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Fludioxonil

Proposed Interim Registration Review Decision
Case Number 7017

March 2018

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Table of Contents

I. INTRODUCTION

This document is the Environmental Protection Agency's (EPA or the Agency) Proposed Interim Registration Review Decision (PID) for fludioxonil (PC Code 071503, case 7017), and is being issued pursuant to 40 CFR sections 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 fludioxonil, can be found in EPA's public docket (EPA-HQ-OPP-2010-1067) 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 the 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 as http://www.epa.gov/pesticide-reevaluation. In 2006, the Agency implemented the registration review program pursuant to FIFRA section 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 a PID for fludioxonil so that it can (1) move forward with aspects of the registration review that are complete and (2) implement interim risk mitigation. The Agency is currently working with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (together, the Services) to develop methodologies for conducting national threatened and endangered (listed) species assessments for pesticides. Therefore, although EPA has not yet fully evaluated risks to listed species, the Agency will complete its listed species assessment and any necessary consultation with the Services for fludioxonil prior to completing the fludioxonil registration review. Likewise, the Agency will complete endocrine screening for fludioxonil, pursuant to the Federal Food, Drug, and Cosmetic Act (FFDCA) section 408(p), before completing registration review. Last, EPA will determine whether pollinator exposure and effects data are necessary to make a final registration review decision for fludioxonil and issue a data call-in (DCI) to obtain any such data prior to completing the fludioxonil registration review. See Appendices C and D, respectively, for additional information on the endangered species assessment and the endocrine screening for the fludioxonil registration review.

Fludioxonil [4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1*H*-pyrrole-3-carbonitrile] is a broad-spectrum contact fungicide and antimicrobial. Fludioxonil belongs to the chemical class of phenylpyrroles, which are derived from a natural antimycotic compound isolated from a soil bacterium. As an antimicrobial, fludioxonil is registered as a materials preservative. Major agricultural pesticide uses of fludioxonil include seed treatment for potatoes, cereal grains, peanuts, rice, cotton, soybeans, popcorn seed. Post-harvest uses include dips, sprays, drenches (*e.g.*, on pome fruits, stone fruits, and carrots); along with other foliar uses such as on ornamentals, turf, Brussels sprouts, strawberries, grapes, pistachios, and potatoes.

Residential use sites for fludioxonil as a conventional pesticide include treatment of ornamentals and residential turf. As an antimicrobial, fludioxonil is used as a preservative in products for residential use such as paint, caulk, and adhesives. Fludioxonil was first registered in 1995 and was not subject to reregistration.

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 fludioxonil 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; the *Proposed Interim Registration Review Decision*, which describes the mitigation measures proposed to address risks of concern and the regulatory rationale for EPA's registration review decision; and, lastly, the *Next Steps and Timeline* for completion of this registration review.

A. Summary of Fludioxonil Registration Review

Pursuant to 40 CFR section 155.50, EPA formally initiated Registration Review for fludioxonil 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 fludioxonil.

- June 2011 – The *Fludioxonil Summary Document*, Human Health Scoping Document, and Environmental Fate and Effects Problem Formulation were posted to the docket for a 60-day public comment period.

- January 2012 – The *Final Work Plan* (FWP) for fludioxonil was issued. During the 60-day comment period for the Human Health Scoping Document and Environmental Fate and Effects Problem Formulation, comments were received from Syngenta and the Northwest Horticultural Council. Anticipated data requirements were modified following review of Syngenta's comments. These comments were addressed in *Fludioxonil; Response to Comments from the Northwest Horticultural Council and Syngenta concerning the Fludioxonil Scoping Document* dated October 27, 2011 and the *Response to the Initial 60-Day Public Comments on "Registration Review – Preliminary Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Assessments for Fludioxonil"* dated November 8, 2011.

- July 2013 – A Generic Data Call-In (GDCI) for fludioxonil was issued for data needed to conduct the registration review risk assessments. All data required by the GDCI have been submitted and evaluated by the EPA.

- December 2017 – The Agency announced the availability of the *Fludioxonil Preliminary Human Health Risk Assessment for Registration Review* and the *Preliminary Environmental Fate and Ecological Risk Assessment* for a 60-day public comment period. Six comments were received from six sources during the comment period. These comments and the Agency's responses are summarized below. The comments did not change the risk assessments or registration review timeline for fludioxonil.

- March 2018 – The Agency completed the PID and will be soon be announcing the availability of the PID in the docket for fludioxonil, for a 60-day public comment period.

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

During the 60-day public comment period for the fludioxonil Draft Risk Assessments, which opened on December 15, 2017 and closed on February 15, 2018, the Agency received public comments from six sources. Comments were submitted by USDA, IR-4, Syngenta, the University of Arizona, and two comments were received by the general public. 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 Registration Review Proposed Interim Decision. The comments did not change the risk assessments or registration review timeline for fludioxonil.

Comments Submitted by USDA in EPA-HQ-OPP-2010-1067-0023

Comment: USDA offered comments on fludioxonil's role in 1) fungicide resistance management; 2) disease management in vegetables, pome and stone fruit, sweet potatoes, lettuce, and berries and small fruits; 3) the impact of select diseases on these crops; and 4) a comparison with other fungicides to treat various crops and diseases. USDA discussed the average application rate and noted that the average number of applications was around 1 annually, with the exception of 1.7 applications annually and 2.7 applications annually on average on caneberries and strawberries, respectively.

EPA Response: The Agency thanks the USDA for the comments and information they provided and considered them in the development of this Proposed Interim Registration Review Decision. EPA agrees with USDA regarding fludioxonil as a beneficial option for use in rotation with other fungicides.

Comments Submitted by IR-4 in EPA-HQ-OPP-2010-1067-0027

Comment: IR-4 cited specific fludioxonil-containing products and described the benefits of fludioxonil for treating post-harvest diseases in specialty crops. Specifically, IR-4 noted the

importance on fludioxonil to control soft rot caused by *Rhizopus stolonifer* and black rot caused by *Ceratocystis jimbriata* in sweet potato. Fludioxonil is also used to treat brown rot, gray mold, and other foliar, stem, and root diseases. Additional specialty crops cited include kiwi, pomegranate, star fruit, sugar apple, and avocado.

EPA Response: The Agency acknowledges that fludioxonil is a useful post-harvest disease management tool and it is registered to treat diseases across a wide range of uses. These comments were considered in the development of this Proposed Interim Decision for fludioxonil.

Comments Submitted by University of Arizona in EPA-HQ-OPP-2010-1067-0032

Comment: The University of Arizona commented on the importance of fludioxonil for uses in select southwest desert cropping systems including potatoes, melons, and lettuce in controlling plant diseases such as *Monosporascus cannonballus* and *Sclerotinia*. The comments described the planting practices for potato seed treatment and the economic contribution of these crops.

EPA Response: EPA appreciates input from the University of Arizona and considered this information for this Proposed Interim Registration Review Decision.

Comments Submitted by Syngenta in EPA-HQ-OPP-2010-1067-0031

Comment: Comments submitted by Syngenta focused on the *Preliminary Environmental Fate and Ecological Risk Assessment* for fludioxonil. Syngenta cited differences in input parameters for the Pesticide Water Calculator (PWC) and the determination of estimated environmental concentrations (EEC).

EPA Response: The Agency addresses these comments in full detail in the *Response to Comments on the Preliminary Environmental Fate and Ecological Risk Assessment for Fludioxonil* and will issue the responses to comments in the docket.

Comments Submitted by members of the public in EPA-HQ-OPP-2010-1067

Comment: Comments submitted by members of the public were brief and expressed concerns for general environmental regulations.

EPA Response: The Agency appreciates all comments and acknowledges the concerns and perspectives on the registration review process for conventional pesticides. Because these comments did not address documents and information pertaining to fludioxonil specifically, they did not influence the outcome of this Proposed Interim Registration Review Decision.

II. USE AND USAGE

Fludioxonil is a non-systemic, contact phenyl-pyrrole fungicide registered for use on a variety of field and vegetable crops, fruit trees, berries, herbs, and grasses. Phenyl-pyrroles inhibit mycelial growth of fungi by targeting signal transduction in the high osmolarity glycerol (HOG)

response pathway. In conventional applications, fludioxonil is mainly used for seed treatment and foliar application against many fungi considered to be pathogenic to plants, such as *Fusarium, Rhizoctonia, Telletia, Helminthosporium, Botrytis. Monilinia and Alternaria,* along with fungi responsible for post-harvest diseases caused by *Monilinia fructicola* and *M. laxa* (brown rot), *Botrytis cinerea* (gray mold), and *Rhizopus stolonifer* (Rhizopus rot). Fludioxonil can be applied as a seed treatment, an at-planting soil application, or by aerial and ground applications including drip irrigation, ground boom spray, fogging, and impregnated material. Post-harvest uses are also allowed on selected fruit and root crops. Fludioxonil is also registered for use in residential areas, including parks, golf courses, athletic fields, residential lawns, ornamentals, and greenhouses. Formulations include emulsifiable concentrates, water dispersible granules, ready-to-use solutions, and pressurized liquids.

For all agricultural uses, the largest markets in terms of seed treatment from 2011 – 2014 were soybeans and cotton, together accounting for 96% of all acres of seed treated with fludioxonil. Annually, an average of 54,000 pounds of fludioxonil were applied to 27.8 million acres via seed treatment. From 2011 – 2015, 58,800 pounds of active ingredient were applied annually via aerial, ground, and chemigation methods to 278,700 acres. Lettuce, strawberries, grapes and caneberries are the largest uses based on acres treated, accounting for 87% of all non-seed treated acres.

Fludioxonil is also registered for use as an antimicrobial pesticide. It is incorporated during the manufacturing process of the following articles: paper, wallboard (drywall and gypsum board) and paperboard products; ceiling tiles; water-based paints, stains, and coatings; latex caulks, sealants, adhesives, and binders; natural and synthetic fibers such as textiles, fabrics, canvas and cordage (not for apparel), carpet backing, boat covers, awnings; and rubber and plastic products (PVC, thermoplastic rubber, foams, etc). Treated articles are for non-food contact.

As of March 2018, there are 102 active conventional and antimicrobial registrations for end-use products containing fludioxonil, including six registrations under FIFRA §24(c) for special local needs (SLN).

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 fludioxonil. For additional details on the human health assessment for fludioxonil, see the *Fludioxonil Preliminary Human Health Risk Assessment for Registration Review,* which is available in the public docket.

1. Risk Summary and Characterization

Dietary (Food + Drinking Water) Risks

An acute dietary exposure assessment was not conducted since an acute endpoint of concern attributable to a single dose was not identified for the general U.S. population or any population subgroup. The highest chronic dietary (food + drinking water) exposure estimate, utilizing unrefined default exposure assumptions including tolerance-level residues and 100 percent of all crops treated with fludioxonil, was for the population subgroup children 1-2 years old, which utilized 71% of the chronic population-adjusted dose (cPAD) for fludioxonil. The Agency found no dietary (food + drinking water) risks of concern for fludioxonil.

Cancer Risks

Fludioxonil is classified as a "Group D chemical – not classifiable as to human carcinogenicity" and, therefore, it is not expected to pose a cancer risk.

Residential Handler Risks

All registered non-antimicrobial fludioxonil end-use product labels with residential use sites (*e.g.*, lawns) require that handlers wear specific clothing (*i.e.*, long-sleeve shirt/long pants) and/or use personal protective equipment (PPE). Therefore, EPA has made the assumption that these products are not for homeowner use and has not conducted a quantitative residential handler assessment.

Residential handler exposures are expected based on registered antimicrobial uses, such as for fludioxonil-treated paints that can be used by residential handlers. For antimicrobials, the paint use is expected to represent the high end of the residential handler exposure potential compared to the other uses of fludioxonil (*e.g.*, caulk, adhesives). No dermal exposure endpoints of concern were identified for fludioxonil, but exposures through inhalation routes do have established endpoints. There were no risks of concern identified for homeowners applying fludioxonil-treated paint (inhalation margins of exposure (MOEs) >15,000; level of concern (LOC) = 100).

Residential Post-Application Risks

Conventional fungicide residential post-application scenarios did not present risks of concern. The quantitative exposure/risk assessment for residential post-application exposures is based on incidental oral exposures to children. MOEs for these scenarios (hand-to-mouth, object-to-mouth, soil-to-mouth) range from 4,600 to 2,100,000 (LOC = 100). There is minimal post-application exposure/contact expected for the registered antimicrobial uses (*e.g.*, paint, carpet backing, awnings, caulk, etc.). In addition, minimal release of vapor is expected based on the low vapor pressure of fludioxonil. Therefore, dermal, inhalation, and incidental oral exposures for the antimicrobial uses have not been quantified.

Spray Drift/Bystander Risks

A quantitative spray drift/bystander risk assessment for fludioxonil was not conducted because the maximum direct spray residential turf application rate is greater than the maximum application rate to a crop/target site multiplied by the adjustment factor for drift for any fludioxonil product. Therefore, residential exposure assessment values are considered protective of bystanders exposed to fludioxonil via spray drift. All MOEs for residential exposures were above the LOC of 100 for adults and children; therefore, no bystander risks of concern from fludioxonil were identified.

Aggregate Risks

No aggregate risks (dietary + residential) were found to be of concern considering all potential exposure durations (*i.e.*, acute, short-term, intermediate-term and chronic). Only short-term and chronic exposure durations are relevant considering available toxicity endpoints (no acute endpoint of concern) and available use patterns for fludioxonil. All short-term aggregate exposure MOEs were greater than 200 (LOC = 100), and since there are no registered uses of fludioxonil that result in intermediate or long-term (chronic) residential exposures, the chronic aggregate risk assessment is equivalent to the chronic dietary (food + drinking water) assessment.

Cumulative Risks

EPA has not made a common mechanism of toxicity to humans finding as to fludioxonil and any other substance and it does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has not assumed that fludioxonil has a common mechanism of toxicity with other substances for this assessment.

Occupational Handler Risks

EPA evaluated potential occupational risks associated with mixing/loading (*i.e.*, handling) and applying of fludioxonil products based on the anticipated use patterns, formulation types, and application methods. A quantitative dermal assessment was not conducted as no toxicological hazard was identified up to the limit dose in the dermal toxicity study. Inhalation risks, however, were assessed.

No occupational inhalation exposure scenarios resulted in risk estimates of concern at baseline personal protective equipment (PPE). MOEs for occupational handlers (inhalation) exposure were at or above the Agency's LOC (100) ranging from 100 to 740,000,000 when handlers utilized current label required PPE (long-sleeved shirt and long pants, shoes plus socks; fogging products also require chemical-resistant gloves, protective eyewear, and respirator).

There are no occupational handler inhalation risk estimates of concern (MOEs $\geq$ 4,500) for the antimicrobial paint uses of fludioxonil with baseline level of personal protection (*i.e.*, no respirator). The paint use is expected to represent the high end of the inhalation exposure potential for the other antimicrobial uses of fludioxonil, and, thus is protective of those uses.

Occupational Post-Application Risks

The term, post-application exposure, or re-entry exposure, is used to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide. Inhalation exposure to handlers resulting from application of pesticides outdoors is likely to result in higher exposure than would be expected for workers entering a previously treated area to conduct various activities. Therefore, it is expected that occupational handler inhalation exposure estimates would be protective of most occupational post-application inhalation exposure scenarios (including the commercial painters).

Based on fludioxonil's uses, short and intermediate-term post-application exposures are expected. The inhalation MOE for post-application exposures to sorters and packers of fruits and vegetables is 5,000 on the day of application with an LOC of 100. Ambient air exposure resulted in an inhalation MOE of 110,000 on the day of application. No post-application scenarios present risks of concern.

Fludioxonil is not a skin sensitizer. It is classified as Toxicity Category IV for skin irritation potential and Toxicity Category III via the dermal route. The Worker Protection Standard restricted entry interval (REI) (40 CFR 156, subpart K) of 12 hours is considered adequate to protect agricultural workers from post-application exposures to fludioxonil. There are no antimicrobial occupational post-application scenarios which present risks of concern.

2. Human Incidents and Epidemiology

Human health incident cases were previously reviewed in 2011 (S. Recore, D384927, 03/01/2011). Based on the low severity and frequency of cases reported to both the Incident Data System (IDS) and the System for Occupational Risk (SENSOR) Pesticides, there does not appear to be a concern at this time that would warrant further investigation.

In the current IDS analysis covering the timeframe from January 1, 2012 to July 13, 2017, 25 cases were reported to Main IDS and 28 cases reported to Aggregate IDS involving fludioxonil. Fourteen cases involving fludioxonil were identified in a query of SENSOR-Pesticides from 1998-2013. Other active ingredients were included in the incidents reported in the Main IDS. For the Aggregate IDS, one incident had no or unknown effect and 27 incidents were classified as minor severity.

Based on the continued low frequency and severity of fludioxonil incidents reported to both systems, there does not appear to be a concern for fludioxonil at this time. The Agency will continue to monitor the incident data and if a concern is triggered, additional analysis will be conducted.

3. Tolerances

The fludioxonil tolerance expressions established in 40 CFR §180.516 should be updated as to incorporate newly revised crop group definitions and correct the number of significant figures in accordance with Agency policy. The proposed changes are listed in Table 1. The U.S. residue definition in plants is harmonized with Canada, Codex, and Mexico; for livestock commodities, the U.S. residue definition is harmonized with Codex, but not Canada. Note that Mexico adopts U.S. tolerances and/or Codex Maximum Residue Limits (MRLs) for its export purposes. Canada and Codex have established MRLs for residues of fludioxonil in/on a number of raw agricultural commodities that are not harmonized with U.S. tolerances. The Agency is not proposing changing the U.S. tolerances for residues of fludioxonil in order to harmonize with the Canadian and/or Codex MRLs at this time as the U.S. patters differ too greatly from the Canadian and/or Codex MRLs.

Table 1. Summary of Recommended Tolerance Revisions for Fludioxonil.

Commodity	Currently Established Tolerance (ppm)	Proposed Tolerance Revisions (ppm)	Comments (*correct commodity definition*)
Bean, dry	0.4	0.40	Correct number of significant figures to be consistent with HED policy.
Bean, succulent	0.4	0.40	Correct number of significant figures to be consistent with HED policy.
Celtuce	-	15	Commodity displaced by the crop group conversion.
Fennel, florence, fresh leaves and stalk	-	15	Commodity displaced by the crop group conversion.
Brassica, head and stem, subgroup 5A	0.70	0.70	Brassica, *head and stem, group 5-16*
Brassica, leafy greens, subgroup 5B	10	10	Brassica *leafy greens subgroup 4-16B*
Kohlrabi	-	2.0	Commodity displaced by the crop group conversion.
Leaf petioles subgroup 4B	15	15	*Leaf petiole vegetable subgroup 22B*
Leafy greens subgroup 4A	30	30	*Leafy greens subgroup 4-16A*
Turnip, greens	10	-	Tolerance should be revoked upon establishment of *Brassica* leafy greens subgroup 4-16B.
Vegetable, root and tuber, group 1, except sugar beet	0.75	0.75	*Vegetable, root and tuber (except sugar beet), subgroup 1B*
Watercress	7.0	-	Tolerance should be revoked upon establishment of Leafy greens, subgroup 4-16A.

4. Human Health Data Needs

The Agency does not anticipate any further data needs for fludioxonil. There were no data deficiencies identified in the toxicological, residue chemistry, or exposure databases.

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 fludioxonil. The amount of fludioxonil used in antimicrobial applications is considerably lower compared to the amount used in conventional applications. A qualitative review indicates a low potential for exposure to non-target organisms from the antimicrobial use of fludioxinil. Sporgard WB (EPA Reg. No. 39967-87), the one antimicrobial product, contains a low amount of fludioxonil (1.92%) that is expected to adhere or remain in the treated products. Wallboard paper, which is the highest use in terms of pounds applied for antimicrobial uses, is not exposed to the outdoors and is therefore not subject to leaching by rainfall. Given the limited potential for exposure to nontarget organisms and the minimal amount of fludioxonil used in antimicrobial applications, ecological risks from exposure due to antimicrobial applications are considered very low and unlikely and were not quantified. Therefore, the potential ecological risks presented in this proposed interim decision are based on the registered conventional, or agricultural uses of fludioxonil. For additional details on the ecological assessment for fludioxonil, see the *Preliminary Environmental Fate and Ecological Risk Assessment for Fludioxonil*, which is available in the public docket.

EPA is currently working with federal partners and other stakeholders to implement an interim approach 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 are finalized, the Agency will complete its endangered species assessment for fludioxonil. 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

Fludioxonil is characterized as slightly-to-practically non-toxic to mammals on an acute exposure basis (LD_{50} >5,000 mg ai/kg-diet). Although the acute toxicity study with mammals had non-definitive results and no effects were observed, acute risk quotients (RQs) were calculated based on the highest dose tested (LD_{50}=5,000 mg/kg-bw) for screening purposes. For the use site with the highest application rate (turf, 0.707 lb ai/A), the highest acute mammalian RQ is 0.04, which is below the LOC for acute risk of 0.50. Thus, potential acute risks to mammals from exposure to the registered uses of fludioxonil on crops are not of concern. Risks based on the seed treatment uses also do not exceed the LOC for acute risk for mammals.

Potential chronic risk estimates for mammals are based on a No Observed Adverse Effect Concentration (NOAEC) of 300 mg ai/kg-diet in which pup body weights were reduced after exposure to fludioxonil in a developmental toxicity study with rats. For the foliar uses, chronic dose-based RQs range from 0.14 -13.0 and exceed the chronic risk LOC of 1.0 for small (20 g), medium (100 g) and large (1,000 g) mammals feeding on most food items (short grasses, tall grasses, broadleaf plants) for the foliar spray uses evaluated. Dietary-based RQ values range from 0.04 to 1.5 and exceed the chronic risk LOC of 1.0 for mammals feeding on short grass for turf and ornamental uses of fludioxonil. Dietary RQs for uses on cole crops, dry beans/peas, grapes, garlic, potatoes and strawberries do not exceed the LOC for chronic dietary risk. Further, post-harvest applications, such as dips and drenches, often take place in a warehouse or location where exposure to the field is limited. Approximately 99% of the total acres treated with fludioxonil are done via seed treatment, and that accounts for 48% of the total pounds applied of fludioxonil annually. Mammalian risks based on the seed treatment uses do not exceed the LOC of 1.0 for chronic risk. As a result, risks to mammals from seed treatments and post-harvest applications are not expected. While potential risks from foliar uses have been identified, given the predominant uses of fludioxonil and current label language requiring spray drift buffers or other restrictions, potential risks from dietary exposure are only expected in a very limited number of scenarios.

Birds, Reptiles, and Terrestrial-Phase Amphibians

Similar to mammals, fludioxonil is also characterized as slightly-to-practically non-toxic to birds (LD_{50} >2,000 mg a.i./kg-bw; LC_{50}: 3,280 mg ai/kg-diet) on an acute exposure basis. Acute risks to birds do not exceed the LOC of 0.5 for non-listed bird species (acute RQs = 0.14 – 0.49).

Potential chronic risk estimates for birds are based on a NOAEC of 303 mg a.i./kg-diet in which effects on embryo viability were observed in the chronic reproduction toxicity study with Northern bobwhite quail. For the foliar uses, chronic dose-based RQs range from <0.01 to 1.5. The RQs for fludioxonil use on ornamentals and turf are 1.5, which exceed the LOC of 1.0 for chronic risk to birds. As noted previously, seed treatment accounts for the majority of the total acres treated with fludioxonil. Avian risks based on the seed treatment uses do not exceed the LOC and potential risk from foliar uses only exceed the LOC for turf and ornamental uses with birds feeding on short grass; therefore, potential risks to birds are considered low.

Invertebrates (honeybees)

Fludioxonil is practically non-toxic to honey bees on an acute exposure basis (LD_{50}>25 µg a.i./bee). The toxicity endpoint for honey bees is non-definitive (*i.e.*, the LD_{50} value is greater than the highest test concentration). RQs were not formally calculated as there is uncertainty as to how much higher exposure would have to be to achieve a definitive LD_{50}. However, if the LD_{50} were assumed to equal 25 µg a.i./bee, the acute contact RQ (0.08) would not exceed the acute risk LOC of 0.4 for the highest application rate (turf application rate: 0.707 lbs. a.i./A). Since there are no data for acute oral toxicity to bees, there is uncertainty regarding acute risk through the oral route.

Although no chronic toxicity was observed in the 10-day study with honey bees, chronic risk was assessed with Bee REX using the results of the feeding study with a NOAEC of 44.06 µg ai/bee. The chronic RQ is 0.52 and does not exceed the chronic LOC of 1.0. Thus, risk to adult honey bees is not a concern. However, acute and chronic toxicity data are lacking for larval honey bees and, therefore, risk cannot be determined.

EPA believes that additional data may be necessary to fully evaluate risks to non-target terrestrial invertebrates, especially pollinators. Although EPA identified the need for certain data to evaluate potential effects to pollinators when initially scoping the registration review for fludioxonil, the problem formulation and registration review DCI for fludioxonil were both issued prior to EPA's issuance of the June 2014 *Guidance for Assessing Pesticide Risks to Bees*[1]. This 2014 guidance lists additional pollinator studies that were not included in the fludioxonil registration review DCI. Therefore, EPA is currently determining whether additional pollinator data are needed for fludioxonil. If the Agency determines that additional pollinator exposure and effects data are necessary to help make a final registration review decision for fludioxonil, then EPA will issue a DCI to obtain these data. The pollinator studies that could be required for fludioxonil are listed in Table 2 below.

Table 2. Potential Pollinator Data Requirements for Fludioxonil

Guideline	Study
850.3020	Acute contact toxicity study with adult honey bees (Tier 1)
Non-Guideline (OECD 213)	Honey bee adult acute oral toxicity (Tier 1)
Non-Guideline (OECD 237)	Honey bee larvae acute oral toxicity (Tier 1)
Non-Guideline	Honey bee adult chronic oral toxicity (Tier 1)
Non-Guideline	Honey bee larvae chronic oral toxicity (Tier 1)
Non-Guideline†	Field trial of residues in pollen and nectar (Tier 2)
Non-Guideline (OECD 75) †	Semi-field testing for pollinators (Tier 2)
850.3040†	Full-Field testing for pollinators (Tier 3)

† The need for higher Tier tests for pollinators will be determined based upon the results of lower Tiered tests and/or other lines of evidence and the need for a refined pollinator risk assessment.

Terrestrial Plants

For terrestrial plants, both seedling emergence and vegetative vigor studies are available. The most sensitive endpoint for plants is the NOAEC of 0.074 lb ai/A, from the seedling emergence study in which the height of corn (*Zea mays*) was adversely affected. An EC_{25} was not available for either monocots or dicots from the seedling emergence study. However, an EC_{25} for dicots (oilseed rape) is available from a vegetative vigor study. The most sensitive dicot species was oilseed rape (*Brassica napus*), based on dry weight with an EC_{25} value of 0.318 lbs ai/A. The terrestrial plant RQs range from <0.01 to 1.1. RQs for listed monocot plants inhabiting semi-aquatic areas only slightly exceed the LOC of 1.0 with use on ornamentals (RQ=1.01) and turf (RQ=1.05). RQs from these uses do not exceed the LOC for dicots (dicot RQ=<0.01). Further, RQs based on spray drift do not exceed the LOC of 1.0 for risk to terrestrial monocots and dicots

[1] http://www2.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf

for applications to any of the registered use sites (RQ=0.15 for monocots, RQ=<0.01 for dicots) at the edge of field.

Aquatic Risks

Fish and Aquatic-Phase Amphibians

On an acute basis, risks of concern were not identified for estuarine/marine fish or freshwater fish as well as for the species which they serve as surrogates, aquatic-phase amphibians. Acute RQs, ranging from 0.01 – 0.17, were below the Agency's LOC of 0.5. Chronic RQ exceedances, however, showed potential risks of concern with an RQ range of <1.0 – 3.0 when considering the buffers to aquatic water bodies that are specified on labels. Reduced hatching success was identified as a chronic toxicity endpoint. With the use of buffers as required by some labels, risks to freshwater fish from use on garlic, strawberries, and Brussels sprouts were reduced to below the LOC. Buffer language on labels includes prohibiting applications within 75 feet of bodies of water (*e.g.*, lakes, reservoirs, rivers, natural ponds, etc.) and restrict cultivation within 10 feet of aquatic areas as to allow a vegetative filter strip. Spray drift buffers reduced RQs for estuarine/marine fish to below the LOC for all uses except ornamentals. Seed treatment uses do not result in aquatic exposure, and no risk to aquatic organisms is presumed for seed treatment uses. Based on the most significant use pattern for fludioxonil and current label language, the Agency considers the extent of potential for risks to fish to be limited.

Freshwater Invertebrates

No acute risks of concern were identified for freshwater invertebrates; all acute RQs were below the Agency's LOC of 0.5 (RQs = 0.01 – 0.09). RQ exceedances were calculated for chronic risks of concern, however, when considering the spray drift buffers required on labels, RQ's range from <1.0 – 3.6. Chronic studies indicated a reduction of body weight in sediment-dwelling midge, *Chironomus dilutus*. The highest RQs were the result of foliar applications of fludioxonil. Conversely, seed treatment uses did not result in measurable aquatic exposures based on preliminary modeling; seed treatment comprises approximately 99% of total acres treated with fludioxonil and 48% of total pounds applied. Thus, risks to aquatic organisms from seed treatment uses is considered negligible. Potential risks from fludioxonil exposure as a result of foliar treatment are expected only for a minimal range of uses and scenarios with foliar spray applications.

Estuarine/Marine Invertebrates

Results of the aquatic risk assessment found that estuarine/marine invertebrates are considered more sensitive to fludioxonil than freshwater invertebrates. Acute RQs ranged from 0.97 – 4.97 when considering use of the currently required spray drift buffers. Chronic RQs, ranged from 2.12 – 10.0 with use of buffers. Chronic tests showed reductions of male body length in mysid shrimp. As with freshwater invertebrates, foliar applications presented the highest potential for risk, whereas no risks are considered present as a result of seed-treatment, the major use of fludioxonil in terms of acres treated.

Aquatic Vascular and Non-Vascular Plants

For aquatic vascular plants, RQ values ranged from 0.02 to 0.12 and do not exceed the LOC of 1.0 for any of the assessed uses. The RQ values for non-vascular plants ranged from 0.04 - 0.28 and are below the LOC. The effect observed in the toxicity studies for non-vascular plants is reduced biomass (growth) and for vascular plants the effect is reduced frond number (growth). The Agency considers risk to aquatic plants from fludioxonil exposure to be low.

2. Ecological Incidents

EPA searched the Environmental Incident Information System (EIIS) database on May 19, 2017 for the timeframe from January 1, 2000 to May 19, 2017 and identified 13 ecological incidents that may have involved exposures to fludioxonil. Incidents in EIIS are defined by a certainty index that describes the likelihood of the pesticide application described resulting in the observed incident. The certainty index defines incidents as "unrelated," "unlikely," "possible," "probable," or "highly probable."

Nine of the thirteen incidents reported plant damage possibly resulting from direct treatments of fludioxonil. However, all but one of the reports included other pesticides which could have caused the damage. The only reported incident involving fludioxonil alone was of damage to a species of plant that is known to be sensitive to fludioxonil. Four of the incidents included reports of dead bees, although all of the reports including bee mortality included possible exposure to chemicals that are more acutely toxic than fludioxonil to bees (*e.g.*, clothianidin, thiamethoxam). Current labels for drench applications identify that foliar or drench applications to some varieties of geraniums may cause stunting or chlorosis (labels have a warning about the sensitivity of impatiens).

3. Ecological and Environmental Fate Data Needs

There are no data gaps for the environmental fate studies. However, only limited data are available to assess the potential toxicity of fludioxonil to bees and the single toxicity acute contact value for formulated fludioxonil is non-definitive. While there are no data to indicate that exposure to fludioxonil will result in direct adverse effects on bees, adult acute and chronic oral toxicity and larval acute/chronic dietary toxicity data are not available. EPA will consider issuing a DCI to obtain pollinator data as a separate action.

C. Benefits Assessment

Fludioxonil is a non-systemic fungicide that inhibits mycelial growth of fungi by inhibition of transport-associated phosphorylation of glucose. As a conventional fungicide, fludioxonil is primarily used as a seed treatment and foliar application to treat pathogenic plant fungi, including *Rhizoctonia*, *Telletia*, *Fusarium*, *Helminthosporium. Alternaria*, *Botrytis*, and *Monilinia*.

Fludioxonil is registered for use on numerous crops including beans, berry crops, leafy vegetables, brassica leafy vegetables, bulb vegetables, tuberous and corm vegetables, corn, pome fruit, citrus, cucurbits, pomegranates, eggplant, tomato litchi, herbs and spices, and ornamentals. Fludioxonil is also registered as a materials preservative for paper, wallboard (drywall and gypsum board) and paperboard products; ceiling tiles; water-based paints, stains, and coatings; latex caulks, sealants, adhesives, and binders; natural and synthetic fibers such as textiles, fabrics, canvas and cordage (not for apparel), carpet backing, boat covers, awnings; and rubber and plastic products (PVC, thermoplastic rubber, foams, etc).

The largest use of fludioxonil as a conventional pesticide is as a seed treatment for soybeans. The wide range of formulations available, ability to use pre- and post-harvest, and the flexibility to use fludioxonil with either ground or aerial equipment, is beneficial to the grower. Fludioxonil represents a useful tool as U.S. growers work to adopt recommendations to use fungicides with different modes of action to manage resistant fungi for the purpose of mitigating the development of fungicide resistance in common agricultural pathogens.

IV. PROPOSED INTERIM REGISTRATION REVIEW DECISION

A. Proposed Risk Mitigation and Regulatory Rationale

The Agency has reviewed the risks and benefits associated with the registered uses of fludioxonil. Risks of concern were not identified for human health when products containing solely fludioxonil are used in accordance with label instructions. At this time, the Agency is proposing advisory spray drift language based on the low likelihood of exceedances to the Agency's levels of concern, the limited scenarios where potential risks are expected to exceed levels of concern, and the benefits of fludioxonil use. However, the addition of the proposed spray drift advisory language is expected to reduce potential exposure to non-target species. In addition, the Agency is also proposing fungicide resistance management language to reduce development of fungicide resistance.

The EPA is also proposing label changes to address generic labeling requirements for Personal Protective Equipment (PPE) for all conventional fludioxonil products and uses (see Appendix B). There is no mitigation proposed for antimicrobial uses.

1. Spray Drift Reduction

EPA is proposing label changes to reduce the potential for off-target spray drift and establish a baseline level of protection against spray drift that is consistent across all fludioxonil 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 proposed 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 fludioxonil. In addition, the use of buffers as required by several labels will further lessen exposure to fludioxonil.

The Agency is proposing standardized spray drift advisory language to be included on all fludioxonil product labels with foliar and post-harvest use sites (see Appendix B). Registrants must ensure that any existing advisory language left on labels does not contradict or modify the new spray drift statements proposed in this proposed interim decision once effective.

2. Fungicide Resistance Management

Pesticide resistance in a pest species develops over time because of selection pressure placed on the population from the repeated use of a single mechanism of action. A few individuals with natural resistance to the pesticide can survive an application of the pesticide. As these individuals reproduce and as each generation is exposed to the pesticide, the proportion of resistant individuals in the population can increase and eventually resistant individuals may dominate the population. The speed at which this genetic shift occurs in the genetic frequency in the population depends on the intensity of the selection pressure. Variance in the intensity of selection pressure depends upon the interaction of characteristics of the chemical, characteristic of the pest species, and characteristics of the crop production system.

The Agency is concerned about resistance issues and considers that managing the development of pesticide resistance, in conjunction with alternative pest management strategies and Integrated Pest Management (IPM) programs, is an important part of sustainable pest management. EPA is proposing resistance-management labeling, as listed in Appendix B, for conventional products containing the fungicide, fludioxonil, in order to provide pesticide users with easy access to important information to help maintain the effectiveness of useful pesticides. Additional information on EPA's guidance for resistance management can be found in PRN 2017-1 at the following website: https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year.

B. Tolerance Actions

The tolerance expression for fludioxonil in 40 CFR §180.516 will be revised to update crop group definitions and correct the number of significant figures for consistency with EPA policy. Refer to Section III.A.3 for details.

C. Proposed Interim Registration Review Decision

In accordance with 40 CFR sections 155.56 and 155.58, the Agency is issuing this Proposed Interim Registration Review Decision. Except for the Endangered Species Act (ESA), Endocrine Disruptor Screening Program (EDSP), and pollinator components of this case, the Agency has made the following Proposed Interim Registration Review Decision: (1) no additional data are required at this time; and (2) changes to the affected registrations or their labeling are needed at this time, as described in Sections IV A and Appendix A.

In this proposed interim registration review decision, EPA is making no human health or environmental safety findings associated with the EDSP screening of fludioxonil, nor is the

Agency making a complete endangered species finding or a complete assessment of effects to pollinators. Although the Agency is not making a complete endangered species finding at this time, the proposed mitigation described in this document is expected to reduce the extent of environmental exposure and may reduce risk to listed species whose range and/or critical habitat co-occur with the use of fludioxonil. The Agency's final registration review decision for fludioxonil will be dependent upon the result of the Agency's ESA assessment, any needed Section 7 consultation with the Services, an EDSP FFDCA section 408(p) determination, and an assessment of non-target exposure to pollinators (bees).

D. Data Requirements

No additional data are anticipated to be needed to be called-in for this chemical at this time. The EPA will consider requiring the submission of pollinator data as a separate action.

V. NEXT STEPS AND TIMELINE

A. Proposed Interim Registration Review Decision

A Federal Register Notice will announce the availability of this proposed interim registration review decision for fludioxonil, and will allow a 60-day comment period on the proposed interim decision. 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, the EPA may issue an interim registration review decision for fludioxonil. However, a final decision for fludioxonil may be issued without the Agency having previously issued an interim decision. A final decision on the fludioxonil registration review case will occur after: (1) an EDSP FFDCA section 408(p) determination, (2) an endangered species determination under the ESA and any needed Section 7 consultation with the Services, and (3) an assessment of non-target exposure to pollinators.

B. Implementation of Mitigation Measures

Once the Interim Registration Review Decision is issued, the fludioxonil registrants must submit amended labels that include the label changes described in Appendix B. The revised labels must be submitted to the Agency for review within 60 days following issuance of the Interim Registration Review Decision.

Appendix A: Summary of Proposed Actions for Fludioxonil

Registration Review Case#: 7017
PC Code: 071503
Chemical Type: Fungicide
Chemical Family: Phenyl-pyrrole
Mode of Action: Protein kinase inhibition

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions	Comment (use to briefly clarify or elaborate on risk or mitigation)
Avian	Residues (at/on site of treatment) Dietary	Ingestion	Chronic	Reproductive	Require advisory spray drift reduction language.	Risks based on the seed treatment uses (which comprise the majority of fludioxonil usage) do not exceed LOCs for acute risk for birds or mammals. Post-harvest applications are likely to be made in a warehouse or away from the field which do not result in non-target exposure.
Mammals	Residues (at/on site of treatment) Dietary	Ingestion	Chronic	Growth effects		

Aquatic	Runoff and spray drift to water and sediment	Respiration Ingestion	Acute Chronic	Reproductive Mortality Growth effects	Require advisory spray drift reduction language.	Seed treatment uses of fludioxonil do not result in measurable aquatic exposure. Post-harvest applications are likely to be made in a warehouse or away from the field which did not result in non-target exposure. Some label language includes spray drift buffers to minimize exposure to aquatic systems.

Appendix B: Proposed Labeling Changes for Conventional Fludioxonil Products

<table>
<tr><th>Description</th><th>Proposed Label Language for Fludioxonil Products</th><th>Placement on Label</th></tr>
<tr><td></td><td>End Use Products</td><td></td></tr>
<tr><td>Mode/Mechanism of Action Group Number</td><td>

Include the name of the ACTIVE INGREDIENT in the first column
Include the word “GROUP” in the second column
Include the MODE OF ACTION CODE in the third column

Include the type of pesticide (i.e., HERBICIDE or FUNGICIDE or INSECTICIDE) in the fourth column

Example:
<table>
<tr><td>FLUDIOXONIL</td><td>CODE</td><td>12
as designated by FRAC</td><td>FUNGICIDE</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>Resistance-management for fungicides and bactericides</td><td>The following general resistance-management labeling statements are recommended for fungicide products containing only a single active ingredient or multiple active ingredients that are from the same mode of action group:

“For resistance management, (name of product) contains a Group (mode of action group number) fungicide. Any fungal population may contain individuals naturally resistant to (name of product) and other Group (mode of action group number) fungicides. A gradual or total loss of pest control may occur over time if these fungicides are used repeatedly in the same fields. Appropriate resistance-management strategies should be followed.”

For products containing two or more active ingredients from different groups, the statement should be modified to reflect the situation. For example:

“For resistance management, please note that (name of product) contains both a Group (mode of action group number)/ [common name] and Group (mode of action group number)/ [common name] fungicide. Any fungal population may contain individuals naturally resistant to (name of product) and other Group (mode of action group number) or Group (mode of action group number) fungicides/. A gradual or total loss of pest control may occur over time if these (fungicides) are used repeatedly in the same fields. Appropriate resistance-management strategies should be followed.”</td><td>Directions for Use</td></tr>
</table>

Description	Proposed Label Language for Fludioxonil Products	Placement on Label
Resistance-management labeling statements for fungicides/bactericides	• Include resistance management label language for fungicides/bactericides from PRN 2017-1 (https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year)	Directions for Use
Updated Respirator Language	For products containing fludioxonil which require respirator language (*e.g.*, foggers): PF 5 respiratory protection (only available for protection from particulates only, low volatility products): "Wear a minimum of a NIOSH-approved filtering facepiece respirator with any N*, R or P filter (TC-84A); OR an elastomeric NIOSH-approved particulate respirator with any N*, R or P filter (TC-84A); OR a NIOSH-approved powered air purifying respirator with an HE filter (TC-21C)." *Drop the "N" option if there is oil in the product's formulation and/or the product is labeled for mixing with oil-containing products. PF 10 respiratory protection: "Wear a minimum of an elastomeric half face NIOSH-approved respirator with" [***Registrant pick product specific option here:*** (1 – low volatility, particulate protection) "any N*, R or P filter (TC-84A), OR a full face NIOSH-approved particulate respirator with any N*, R or P filter (TC-84A); OR a NIOSH-approved powered air purifying respirator with an HE filter (TC-21C)." (2 – organic vapor and particulate protection) "organic vapor (OV) cartridges and a combination N*, R, or P filter (TC-84A); OR a NIOSH-approved gas mask with an OV canister (TC-14G); OR a NIOSH-approved powered air purifying respirator with an OV cartridge and combination HE filter (TC-23C)." (3-organic vapor only) "organic vapor (OV) cartridges (TC-23C); OR a NIOSH-approved full face respirator with OV cartridges; OR a gas mask with an OV canister; OR a powered air purifying respirator with an OV cartridge." *Drop the "N" option if there is oil in the product's formulation and/or the product is labeled for mixing with oil-containing products.	In the Personal Protective Equipment (PPE) within the Precautionary Statements
Updated Gloves Statement	For products containing fludioxonil which require glove statements, outdated glove statements must be updated to identify the appropriate glove type on the label, per the Label Review Manual (LRM) (Chapter 10). Registrants can no longer reference LRM category charts.	In the Personal Protective Equipment (PPE) within the Precautionary Statements

Description	Proposed Label Language for Fludioxonil Products	Placement on Label
Advisory Spray Drift Management Language for all conventional products with foliar and post-harvest use sites.	**"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 Fludioxonil 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."	
Advisory Spray Drift Management Language for products that allow boom-less ground sprayer applications	**"SPRAY DRIFT** **Boom-less Ground Applications:** • Setting nozzles at the lowest effective height will help to reduce the potential for spray drift."	Directions for Use, just below the Spray Drift box, under the heading "Spray Drift Advisories"
Advisory Spray Drift Management Language for products that allow applications with handheld technologies	**"SPRAY DRIFT** **Handheld Technology Applications:** • Take precautions to minimize spray drift."	Directions for Use, just below the Spray Drift box, under the heading "Spray Drift Advisories"

Appendix C: Endangered Species Assessment

In November 2013, the EPA, along with the Services 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. The Interim Approaches were developed jointly by the agencies in response to the National Academy of Sciences' (NAS) recommendations and reflect a common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. The NAS report[2] outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the ESA and FIFRA.

As part of a phased, iterative process for developing the Interim Approaches, the agencies will also consider public comments on the Interim Approaches in connection with the development of upcoming Registration Review decisions. The details of the joint Interim Approaches are contained in the white paper *Interim Approaches for National-Level Pesticide Endangered Species Act (ESA) Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report*[3], dated November 1, 2013.

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, the ecological risk assessment supporting this Proposed Interim Decision for fludioxonil 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 proposed interim decision 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 fludioxonil. This assessment will allow EPA to focus its future evaluations on the types of species where the potential for effects exists once the scientific methods being developed by the agencies have been fully vetted. Once the agencies have fully developed and implemented the scientific methodology for evaluating risks for listed species and their designated critical habitats, these methods will be applied to subsequent analyses for fludioxonil 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,

[2] *Assessing Risks to Endangered and Threatened Species from Pesticides.* Available at http://www.nap.edu/catalog.php?record_id=18344
[3] Available at http://www2.epa.gov/endangered-species/assessing-pesticides-under-endangered-species-act#report

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 fludioxonil, 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 section 408(p), fludioxonil 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 section 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[4] 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. Fludioxonil 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, please visit our website.[5]

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

[4] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[5] http://www.epa.gov/endo/