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Carboxin and Oxycarboxin

Proposed Interim Registration Review Decision
Case Number 0012

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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 Carboxin (PC Code 090201) and Oxycarboxin (PC Code 090202) (case 0012) and is being issued pursuant to 40 CFR §§ 155.56 and 155.58. These chemicals are being reviewed together because oxycarboxin is a transformation product of carboxin, and both chemicals have registered pesticide uses. 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 carboxin and oxycarboxin can be found in EPA's public dockets for this case at (EPA-HQ-OPP-2004-0124: "Carboxin; Risk Assessments; Notice of Availability") and (EPA-HQ-OPP-2015-0144: "Carboxin and Oxycarboxin Registration Review") at www.regulations.gov.

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

EPA is issuing a PID for carboxin and oxycarboxin 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). The Agency is currently working with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (collectively referred to as, "the Services") to improve the consultation process for national threatened and endangered (listed) species for pesticides in accordance with the Endangered Species Act (ESA) § 7. Therefore, although EPA has not yet fully evaluated risks to federally listed species (hereafter referred to as "listed" species), the Agency will complete its listed species assessment and any necessary consultation with the Services for carboxin and oxycarboxin prior to completing the carboxin and oxycarboxin registration review. Likewise, the Agency will complete endocrine screening for carboxin and oxycarboxin, pursuant to the Federal Food, Drug, and Cosmetic Act (FFDCA) § 408(p), before completing registration review. See Appendices C and D, respectively, for additional information

on the listed species assessment and the endocrine screening for the carboxin and oxycarboxin registration review.

Carboxin and oxycarboxin are oxathiin-carboxamide class fungicides which are systemic in plants and are used on a variety of agricultural and ornamental crops. Their systemic nature makes them valuable for controlling seed-borne and seedling diseases, primarily *Basidiomycete* pathogens such as rusts, smuts, and bunts. Products containing carboxin are registered for use as a seed treatment on crops that include wheat, barley, oats, corn, cotton, peanuts, soybeans, safflower, beans, and as a dip for ornamental bulbs and corms. Carboxin can be applied to seeds at commercial seed treatment facilities and through on-farm seed treatment applications. There are no other agricultural or non-agricultural uses for carboxin. Oxycarboxin has a single agricultural use and is only applied to foliage on ornamental plants inside greenhouses to control rust diseases. There are no registered residential uses for carboxin or oxycarboxin. Carboxin was first registered in 1968 and oxycarboxin was first registered in 1971. The Reregistration Eligibility Decision (RED) for both chemicals was completed in 2004. Carboxin and oxycarboxin currently have one technical registrant, MacDermid Agricultural Solutions, Inc.

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 carboxin and oxycarboxin are 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 Carboxin and Oxycarboxin Registration Review

Pursuant to 40 CFR § 155.50, EPA formally initiated registration review for carboxin and oxycarboxin 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 carboxin and oxycarboxin.

- March 2015 – The *Carboxin and Oxycarboxin Preliminary Work Plan* (PWP) (dated March 12, 2015); *Carboxin and Oxycarboxin: Human Health Scoping Document in Support of Registration Review* (dated February 24, 2015); and *Preliminary Problem Formulation for the Drinking Water and Ecological Risk Assessments of Carboxin and Oxycarboxin* (dated March 11, 2015)*;* were posted to the docket for a 60-day public comment period (posted in Docket #: EPA-HQ-OPP-2015-0144).

- September 2015 – The *Carboxin and Oxycarboxin Final Work Plan (FWP)* (dated September 11, 2015) was issued and posted to the docket along with the *EFED Response to Comments on the Problem Formulation for the Registration Review of Carboxin/Oxycarboxin* (dated July 15, 2015) (Posted in Docket #: EPA-HQ-OPP-2015-0144). The FWP included a description of public comments on the *Carboxin and*

Oxycarboxin Preliminary Work Plan. Comments were received from the Center for Biological Diversity, Physicians for Responsible Medicine, the FIFRA Endangered Species Task Force; and MacDermid Agricultural Solutions, Inc., the technical registrant. There were no comments that resulted in changes to the regulatory timeline or anticipated risk assessments. The registrant indicated their intent to amend the label for oxycarboxin to read "for use in enclosed commercial greenhouses", as recommended in the *Preliminary Problem Formulation for the Drinking Water Ecological Risk Assessments of Carboxin and Oxycarboxin*, which eliminated the need for several ecological toxicity studies. No other comments resulted in changes to the anticipated data requirements.

- September 2016 – Generic Data Call-In (GDCI) notices for carboxin (GDCI-090201-1538) and oxycarboxin (GDCI-090202-1539) were issued for data needed to conduct the registration review risk assessments (posted in Docket #: EPA-HQ-OPP-2004-0124). All required data were submitted or waived. The Subchronic Inhalation Study (870.3465) was waived with the addition of an APF10 respirator to several occupational scenarios. Based on the results of the Tier 1 honey bee data (i.e., laboratory studies) submitted and other lines of evidence, EPA has decided that additional higher tier (Tier 2 and 3) honey bee data (*i.e.* semi-field/field studies) are not needed. See Section III for details.

- February 2020 – The Agency announced the availability of the following preliminary human health and ecological risk assessments and supporting documents for a 60-day public comment period (posted in Docket #: EPA-HQ-OPP-2004-0124):
    - *Carboxin and Oxycarboxin: Draft Human Health Risk Assessment for Registration Review* (dated December 10, 2019)
    - *Carboxin: Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments in Support of Registration Review* (dated December 10, 2019)
    - *Carboxin and Oxycarboxin: Occupational and Residential Exposure and Risk Assessment in Support of Registration Review* (dated December 10, 2019)
    - *Carboxin and Oxycarboxin: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment* (dated June 12, 2019)
    - *Carboxin and Oxycarboxin: Draft Ecological Risk Assessment for Registration Review* (dated May 29, 2019)

  The Agency received comments from four sources. These comments and the Agency's responses are summarized below. The comments led to revisions to the occupational risk assessments for carboxin but did not change the registration review timeline for carboxin and oxycarboxin.

- September 2020 – The Agency is now announcing the availability of the PID in the docket for carboxin and oxycarboxin for a 60-day public comment period (Docket #: EPA-HQ-OPP-2015-0144). Along with the PID, the following documents are also posted to the carboxin and oxycarboxin docket and are available for public comment:
    - *Carboxin/Oxycarboxin: Response to Comments on the Human Health Draft Risk Assessment for Registration Review* (dated August 20, 2020)
    - *Response to United States Department of Agriculture (USDA) Comments on the Preliminary Environmental Fate and Ecological Risk Assessment for Carboxin and Oxycarboxin* (dated September 2, 2020).

- *Carboxin and Oxycarboxin Use, Benefits, and Impacts Assessment (PC Code# 090201; 090202)*, (dated September 18, 2020).

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

During the 60-day public comment period for the Carboxin and Oxycarboxin Draft Risk Assessments, which opened on February 4, 2020 and closed on April 4, 2020, the Agency received public comments from four sources. Comments were submitted by the technical registrant, MacDermid Agricultural Solutions, Inc.; the United States Department of Agriculture, Office of Pest Management Policy; the American Seed Trade Association (ASTA); and an anonymous public commenter. Substantive comments, comments of a broader regulatory nature, and the Agency's responses to those comments are summarized below. The Agency thanks all contributors for their comments and has considered them in developing this PID.

Comment Submitted by MacDermid Agricultural Solutions, Inc. in EPA-HQ-OPP-2004-0124-0044

Comment: The technical registrant, MacDermid, commented on the human health risk assessment's recommendation that APF10 respirators should be required for eight occupational scenarios involving commercial seed treatment with carboxin to ensure acceptable levels of risk. The registrant indicated that if risk estimates use typical application and seed treatment rates, rather than the maximum label application rates (as used in the human health risk assessment), three of the eight occupational exposure scenarios identified by the Agency should have acceptable levels of risk and should not require the use of APF10 respirators.

EPA Response: The Agency's response to these concerns can be found in the memorandum *Carboxin/Oxycarboxin: Response to Comments on the Human Health Draft Risk Assessment for Registration Review* (dated August 20, 2020), publishing simultaneously with this PID. EPA agrees with the registrant's calculations for the carboxin occupational handler exposure scenarios using a revised application rate for cereal grains (barley, oats, triticale, and wheat) and a revised amount of seeds treated per day for dried beans and soybeans. Based on the revised calculations, the Agency no longer considers these three scenarios to be of concern. However, the exposure estimate in the risk assessment for the scenario involving succulent beans (lima, snap) already uses the typical rates and continues to exceed the Agency's Level of Concern (LOC).

Comment Submitted by the United States Department of Agriculture (USDA) in EPA-HQ-OPP-2004-0124-0045

Comment: USDA noted that carboxin products provide effective treatment for a wide variety of crops – often in combination with other chemicals – and are important to the seed treatment industry. In the ecological risk assessment, USDA suggested that the Agency revise calculations using data from the National Agricultural Statistics Service (NASS) for seeding rates and application rates, which are more typical of field conditions and are lower than the maximum label rates used in the draft risk assessments. For the human health draft risk assessments, USDA suggested that the Agency refine assumptions about the amount of seed treated per day; suggested labeling language for the 4-month plant back intervals (PBIs) to ensure growers

clearly understand which registered crops may be planted back immediately; and recommended EPA incorporate updated data from a recent study of backpack and handgun pesticide application into the oxycarboxin risk mitigation plan. USDA also recommended that EPA work with the registrant to ensure that product labeling updates are included on labels for commercially treated seed (*e.g.*, seed bag tags) to ensure that planting is conducted in accordance with the mitigation on the pesticide labels.

EPA Response: The Agency's full responses to USDA can be found in the memoranda *Carboxin/Oxycarboxin: Response to Comments on the Human Health Draft Risk Assessment for Registration Review* (dated August 20, 2020); and *Response to United States Department of Agriculture (USDA) Comments on the Preliminary Environmental Fate and Ecological Risk Assessment for Carboxin and Oxycarboxin* (dated September 2, 2020). To summarize:

- EPA revised assumptions on the application rate and amount of seed treated per day for the occupational scenarios in the human health risk assessment involving commercial treatment of seed with carboxin on cereal grains, beans, and soybeans. The full response is provided above to the previous comment from the technical registrant, MacDermid.
- EPA thanks the USDA for the suggested PBI language and has incorporated the recommendation into the proposed PBI language in this PID (see Section IV.A.)
- EPA revised the risk estimate for the application of oxycarboxin to ornamentals in greenhouses using mechanically pressurized handguns. The margin of exposure (MOE) improved from 330 to 510, but without an APF10 respirator still exceeds the LOC.
- EPA thanks USDA for comments on the ecological risk assessment. EPA maintains that the modeling assumptions made are protective and consistent with approved scientific policy on risk assessments. Use of the suggested NASS data would not affect the overall risk profile of carboxin to foraging birds and mammals. EPA has provided an updated table in the response to the USDA's comments with corrections to the maximum annual application rates for soybeans, succulent beans, and cotton.
- EPA appreciates USDA's recommendation that labeling updates also be placed on bag tags for commercially treated seed. EPA has incorporated this recommendation into the "Treated Seed Labeling" updates (see Section IV.A. and Appendix B).

Comment Submitted by the American Seed Trade Association (ASTA) in EPA-HQ-OPP-2004-0124-0043

Comment: ASTA describes the history and importance of carboxin as a fungicidal seed treatment with systemic activity, its importance to resistance management through complementary use with other fungicidal seed treatment chemicals, and its usefulness for a wide variety of crops at low cost. ASTA notes that carboxin plays a major role in facilitating the global seed trade and its use is required for the export of corn seeds to several countries. ASTA also highlights the usefulness of carboxin products on dry beans/pulses, peanuts, soybeans, and corn/sweet corn, four of its more common uses.

EPA Response: EPA thanks ASTA for their comment regarding the benefits and importance of carboxin and has taken it into consideration in the PID.

II. USE AND USAGE

Carboxin is a systemic seed treatment fungicide used to control soil-borne seed and seedling diseases on barley, beans, canola, corn, cotton, grasses grown for seed, oats, onions, peanuts, peas, rice, rye, safflower, clary sage, soybeans, triticale, and wheat. Carboxin is also used as an ornamental (bulbs/corms) dip treatment to control *Rhizoctonia* root rot. Formulations include dust and flowable, emulsifiable, and soluble concentrates, as well as ready-to-use liquids. Carboxin is applied to seeds prior to planting both by commercial seed treaters and on-farm applicators. Oxycarboxin is wettable powder fungicide used as a foliar spray to control rust diseases of ornamentals grown in greenhouses.

There are limited usage data available for pesticidal seed treatments, including carboxin. Carboxin was widely used in the past as a seed treatment fungicide on cotton, peanuts, soybeans, and wheat[1]. However, reliable national level carboxin usage data were not found for any of the registered uses because they are either not surveyed (barley, beans/peas, clary sage, grasses grown for seed, oats, ornamentals, rye, safflower, and triticale) or surveyed but no reliable carboxin usage data were found (canola, corn, cotton, onions, rice, soybeans, and wheat). On the state level, recent data from California show that the predominant use of carboxin is on dry onions where an average of 500 lb ai were applied annually between 2013 and 2017. Small amounts of carboxin were also used in California on peas and dried beans during the same period[2]. No reports of carboxin usage were found for other states.

Current oxycarboxin usage information is not available.

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 carboxin and oxycarboxin. For additional details on the human health assessment for carboxin and oxycarboxin, see the *Carboxin and Oxycarboxin: Draft Human Health Risk assessment for Registration Review,* which is available in the public docket, EPA-HQ-OPP-2004-0124.

The anticipated exposure pathways from carboxin include dietary (food and water) and occupational exposure. Application of carboxin as a seed treatment may lead to human exposure through residue uptake into crops or runoff of residues from treated seed into surface- and ground-water sourced drinking water. Dermal and inhalation exposures are expected for occupational handlers engaged in commercial and on-farm seed treatment, seed planting, and from dipping ornamental corms/bulbs. Anticipated exposure pathways for oxycarboxin include

[1] Kynetec USA, Inc. 2019. "The AgroTrak Study from Kynetec USA, Inc." Database Subset: 2010-2014.
[2] California Department of Pesticide Regulation. 2013-2017.

occupational dermal and inhalation exposure to handlers and post-application dermal exposures from applications to ornamental plants. Dietary (food and water) exposure to oxycarboxin is not anticipated since it is not registered on food/feed crops, and it is only applied inside greenhouses.

1. Risk Summary and Characterization

The Agency found potential human health risks of concern for eight occupational handler scenarios involving the application of carboxin in commercial seed treatment facilities, and one occupational scenario involving the use of mechanically pressurized handguns to apply oxycarboxin in greenhouses. The Agency found no other human health risks of concern from registered uses of carboxin and oxycarboxin.

Dietary (Food + Water) Risks
The human health risk assessment did not identify any risks of concern from dietary exposure to carboxin. An acute dietary risk assessment for carboxin was not necessary because no acute endpoint attributable to a single dose was identified. The carboxin chronic dietary exposure and risk estimates are not of concern for the general U.S. population or any population subgroups (<100% of the chronic population adjusted dose (cPAD)). The most highly exposed population subgroup is children 1-2 years old at 74% of the cPAD.

Carboxin is classified as "Not Likely to be Carcinogenic to Humans." Quantification of cancer risk was not necessary.

Dietary exposure (food and water) from oxycarboxin is not anticipated because it is only registered for use in enclosed greenhouses for applications to ornamental plants. Therefore, there is not a dietary risk from the use of oxycarboxin.

Residential Handler and Residential Post-Application Risks
Because there are no registered or proposed residential uses for carboxin and oxycarboxin, a residential exposure assessment has not been conducted. Any potential residential exposure from consumers handling bulbs treated with carboxin is negligible due to the intermittent nature of this contact, and no dermal toxicity endpoint was selected for carboxin.

Bystander Risks
All registered uses of carboxin (*i.e.*, seed treatments) are not expected to result in spray drift, and all uses of oxycarboxin are indoors. Therefore, spray drift exposures to the chemicals have not been assessed.

Aggregate Risks
The aggregate risk assessment considers estimates from dietary (food + drinking water) and residential exposures. Since there are no residential uses, all aggregate exposures to carboxin are equivalent to dietary exposure estimates. Due to the lack of an acute dietary endpoint, EPA did not conduct an acute dietary risk assessment, and therefore did not conduct an acute aggregate risk assessment. The chronic risk estimates for all populations resulting from aggregate exposure to carboxin in food and drinking water are below the level of concern (<100% cPAD). Since

carboxin is classified as "Not Likely to be Carcinogenic to Humans," quantification of cancer aggregate risk was not necessary.

Cumulative Risks
EPA has not made a common mechanism of toxicity to humans finding, and therefore has not assumed that carboxin or oxycarboxin have a common mechanism of toxicity with other substances.

Occupational Handler Risks
Based on anticipated use patterns, types of equipment and techniques used, and current labeling, the registered uses of carboxin and oxycarboxin can be expected to lead to occupational handler exposure. The Agency conducted only an assessment of inhalation exposure and risk. A dermal endpoint was not selected because effects were only seen at the limit dose of 1000 mg/kg/day, which is not relevant for human health risk assessments.

A sub-chronic inhalation study was not available for carboxin and oxycarboxin and is normally required to select an endpoint. In the absence of this study, a sub-chronic oral toxicity study in rats was used to select short- and intermediate-term inhalation exposure endpoints, resulting in a NOAEL of 5.5 mg/kg/day (selected as the point of departure) and a LOAEL of 10.5 mg/kg/day. The LOAEL is based on an increased kidney histopathology and chronic progressive neuropathy in male rats. For occupational scenarios, the LOC selected is 1000 (10X for interspecies extrapolation, 10X for intraspecies extrapolation, and a 10X database uncertainty factor (UF_{DB})) for the lack of a sub-chronic inhalation toxicity study. Inhalation toxicity is assumed to be equivalent to oral toxicity based on route-to-route extrapolation using a weight of evidence approach[3].

No risks of concern were identified for the majority of carboxin occupational exposure scenarios evaluated, which include workers performing on-farm seed treatment, planting seed, and dipping ornamental bulbs/corms.

In the DRA, risks of concern were identified for several occupational handler inhalation exposure scenarios during commercial seed treatment with carboxin, with MOEs ranging from 620 to 980 (LOC = 1000). Based on comments received, the Agency revised the application rate and amount of seeds treated per day for several scenarios to refine the MOEs, which improved the MOEs for two scenarios.

The final eight scenarios that numerically exceed the LOC (MOEs < 1000) are listed below. Scenarios assume workers wear baseline attire (*i.e.*, long-sleeved shirt, long pants, socks, and shoes) and chemical-resistant gloves. Exposure would be within acceptable levels and not be of concern (*i.e.*, with MOEs ≥ 1000) if a respirator with a 10X assigned protection factor (APF10) is worn.

[3] See Louden, R. September 20, 2019. Carboxin/Oxycarboxin: Summary of Hazard and Science Policy Council (HASPOC) Meeting on September 19, 2019: Recommendations on the Need for a Subchronic Inhalation Study. TXR No. 0057945.

Carboxin

- ***Commercial seed treatment (multiple activities) for liquid-formulated products:*** Activities involve cleaning and maintenance of seed treatment equipment (*e.g.*, scraping, wiping, brushing, and vacuuming of the mixing, delivery, or treatment chamber using compressed air and/or pressurized water) (LOC = 1000).
    - **Corn (field and sweet):** the estimated inhalation MOE of 620 increases to 6,200 with the addition of an APF10 respirator.
    - **Beans (dried type):** the estimated inhalation MOE of 980 increases to 9,800 with the addition of an APF10 respirator.
    - **Succulent beans (lima, snap)**: the estimated inhalation MOE of 810 increases to 8,100 with the addition of an APF10 respirator.
    - **Soybeans:** the estimated inhalation MOE of 980 increases to 9,800 with the addition of an APF10 respirator.

- ***Commercial seed treatment (mixing/loading) for dust-formulated products*** (LOC = 1000):
    - **Barley, oats, and wheat:** the estimated inhalation MOE of 890 increases to 8,900 with the addition of an APF10 respirator.
    - **Beans (dried type) and succulent beans (lima, snap):** the estimated inhalation MOE of 750 increases to 7,500 with the addition of an APF10 respirator.
    - **Peas (dried type, succulent)[4]:** the estimated inhalation MOE of 750 increases to 7,500 with the addition of an APF10 respirator.
    - **Soybeans**: the estimated inhalation MOE of 900 increases to 9,000 with the addition of an APF10 respirator.

For oxycarboxin, the occupational handler inhalation MOEs were also estimated using the oral POD of 5.5 mg/kg/day for use on greenhouse ornamentals. Of the three scenarios assessed, only the following scenario has a risk of concern without the use of an APF10 respirator:

Oxycarboxin

- ***Mixing/loading/applying with a mechanically pressurized handgun (greenhouse ornamentals, wettable powder)*** (LOC = 1000): the estimated inhalation MOE of 510 increases to 5,100 with addition of APF10 respirator.

Occupational Post-Application Risks

An occupational post-application inhalation exposure assessment is not necessary for carboxin or oxycarboxin because exposure is expected to be negligible. Assessments carried out for seed treaters, sprayers, and secondary handlers (*i.e.*, seed planters) are expected to be protective of any low-level post-application inhalation exposure that could result from registered applications.

For carboxin and oxycarboxin, dermal post-application exposure is expected but was not quantified because a dermal exposure endpoint was not selected. Occupational post-application

[4] Carboxin use on peas is currently listed on some labels but not supported by a tolerance. If a tolerance is established and this use is re-approved, this peas scenario would require an APF10 respirator to not be of concern.

exposure is not expected following applications to treated ornamental corms/bulbs because the packaging process is automated and does not require contact with the treated corms/bulbs.

Labeled carboxin and oxycarboxin restricted entry intervals (REIs) range from 12 to 24 hours and are considered protective of post-application exposure.

2. Human Incidents and Epidemiology

The Agency previously reviewed carboxin and oxycarboxin incidents in 2014 and found a low frequency and severity of carboxin and oxycarboxin incidents that did not warrant further investigation.

In 2019, for registration review, the Agency conducted a review of human health incidents related to carboxin and oxycarboxin reported to the Incident Data System (IDS) and National Institute for Occupational Safety and Health (NIOSH) Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides databases. The analysis of IDS data from January 1, 2014 to May 2, 2019 identifies no carboxin- or oxycarboxin-related incidents in the Main IDS. One carboxin incident was reported to the Aggregate IDS and classified as minor severity.

A query of SENSOR-Pesticides from 2010-2015 found no cases involving oxycarboxin and one case involving carboxin. This case was low in severity with dermal symptoms reported. The case involved multiple pesticide products and active ingredients, making it uncertain whether carboxin caused the incident.

Based on the continued low frequency and severity of carboxin and oxycarboxin incidents reported to both IDS and SENSOR-Pesticides, there does not appear to be a concern. The Agency will continue to monitor the incident information, and additional analysis will be conducted if a concern is triggered.

3. Tolerances

Tolerances for carboxin are established at 40 CFR § 180.301. The tolerance expression needs to be updated to appropriately cover the metabolites and degradates of carboxin and to specify the residues to be measured for each commodity for enforcement purposes. The Agency anticipates revising the tolerance expression to read:

> "Tolerances are established for residues of carboxin, 5,6-dihydro-2-methyl-*N*-phenyl-1,4-oxathiin-3-carboxanilide, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only those carboxin residues convertible to aniline, expressed as the stoichiometric equivalent of carboxin, in or on the following raw agricultural commodities."

The Agency proposes the following changes to the tolerances for carboxin under 40 CFR §180.301, summarized in Table 1 below. The Agency will use its FFDCA authority to initiate these changes.

- Based on supervised field trials conducted on wheat seeds with carboxin, the Agency recommends a tolerance level of 0.2 ppm for residues in/on *barley, hay*; *oat, hay*; and *wheat, hay*.
- Based on total radioactive residue data from a cottonseed metabolism study, the Agency proposes a tolerance level of 3 ppm for residues in/on *cotton, gin byproducts*.

Table 1. Carboxin 40 CFR §180.301: Summary of Proposed Tolerance Actions

Commodity	Established Tolerance (ppm)	Proposed Tolerance (ppm)	Comments
(a) General			
Barley, hay	-	0.2	Tolerance translation from wheat, hay.
Cotton, gin byproducts	-	3	Cropp-Kohlligian, B., 2/5/2015, D425015
Oat, hay	-	0.2	Tolerance translation from wheat, hay.
Rapeseed, seed	-	0.03	Commodity definition revision
Canola, seed	0.03	Remove	
Wheat, hay	-	0.2	Morton, T., 4/3/2003, D269533

Several carboxin labels are currently registered with approved uses on peas (dry and succulent) and rye, even though no tolerances are established for these commodities. EPA is currently working with the registrant to correct these labels and resolve the missing tolerances.

Oxycarboxin is not registered for use on food/feed crops; therefore, no tolerances or tolerance actions are needed.

International Harmonization

Codex has not established any maximum residue limits (MRLs) for carboxin in/on any commodities. Mexico adopts United States tolerances and/or Codex MRLs for its export purposes. Canada has established several MRLs in crop commodities that have been harmonized with established U.S. tolerances (*e.g.*, barley, corn, oats, rice, triticale, wheat, rapeseed, and mustard seed). However, Canadian MRLs for carboxin in/on legume vegetable commodities are lower than U.S. tolerances for dry and succulent beans due to the use of different data sets (Canadian 0.03 ppm vs. U.S. 0.2 ppm). The U.S. field trial data also combined multiple residues of concern and had detectable residue levels above the Canadian MRL. Due to these factors, the U.S. cannot lower these tolerances to harmonize with Canada, which may cause trade irritancy.

Residue uptake in rotational crops

An adequate confined rotational crop study found that carboxin residues were taken up by wheat, beets, and lettuce four months after treatment[5]. To reduce the risk of residue uptake in rotational

[5] Morton, T. August 7, 2003. Tolerance Reassessment Eligibility Document (TRED) of Carboxin (PC Code 090201): Product and Residue Chemistry Considerations. Reregistration Case 0012. DP Barcode: D289853. Original Residue Study MRID: 00003114.

crops, the Agency recommends that a minimum four-month plant-back interval (PBI) be specified for all crops that are not registered for use with carboxin, and that this PBI be required for all carboxin end-use product labels, including on treated seed labels (*e.g.* seed bag tags). See Section IV for the proposed label language.

4. Human Health Data Needs

All required human health data have been submitted except for the subchronic inhalation toxicity study (Guideline No. 870.3465). In the absence of this study, the Agency applied a 10X database uncertainty factor (UF_{DB}) for assessing occupational inhalation exposure. With the addition of an APF10 respirator, risk concerns will be mitigated. With the addition of the respirator requirement to the labels for these carboxin and oxycarboxin exposure scenarios, the Agency is able to waive the subchronic inhalation study requirement[6].

The current analytical reference standard for carboxin, available in EPA's National Pesticide Standards Repository (NPSR), expired on March 31, 2020; an updated reference standard must be submitted. The registrant is also required to submit an analytical standard for aniline (currently lacking in the NSPR), because the tolerance level of carboxin is determined by measuring only those carboxin residues convertible to aniline and expressed as carboxin. Instructions for submission are available in Appendix G of the *Carboxin and Oxycarboxin: Draft Human Health Risk Assessment for Registration Review* (dated December 10, 2019), Appendix G, available in docket #: EPA-HQ-OPP-2004-0124.

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 carboxin and oxycarboxin. For additional details on the ecological assessment for carboxin and oxycarboxin, see *Carboxin and Oxycarboxin: Draft Ecological Risk Assessment for Registration Review* (dated May 29, 2019), which is available in the public docket #: EPA-HQ-OPP-2004-0124.

EPA is currently working with its 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 carboxin and oxycarboxin. See Appendix C for more details. As such, potential risks for non-listed species only are described below.

[6] Louden, R. September 20, 2019. Carboxin/Oxycarboxin: Summary of Hazard and Science Policy Council (HASPOC) Meeting on September 19, 2019: Recommendations on the Need for a Subchronic Inhalation Study. TXR No. 0057945.

1. Risk Summary and Characterization

Risk quotients (RQ) were compared against the Agency's LOCs to estimate potential risks. The RQ is the ratio of the exposure estimates to the toxicity endpoint. RQs above the LOC represent potential risks of concern. LOC exceedances are one line of evidence used by EPA to describe the potential risks posed by a pesticide to non-target organisms. For carboxin, the Agency identified potential chronic risks of concern for birds and mammals foraging on fields with treated seeds.

Terrestrial Risks

Mammals, Birds, Reptiles, and Terrestrial-Phase Amphibians

EPA did not identify any acute risks of concern for mammals, birds, reptiles, and terrestrial-phase amphibians following acute exposure to carboxin at currently labeled rates. Exposure to birds is used as a surrogate for potential exposure for reptiles and terrestrial-phase amphibians. Therefore, acute risk to these taxa is also not anticipated.

EPA identified potential chronic risks of concern (LOC=1.0) to mammals based on consumption of carboxin-treated seeds. The endpoints selected were based on a maximum 46.5% inhibition in parental body weight in male rats resulting in a LOAEL of 200 mg a.i./kg-diet and a NOAEL of 20 mg a.i./kg-diet. Using the NOAEL and a calculation of the amount of carboxin available per square foot from this highest application rate (pearl onions), chronic dietary-based RQs were 723, 618, and 331 for small, medium, and large mammals, respectively, and exceed the LOC of 1.0. Other assumptions still resulted in risk exceedances. Using the LOAEL, chronic RQs for small, medium, and large mammals are 72.3, 61.8, and 33.1, respectively. Chronic RQs using the lowest labeled application rates (0.0082 lb a.i./A/yr on canola) ranged from 96.4 to 44.1 for small to large mammals.

This assessment assumes that enough seeds are available at the surface for mammals to consume. Seed treatment analysis estimated that the number of seeds needed to trigger a chronic risk of concern ranges from 1 to 154 seeds depending on the application rate and the size of the mammal.

EPA identified potential chronic risks of concern for birds based on consumption of carboxin-treated seeds. The endpoints selected are based on an observed 22% decrease in eggs laid and 6.1% decrease in female body weight, resulting in a LOAEC of 700 mg a.i./kg-diet and a NOAEC of 70 mg a.i./kg-diet. Chronic RQs range up to 107 using the NOAEC and 10.7 using the LOAEC (LOC = 1.0). This assessment assumes that enough seeds are available at the surface for birds to consume. Seed treatment analysis estimated that the number of seeds needed to trigger a chronic risk of concern ranges from 2 to 771 depending on the application rate and the size of the bird.

Although oxycarboxin is slightly toxic to birds on an acute exposure basis, EPA did not identify any acute or chronic risks of concern to birds or mammals from exposure to oxycarboxin due to its restriction to indoor use in greenhouses only.

Terrestrial Invertebrates (Honey Bees)

Honey bees (*Apis mellifera*) are used as surrogates for both *Apis* and non-*Apis* bees. The potential for adverse effects from exposure to carboxin or oxycarboxin from currently registered uses is considered low.

Available data indicate that carboxin is practically non-toxic to adult honey bees on an acute oral exposure basis and moderately toxic on an acute contact exposure basis. The acute risk LOC (0.4) was not exceeded for either adult or larval honey bees (RQs ≤ 0.01).

Chronic risk estimates for both adult and larval bees do not exceed their respective levels of concern. For adult honey bees, an RQ of 0.02 (LOC = 1.0) was estimated for potential chronic dietary risk. For larval honey bees, the RQ was 0.08 (LOC = 1.0). These assessments are made assuming the maximum allowable label rates of 0.825 lb a.i./A/yr. The endpoint for adult honey bees was based on a 22% reduction in food consumption at the LOAEL of 18 µg a.i./bee/day (NOAEL = 9.2 µg a.i./bee/day). The endpoint for larval honey bees was based on a 10.3% reduction in mean weight of adults at emergence at the LOAEL of 3.8 µg a.i./larva/day (NOAEL = 1.5 µg a.i./larva/day).

Although the likelihood of carboxin exposure to bees from treated seed is considered low, EPA recognizes that during planting, treated seed coating can be abraded and form dusts (known as dust-off) which can drift off-site and represent a route of exposure for bees. The extent of dust-off exposure was not quantified due to its dependence on multiple factors (*e.g.*, seed surface texture, weather conditions, seeding equipment, sticking agents). Therefore, although carboxin is classified as moderately toxic to honey bees on an acute contact exposure basis, risk estimates from contact exposure were not calculated.

While available data indicate oxycarboxin is moderately toxic to honey bees on an acute contact basis, the limitation of its use to greenhouses makes ecological exposure unlikely. While there may be potential concern to honey bees brought into greenhouses to provide pollination services, the risk assessment for carboxin is considered protective of oxycarboxin exposure.

To determine the need for additional higher-tier pollinator data, the Agency has synthesized the information discussed earlier in this document, and summarized its determination below:

> Carboxin and oxycarboxin are systemic oxathiin class fungicides used as seed treatments (carboxin) or foliar applications (oxycarboxin) on a variety of agricultural and ornamental crops. The compounds target mitochondria by inhibiting the succinate-ubiquinone oxidoreductase system of electron transport. The full suite of honey bee Tier 1 toxicity data are available for carboxin. Since oxycarboxin is generally less toxic than carboxin, toxicity data for the latter serve as a surrogate for oxycarboxin. There is one bee kill incident associated with the use of carboxin; however, multiple pesticide residues were detected and the certainty that carboxin was associated with the incident was categorized as unlikely. Acute and chronic risk estimates are below their respective levels of concern (LOCs) for both chemicals; therefore, based on the current uses of carboxin as

a seed treatment and foliar uses of oxycarboxin in shade houses, no additional bee data are recommended at this time.

Terrestrial Plants

The Agency did not calculate risk quotients for terrestrial plants because methods have not been established to assess risks from seed treatments. The weight of evidence indicates carboxin's chemical class exhibits relatively low toxicity to terrestrial plants. Given the low expected exposure from carboxin's sole use as a seed treatment, the potential for adverse effects to non-target terrestrial plants is expected to be low.

Aquatic Risks

Freshwater Fish (Freshwater and Estuarine/Marine), Aquatic-Phase Amphibians, and Aquatic Invertebrates (Freshwater and Estuarine/Marine)

Based on available data, there are no acute or chronic risks of concern for freshwater or estuarine/marine fish nor for aquatic-phase amphibians (using freshwater fish as surrogates). Similarly, there are no acute or chronic risks of concern to freshwater or estuarine/marine invertebrates. For all these taxa, RQs are well below the acute risk LOC of 0.5 and the chronic risk LOC of 1.0.

Aquatic Vascular and Non-Vascular Plants

Based on available data on duckweed, freshwater and marine diatoms, and green algae, there are no risks of concern for vascular or non-vascular aquatic plants. Potential risks to aquatic plants are estimated using the 1-in-10 year daily average concentration based on exposure from runoff and erosion. Across all uses evaluated, RQ values do not exceed the LOC of 1.0 for risks to non-listed species of aquatic vascular (RQs $\leq$ 0.07) and non-vascular plants (RQs $\leq$ 0.13).

2. Ecological Incidents

The Incident Data System (IDS) is an internal EPA database that provides information from reports of ecological incidents associated with the use of specific pesticides. The Agency searched the IDS to include all reports in the database dating from registration of carboxin and oxycarboxin up until February 28, 2019. Two incidents were listed for carboxin. One occurred outside of the United States and is categorized as unlikely because it was difficult to ascribe the reported impacts to carboxin due to the presence of multiple pesticides in the samples taken. In the other incident, a farmer treated soybean seeds with a product containing both carboxin and permethrin and reported yield decreases in 142 acres of soybeans planted. An aggregate search found 8 minor incidents involving humans, 2 unspecified incidents involving domestic animals, and 1 moderate incident involving domestic animals. No incidents involving oxycarboxin were reported.

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

The ecological and environmental fate database is complete, and no additional data are required to support this registration review decision. Given the limited use of carboxin primarily as a seed treatment, and the use of oxycarboxin only inside greenhouses, EPA is not requiring additional honey bee data.

C. Benefits Assessment

The first generation succinate dehydrogenase inhibitor (SDHI) fungicide carboxin is generally effective as a seed treatment against seed and seedling diseases caused by basidiomycete fungi, such as loose smut, common bunt of wheat, covered smut, scab seedling blight, flag smut, as well as some seedling diseases[7,8]. The crop sections below discuss benefits of carboxin for specific crops; these crops were selected for discussion due to relatively high usage and/or because of mitigation options being considered.

- **Corn:** There are several fungal species that cause seed rots and seedling blights in corn; seed treatments are important for the insurance of a healthy crop stand[9].

- **Cotton:** Systemic fungicides, such as carboxin, are typically combined with protectant fungicides such as captan for greater seed protection[10]. Cotton seed treatments are used to prevent seedling disease, as well as using high quality seed and in-furrow fungicide treatments[11].

- **Onion:** Carboxin is used as a seed treatment to treat for smut (*Urocystis magica*)[12]. All current control options (seed treatments, in-furrow, and fumigants), including carboxin, provide only fair control of smut.

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[7] McKay, A H., Hagerty, G. C., Follas, G. B., Moore, M. S., Christie, M. S., and Beresford, R. M. 2011. Succinate dehydrogenase inhibitor (SDHI) fungicide resistance prevention strategy. New Zealand Plant Protection 64:119-124. http://nzpps.org/journal/64/nzpp_641190.pdf

[8] Schultz, D. and French, R. D. 2011. Fungicide seed treatment decisions for use on winter wheat. Texas A&M University Extension. http://amarillo.tamu.edu/files/2010/11/WheatFungSeedTrtPLPAWhtSd011-1.pdf

[9] Robertson, A. 2020. Potential disease problems in corn following corn. Iowa State University. Retrieved from: https://crops.extension.iastate.edu/encyclopedia/potential-disease-problems-corn-following-corn.

[10] Koenning, S. Undated. Cotton seedling diseases. North Carolina State University Extension. http://www.ces ncsu.edu/depts/pp/notes/Cotton/cdin1/cdin1.htm

[11] Isakeit, T. 2016. Managing Seedling Diseases in Cotton. Texas A&M System. AgriLife Extension. Retrieved from: http://cotton.tamu.edu/Nematodes/Management%20of%20seedling%20diseases%20of%20cotton_2016.pdf

[12] Schwartz, H. 2012. Pest Management Strategic Plan for Dry Bulb Storage Onions in the United States. Western Integrated Pest Management Center. Retrieved from: https://ipmdata.ipmcenters.org/source_report.cfm?view=yes&sourceid=972

- **Peanut:** Anco (2017)[13] recommends that all peanut seed should be treated with fungicide to reduce the incidence of seed-transmitted and soil-borne diseases. Treated seed generally provide improved germination, seedling rot inhibition, and can help prevent field-contamination of fungal pathogens[14].

- **Pea:** Crop rotation has been ineffective in controlling *Rhizoctonia* and there are no resistant cultivars available; therefore, seed treatments are important for the control of this disease in peas[15].

- **Soybean:** Damping off and seedling rots, including *Rhizoctonia*, can be problematic seedling diseases; carboxin is one of several seed treatments available[16,17]. Soybean seed treatments are recommended when conditions indicate that seedling diseases may be a problem either due to past experience in the field or because of impending weather causing cool wet soils at planting. Seed treatments are also advised when planting seeds of marginal quality[18].

- **Wheat:** Carboxin, plus captan or thiram, is recommended for the control of smuts and seedling blights[19]. In wheat, fungicide treatments may help seed with low germination rates (less than 90%) improve stand establishment[20].

- **Rye:** Carboxin is recommended for the control of smuts and seedling blights[21,22].

Carboxin offers control of pathogens that reduce quality and yield in numerous use sites. In use sites such as onions, and rye, there are limited alternatives and, therefore, carboxin may be more

[13] Anco, D. 2017. Peanut Disease Management. South Carolina Pest Management Handbook for Field Crops. Retrieved from: https://www.clemson.edu/extension/agronomy/pestmanagement17/Peanut%20disease%20control.pdf

[14] Spears, J. F., Jordan, D. L., and Bailey, J. E. 2002. Peanut seed production: A guide for producers of Virginia-type peanut seed. North Carolina State University Extension Publ. AG-622. http://www.peanut ncsu.edu/PDFFiles/004968/Peanut_Seed_Production_Guide.pdf

[15] Markell, S., Pasche, J., & Porter, L. 2016. Pea Disease Diagnostic Series. North Dakota State University Extension Service. Retrieved from: https://www.ag.ndsu.edu/publications/crops/pea-disease-diagnostic-series/pp1790.pdf

[16] Giesler, L. J. and Ziems, A. D. 2008. Seed treatment fungicides for soybeans. University of Nebraska Extension. http://ianrpubs.unl.edu/pages/publicationD.jsp?publicationId=1007

[17] Osborne, L. and Ruden, K. 2011. Seed treatment fungicide options for soybeans in South Dakota. South Dakota State University Extension Publ. FS966. http://pubstorage.sdstate.edu/AgBio_Publications/articles/FS966.pdf

[18] Koenning, S., Ferguson, J. and Dunphy, E. J. 2000. Soybean seed and seedling diseases. North Carolina State University Extension. http://www.ces ncsu.edu/depts/pp/notes/Soybean/soy002/soy002.htm

[19] Gunter, D. 2018. Small Grain Disease Control. South Carolina Pest Management Handbook for Field Crops. https://www.clemson.edu/extension/agronomy/pestmanagementhandbook18/SmallGrainsDiseaseControl18.pdf

[20] DeWolf, E. 2013. Fungicide seed treatments for wheat. No-Till Farmer. Oct. 7, 2013. https://www no-tillfarmer.com/articles/2275-fungicide-seed-treatments-for-wheat

[21] Gunter, D. 2018. Small Grain Disease Control. South Carolina Pest Management Handbook for Field Crops. https://www.clemson.edu/extension/agronomy/pestmanagementhandbook18/SmallGrainsDiseaseControl18.pdf

[22] Day, J. L. and Coy, A. E. (eds.). 2014. 1999-2000 Small Grains Performance Tests. University of Georgia Extension. Retrieved from: https://extension.uga.edu/publications/detail html?number=RR666

critical. For use sites such as cotton and soybean, there are more alternative chemistries available and therefore the importance of carboxin may be more limited.

IV. PROPOSED INTERIM REGISTRATION REVIEW DECISION

A. Proposed Risk Mitigation and Regulatory Rationale

For carboxin, EPA identified potential human health risks of concern from occupational handler exposure; and potential ecological risks of concern to non-listed birds, reptiles, terrestrial-phase amphibians and mammals foraging on treated seeds. For oxycarboxin, EPA identified potential human health risks of concern from occupational handler exposure but did not identify any ecological risks of concern. In evaluating potential risk mitigation for carboxin and oxycarboxin, the Agency considered the risks, benefits, and use patterns of these compounds.

To address the potential risks identified, EPA is proposing the following mitigation measures and label changes:

- Require the use of an APF10 respirator for 6 specific occupational scenarios of concern involving the use of carboxin in commercial seed treatment facilities and one occupational scenario of concern involving the foliar application of oxycarboxin to ornamentals inside greenhouses.
- Require updated mandatory label language on seed management and planting to mitigate the risk of consumption of treated seed by non-listed birds and mammals.
- On all end-use product labels, including treated seed labels (*e.g.* seed bag tags), require a 4-month Plant-Back Interval (PBI) for all crops not specifically registered for use with carboxin.

In addition, EPA is proposing the following label changes to address generic labeling requirements for all carboxin and oxycarboxin products and uses:

- Updated glove statements
- Updated groundwater and surface water advisory language
- Fungicide resistance management language

The technical registrant has not objected to any of the proposed label changes outlined in Appendix A and B.

1. Require APF10 respirator for specific occupational scenarios

Respirator Requirement for Carboxin and Oxycarboxin Handlers

To mitigate potential inhalation risk to occupational handlers in several occupational scenarios, the Agency is proposing an APF10 respirator for the following oxycarboxin scenario covered by

the Worker Protection Standard[23] (WPS), which requires fit testing, training, and a medical evaluation:

Oxycarboxin

- **Mixing/loading/applying wettable powders with a mechanically pressurized handgun to greenhouse ornamentals** (LOC = 1000): the estimated inhalation MOE of 510 increases to 5,100 with addition of an APF10 respirator.

The following scenarios for carboxin in commercial seed treatment facilities are not covered by the WPS. Therefore, the Agency is proposing an APF10 respirator requirement that is equivalent to scenarios under WPS, requiring testing, training, and a medical evaluation for all occupational handlers required to wear a respirator and following requirements set by the Occupational Safety and Health Administration (OSHA) (see 29 CFR Part 1910.134).

In addition, EPA determined that of the scenarios described in Section III.A.1, two scenarios with MOEs of 980 (LOC = 1000) are not of concern due to the protective nature of the risk assessment and uncertainty factors incorporated into the estimates. These scenarios are beans (dried type) and soybeans, for *liquid-formulated products, multiple activities.* EPA is not proposing a respirator for these use sites. The revised list of six carboxin commercial seed treatment scenarios for which EPA is proposing an APF10 respirator are provided below:

Carboxin

- ***Commercial seed treatment (multiple activities) for liquid-formulated products:*** activities include cleaning and maintenance of seed treatment equipment, such as scraping, wiping, brushing, and vacuuming of the mixing, delivery, or treatment chamber using compressed air and/or pressurized water (LOC = 1000)
    - **Corn (field and sweet):** the estimated inhalation MOE of 620 increases to 6,200 with addition of an APF10 respirator.
    - **Succulent beans (lima, snap):** the estimated inhalation MOE of 810 increases to 8,100 with the addition of an APF10 respirator.
- ***Commercial seed treatment (mixing/loading) for dust-formulated products*** (LOC = 1000):
    - **Barley, oats, and wheat:** the estimated inhalation MOE of 890 increases to 8,900 with the addition of an APF10 respirator.
    - **Beans (dried type) and succulent beans (lima, snap):** the estimated inhalation MOE of 750 increases to 7,500 with the addition of an APF10 respirator.
    - **Peas (dried type, succulent)[24]:** the estimated inhalation MOE of 750 increases to 7,500 with the addition of an APF10 respirator.
    - **Soybeans**: the estimated inhalation MOE of 900 increases to 9,000 with the addition of an APF10 respirator.

[23] 40 CFR 170

[24] Carboxin use on peas is currently listed on some labels but not supported by a tolerance. If a tolerance is established and this use is re-approved, this peas scenario would require an APF10 respirator to not be of concern.

EPA has recently required fit testing, training, and medical evaluations[25] for all handlers who are required to wear respirators and whose work falls within the scope of the WPS[26]. If a carboxin or oxycarboxin handler currently does not have a respirator, an additional cost will be incurred by the handler or the handler's employer, which includes the cost of the respirator plus the cost for a respirator fit test, training, and medical exam.

Respirator costs are extremely variable depending upon the protection level desired, disposability, comfort, and the kinds of vapors and particulates being filtered. Based on available information that EPA has, the cost of the respirators (whether disposable or reusable) is relatively minor in comparison to the fit-test requirement under the Worker Protection Standard. The Agency expects that the average cost of a particulate filtering facepiece respirator is lower than the average cost of an elastomeric half-mask respirator. The cost of a respirator fit test, training and medical exam was estimated to be about $180 annually[27]. However, if a carboxin or oxycarboxin handler typically uses other chemicals requiring a respirator in the production system or as part of the business, additional fit testing is not needed. The handler or employer may only incur the cost of purchasing filters for the respirator on a more frequent basis. Respirator fit tests are currently required by the Occupational Safety and Health Administration (OSHA) for other occupational settings to ensure proper protection[28].

EPA acknowledges that requiring a respirator and the associated fit testing, training, and medical evaluation places a burden on handlers or employers. However, the proper fit and use of respirators is essential to accomplish the protections respirators are intended to provide. In estimating the inhalation risks, and the risk reduction associated with different respirators, EPA's human health risk assessments assume National Institute for Occupational Safety and Health (NIOSH) protection factors (*i.e.*, respirators are used according to OSHA's standards). If the respirator does not fit properly, use of carboxin or oxycarboxin may cause unreasonable adverse effects on the pesticide handler.

2. Updated Gloves Statement

The Agency is proposing an update to gloves statements to be consistent with Chapter 10 of the Label Review Manual. In particular, the Agency is proposing the removal of reference to specific categories in EPA's chemical-resistance category selection chart and requiring that labels specify the appropriate glove types to use. For example, the chemical-resistant glove statements in the label should remove "such as" language and not state the solvent category, but rather add all acceptable glove types that provide high-level chemical resistance for the solvent category as

[25] Fit testing, training, and medical evaluations must be conducted according to OSHA regulations 29 CFR § 1910.134, 29 CFR § 1910.134(k)(1)(i) through(vi), and 29 CFR § 1910.134, respectively.
[26] 40 CFR 170 (see also Appendix A of Chapter 10 of the Label Review Manual, available at https://www.epa.gov/pesticide-registration/label-review-manual.
[27] Economic Analysis of the Agricultural Worker Protection Standard Revisions. Biological and Economic Analysis Division, Office of Pesticide Programs, U.S. EPA. 2015. p. 205. Available at www.regulations.gov, docket number EPA-HQ-OPP-2011-0184-2522.
[28] 29 CFR § 1910.134

mentioned in Table 3 of Chapter 10 of the Label Review Manual[29]. This minor clarification does not fundamentally change the personal protective equipment that workers are currently required to use.

3. Updated Mandatory Seed Management and Planting Language

While all carboxin end-use product labels already include some mandatory language on managing treated seeds to avoid consumption by birds or wildlife (*e.g.*, to "cover and collect spilled seeds"), the language is inconsistent and variable across product formulations. To ensure consistent, clear, and enforceable language across all carboxin product labels to mitigate the risk that wildlife consume treated seed, the following language is proposed under the "Directions for Use" and "Treated Seed Labeling" sections:

> "Do not plant treated seeds by broadcasting to the soil surface. Treated seed exposed on soil surfaces may be hazardous to birds or mammals. Cover or collect seed spilled during loading. If seeds are not thoroughly incorporated by the planter during planting, additional incorporation may be required to thoroughly cover exposed seeds."

This language is expected to have limited impact on growers as most crops registered for carboxin do not rely on broadcast applications. For crops where broadcast applications are important, growers may need to rely on alternative seed treatment options, if available, or invest in different planting equipment which could result in additional cost.

4. Updated Language on Plant-Back Intervals (PBIs)

Several end-use product labels currently have plant-back intervals (PBIs) set for rotational crops that are too short to avoid the risk of carboxin residue uptake in unregistered crops. PBIs of at least 4 months are required for all crops that are not registered for use with carboxin. PBIs longer than 4 months may also be set for specific crops as needed to account for other active ingredients. The following language is proposed for all end-use product labels, including treated seed labels (*e.g.* seed bag tags), under the "Directions for Use" and "Treated Seed Labeling" sections:

> "Areas planted with carboxin-treated seed may be replanted immediately with barley, beans (dry shelled and succulent), canola, corn (field, sweet, pop), cotton, oat, onion (bulb), peanuts, rape seed, rice, safflower, soybean, triticale, or wheat. Do not plant any other crop not listed above in the treated area for at least four months after treated seeds are planted."

If additional crops become approved for food use with carboxin and have tolerances established, they may be added to the list of crops in the statement above. Because carboxin is applied as a seed treatment at the beginning of the crop cycle, and all registered crops have cycles greater

[29] US EPA. March 2018. Office of Pesticide Programs. Label Review Manual. https://www.epa.gov/pesticide-registration/label-review-manual

than four months, a four-month PBI is not expected to impact growers, except in the rare instance following a crop failure where a grower may wish to plant a different crop not registered for use with carboxin.

5. Updated Groundwater and Surface Water Advisory Language

While some carboxin product labels already include advisory language on minimizing runoff of pesticide residue into surface water, because carboxin has been detected in groundwater, the Agency is proposing updated language in accordance with current EPA policy to be standardized across all end-use labels in the "Environmental Hazards" section. EPA proposes the addition of groundwater and surface water advisory language to labels to encourage grower awareness and best practices (*e.g.*, use of vegetative buffer strips and avoiding planting of treated seed within 48 hours of expected rainfall) to reduce the risk of potential inflows of carboxin and its degradates into groundwater and surface water after application. The updated proposed language to be included is provided in Appendix B under "Groundwater and Surface Water Runoff Label Advisories".

6. Pesticide Resistance Management

Pesticide resistance occurs when genetic or behavioral changes enable a portion of a pest population to tolerate or survive what would otherwise be lethal doses of a given pesticide. The development of such resistance is influenced by a number of factors. One important factor is the repeated use of pesticides with the same mode (or mechanism) of action. This practice kills sensitive pest individuals but allows less susceptible ones in the targeted population to survive and reproduce, thus increasing in numbers. These individuals will eventually be unaffected by the repeated pesticide applications and may become a substantial portion of the pest population. An alternative approach, recommended by resistance management experts as part of integrated pest management (IPM) programs, is to use pesticides with different chemical modes (or mechanisms) of action against the same target pest population. This approach may delay and/or prevent the development of resistance to a particular mode (or mechanism) of action without resorting to increased rates and frequency of application, possibly prolonging the useful life of pesticides.

EPA is proposing resistance-management labeling, as listed in Appendix B, for products containing carboxin and oxycarboxin, 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 at the following website: https://www.epa.gov/pesticide-registration/prn-2017-1-guidance-pesticide-registrants-pesticide-resistance-management.

B. Tolerance Actions

The following updates to tolerances for carboxin are proposed:

- The tolerance expression under 40 CFR §180.301 should be revised to appropriately cover carboxin metabolites and residues and specify residues to be measured for each commodity for enforcement purposes.
- Tolerances for several commodities need to be established based on review of existing residue data, and one tolerance needs to be revised based on a commodity definition revision.
- Refer to Section III.A.3 for details.

The Agency will use its FFDCA rulemaking authority to make the needed changes to the tolerances.

C. Proposed Interim Registration Review Decision

In accordance with 40 CFR §§ 155.56 and 155.58, the Agency is issuing this PID. Except for the Endocrine Disruptor Screening Program (EDSP) and the Endangered Species Act (ESA) components of this case, the Agency has made the following proposed interim decision: (1) no additional data are required at this time; and, (2) changes to the affected registrations and their labeling are needed at this time, as described in Section IV.A and Appendices A and B.

In this PID, the Agency is making no human health or environmental safety findings associated with the EDSP screening of carboxin and oxycarboxin, nor is it making a complete endangered species finding. 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 carboxin and oxycarboxin. The Agency's final registration review decision for carboxin and oxycarboxin will be dependent upon the result of the Agency's ESA assessment and any needed § 7 consultation with the Services and an EDSP FFDCA § 408(p) determination.

D. Data Requirements

A Generic Data Call-In (DCI) was issued for carboxin and oxycarboxin for data needed to conduct the registration review risk assessments. All data requirements have been satisfied or waived. The Agency does not anticipate calling-in additional data for registration review of carboxin and oxycarboxin.

Reference Standards

- The analytical reference standard for carboxin has expired and must be submitted to EPA's National Pesticide Standards Repository (see https://www.epa.gov/pesticide-analytical-methods/national-pesticide-standard-repository).
- The Agency proposes to require an analytical reference standard for the carboxin metabolite aniline to be submitted to the National Pesticides Standards Repository.

V. NEXT STEPS AND TIMELINE

A. Proposed Interim Registration Review Decision

A Federal Register Notice will announce the availability of this PID for carboxin and oxycarboxin 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 carboxin and oxycarboxin. However, a final decision for carboxin and oxycarboxin may be issued without the Agency having previously issued an interim decision. A final decision on the carboxin and oxycarboxin 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 carboxin and oxycarboxin 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 Carboxin and Oxycarboxin

Registration Review Case#: 0012
PC Code: Carboxin (PC Code 090201) and Oxycarboxin (PC Code 090202)
Chemical Type: Fungicide
Chemical Family: Oxathiin-carboxamide class systemic fungicides
Mode of Action: Inhibition of the succinate-ubiquinone oxidoreductase system of the mitochondrial electron transfer chain

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Avian	Dietary	Ingestion	Chronic	Developmental	Require updated mandatory seed management and planting language
Mammals	Dietary	Ingestion	Chronic	Developmental	Require updated mandatory seed management and planting language
Occupational Handlers • Carboxin: Mixing, loading, cleaning, and maintenance activities in commercial seed treatment facilities • Oxycarboxin: mechanically pressurized handgun applications in greenhouses	Air	Inhalation	Sub-chronic	Inhalation toxicity	Require use of APF10 respirator

Appendix B: Proposed Labeling Changes for Carboxin and Oxycarboxin Products

<table>
<tr><th>Description</th><th>Proposed Label Language for Carboxin Products</th><th>Placement on Label</th></tr>
<tr><td></td><td>End Use Products</td><td></td></tr>
<tr><td>Mode 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 OF ACTION CODE in the third column
Include the type of pesticide (i.e., HERBICIDE or FUNGICIDE or INSECTICIDE) in the fourth column
Example: See page 7 of PR Notice 2017-1: https://www.epa.gov/sites/production/files/2017-09/documents/prn-2017-1-pesticide-resistance-management-labeling.pdf

<table><tr><td>CARBOXIN</td><td>GROUP</td><td>7</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>Updated Gloves Statement</td><td>Update the gloves statements to be consistent with Chapter 10 of the Label Review Manual. In particular, remove reference to specific categories in EPA’s chemical-resistance category selection chart and list the appropriate chemical-resistant glove types to use.</td><td>In the Personal Protective Equipment (PPE) within the Precautionary Statements and Agricultural Use Requirements, if applicable</td></tr>
<tr><td>Respirator Language (https://www.epa.gov/pesticide-registration/label-review-manual-chapter-10-revised-</td><td>For liquid formulations, the following additional language must be added:

“FOR COMMERCIAL SEED TREATMENT APPLICATIONS TO CORN (FIELD AND SWEET) AND SUCCULENT BEANS (LIMA, SNAP),
Workers carrying out activities involving cleaning and maintenance of seed treatment equipment, including but not limited to scraping, wiping, brushing, and vacuuming of the mixing, delivery, or treatment chamber using compressed air and/or pressurized water, must also:</td><td>In the Personal Protective Equipment (PPE) within the Precautionary Statements</td></tr>
</table>

Description	Proposed Label Language for Carboxin Products	Placement on Label
respirator-descriptions-public-comment) **required for products:** 1) Formulated as a liquid 2) Registered for use on corn (field and sweet) and succulent beans (lima, snap)	[**Note to registrant**: If your end-use product only requires protection from particulates only (low volatility), use the following language:] "Wear a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N*, R or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N*, R or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters." *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. [**Note to registrant:** For respiratory protection from organic vapor a**nd** particulates (or aerosols), use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half-mask respirator with organic vapor (OV) cartridges and combination N*, R, or P filters; OR a NIOSH-approved gas mask with OV canisters; OR a NIOSH-approved powered air purifying respirator with OV cartridges and combination HE filters." [**Note to registrant:** For products requiring protection for organic vapor only, use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half-mask respirator with organic vapor (OV) cartridges; OR a NIOSH-approved full-face respirator with OV cartridges; OR a gas mask with OV canisters; OR a powered air purifying respirator with OV cartridges." *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.	
Respirator Language (https://www.epa.gov/pesticide-registration/label-review-manual-chapter-10-revised-respirator-descriptions-public-comment) **required for products:** 1) Formulated as a dust 2) Registered for use on barley,	*For dust formulations, the following additional language must be added:* **"FOR COMMERCIAL SEED TREATMENT APPLICATIONS TO BARLEY, OATS, WHEAT, BEANS (DRIED TYPE), SUCCULENT BEANS (LIMA, SNAP), AND SOYBEANS,** **Mixers and loaders must also:** [**Note to registrant**: If your end-use product only requires protection from particulates only (low volatility), use the following language:] "Wear a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N*, R or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N*, R or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters." *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

Description	Proposed Label Language for Carboxin Products	Placement on Label
oats, wheat, beans (dried type), succulent beans (lima, snap), and soybeans	[**Note to registrant:** For respiratory protection from organic vapor a**nd** particulates (or aerosols), use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half-mask respirator with organic vapor (OV) cartridges and combination N*, R, or P filters; OR a NIOSH-approved gas mask with OV canisters; OR a NIOSH-approved powered air purifying respirator with OV cartridges and combination HE filters." [**Note to registrant:** For products requiring protection for organic vapor only, use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half-mask respirator with organic vapor (OV) cartridges; OR a NIOSH-approved full-face respirator with OV cartridges; OR a gas mask with OV canisters; OR a powered air purifying respirator with OV cartridges." *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.	
Respirator Fit Testing Requirements for Non-WPS Uses: Applies to all scenarios requiring respirators in commercial seed treatment facilities	**"Respirator fit testing, medical qualification, and training** Using a program that conforms to OSHA's requirements (see 29 CFR Part 1910.134), employers must verify that any handler who uses a respirator is: • Fit-tested and fit-checked, • Trained, and • Examined by a qualified medical practitioner to ensure physical ability to safely wear the style of respirator to be worn. A qualified medical practitioner is a physician or other licensed health care professional who will evaluate the ability of a worker to wear a respirator. The initial evaluation consists of a questionnaire that asks about medical conditions (such as a heart condition) that would be problematic for respirator use. If concerns are identified, then additional evaluations, such as a physical exam, might be necessary. The initial evaluation must be done before respirator use begins. Handlers must be reexamined by a qualified medical practitioner if their health status or respirator style or use conditions change. Upon request by local/state/federal/tribal enforcement personnel, employers must provide documentation demonstrating how they have complied with these requirements."	In the Personal Protective Equipment (PPE) within the Precautionary Statements
Groundwater and Surface Water Label Advisories	"Carboxin and its degradates are known to leach through soil into groundwater under certain conditions as a result of label use. This chemical may leach into groundwater if used in areas where soils are permeable, particularly where the water table is shallow" "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 high potential for reaching surface water via runoff for several months or more after application."	"Environmental Hazards" and "Treated Seed Labeling" sections

Description	Proposed Label Language for Carboxin Products	Placement on Label
	"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 carboxin and carboxin sulfoxide 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."	
Updated Seed Management and Planting language	"Do not plant treated seeds by broadcasting to the soil surface. Treated seed exposed on soil surfaces may be hazardous to birds or mammals. Cover or collect seed spilled during loading. If seeds are not thoroughly incorporated by the planter during planting, additional incorporation may be required to thoroughly cover exposed seeds."	"Directions for Use" and "Treated Seed Labeling" sections
Updated Rotational Plant-back Interval (PBI) Language	For all end-use products labels, including treated seed labels (*e.g.* seed bag tags) a minimum four-month plant-back interval must observed for all crops not registered for carboxin. The registrant may set PBIs longer than 4 months for different crops to account for other active ingredients if needed. The following language is proposed: "Areas planted with carboxin-treated seed may be replanted immediately with barley, beans (dry shelled and succulent), canola, corn (field, sweet, pop), cotton, oat, onion (bulb), peanuts, rape seed, rice, safflower, soybean, triticale, or wheat. Do not plant any other crop not listed above in the treated area for at least four months after treated seeds are planted."	"Directions for Use" and "Treated Seed Labeling" sections
Resistance-management for fungicides	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, prior to directions for specific crops

<table>
<tr><th>Description</th><th>Proposed Label Language for Oxycarboxin Products</th><th>Placement on Label</th></tr>
<tr><td></td><td>End Use Products</td><td></td></tr>
<tr><td>Mode 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 OF ACTION CODE in the third column
Include the type of pesticide (i.e., HERBICIDE or FUNGICIDE or INSECTICIDE) in the fourth column
Example: See page 7 of PR Notice 2017-1: https://www.epa.gov/sites/production/files/2017-09/documents/prn-2017-1-pesticide-resistance-management-labeling.pdf

<table><tr><td>OXYCARBOXIN</td><td>GROUP</td><td>7</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>
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<tr><td>Respirator Language (https://www.epa.gov/pesticide-registration/label-review-manual-chapter-10-revised-respirator-</td><td>For wettable powder formulations, the following additional language must be added:

“FOR APPLICATIONS TO GREENHOUSE ORNAMENTALS USING MECHANICALLY PRESSURIZED HANDGUNS,
Mixers, loaders, and applicators must also:

[Note to registrant: If your end-use product only requires protection from particulates only (low volatility), use the following language:]</td><td>In the Personal Protective Equipment (PPE) within the Precautionary Statements</td></tr>
</table>

Description	Proposed Label Language for Oxycarboxin Products	Placement on Label
descriptions-public-comment) Applies to all products applied using mechanically pressurized handguns inside greenhouses	"Wear a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N*, R or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N*, R or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters." *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. [**Note to registrant:** For respiratory protection from organic vapor **and** particulates (or aerosols), use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half-mask respirator with organic vapor (OV) cartridges and combination N*, R, or P filters; OR a NIOSH-approved gas mask with OV canisters; OR a NIOSH-approved powered air purifying respirator with OV cartridges and combination HE filters." [**Note to registrant:** For products requiring protection for organic vapor only, use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half-mask respirator with organic vapor (OV) cartridges; OR a NIOSH-approved full-face respirator with OV cartridges; OR a gas mask with OV canisters; OR a powered air purifying respirator with OV cartridges." *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.	
Resistance-management for fungicides	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, prior to directions for specific crops

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.[30] 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.[31]

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 carboxin and oxycarboxin 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 carboxin and oxycarboxin. This will allow EPA to focus its future evaluations on the types of species where the potential for effects exists once the Revised

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

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

Method has been fully implemented. Once that occurs, the Revised Method will be applied to subsequent analyses for carboxin and oxycarboxin 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 carboxin and oxycarboxin, 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), carboxin and oxycarboxin are 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,[32] 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. Carboxin and oxycarboxin are 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 the EPA website.[33]

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

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