced biomass, cell density, and growth rate.

2. Ecological Incidents

A review of ecological incidents was conducted on July 23, 2020 to identify reported incidents in the Agency's Incident Data System (IDS). There are 51 reported incidents. All incidents were related to terrestrial plants. The majority of plant incidents were from herbicide carry-over onsite, where growers reported phytotoxicity after rotating treated fields to a new crop. The majority (61%) of the reported incidents were the result of a registered use with all but two incidents assigned a certainty index of either possible or probable. The OPP Aggregate Incident Reports database was also searched on July 23, 2020. A total of 28 aggregate plant incidents were reported, however no further information is available on the aggregate incidents

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.

3. Ecological and Environmental Fate Data Needs

Several ecological fate and effects studies were required in GDCI-000692-1678. Three guideline 835.4100 aerobic soil metabolism studies (MRIDs 46801709, 46801710, and 46801711) were submitted and classified as acceptable. Data on one soil is needed to complete the guideline 835.4100 requirement. Due to the low risk for *Apis* and non-*Apis* bees posed by currently registered uses of pyrasulfotole, the Agency is not recommending submission of additional Tier 2 and Tier 3 honey bee data at this time.

C. Benefits Assessment

Pyrasulfotole is a member of the Group 27 herbicides and works by blocking enzymatic activity of HPPD, which functions to catabolize tyrosine (tyrosine breakdown products are necessary for the synthesis of chlorophyll). Pyrasulfotole is used to control an array of annual broadleaf weeds after weed emergence. The herbicide can be applied to actively growing crops. It may be applied to conservation reserve program acres and grasses grown for seed anytime from preemergence to established grass. Pyrasulfotole was the first HPPD herbicide available for use in production of grains.[11] It provides a useful mechanism of action in small grains to control wild buckwheat,

[11] BCP. 2016. BEAD Chemical Profile (BCP) for Registration Review: Pyrasulfotole (000692). Biological and Economic Analysis Division (BEAD) memorandum. Leonard Yourman, Jihad Alsadek, Stephen Smearman. June 15, 2016.

common lambsquarters, redroot pigweed, and volunteer canola.[11,12] It is typically mixed with another herbicide (bromoxynil) to broaden the spectrum of weed control in winter wheat[13] and provides control of annual cocklebur, lambsquarters, nightshade, pigweed, ragweed, velvetleaf, wild mustard, and chickweed.[8,9] Pyrasulfotole can be used as a part of a weed resistance management program to supply a different mechanism of action, especially where resistance is known to acetolactate synthase (ALS) inhibitors, phenoxy, and glyphosate herbicides.[12]

IV. PROPOSED INTERIM REGISTRATION REVIEW DECISION

A. Proposed Risk Mitigation and Regulatory Rationale

The Agency has identified risks of concern to mammals and non-target terrestrial dicot plants from currently registered pyrasulfotole uses. Proposed mitigations to address these risks include mandatory spray drift management; a non-target organism advisory; and surface and ground water advisories. EPA is also proposing weed resistance management labeling consistent with all herbicide products, and advisory spray drift statements which are consistent with all pesticide products.

1. Spray Drift Management

The Agency is proposing label changes to reduce off-target spray drift and establish a baseline level of protection against spray drift that is consistent across all pyrasulfotole products. Reducing spray drift will reduce the extent of environmental exposure and risk to non-target plants and animals. Although the Agency is not making a complete endangered species finding at this time, these label changes are expected to reduce the extent of exposure and may reduce risk to listed species whose range and/or critical habitat co-occur with the use of pyrasulfotole.

The Agency is proposing the following spray drift mitigation language to be included on all pyrasulfotole product labels for products applied by liquid spray application. The proposed spray drift language is intended to be mandatory, enforceable statements and supersede any existing language already on product labels (either advisory or mandatory) covering the same topics. The Agency is also providing recommendations which allow pyrasulfotole registrants to standardize all advisory language on pyrasulfotole product labels. Registrants must ensure that any existing advisory language left on labels does not contradict or modify the new mandatory spray drift statements proposed in this PID, once effective.

- Applicators must not spray during temperature inversions.
- For aerial applications, do not apply when wind speeds exceed 15 mph at the application site. If the windspeed is greater than 10 mph, the boom length must be 65% or less of the wingspan for fixed wing aircraft and 75% or less of the rotor diameter for helicopters. Otherwise, the boom length must be 75% or less of the wingspan for fixed-wing aircraft and 90% or less of the rotor diameter for helicopters.

[12] Mahoney KJ, McNaughton KE, Sikkema PH. 2016. Control of glyphosate-resistant horseweed in winter wheat with pyrasulfotole premixed with bromoxynil. Weed Technology 30:291-296. http://www.bioone.org/doi/1O.l614/WT-D-15-00046.1.
[13] Crummett D. 2008. Small grains get help from Huskie. Prairie Farmer, January 2008.

- For aerial applicators, if the windspeed is 10 miles per hour or less, applicators must use ½ swath displacement upwind at the downwind edge of the field. When the windspeed is between 11-15 miles per hour, applicators must use ¾ swath displacement upwind at the downwind edge of the field.
- For aerial applications, the release height must be no higher than 10 feet from the top of the crop canopy or ground, unless a greater application height is required for pilot safety.
- For ground boom applications, apply with the release height no more than 4 feet above the ground or crop canopy.
- For ground applications, do not apply when wind speeds exceed 15 miles per hour at the application site.
- For ground boom and aerial applications, select nozzle and pressure that deliver fine or coarser droplets in accordance with American Society of Agricultural & Biological Engineers (ASABE) Standard 572 (for ground application) or ASABE S641 (for aerial application).

Impacts of Select Spray Drift Mitigation

All but one of the currently registered products contain pyrasulfotole co-formulated with bromoxynil. None of the new mitigations being proposed for pyrasulfotole are more restrictive than current mitigations required for application of bromoxynil. For instance, bromoxynil has a maximum wind speed for ground applications of 10 miles per hour, which is more restrictive than the proposed 15 miles per hour maximum wind speed for ground applications of pyrasulfotole. As pyrasulfotole appears to be applied almost exclusively as a premix with bromoxynil and the new mitigations being proposed for pyrasulfotole are less restrictive than the mitigations currently imposed on bromoxynil, the potential mitigations being considered for pyrasulfotole should not restrict grower ability to use pyrasulfotole relative to the current use of pyrasulfotole products. The proposed spray drift labeling could affect use of the pyrasulfotole-only registration (EPA reg. no. 264-1024). The proposed "fine or coarser" droplet size could provide greater flexibility for tank-mixing both the pyrasulfotole-only registration as well as premixes of pyrasulfotole and bromoxynil.

2. Herbicide Resistance Management

On August 24, 2017, EPA finalized a Pesticide Registration Notice (PRN) on herbicide resistance management.[14] Consistent with the Notice, EPA is proposing the implementation of herbicide resistance measures for existing chemicals during registration review, and for new chemicals and new uses at the time of registration. In registration review, herbicide resistance elements will be included in every herbicide PID.

The development and spread of herbicide resistant weeds in agriculture is a widespread problem that has the potential to fundamentally change production practices in U.S. agriculture. While herbicide resistant weeds have been known since the 1950s, the number of species and their

[14] PRN 2017-2, "Guidance for Herbicide Resistance Management Labeling, Education, Training, and Stewardship". Available at https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year

geographical extent, has been increasing rapidly. Currently there are over 250 weed species worldwide with confirmed herbicide resistance. In the United States, there are over 155 weed species with confirmed resistance to one or more herbicides.

Management of herbicide resistant weeds, both in mitigating established herbicide resistant weeds and in slowing or preventing the development of new herbicide resistant weeds, is a complex problem without a simple solution. Coordinated efforts of growers, agricultural extension, academic researcher, scientific societies, pesticide registrants, and state and federal agencies are required to address this problem.

EPA is proposing measures for the pesticide registrants to provide growers and users with detailed information and recommendations to slow the development and spread of herbicide resistant weeds. This is part of a more holistic, proactive approach recommended by crop consultants, commodity organizations, professional/scientific societies, researchers, and the registrants themselves.

3. Non-Target Organism Advisory Statement

The Agency is also proposing the addition of a non-target organism advisory. The protection of pollinating organisms is a priority for the Agency. Pyrasulfotole may negatively impact forage and habitat of pollinators and other non-target organisms. It is the Agency's goal to reduce spray drift whenever possible and to educate growers on the potential for indirect effects on the forage and habitat of pollinators and other non-target organisms. Therefore, EPA is proposing a non-target organism advisory to be placed on pyrasulfotole labels to address this potential concern. See Appendix B for the proposed non-target organism advisory.

4. Groundwater and Surface Water Advisories

The Agency is proposing surface water and groundwater advisories for pyrasulfotole because the environmental fate characteristics indicate that products containing pyrasulfotole might be transported to surface water and groundwater. This language is consistent with current labeling practices as noted in the Agency's Label Review Manual.[15]

The Agency identified potential risk to non-target plants from use of groundwater-derived irrigation water. The proposed groundwater advisory includes a statement to warn users not to apply pyrasulfotole in soils that are very permeable, to prevent the potential contamination of aquifers and other sources of irrigation water:

"Users are advised not to apply pyrasulfotole where soils have a rapid to very rapid permeability (such as loamy sand to sand) and the water table of an underlying aquifer is shallow or to soils containing sinkholes over limestone bedrock, severely fractured surfaces, and substrates which would allow direct introduction into an aquifer. Your local agricultural agencies can provide further information on the type of soil in your area and the location of groundwater."

[15] https://www.epa.gov/pesticide-registration/label-review-manual

See Appendix B for the proposed water advisories.

B. Tolerance Actions

The Agency anticipates modifying several pyrasulfotole tolerances, as described in Section III.A.3. Anticipated tolerance actions include commodity definition revisions and the removal of trailing zeros to be consistent with OECD Rounding Class Practice. The Agency will use its FFDCA rulemaking authority to make the needed changes to the tolerances. These changes are needed to satisfy the "no risk" FFDCA standard.

C. Proposed Interim Registration Review Decision

The Agency is issuing this PID in accordance with 40 CFR §§ 155.56 and 155.58. The Agency has made the following proposed interim decision: 1) Except for the remaining outstanding guideline 835.4100 aerobic soil metabolism study in one soil, EPA proposes that no additional date are required at this time; and 2) EPA proposes that pyrasulfotole does not meet the registration standard without the changes to the affected registrations and their labeling, proposed in Section IV and Appendices A and B. The Agency conducted detailed human health and ecological risk assessments. EPA did not identify any human health risks of concern. The Agency identified potential risks to mammals and non-target terrestrial plants. The Agency proposes to address risks to non-target organisms with mandatory spray drift management measures. EPA also determined that continuing to register pyrasulfotole provides benefits to growers with croplands experiencing weed resistance to ALS inhibitors, phenoxy and glyphosate herbicides by supplying a different mechanism of action for use in weed management programs.

During registration review, EPA considers whether a pesticide registration "continues to satisfy the FIFRA standard for registration."[16] Here, EPA proposes that pyrasulfotole does not meet the FIFRA registration standard without the changes to the affected registrations and their labeling described in Section IV.A and Appendices A and B. The spray drift management measures proposed herein are intended to reduce off-target drift and reduce exposure to non-target organisms, while maintaining the benefits of pyrasulfotole.

EPA has determined that there is no human dietary risk from registered uses of pyrasulfotole that is inconsistent with the FFDCA safety standard. Taking into consideration the available information on toxicity and exposure, EPA assessed pyrasulfotole's potential aggregate risks,

[16] 40 C.F.R. § 155.40(a); 7 U.S.C. § 136a(c)(5); *see also* 7 U.S.C. §§ 136(bb) (defining "unreasonable adverse effects on the environment" as encompassing both "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" [FIFRA's risk-benefit standard] **and** "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]"). In a PID, EPA sets out a proposed interim decision that includes EPA's "proposed findings with respect to the FIFRA standard for registration and describe the basis for such proposed findings." 40 C.F.R. §§ 155.56, 155.58(b)(1).

including dietary (food and water) and non-occupational residential exposures, and found no risks exceeding the Agency's levels of concern.[17]

EPA proposes to conclude that there is a reasonable certainty that no harm will result from aggregate exposure to pyrasulfotole, including all anticipated dietary exposures and all other exposures for which there is reliable information. Therefore, the pyrasulfotole residues are safe. EPA intends to modify existing tolerances to remove trailing zeros to be consistent with current rounding practices and revise commodity definitions to reflect current crop groupings.

In this PID, the Agency is not making any human health or environmental safety findings associated with the Endocrine Disruptor Screening Program (EDSP) screening of pyrasulfotole. Similarly, the Agency is not making a complete endangered species finding, though the proposed mitigation is expected to reduce the extent of environmental exposure and may reduce risk to listed species whose range or critical habitat co-occur with the use of pyrasulfotole. The Agency will complete a listed-species assessment and any necessary Endangered Species Act (ESA) Section 7 consultation with the Services, and make an EDSP determination before issuing a final registration review decision for pyrasulfotole. For more information, see Appendices C and D.

D. Data Requirements

GDCI-000692-1678 was issued for pyrasulfotole for data needed to conduct the registration review risk assessments. All data requirements have been satisfied with the exception of a guideline 835.4100 aerobic soil metabolism study. One of the three available aerobic soil metabolism studies (MRID 46801711) was conducted using a German soil; when the study was submitted, insufficient information was provided about the German soil to make a comparison to soils in the United States. The registrant has since provided supplemental information to address the deficiencies in the German soil study and the study is now classified as acceptable. The guideline requires the testing of four soils and only three soils, including the German soil, have been tested; data for an additional soil study therefore must be submitted by the registrant.

Of the available Tier 1 honey bee data, the pyrasulfotole effects database only lacks the acute larval toxicity study; however, this is not considered a data gap because information from the larval chronic toxicity study was used to derive a surrogate acute endpoint. Acute and chronic RQs are below the Agency's level of concern for both adult and larval bees. No incidents involving bees are reported in the IDS for registered uses of pyrasulfotole as of December 2020. Due to the low risk for individual bees posed by currently registered uses of pyrasulfotole, the Agency is not recommending submission of additional Tier 2 or 3 bee data at this time.

V. NEXT STEPS AND TIMELINE

[17] 2020. Pyrasulfotole Human Health Draft Risk Assessment for Registration Review. Health Effects Division, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention, United States Environmental Protection Agency. Joshua Godshall, Anwar Dunbar, Oluwaseun Gbemigun. September 18, 2020.

A. Proposed Interim Registration Review Decision

A Federal Register Notice will announce the availability of this PID for pyrasulfotole and will allow a 60-day comment period. If there are no significant comments or additional information submitted to the docket during the comment period that leads the Agency to change its proposed interim decision, EPA may issue an interim registration review decision for pyrasulfotole. However, a final decision for pyrasulfotole may be issued without the Agency having previously issued an interim decision. A final decision on the pyrasulfotole registration review case will occur after: (1) an EDSP FFDCA § 408(p) determination, and (2) an endangered species determination under the ESA and any needed § 7 consultation with the Services.

B. Implementation of Mitigation Measures

Once the Interim Registration Review Decision is issued, the pyrasulfotole registrants must submit amended labels that include the label changes described in Appendices A and B. 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.

Appendix A: Summary of Proposed Actions for Pyrasulfotole

Registration Review Case#: 7272
PC Code: 000692
Chemical Type: Herbicide
Chemical Family: Pyrazoles
Mechanism of Action: Inhibition of Hydroxyphenyl Pyruvate Dioxygenase (HPPD)

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions	Comment
• Mammals	• Dietary	• Ingestion	• Chronic	• Increase in time to maturity (3 days)	• Spray drift management • Non-target organism advisory	
• Terrestrial plants (dicots)	• Spray drift • Runoff	• Root absorption • Foliar absorption	• N/A	• Reduced dry weight	• Spray drift management	Risks from spray drift extends to 33 ft from the edge of the field for ground application and 256 ft for aerial application.

Appendix B: Proposed Labeling Changes for Pyrasulfotole Products

<table>
<tr><th>Description</th><th>Proposed Label Language for Pyrasulfotole Products</th><th>Placement on Label</th></tr>
<tr><td></td><td>End Use Products</td><td></td></tr>
<tr><td>Mechanism of Action Group Number</td><td>Note to registrant:
Include the name of the ACTIVE INGREDIENT in the first column
Include the word “GROUP” in the second column
Include the MODE/MECHANISM/SITE OF ACTION CODE in the third column (for fungicides this is the FRAC Code, and for insecticides this is the Primary Site of Action; for Herbicides this is SITE OF ACTION)
Include the type of pesticide (i.e., HERBICIDE) in the fourth column.
<table><tr><td>PYRASULFOTOLE</td><td>GROUP</td><td>27</td><td>HERBICIDE</td></tr></table></td><td>Front Panel, upper right quadrant.
All text should be black, bold face and all caps on a white background, except the mode of action code, which should be white, bold face and all caps on a black background; all text and columns should be surrounded by a black rectangle.</td></tr>
<tr><td>Non-target Organism Advisory</td><td>“NON-TARGET ORGANISM ADVISORY: This product is toxic to plants and may adversely impact the forage and habitat of non-target organisms, including pollinators, in areas adjacent to the treated site. Protect the forage and habitat of non-target organisms by following label directions intended to minimize spray drift.”</td><td>Environmental Hazards</td></tr>
<tr><td>Surface Water Advisory</td><td>“This product may impact surface water quality due to runoff of rain water. This is especially true for poorly draining soils and soils with shallow ground water. This product is classified as having a medium potential for reaching both surface water and aquatic sediment via runoff for several months or more after application. A level, well-maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential loading of pyrasulfotole from runoff water and sediment. Runoff of this product will be reduced by avoiding applications when rainfall or irrigation is expected to occur within 48 hours.”</td><td>Environmental Hazards</td></tr>
<tr><td>Groundwater Advisory</td><td>“This chemical has properties and characteristics associated with chemicals detected in groundwater. This chemical may leach into groundwater if used in areas where soils are permeable, particularly where the water table is shallow.

Users are advised not to apply pyrasulfotole where soils have a rapid to very rapid permeability (such as loamy sand to sand) and the water table of an underlying aquifer is shallow or to soils containing sinkholes over limestone bedrock,</td><td>Environmental Hazards</td></tr>
</table>

Description	Proposed Label Language for Pyrasulfotole Products	Placement on Label
	severely fractured surfaces, and substrates which would allow direct introduction into an aquifer. Your local agricultural agencies can provide further information on the type of soil in your area and the location of groundwater."	
HERBICIDE RESISTANCE MANAGEMENT: Weed Resistance Management	Include resistance management label language for herbicides from PRN 2017-1 and PRN 2017-2 (https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year)	Directions for Use, prior to directions for specific crops under the heading "WEED RESISTANCE-MANAGEMENT"
Spray Drift Management Application Restrictions for all products delivered via liquid spray application and allow aerial application	**"MANDATORY SPRAY DRIFT MANAGEMENT** **Aerial Applications**: • Do not release spray at a height greater than 10 ft above the ground or vegetative canopy, unless a greater application height is necessary for pilot safety. • Applicators are required to use a fine or coarser droplet size (ASABE S641). • If the windspeed is 10 miles per hour or less, applicators must use ½ swath displacement upwind at the downwind edge of the field. When the windspeed is between 11-15 miles per hour, applicators must use ¾ swath displacement upwind at the downwind edge of the field. • Do not apply when wind speeds exceed 15 mph at the application site. If the windspeed is greater than 10 mph, the boom length must be 65% or less of the wingspan for fixed wing aircraft and 75% or less of the rotor diameter for helicopters. Otherwise, the boom length must be 75% or less of the wingspan for fixed-wing aircraft and 90% or less of the rotor diameter for helicopters. • Do not apply during temperature inversions."	Directions for Use, in a box titled "Mandatory Spray Drift Management" under the heading "Aerial Applications" Placement for these statements should be in general directions for use, before and use-specific directions for use.
Spray Drift Management Application Restrictions for products that are applied as liquids and allow ground boom applications	**"MANDATORY SPRAY DRIFT MANAGEMENT** **Ground Boom Applications:** • User must only apply with the release height recommended by the manufacturer, but no more than 4 feet above the ground or crop canopy. • Applicators are required to use a fine or coarser droplet size (ASABE S572). • Do not apply when wind speeds exceed 15 mph at the application site. • Do not apply during temperature inversions."	Directions for Use, in a box titled "Mandatory Spray Drift Management" under the heading "Ground Boom Applications"

Description	Proposed Label Language for Pyrasulfotole Products	Placement on Label
Advisory Spray Drift Management Language for all products delivered via liquid spray application	**"SPRAY DRIFT ADVISORIES** THE APPLICATOR IS RESPONSIBLE FOR AVOIDING OFF-SITE SPRAY DRIFT. BE AWARE OF NEARBY NON-TARGET SITES AND ENVIRONMENTAL CONDITIONS. **IMPORTANCE OF DROPLET SIZE** An effective way to reduce spray drift is to apply large droplets. Use the largest droplets that provide target pest control. While applying larger droplets will reduce spray drift, the potential for drift will be greater if applications are made improperly or under unfavorable environmental conditions. **Controlling Droplet Size – Ground Boom** ***(note to registrants:*** *remove if ground boom is prohibited on product labels)* • Volume - Increasing the spray volume so that larger droplets are produced will reduce spray drift. Use the highest practical spray volume for the application. If a greater spray volume is needed, consider using a nozzle with a higher flow rate. • Pressure - Use the lowest spray pressure recommended for the nozzle to produce the target spray volume and droplet size. • Spray Nozzle - Use a spray nozzle that is designed for the intended application. Consider using nozzles designed to reduce drift. **Controlling Droplet Size – Aircraft** ***(note to registrants:*** *remove if aerial application is prohibited on product labels)* • Adjust Nozzles - Follow nozzle manufacturers' recommendations for setting up nozzles. Generally, to reduce fine droplets, nozzles should be oriented parallel with the airflow in flight. **BOOM HEIGHT – Ground Boom** ***(note to registrants:*** *remove if ground boom is prohibited on product labels)* For ground equipment, the boom should remain level with the crop and have minimal bounce. **RELEASE HEIGHT - Aircraft** ***(note to registrants:*** *remove if aerial application is prohibited on product labels)* Higher release heights increase the potential for spray drift. **SHIELDED SPRAYERS** Shielding the boom or individual nozzles can reduce spray drift. Consider using shielded sprayers. Verify that the shields are not interfering with the uniform deposition of the spray on the target area. **TEMPERATURE AND HUMIDITY** When making applications in hot and dry conditions, use larger droplets to reduce effects of evaporation. **TEMPERATURE INVERSIONS**	Directions for Use, just below the Spray Drift box, under the heading "Spray Drift Advisories"

Description	Proposed Label Language for Pyrasulfotole Products	Placement on Label
	Drift potential is high during a temperature inversion. Temperature inversions are characterized by increasing temperature with altitude and are common on nights with limited cloud cover and light to no wind. The presence of an inversion can be indicated by ground fog or by the movement of smoke from a ground source or an aircraft smoke generator. Smoke that layers and moves laterally in a concentrated cloud (under low wind conditions) indicates an inversion, while smoke that moves upward and rapidly dissipates indicates good vertical air mixing. Avoid applications during temperature inversions. **WIND** Drift potential generally increases with wind speed. AVOID APPLICATIONS DURING GUSTY WIND CONDITIONS. Applicators need to be familiar with local wind patterns and terrain that could affect spray drift."	

Appendix C: Endangered Species Assessment

In 2013, EPA, along with the Fish and Wildlife Service (FWS), the National Marine Fisheries Service (NMFS), and the United States Department of Agriculture (USDA) released a summary of their joint Interim Approaches for assessing risks to endangered and threatened (listed) species from pesticides. These Interim Approaches were developed jointly by the agencies in response to the National Academy of Sciences' (NAS) recommendations that discussed specific scientific and technical issues related to the development of pesticide risk assessments conducted on federally threatened and endangered species.

Since that time, EPA has conducted biological evaluations (BEs) on three pilot chemicals representing the first nationwide pesticide consultations (final pilot BEs for chlorpyrifos, malathion, and diazinon were completed in January 2017). These initial pilot consultations were envisioned to be the start of an iterative process. The agencies are continuing to work to improve the consultation process. For example, after receiving input from the Services and USDA on proposed revisions to the pilot interim method and after consideration of public comments received, EPA released an updated *Revised Method for National Level Listed Species Biological Evaluations of Conventional Pesticides* (i.e., Revised Method) in March 2020.[18] During the same timeframe, EPA also released draft BEs for carbaryl and methomyl, which were the first to be conducted using the Revised Method.

Also, a provision in the December 2018 Farm Bill included the establishment of a FIFRA Interagency Working Group (IWG) to provide recommendations for improving the consultation process required under section 7 of the Endangered Species Act for pesticide registration and Registration Review and to increase opportunities for stakeholder input. This group includes representation from EPA, NMFS, FWS, USDA, and the Council on Environmental Quality (CEQ). Given this new law and that the first nationwide pesticide consultations were envisioned as pilots, the agencies are continuing to work collaboratively as consistent with the congressional intent of this new statutory provision. EPA has been tasked with a lead role in this group, and EPA hosted the first Principals Working Group meeting on June 6, 2019. The recommendations from the IWG and progress on implementing those recommendations are outlined in reports to Congress.[19]

Given that the agencies are continuing to work toward implementation of the Revised Method to assess the potential risks of pesticides to listed species and their designated critical habitat, the ecological risk assessment supporting this PID for pyrasulfotole does not contain a complete ESA analysis that includes effects determinations for specific listed species or designated critical habitat. Although EPA has not yet completed effects determinations for specific species or habitats, for this PID, EPA's evaluation assumed, for all taxa of non-target wildlife and plants, that listed species and designated critical habitats may be present in the vicinity of the application of pyrasulfotole. This will allow EPA to focus its future evaluations on the types of species where the potential for effects exists once the Revised Method has been fully

[18] https://www.regulations.gov/document?D=EPA-HQ-OPP-2019-0185-0084

[19] https://www.epa.gov/endangered-species/reports-congress-improving-consultation-process-under-endangered-species-act

implemented. Once that occurs, the Revised Method will be applied to subsequent analyses for pyrasulfotole as part of completing this registration review.

Appendix D: Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, sub-chronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision for pyrasulfotole, the EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA § 408(p), pyrasulfotole is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA § 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The Agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013,[20] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. Pyrasulfotole is not on either list. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, visit EPA website.[21]

[20] See http://www regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[21] https://www.epa.gov/endocrine-disruption

In this PID, EPA is making no human health or environmental safety findings associated with the EDSP screening of pyrasulfotole. Before completing this registration review, the Agency will make an EDSP FFDCA § 408(p) determination.