NEW YORK STATE DEPARTMENT OF ENVIRONMENTAL CONSERVATION

Division of Materials Management, Bureau of Pesticides Management
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February 22, 2019

VIA E-MAIL (Company # 67690)

Dr. Laurent Mezin
SePro Corporation
11550 N. Meridian Street, Suite 600
Carmel, Indiana 46032-4565

Re: **Registration of Special Local Need (SLN) Labeling for ProcellaCOR EC (EPA Reg. No. 67690-80) for Use on Aquatic Weeds. Contains the Active Ingredient: Florpyrauxifen-benzyl (chemical code: 030093).**

Dear Dr. Mezin:

The New York State Department of Environmental Conservation (Department) has reviewed the application and data package for the above-referenced product, received on July 30, 2018, along with additional data received in response to the Department's incompleteness decision letter dated September 25, 2018. The above referenced product contains the active ingredient florpyrauxifen-benzyl which has not previously been registered in New York State and is considered a new active ingredient requiring full technical review to ensure protection of human health and state environmental resources, prior to registration and use in New York State.

The active ingredient florpyrauxifen-benzyl is contained in the product ProcellaCOR EC at 2.7% and is a selective systemic herbicide for management of freshwater aquatic vegetation in slow-moving/quiescent waters with little or no continuous outflow, or to slow-moving/quiescent areas of rivers. ProcellaCOR EC is absorbed by aquatic vascular plants through emergent or floating leaves and from water surrounding submersed plant shoots and leaves. The product is best used to control plants with high uptake rates in spot or partial treatment designs in which exposure times are relatively short. ProcellaCOR EC has been determined to be efficacious in controlling invasive plants including Eurasian water milfoil while not impacting many native species.

The net contents and application information are expressed as Prescription Dose Unit or PDU. The conversion for PDU is given on the front panel of the label as 1 PDU is equal to 3.2 fluid ounces of product. However, the application directions are based on 1 PDU being equal to 3.17 fluid ounces. The registrant has been informed that at the next printing of the label, the net contents must be expressed in conventional American units of fluid ounces, pints, quarts, and gallons as required by 40 CFR 156.10(d)(2).

ProcellaCOR EC is labeled for use on selected vascular aquatic plants either as a foliar spray on emergent weeds or in-water application to submersed, emersed, or floating weeds. The maximum application rate for foliar spraying of plants either standing or floating in water, is 10 PDU (31.7 fl. oz.) per acre per treatment or 20 PDU (63.4 fl. oz.) per acre annually. The maximum in-water application rate to submersed, emersed, or floating weeds is 25 PDU (79.25 fl. oz.) per application with a limit of three applications allowed per year. Application of one PDU (3.17 fl. oz.) per acre-foot of water is approximately 1.91 ppb florpyrauxifen-benzyl and the maximum dose of 25 PDU (79.25 fl. oz.) is approximately 47.8 ppb of the active ingredient per acre-foot of treatment area.

ProcellaCOR EC was granted reduced risk status from the U.S. Environmental Protection Agency as the overall profile for ProcellaCOR EC, when compared with the registered alternatives for aquatic weed control, is more favorable as it pertains to human health. In addition, ProcellaCOR EC demonstrates an alternate mode of action from any other aquatic herbicide which when used in integrated pest management (IPM) strategies will limit weed resistance. The application rate is orders of magnitude less than many other aquatic herbicides and the maximum application rate of 25 PDU per acre-foot is less than the New York State Drinking Water Standard for non-specific organic contaminants maximum allowed concentration of 50 ppb.

The product application was determined to be complete on November 6, 2018 and fully reviewed regarding human health as well as ecosystem health. There were no objections to the registration of this product in New York State (detailed reviews are provided in the Appendix). However, the federally approved ProcellaCOR EC labeling that has been provided to the Department is not as restrictive as the state requirements to permit application in aquatic sites. Therefore, the Department will register these requirements as provided on Special Local Need (SLN) labeling which must be in the possession of the applicator when using ProcellaCOR EC. The following stated concerns will be addressed on the SLN labeling and the ProcellaCOR EC product labeling will only be used in conjunction with this SLN labeling:

- The Department's Bureau of Ecosystem Health (BEH) has expressed concerns regarding the potential of this product to impact ecosystem health if applied aerially over large areas. The BEH does not support the aerial application of this product as an appropriate method to control target weeds. The BEH recommends that requests to apply ProcellaCOR EC by aerial application be supported by adequate justification of significant localized need.

- The ProcellaCOR EC container labeling that has been provided to the Department has certain Use Restrictions that the Department finds vague and potentially unenforceable, and in need of clarification and qualification. Therefore, for the purposes of watering livestock and irrigating field crops, greenhouse, nursery, or hydroponically grown crops, treated water must be analyzed and determined to be less than 1 ppb active ingredient or determined by a Department approved model, to have degraded/diluted to below 1 ppb.

- The container net contents and Prescription Dose Unit (PDU) conversion are clarified in appropriate fluid ounces.

- The application methods for in-water applications are clarified to include the emersed weed species that are listed in Table 3 of the container label.

The Department has **registered the SLN labeling (SLN NY-190001)** for ProcellaCOR EC (EPA Reg. No. 67690-80) as a restricted use product as required by 6NYCRR Part 326.2(h) for any pesticide labeled for direct application to or in surface waters. Enclosed for your records are copies of the Certificate of Pesticide Registration and stamped "Accepted for Registration" SLN labeling for this product. The container labeling has been stamped "Accepted for Registration Only in Conjunction with New York State Specific Supplemental Labeling." Please note the "yes" under the "restriction" column on the enclosed Certificate of Pesticide Registration and the "Classified for Restricted Use in New York State" stamp on the attached SLN and product labeling. As such, this product is restricted in its purchase, distribution, sale, use and possession in New York State. Furthermore, this product may only be purchased and used by a certified applicator in New York State.

The New York State Department of Environmental Conservation Regulations 6NYCRR Part 326.3(a) state: "It shall be unlawful for any person to distribute, sell, offer for sale, purchase for the purpose of resale, or possess for the purpose of resale, any restricted pesticide unless said person shall have applied for, and been issued a commercial permit." Should you require information to obtain a commercial permit, please contact the Pesticide Reporting and Certification Section, at (518) 402-8748.

The Pesticide Reporting Law within Environmental Conservation Law Article 33 Title 12 requires all certified commercial pesticide applicators to report information annually to the Department regarding each pesticide application they make. **Commercial pesticide retailers are required to report all sales of restricted pesticide products and sales of general use pesticide products to private applicators for use in agricultural crop production.** If no sales are made within New York State, a report must be filed with the Department indicating this is the case.

If you need information relating to the Pesticide Reporting Law, or annual report forms, please visit the Department's website at: http://www.dec.ny.gov/chemical/27506.html, or call (518) 402-8748.

Please note that a proposal by SePro Corporation or any other registrant, to register a product that contains florpyrauxifen-benzyl, and whose labeled uses are likely to increase the potential for significant impact on humans, non-target organisms, or the environment, would constitute a major change in labeling. Such an application must be accompanied by a new application fee and meet the requirements listed on our website. This information, as well as forms, can be accessed at: http://www.dec.ny.gov/chemical/8528.html.

Please contact the Pesticide Product Registration Section at (518) 402-8768, if you have any questions regarding this letter.

Sincerely,

/s/

Scott Menrath, P.E.
Director
Bureau of Pesticides Management

Enclosures

APPENDIX

HUMAN HEALTH ASSESSMENT

The New York State Department of Health (DOH) reviewed the application and supporting data submitted by SePro Corporation to register the pesticide product ProcellaCOR EC (EPA Reg. No. 67690-80) in New York State. This product contains the new active ingredient florpyrauxifen-benzyl (benzyl-4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-pyridine-2-carboxylate) and is labeled as a selective, systemic herbicide for the management of freshwater aquatic vegetation in slow-moving, quiescent water with minimal outflow.

Acute Toxicity

Neither florpyrauxifen-benzyl nor ProcellaCOR EC was very toxic in acute oral, dermal or inhalation exposure studies in laboratory animals. The active ingredient and formulated product were moderate eye irritants, but not skin irritants (tested on rabbits). In addition, florpyrauxifen-benzyl was a weak skin sensitizer, but ProcellaCOR EC was not (tested on guinea pigs).

Subchronic/Chronic/Developmental/Reproductive Toxicity

Florpyrauxifen-benzyl did not cause any toxic effects in neurotoxicity, immunotoxicity, subchronic, chronic, or developmental/reproductive feeding studies in laboratory animals (rats, mice and dogs) at the highest doses tested. In addition, florpyrauxifen-benzyl did not cause any carcinogenic effects in rats or mice and was negative in a number of genotoxicity studies. Based on these results, the U.S. Environmental Protection Agency (U.S. EPA) classified florpyrauxifen-benzyl as “not likely to be carcinogenic to humans.” Additionally, the U.S. EPA did not conduct dietary, occupational, or residential post-application quantitative human health risk assessments since toxicity endpoints for florpyrauxifen-benzyl were not determined from animal studies.

Drinking Water/Groundwater Standards

There are no chemical-specific federal or New York State drinking water/groundwater standards for florpyrauxifen-benzyl. Based on its chemical structure, this chemical falls under the 50 micrograms per liter (µg/L) New York State drinking water standard for “unspecified organic contaminants” (10 NYCRR Part 5, Public Water Systems).

Summary

The available information on florpyrauxifen-benzyl and the formulated product ProcellaCOR EC indicates that they are not acutely toxic and the active ingredient is not carcinogenic, genotoxic, neurotoxic, or teratogenic. Due to a complete lack of toxic

effects for florpyrauxifen-benzyl, the U.S. EPA did not conduct dietary, occupational, or post-application residential risk assessments for the labeled use of ProcellaCOR EC. Although the formulated product was a moderate eye irritant, the protective eyewear required on the product label for handlers of ProcellaCOR EC should mitigate any potential eye irritation from its use.

NYS DOH Recommendation

The risks to human health from the use of ProcellaCOR EC in slow-moving, quiescent water bodies to control undesirable or invasive freshwater aquatic vegetation appears to be minimal. Florpyrauxifen-benzyl is a systemic herbicide with a half-life range of < 1 day to 6 days, depending on the route of degradation. The major degradation products have longer half-lives than the parent, however, they are expected to have similar or lower toxicity profiles than florpyrauxifen-benzyl. The ProcellaCOR EC label contains restrictions on the use of treated water for irrigation purposes and watering livestock, due to the herbicidal activity of the product, but does not contain restrictions regarding the use of treated water for recreational purposes, including swimming and fishing. The label does not include set-back requirements for potable water intakes, however, the maximum labeled use rate does not exceed the 50 µg/L New York State generic drinking water standard for this chemical.

Given the limited risks to workers and the general public, we do not object to the registration of ProcellaCOR EC in New York State. However, we believe measures (both in terms of planning and laboratory quantification) to ensure that ProcellaCOR EC applications do not result in potable water concentrations of florpyrauxifen-benzyl in excess of 50 µg/L, as well as other site-specific considerations (e.g., public notification, provisions of alternate drinking water, etc.), should be addressed as part of the NYS DEC aquatic pesticide application permitting process.

ECOTOXICITY ASSESSMENT

Background

The Department's Division of Fish and Wildlife (DFW) Bureau of Ecosystem Health (BEH) reviewed the application and supporting data for the new active ingredient florpyrauxifen-benzyl as formulated in the aquatic herbicide ProcellaCOR EC (EPA reg. # 67690-80) developed by SePRO Corporation. The product is intended for management of freshwater aquatic vegetation with good selectivity for common invasive species in the U.S. including the Eurasian watermilfoil. The active ingredient (a.i.) florpyrauxifen-benzyl belongs to the Group 4 herbicides, which are synthetic auxins that interfere with normal plant cell growth. Florpyrauxifen-benzyl is a systemic herbicide and appears to be most active against cells in the meristem. Its selectivity against different plant species is likely dependent on the effectiveness of the translocation of the a.i. to the meristem after contact. The exact mechanism of its toxicity to target organisms is not clear but it has been shown to affect multiple molecular and cellular processes during cell division.

ProcellaCOR EC is a liquid formulation containing 2.7% florpyrauxifen-benzyl. The label allows foliar application on emergent aquatic plants and in-water treatment of submerged plants. Spot and partial treatment designs for in-water treatment are claimed to be effective. The maximum single application rate for in-water treatment is 25.0 prescription dose units (PDU, equivalent to 0.0052 lb. a.i.) per acre-foot with no more than three applications per year. Foliar applications to emergent vegetation are allowed at the maximum single application rate of 10 PDU per acre and the maximum annual application rate of 20 PDU. The minimum interval between two consecutive applications is 14 days. The label also contains instructions for ground and aerial applications, but these application methods do not appear to be consistent with the intended use of this product as a highly effective and selective systemic herbicide for aquatic vascular plant management. The chemical properties for florpyrauxifen-benzyl are listed in **Table 1** and recommended application patterns are listed in **Table 2**.

Toxicity information

Florpyrauxifen-benzyl mimics the action of auxin, a class of plant hormones that play a key role in plant growth and development. Auxins are involved in the regulation of plant cell division and elongation and their synthesis and actions are found to be most active in the apical (e.g., roots and shoots) meristem cells, and these cells are also the main targets of florpyrauxifen-benzyl. Exposure to this a.i. can stimulate the elongation and division of meristem cells, which lead to uncontrolled tissue growth and eventually death of the plant. The mode of action of this a.i. also determines effectiveness only when adequate dosage is present in the meristem, which is not usually directly exposed to the environmental media. A study conducted by the registrant showed that although rapid uptake of the a.i. through leaves occurred in all plants tested, significant inter-species differences were observed in the metabolism of the a.i. and its translocation to the meristem. It was concluded that these inter-species differences determine the relative sensitivity of a plant species to florpyrauxifen-benzyl. The registrant also demonstrated that certain invasive aquatic plant species were particularly sensitive to the a.i. while a significant number of the native species showed much higher tolerance. These findings make florpyrauxifen-benzyl a promising alternative to non-selective aquatic herbicides such as copper sulphate. Nonetheless, the information on this product's selectivity was almost exclusively empirical. Any non-target plant that has not been tested against this a.i. may still be susceptible. An effective method for reliably predicting sensitivity of untested native plants is not available. Elucidating the biochemical mechanism of transportation and metabolism of the a.i. in aquatic plants may help with the development of such a method.

Acute toxicity from florpyrauxifen-benzyl and its major metabolites to freshwater aquatic invertebrates and fish is low. The low solubility of the technical grade active ingredient (TGAI) in water, limited the concentrations tested in fresh water invertebrate and fish studies to below 60 µg a.i./L. Definitive LC/EC50s were not reported as they were above the highest concentrations tested for all species studied. Sublethal effects were observed in rainbow trout at concentrations of 12.3 µg a.i./L and above. All major

metabolites showed very low acute toxicity to aquatic organisms as well, with no definitive LC/EC50s reported. Chronic toxicity from TGAI and its metabolites were also low to freshwater aquatic invertebrates and fish. There were no statistically significant effects observed in studies with TGAI. Only one study in daphnia using the metabolite X11438848 reported statistically significant reproductive effects at 52.9 mg a.i./L.

Marine aquatic organisms did not appear to be significantly affected by acute exposure to florpyrauxifen-benzyl, with no definitive LC/EC50s identified in invertebrate and fish studies with TGAI or its major metabolites. However, concern for chronic toxicity in marine invertebrates could not be eliminated completely. Biologically significant adverse effects were observed in mysids at concentrations as low as 1.1 µg a.i./L and a NOAEC was not established. There were no indications of chronic toxicity effects in fish based on the available studies.

Information concerning toxicity to benthic invertebrates was limited. However, one 10-day sub-chronic study reported statistically significant non-lethal effects in freshwater midge at 4.32 µg a.i./L TGAI in pore-water, which was the lowest concentration tested. Chronic toxicity from two metabolites, X12300837 (hydroxy benzyl) and X11966341(hydroxy-acid), were also studied. No statistically significant effects were observed except delayed emergence in males exposed to 350 mg/kg of X11966341.

Data from studies submitted by the registrant showed no evidence of significant acute or chronic toxicity to avian and mammalian species from florpyrauxifen-benzyl. Toxicity to birds and mammals from major metabolites could not be evaluated as no relevant data were submitted.

Only acute toxicity data for honeybees were available and they appear to indicate a negligible effect from florpyrauxifen-benzyl TGAI when bees were exposed orally (LD50 > 105.4 µg a.i./bee) or by contact (LD50 > 100 µg a.i./bee). Information on chronic toxicity of the a.i. to honeybees was not available at the time of this review.

Environmental fate

Florpyrauxifen-benzyl has low solubility in water (0.015 µg/mL) and a relatively high K_{ow} (5.5 at pH=7). This suggests that the a.i., intended for use mostly in aquatic ecosystems, may have a high tendency to partition into the sediment or the biota. Nonetheless, it has been demonstrated that the a.i. degraded efficiently in aquatic and soil systems. Under laboratory conditions, aerobic and anaerobic aquatic metabolism half-lives are 5.1 days and 2.2 days, respectively. It is relatively more stable in soil, with aerobic and anaerobic metabolism half-lives at 21.5 days and 28.9 days, respectively. Field dissipation tests yielded similar results for aquatic systems, reporting a half-life of 1.4-2.3 days at the maximum single application rate of 50 ppb for in-water treatment. There is a likelihood that the a.i. may be more persistent in the sediment. However, deposition in the sediment may be manageable by using low application rates and spot treatment design. Three of the major metabolites are considered of ecological concern:

florpyrauxifen-acid (X11438848), florpyrauxifen-hydroxy benzyl (X12300837), and florpyrauxifen-hydroxy acid (X11966341). For the intended aquatic use, X11438848 appeared to be the major metabolite based on field dissipation studies. The metabolites are more persistent than the a.i. in water. The half-life for the terminal metabolite X11966341 after in-water treatment was estimated to be between 53-121 days.

Overall, florpyrauxifen-benzyl and its major metabolites are not expected to be persistent in the environment at typical application rates. Spot and partial treatment design may further reduce the likelihood of their accumulation at high levels in the sediment and soil.

Ecological toxicity risk modeling

Potential toxicity risk to non-target fish and wildlife species under labeled use were identified using the Pesticide Screening System (PSS) tool. This model estimates possible exposure levels of various representative species to the active ingredient when the product is used at application rates recommended in the label. A likely adverse effect to an exposed organism is suggested when the estimated exposure level exceeds the toxicity threshold(s) reported by the registrant.

The maximum seasonal application rates listed on the label were not used to calculate pesticide residue levels after a series of applications within a season. Instead, the maximum single application rate, maximum number of repeat applications, minimum re-application intervals, and field dissipation rates were used to predict the equivalent maximum seasonal application rate of pesticide after the last application. This method takes into account the degradation that would occur between applications. The calculation is accomplished by the PSS Max Application Rate Calculator operation of the PSS. It takes the single application rate in lbs. AI/acre, and using the field dissipation rate half-life, estimates the percentage of AI applied that will remain after the dissipation that will occur during the interval between consecutive applications. This quantity of a.i. is added to the amount applied in subsequent applications.

The label for ProcellaCOR EC allows up to three in-water treatments per year at 0.13 lb a.i./acre-foot (approx. 50 ppb) and no more than two treatments per year for foliar treatment at the maximum single application rate of 0.052 lb a.i./acre. The minimum interval between two consecutive treatments is 14 days.

The risk assessment models calculate risk quotients (RQs) for different organisms by dividing potential exposure levels by toxicity thresholds extracted from the USEPA Data Evaluation Record (DER) or study reports. For terrestrial risk assessment, the model estimates the residues likely to be present on treated vegetation for any given application scenario. For aquatic risk assessment, the model calculates the concentration of florpyrauxifen-benzyl likely to occur in the water column in test ponds of different volumes, using different runoff scenarios. RQs are calculated for both the upper toxicity threshold (LC50, EC50, LOEC, or LOEL) and the lower toxicity threshold (NOEC or NOEL). The one exception is the chronic mammalian dose-based model,

which uses the maximum acceptable toxicity concentration (MATC) as the toxicity threshold. The MATC is the geometric mean of the LOEL and NOEL. If the RQ is greater than 1.0, the organism would be exposed to levels higher than the toxicity threshold and adverse effects would be likely to occur. If the RQ is less than 1.0, then the likely exposure level is below the toxicity threshold, and severe toxicity is not anticipated. Results from the toxicity modeling are listed in Appendix II and discussed below.

Avian and mammalian toxicity modeling

The product is intended for aquatic use only. High residue levels in plants located in areas away from target waterbodies are not expected. Exposure to florpyrauxifen-benzyl through consumption of aquatic organisms from treated waterbodies is possible but studies submitted by the registrant indicated quick metabolism and excretion of the a.i. from freshwater species, thus bioaccumulation is not expected. Another likely exposure route for terrestrial vertebrates like birds and mammals is through drinking treated water. However, the most sensitive NOED for avian species was reported in Bobwhite quail at 398 mg/kg bw/day. At the maximum single application rate of 50 ppb, an adult quail with a bodyweight of 0.15 kg would need to consume 1194 L of water to reach that dosage, which is highly unrealistic. Toxicity data for mammals also suggested environmental exposure to florpyrauxifen-benzyl was unlikely to exceed the most sensitive NOED.

Aquatic toxicity modeling

For aquatic organisms, only the direct application scenario was modeled. However, definitive results were not acquired for most freshwater fish and invertebrate species because toxicity effects were not observed below the a.i. solubility limit. Exceedance of non-definitive endpoints were not considered reliable indicators of toxicity risk. The modeling results indicated no realistic toxicity concern for freshwater fish and invertebrate species. For algae and cyanobacteria, only acute NOECs were exceeded.

Pollinators

The intended use pattern of this product would indicate that direct contact or oral exposure at toxic levels is not likely if only spot or partial in-water treatment designs are used.

Risk assessment

The results from toxicity studies indicated overall low toxicity from florpyrauxifen-benzyl to most of the non-target animal species except benthic invertebrates and marine aquatic invertebrates. However, environmental fate studies showed no evidence of long term accumulation of the a.i. in the sediment and the product is intended to be used in freshwater systems only. The risk assessment modeling only detected

exceedance of acute NOECs for algae and cyanobacteria and no definitive acute LC/IC50s were reported for these organisms. If the treatment method is limited to spot and partial treatment and considering that florpyrauxifen-benzyl would dissipate quickly after application, effects to these organisms may be sufficiently reduced to levels of minimum ecological impact.

Toxicity data would suggest that there may be a higher risk to non-target aquatic and terrestrial vascular plants from environmental exposure to florpyrauxifen-benzyl. However, additional information from the registrant demonstrated apparent selective toxicity to invasive aquatic vascular plants. Tolerance of the a.i. was confirmed in a few common native plant species, but not all non-target plants were tested. All sensitivity data currently available is empirical. According to one study of the effects on aquatic macrophytes reviewed by OECD, the sensitivity of a plant was most likely determined by the ability of the a.i. to penetrate the meristem rapidly to achieve the biologically active dosage. The study also showed different species exhibit a gradience in tolerance, indicating that species categorized as “selective plants” may not be completely protected from the toxicity of the a.i. As a matter of fact, there has been reported incidences where the use of Rinskor, another herbicide product containing florpyrauxifien-benzyl and intended to be used for weed control in rice fields, damaged rice plants.

Therefore, caution must be taken if the areas to be treated host non-target plant species with no tolerance information available. Moreover, the well-demonstrated selectivity of florpyrauxifen-benzyl towards invasive species at relatively low application rates make it a promising tool for the management and restoration of the local aquatic flora. However, its effectiveness in esthetic use against native species is questionable. When used in invasive species management, an appropriate management plan should be developed. Aerial and ground applications, allowed by the label, over large areas should be avoided. Destruction of vegetation on a large scale, regardless of native or invasive species, can have disastrous ecological consequences, such as fish kills due to oxygen deprivation or loss of food and shelter. Spot and partial treatment designs should be recommended for most cases to allow effective management of invasive aquatic plants as well as maintaining healthy ecosystems.

Conclusion

Based on the information available, the BEH did not identify significant risk for ecotoxicological impacts from the labeled use of ProcellaCOR EC. BEH is concerned about allowing large scale aerial and ground applications of this product over much of the water body and surrounding riparian areas. These methods may not be more effective than spot and partial treatment designs but could have more indirect impact on the biota of these waterbodies. BEH does not object to the registration of the product but recommends additional site-specific review of treatment plans that specify aerial or large-scale ground application, for example treatment of one-third or more of the water body, to limit impact to native plants, fish and invertebrates.

Table 1. Physical/chemical characteristics of florpyrauxifen-benzyl

Parameter	Florpyrauxifen-benzyl
Empirical formula:	$C_{20}H_{14}C_{l2}F_2N_2O_3$
Molecular weight:	439.24 g/mol
Density (20°C):	0.202 g/mL
Water solubility (20°C):	0.015 µg/mL
Log K_{ow} (20°C):	5.5±0.04

Table 2. Active ingredients and application rates for product proposed for registration in New York State.

Treatment method*	Max single app. rate	Max # of apps/season*	Max seasonal app. rate	Min # of days between repeat apps
In-water treatment (lbs.AI/acre-ft)	0.13	3	0.39	14
Foliar applications (lbs.AI/acre)	0.052	2	0.104	14

*If not given on the label, the maximum number of applications was estimated by dividing the seasonal application rate by the smallest single application rate for each crop on the label.

Table 3. Summary of the ecotoxicological testing conducted with florpyrauxifen-benzyl. When multiple tests of the same type were conducted, only the most sensitive test result is reported here. These are the toxicity data utilized in risk assessment modeling.

Organism	Test/Study Type	LC50/EC50/ or LOEL/LOEC	NOEL/NOEC
Mammalian			
Rat	Acute oral	>5000 mg/kg bw	
Rat	90 day feeding	>1000 mg/kg/day	1000 mg/kg/day
Rat	2 generation reproduction	>300 mg/kg/day	300 mg/kg/day
Mouse	78 week chronic/ carcinogenicity	>800 mg/kg/day	800 mg/kg/day
Avian			
Bobwhite quail	Acute oral	>2500 mg/kg/day	2500 mg/kg/day
Zebra finch	Acute oral	>2250 mg/kg/day	2250 mg/kg/day
Bobwhite quail	5 day dietary	>5640 mg/kg/day	5640 mg/kg/day
Mallard duck	5 day dietary	>5640 mg/kg/day	5640 mg/kg/day
Bobwhite quail	Avian reproduction	999 mg/kg/day	398 mg/kg/day
Mallard duck	Avian reproduction	>999 mg/kg/day	999 mg/kg/day
Aquatic – freshwater fish			
Rainbow trout (*Oncorhynchus mykiss*)	96 hour acute	>0.049 mg/L	0.049 mg/L

Organism	Test/Study Type	LC50/EC50/ or LOEL/LOEC	NOEL/NOEC
Carp (Cyprinus carpio)	96 hour acute	>0.0414 mg/L	0.0414 mg/L
Fathead minnow (Pimephales promelas)	32 day early life stage	>0.0518 mg/L	0.0518 mg/L
Aquatic – freshwater invertebrates			
Daphnia magna	96 hour acute	>0.0626 mg/L	0.0626 mg/L
	21 day life cycle	>0.0385 mg/L	0.0385 mg/L
Marine/Estuarine			
Sheepshead minnow (*Cyprinodon variegatus*)	96 hour acute	>0.0403 mg/L	0.0403 mg/L
Mysid shrimp (*Americamysis bahia*)	96 hour acute	>0.026 mg/L	0.026 mg/L
	Chronic toxicity test	0.0518 mg/L	<0.0518 mg/L
Oyster larvae (*Crassostrea virginica*)	96 hour shell deposition	>0.0251 mg/L	0.0251 mg/L
Aquatic Plants			
Aquatic macrophyte – *Lemna gibba*	7 day EC_{50}	>0.0414 mg/L	0.0414 mg/L
Green algae – *Pseudokirchneriella subcapitata*	72 hour EC_{50}	>0.0612 mg/L	0.0298 mg/L
Blue-green algae *Anabaena flos-aquae*	96 hour EC_{50}	>0.0513 mg/L	0.0285 mg/L
FW diatom – *Navicula pelliculosa*	96 hour EC_{50}	>0.0565 mg/L	0.0124 mg/L
Marine diatom – *Skeletonema costatum*	96 hour EC_{50}, cell density	>0.0389 mg/L	0.0124 mg/L
Terrestrial invertebrates			
Honeybee	Acute contact	>0.100 mg a.i./bee	0.100 mg a.i./bee
	Oral	>0.1054 mg a.i./bee	0.1054 mg a.i./bee
Aquatic – sediment			
Chironomus tentans	whole sediment 10-day toxicity test	>0.0346 mg a.i./L	0.0346 mg a.i./L

Appendix II
Fish Direct Application Toxicity Assessment for
Florpyrauxifen-benzyl

This program evaluates the toxicity of a direct application of Florpyrauxifen-benzyl to biota in a pond with a surface area of one acre and a depth of either 0.5 feet or one foot.
If the concentration of Florpyrauxifen-benzyl in the water exceeds a toxicity threshold, the model prints EXCEEDED next to the corresponding aquatic organism. If a toxicity threshold is not exceeded, the model prints SAFE.

Depth of pond = 1 ft.

Application rate = 0.13 lbs AI/acre

The water column concentration of Florpyrauxifen-benzyl = 4.780507E-02 mg/L; **Module not solubility limited**.

Florpyrauxifen-benzyl solubility limit = 0.015 mg/l

SPECIES	EC/LC50 mg/L	NOEC mg/L
Common carp	> 0.0414	0.0414
Rainbow trout >	> 0.049	0.490
Daphnia magna >	> 0.0626	0.0626
Sheepshead minnow >	> 0.0403	0.0403
Mysid shrimp >	> 0.026	0.026
Oyster >	> 0.0251	0.0251
Lemna gibba>	> 0.0414	0.0414
P. subcapitata	> 0.0612	EXCEEDED
Anabaena flos-aquae>	> 0.0513	EXCEEDED
Navicula pelliculosa>	> 0.0565	EXCEEDED
Skeletonema costatum>	> 0.0389	EXCEEDED

STATE OF CONNECTICUT
DEPARTMENT OF PUBLIC HEALTH

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TOCOLOGY OVERVIEW AND ASSESSMENT FOR SELECTED HERBICIDES:
Procellacor within Drinking Water Watersheds
Environmental Health Section, October 2018

Through the Memorandum of Understanding between the Connecticut Department of Energy and Environmental Protection and the Drinking Water Section of the Connecticut Department of Public Health (CTDPH) regarding the use of pesticides in drinking water management areas, CTDPH's Environmental and Occupational Health Assessment program has reviewed the proposed use of Procellacor. This CTDPH evaluation is intended to inform the process by providing a toxicity and environmental fate review.

In summary, our findings are that Procellacor has low mammalian toxicity and no clear indication of carcinogenicity, mutagenicity or ability to cause reproductive effects, especially at the low environmental concentrations possible from its proper application. Procellacor's environmental degradation time is short, indicating that there is a low probability of detecting the parent compound in drinking water. Degradation time is longer however for hydroxyl acid breakdown product which also sequesters in plant sugars. Despite the uncertainty around the environmental persistence of Procellacor's degredates, the CTDPH does not believe that the use of this herbicide in watershed areas will adversely impact drinking water supplies or human health when used in accord with US EPA label instructions.

PRODUCT INFORMATION

Active Ingredient: Florpyrauxifen-benzyl (2.7%)
CAS #: 1390661-72-9
Trade Name: PROCELLACOR EC
EPA Reg # 67690-80 (February 27, 2018) Decision No. 534950
Application methods and rates:

- For in-water applications, the maximum single application rate is 80 fluid ounces product per acre-foot of water with a limit of three applications per year.
- For aquatic foliar applications, do not exceed 32 fluid ounces product per acre for a single application and do not apply more than 64 fluid ounces product total per acre per year.

Inactive Ingredients:

- Ethylhexanol (2.1 %)
- Methanol (0.9%)
- Unreported (94.3%)

Use Restrictions:

- There are no restrictions for recreational purposes, including swimming and fishing.
- Allow 14 days or greater between applications.

MECHANISM OF HERBICIDAL ACTIVITY

Procellacor belongs to the arylpicolinate group of synthetic auxin herbicides. This herbicide mimics the effect of a persistent high dose of the natural plant hormone auxin, causing over-stimulation of specific auxin-regulated genes which results in the disruption of several growth processes in susceptible plants.

ENVIRONMENTAL FATE AND PERSISTANCE

Water Column:
Procellacor has a low water solubility (about 15 µg/L) and is rapidly hydrolyzed in surface water with a half-life of 1.3 days at pH 9. When exposed to direct sunlight, the photolytic half-life approximately 0.1 days.

Soils and Sediments:
Procellacor log Koc values are approximately 5.4 to 5.5, indicating that the compound will bind to organic carbon of soils with high affinity. The compound degrades in aerobic soil with half-lives ranging from 2.5 to 34 days. Anaerobic soil metabolism rates are similar to the aerobic rates. The parent compound is thus not expected to accumulate in the sediments of treated lakes.

Environmental Degradants:
The primary degradation pathway in aerobic and anaerobic sediments and the water column is through cleavage of the benzyl ester parent to form the acid metabolite (X11438848). (The degradation scheme is outlined in the Appendix.) The acid metabolite exhibits moderate mobility potential, with an average Koc value of 115 mL/g. In acidic environments, the ester moiety is spared and the methyl-ether group cleaved to form an alcohol (X12300837). This compound has a low water leaching potential (Koc value is 2727 mL/g) as it binds tightly to soil. It is thus not expected to be a concern in surface water. Procellacor (XDE-848 benzyl ester) is also degraded by sunlight. The dechlorinated acid degradant of photolysis, X12393505 and the aforementioned primary hydrolysis product have similar leaching potentials. Both the acid and the alcohol compounds are further degraded to a hydroxyl acid (X11966341). This hydroxyl acid metabolite has a geometric mean water/organic carbon partition coefficient (Koc) of 61.2 (Volume 3 – Annex CA - B.8 – Page 147), indicating that this compound is mobile in the aquatic environment. The hydroxyl metabolite is also moderately persistent in the environment. The water half-life (DT50) in a water/sediment system ranged from 37.3 to 87.9 days (Volume 3 – Annex CA - B.8 – Page 237). The list of Procellacor degradants that could be present in surface waters therefore includes; X11438848 (XDE-848 acid), X12131932 (dechlorinated XDE-848 BE), X12393505 (dechlorinated XDE-848 acid), and X11966341 (hydroxyl acid).

Degradation times for the first three aforementioned degradants are short, while the degradation time for the hydroxyl acid is greater and may be prolonged. The prolonged effect is likely due to sequestration with plant sugars (e.g.; cellulose) via conjugation of the hydroxyl acid with glucose. Significant portions of the hydroxyl acid metabolite were converted to either a glucose conjugate (X12431091) or a glucose-malonic acid conjugate (X12431475) in treated crops (Volume 1 – Level 1 – Page 41).

The X11966341 (hydroxyl acid) degradant is formed in significant quantities relative to the applied dose. When radiolabeled Procellacor was applied to the water layer in aerobic flooded soil systems, the maximum total system concentration of X11966341 was 64% of the applied radioactivity (Volume 1 – Level 1 – Page 44).

While the parent compound is unlikely to be a contaminant of concern in drinking water, this has not been demonstrated for the X11966341 (hydroxyl acid) degradant. Further work should investigate this degradant's fate and persistence in the aquatic environment.
Furthermore, as the hydroxyl degradant is known to sequester in plant sugars, the possibility that decomposition could release this degradant into the water column should be evaluated.

TOXICOKINETICS

Mammalian absorption and elimination:
Excretion is primarily via feces (> 51%) and urine (8-42%) with the majority eliminated within 24 hr. Plasma elimination of Procellacor is biphasic with a rapid declining plasma alpha phase ($t_{1/2\alpha}$=~2 hours) and a more slowly declining beta phase plasma half-life ($t_{1/2}$= 27-51 hours) in both male and female rats. The fraction eliminated in the urine was higher in the lower dose groups, consistent with higher absorption at lower doses. This kinetic non-linearity is consistent with either reduced absorption or higher biliary elimination at the high dose, as possible reasons for reduced renal elimination at the high dose. Based on relatively low percent recoveries in the liver and in bile samples the non-linearity appears to be a result of reduced absorption of Procellacor at higher dose levels.

Mammalian metabolism:
The kinetic profile of Procellacor was consistent across the species in rats, mice, dogs and rabbits, with a rapid systemic absorption and complete hydrolysis of the absorbed fraction to the acid metabolite (X11438848) and other minor metabolites. There was no Procellacor detected in the urine, blood or liver samples across species suggesting that the systemic exposure is primarily to the acid metabolite (X11438848). The hydroxyl acid metabolite (X11966341) is a small percentage of the dose and is eliminated through conjugation. As a percentage of the dose, the sum of the hydroxyl acid and its conjugate is less than 5%.

The European Union, in their assessment, considered the hydroxyl acid (X11966341) toxicity to be covered by the toxicological database of the parent compound (Volume 1 – Level 1 – Page 33). Though this assumption cannot presently be refuted, the lack of toxicity data for this specific degradant represents a significant gap in the toxicology database because, as per the discussion in the section on environmental degradants, the hydroxyl acid (X11966341) is the contaminant of greatest concern for surface water.

Results from in vitro comparative metabolism study have shown that Procellacor was highly metabolized in liver microsomes from rat, mouse, dog, rabbit, and human donors. No unique metabolites were formed in human microsomal incubations compared to rat, mouse, rabbit or dog microsomal incubations.

Mammalian distribution:
Procellacor is well metabolized primarily in to a single metabolite XDE-848 acid (X11438848), and readily eliminated in urine and feces from the rat, with almost no tissue residues. In necropsied test animals, the concentrations of Procellacor were highest, by far, in the GI tract, followed by urinary bladder, plasma, kidney and liver.

When goats were dosed with radiolabeled Procellacor at 10 mg/kg dry feed in the diet for 7 consecutive days, approximately 80% of applied test material was recovered. Of the radioactivity recovered, > 99% was eliminated from the animals through the feces and urine. Less than 1% of recovered radioactivity was detected in the edible tissues and milk. Only the liver and kidney tissues contained > 0.010 mg/kg. Edible tissues and milk contained < 0.010 mg/kg. Parent compound distribution is thus limited primarily to within the portal of entry and primary excretion tissues.

Maximum Tolerated Dose:
The inflection point for onset of a sublinear relationship between administered dose and systemic concentration is a benchmark which represents the kinetically derived maximum dose (KMD). In test animals exposed to Procellacor, this inflection point is between 300 and 1000 mg/kg*day. The highest dose tested in registration studies is within this range and justifiably represents the practical limit on administered dose.

TOXICOLOGY DATABASE

Tumor Effect:
In a long-term study, the incidence of adenocarcinoma of the rat mammary gland was 0/50, 0/6, 1/11, and 2/50 in males given 0, 10, 50 or 300 mg/kg/day, respectively (Two-Year Chronic Toxicity/Oncogenicity Study in F344/DuCrl Rats. In Volume 3 – Annex CA - B.3 – Page 222). This dose response has been identified as possibly indicative of a data gap and has led some reviewers to consider 50 mg/kg*day the NOAEL for an endocrine effect. (European Food Safety Authority (2018) https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2018.5378) Others however have noted that the minimally higher incidence of mammary gland adenocarcinomas in males given the high-dose of 300 mg/kg/day was not statistically significant, and while effects on mammary gland including mammary tumors are most commonly seen in female rats, study, there were no treatment-related effects on the mammary gland of females at any dose in this study, and no females from either the control or treatment groups had an adenocarcinoma of the mammary gland.

While this response to Procellacor may represent a data gap, the response was positive in just a single test animal in the 50 mg/kg group, and the effect is not dose-dependent. Though the result is most likely an artifact, the small number of test animals in the 10 and 50 mg/kg*day groups highlights a weakness in the study.

TUMOR EFFECT OR THRESHOLD							
*LOAEL (mg/kg*day)*	*NOAEL (mg/kg*day)*	*Doses (mg/kg*day)*	*Route of Exposure*	*Tumor Endpoint*	*N (initial)*	*# Dosing Days*	*Model*
none	>300	0,10,50,300	Diet	no significant tumor result *	50/(sex* group)	760	Rat
none	>800(F),>1000(M)	0,50,200,800(F), 1000(M)	Diet	no significant tumor result	50/(sex* group)	547	Mouse

* Dose response for interstitial cell adenomas of the testes was within the range of historical controls.

Sub-Chronic Exposure Studies

Short-term dietary toxicity studies in F344 rats, CD-1 mice, and Beagle dogs were conducted. There were no treatment-related effects on clinical signs, body weights, body weight gains, feed consumption, ophthalmology, hematology, prothrombin time, clinical chemistry parameters, urinalysis, organ weights, and gross or histopathologic observations. There was no evidence of short-term toxicity when Procellacor was administered up to a limit dose of 1000 mg/kg/day for 28 days or 90 days in rats, mice or dogs.

SYSTEMIC EFFECT OR THRESHOLD (SUBCHRONIC)								
*HDT (mg/kg*day)*	*LOAEL (mg/kg*day)*	*NOAEL (mg/kg*day)*	*Doses (mg/kg*day)*	*Effect*	*Route of Exposure*	*# Dosing Days*	*Model*	*N (initial)*
1000	none	>1000	0,250,500,1000	No effect	Diet	28	Rat	5 each sex/grp
1000	none	>1000	0,250,500,1000	No effect	Diet	28	Mouse	5 each sex/grp
1000	none	>1000	500, 1000	5% d bw, hd	Diet	28	Dog	2 male, 4 female
1000	none	>1000	0,100, 300, 1000	No effect	Diet	90	Rat	5 each sex/grp
1000	none	>1000	0,100,300,1000	F HDT: 9.6% d bw & 31% d bwg	Diet	90	Mouse	10 each sex/grp
1008	none	>1008	0,106,336,1008	No effect	Diet	90	Dog	4 each sex/grp

Chronic Exposure Studies

In the rat study there were no statistically significant or treatment-related changes in final body weights or any of the organ weights of males or females at any dose level as compared to the respective controls. There were no treatment-related histopathological observations in any of the organs/tissues examined.

In the mouse study there were no treatment-related differences in body weights/body weight gains of males or females between any of the treatment groups as compared to their respective controls. There were no treatment-related histopathologic observations in males or females at any dose level.

SYSTEMIC EFFECT OR THRESHOLD (CHRONIC)							
*HDT (mg/kg*day)*	*LOAEL (mg/kg*day)*	*NOAEL (mg/kg*day)*	*Doses (mg/kg*day)*	*Effect*	*Route of Exposure*	*# Dosing Days*	*Model*
300	none	>300	0,10,50,300 *	none	Diet	365	Rat
800(F),1000(M)	none	>800(F), >1000(M)	0,50,200,800(F), 1000(M)	none	Diet	547	mouse

* Above kinetically derived maximum dose

Reproductive

There were no treatment-related effects in clinical observations, body weights, feed consumption, reproductive function, litter size, prenatal/early neonatal growth and survival of the offspring, organ weights, gross pathology or histopathology in either sex at all dose levels tested.

REPRODUCTIVE EFFECT OR THRESHOLD								
*Doses (mg/kg*day)*	*Parental LOAEL, devel/repro (mg/kg*day)*	*Parental NOAEL, devel/repro (mg/kg*day)*	*Offspring LOAEL, devel/repro (mg/kg*day)*	*Offspring NOAEL, devel/repro (mg/kg*day)*	*Route of Exposure*	*Subject N*	*Note*	*Model*
0,100,300, 1000	none	1000	none	1000	Diet	10/(sex*group)	Screening study	Rat
0,10,50,300	none	300	none	300	Diet	25/(sex*group)	Dietary Two-Generation Reproduction	Rat

Developmental

In rats, administration of Procellacor in the diet at 975 mg/kg*day, the KMD, produced no treatment-related maternal toxicity and no indication of embryo/fetal toxicity or teratogenicity.

In rabbits, administration of Procellacor in the diet at 1042 mg/kg*day, the KMD, produced no treatment related maternal toxicity and no indication of embryo/fetal toxicity or teratogenicity.

DEVELOPMENTAL EFFECT OR THRESHOLD										
*HDT (mg/kg*day)*	*Doses (mg/kg*day)*	*Maternal LOAEL (mg/kg*day)*	*Maternal NOAEL (mg/kg*day)*	*Effect, maternal*	*Offspring LOAEL (mg/kg*day)*	*Offspring NOAEL (mg/kg*day)*	*Effect, developmental*	*Route of Exposure*	*Model*	*Study N*
975	0,975	none	975	none	none	975	none	Diet	Rat	24/(group)
1042	0,1042	none	1042	none	none	1042	no sig ef treat *	Diet	Rabbit	24/(group)

* The effect on percent postimplantation loss was above historical controls but statistically insignificant

TOXICOLOGY SUMMARY

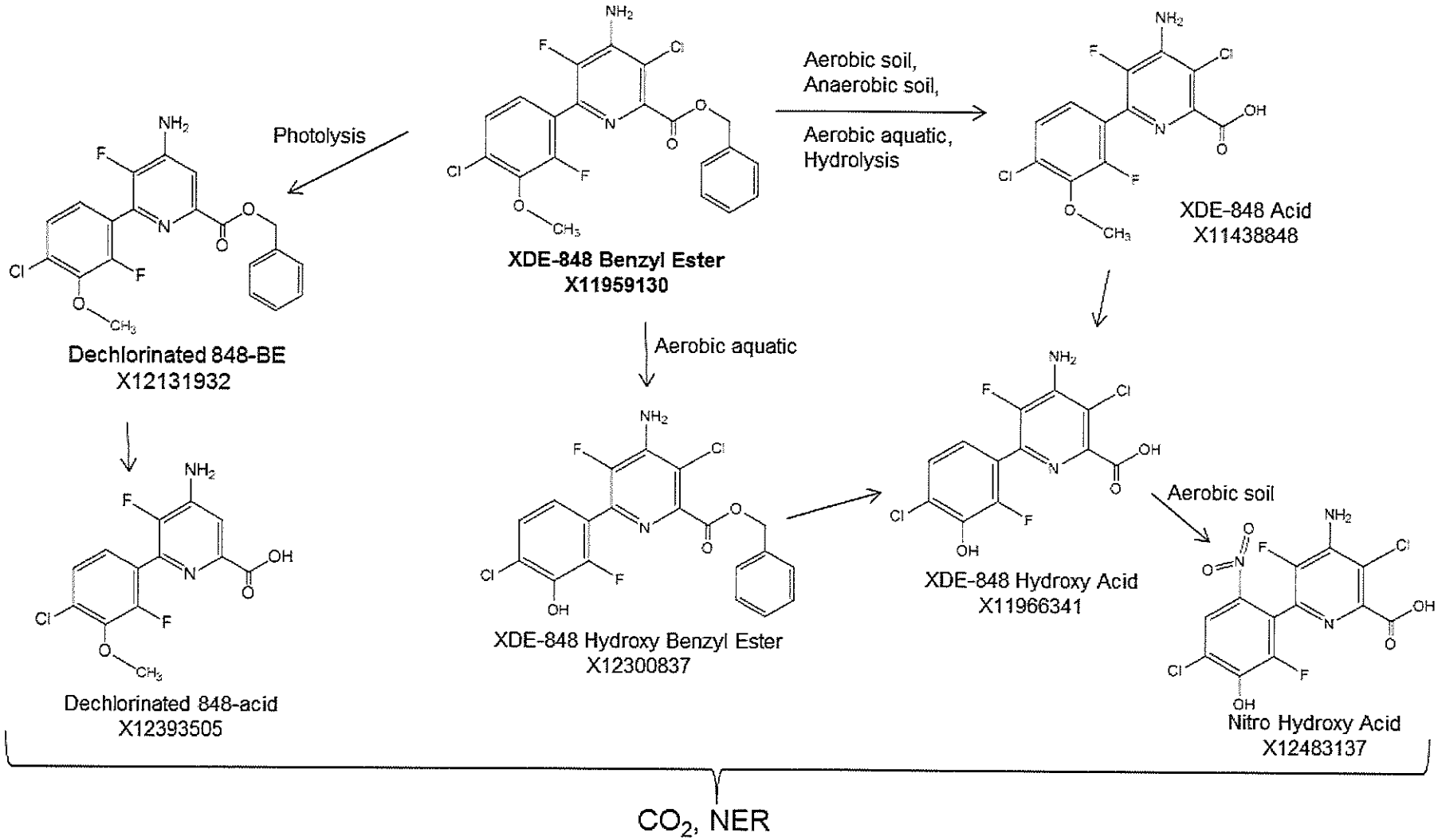
The toxicology database for the parent compound, Procellacor (XDE-848 benzyl ester), is nearly complete with the exception of some uncertainty focused at the low denominators in the 10 and 50 mg/kg*day groups in the long-term toxicity study. (See the section on tumor effect.) Overall, the parent compound is poorly absorbed in mammalian systems, and distribution is limited to the organs of excretion.

The available mammalian toxicology database for this herbicide understandably focuses almost exclusively on the parent compound. Within this report's scope (use around drinking water supplies), this is a limitation because the parent compound is not the most persistent in the aquatic environment. The hydroxyl acid degradant (X11966341) therefore presents the greatest exposure potential within the drinking water exposure scenario.

SOURCES

The information referenced in this report was obtained from the European Food Safety Authority; "Public consultation on the active substance florpyrauxifen-benzyl - Updated: 28 July 2017", available at https://www.efsa.europa.eu/en/consultations/call/170705. Information from the relevant US EPA docket was also reviewed (https://www.regulations.gov/docket?D=EPA-HQ-OPP-2016-0560).

Appendix: Route of Degradation of Procellacor (XDE-848 BE) in the Environment (Volume 1 – Level 1 – Page 82)



Final Registration Decision on the New Active Ingredient Florpyrauxifen-benzyl

Approved by: Richard P Keigwin, Jr

Richard P. Keigwin, Jr., Acting Director

Office of Pesticide Programs

Date: 9/8/2017

Summary

This document announces that the U.S. Environmental Protection Agency (EPA) is granting an unconditional registration under Section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for the new active ingredient florpyrauxifen-benzyl (XDE-848 benzyl ester or Rinskor™; 2-Pyridinecarboxylic acid, 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-, phenylmethyl ester).

Florpyrauxifen-benzyl, an herbicide, is for use on rice (pre- and post-flooding) for post-emergence grass, sedge, and broadleaf weed control in Arkansas, Florida, Louisiana, Mississippi, Missouri, South Carolina, Tennessee and Texas; and for national use on freshwater aquatic sites, including foliar application to emergent aquatic vegetation (foliar-aquatic) or direct application to water body (in-water) use sites. The aquatic use is intended for management of freshwater aquatic vegetation in slow-moving/quiescent waters with little or no continuous outflow in ponds, lakes, reservoirs, freshwater marshes, wetlands, bayous, drainage ditches, and non-irrigation canals, including shoreline and riparian areas in or adjacent to these sites, as well as, management of invasive freshwater aquatic vegetation in slow-moving/quiescent areas of rivers (coves, oxbows or similar sites). Target plants for the aquatic use include invasive species such as hydrilla (*Hydrilla verticillata*), Eurasian watermilfoil *(Myriophyllum spicatum*), and crested floating heart (*Nymphoides cristata*). Tolerances on rice, freshwater fish, and shellfish (crustacean and mollusc) are being proposed to support these uses.

Florpyrauxifen-benzyl will be formulated as one technical product (Rinskor™ Technical) and four end-use products. GF-3480, GF-3206, and GF-3565 are proposed for use on rice only and GF-3301 is proposed for use on the rice and aquatic uses. The Rinskor™ Technical contains 94.6% florpyrauxifen-benzyl. The end-use product GF-3206 contains 2.7% florpyrauxifen-benzyl. The end-use product GF-3301 contains 26.5% florpyrauxifen-benzyl. The end-use product GF-3565 contains 1.3% florpyrauxifen-benzyl and 2.1% penoxsulam. The end-use product GF-3480 contains 2.13% florpyrauxifen-benzyl and 10.64% cyhalofop-butyl.

Although florpyrauxifen-benzyl is a new active ingredient, penoxsulam and cyhalofop-butyl, the co-formulated active ingredients in GF-3565 or GF-3480, respectively, are both currently registered active ingredients with labeled use on rice. Since penoxsulam and cyhalofop-butyl will be co-formulated in products only proposed for use on rice, no new exposures for these active ingredients are being considered with this registration action, and no new assessments were performed for penoxsulam and cyhalofop-butyl. Therefore, this document discusses the results of the EPA's findings on the assessment of the new active ingredient florpyrauxifen-benzyl and its use in rice and aquatic (in-water and foliar) use sites.

Background

On September 15, 2015, the EPA received an application from Dow AgroSciences (DAS) to register products containing the new active ingredient florpyrauxifen-benzyl (CAS No. 1390661-72-9), a post emergence herbicide, for use on rice fields (Labeled for use only in Arkansas, Florida, Louisiana, Mississippi, Missouri, South Carolina, Tennessee and Texas) and for aquatic applications (in-water and foliar) for management of freshwater aquatic vegetation. The application also requested the establishment of tolerances for residues resulting from these uses.

Florpyrauxifen-benzyl is a new synthetic auxin (plant hormone) and belongs to the arylpicolinate class of herbicides (WSSA Group 4; HRAC Group O). Florpyrauxifen-benzyl, like other synthetic auxins, mimics the plant growth hormone auxin, resulting in the disruption of growth processes in susceptible plants. Florpyrauxifen-benzyl undergoes de-esterification to its corresponding free acid florpyrauxifen (also known as XDE-848 acid). Alternatively, depending on the environmental conditions, florpyrauxifen-benzyl can undergo demethylation to yield XDE-848 benzyl hydroxy, which then can hydrolyze to form XDE-848 hydroxy acid.

The product labels specify that florpyrauxifen-benzyl is to be applied as a post-emergent herbicide on rice with a maximum single application rate of 0.027 lb a.i./A. Two foliar spray applications for rice are allowed per year, with a maximum yearly rate of 0.0525 lb a.i./A. The preharvest interval (PHI) is 60 days. One end use product (GF-3301) can be applied directly to water or sprayed into emergent foliage of aquatic plants for purposes of freshwater aquatic vegetation management. For the in-water aquatic use, the concentration of the active ingredient in the volume of water must be calculated. Three applications a year are permitted, with a maximum active ingredient concentration of 50 ppb per application. For the aquatic foliar application, the maximum single application rate is 0.0527 lb a.i./A, with a maximum of two applications per year (maximum of 0.1054 lbs a.i./A/year). For both the rice and aquatic uses, applications can be made using aerial or ground equipment. A 14-day interval is required between treatments.

On February 8, 2016, florpyrauxifen-benzyl was granted Reduced Risk status for both the rice and aquatic uses based predominantly on reduced risk to human health when compared to registered alternatives.

Evaluation of Risk to Human Health and the Environment

In evaluating a pesticide registration application, the EPA assesses a wide variety of exposure information *(i.e.,* where and how the pesticide is used), environmental fate studies *(i.e.,* how the chemical will move in the environment) and toxicity studies *(i.e.,* effects on humans and other non-target organisms) to determine the likelihood of adverse effects (*i.e.,* risk) from exposures

associated with the proposed use of the product. Risk assessments are developed to evaluate the environmental fate of the compound as well as how it might affect a wide range of non-target organisms including humans, terrestrial and aquatic wildlife and plants. On the basis of these assessments, the EPA evaluates and, as appropriate, approves language for each pesticide label to ensure the directions for use and safety measures are appropriate to mitigate any potential risk. The pesticide's label helps to communicate essential limitations and mitigations that are necessary for public safety. It is a violation of federal law to use a pesticide in a way that conflicts with the label.

Assessment of Risk to Human Health

The EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. The EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The toxicology database for florpyrauxifen-benzyl is considered complete and no additional data are required at this time.

Toxicological Profile

One of the unique features for this herbicide is that, with oral administration, the maximum absorption occurs at approximately 300 mg/kg, above which the blood level of the test material remains constant. Hence, 300 mg/kg is considered as the kinetically-derived maximum dose. The absorbed florpyrauxifen-benzyl was rapidly metabolized, and the parent compound was essentially undetectable in the majority of blood samples, but it was found in large quantities in feces indicating much of the administered dose is not absorbed. The majority of the administered dose was eliminated within the first 24 hours post-dosing.

Single or repeated dose studies performed by any routes and durations of exposure produced no adverse effect following florpyrauxifen-benzyl treatment at or above the limit dose (1000 mg/kg/day) or the kinetically derived maximum dose. Chronic administration of florpyrauxifen-benzyl did not show any carcinogenicity potential in rats and mice, and it was not genotoxic. Florpyrauxifen-benzyl is of very low acute toxicity by the oral, dermal and inhalation routes of exposure. It is not an irritant to eyes or skin but demonstrated only a weak dermal sensitization potential in mouse local lymph node assay.

Since no adverse toxicity was found in the available toxicology database, toxicity endpoints and points of departure for risk assessment were not selected for florpyrauxifen-benzyl exposure scenarios, and a quantitative risk assessment was not conducted. Instead, a qualitative human health risk assessment has been conducted to support the proposed uses of florpyrauxifen-benzyl.

Residues in Food and Drinking Water

The submitted residue chemistry studies are adequate for establishing appropriate tolerance levels for enforcement and for purposes of risk assessment. The recommended residues of concern for the risk assessment and tolerance expression in crops are the parent florpyrauxifen-benzyl and its acid metabolite, florpyrauxifen (XDE-848 acid) only.

There is potential for exposure to florpyrauxifen-benzyl from food and drinking water based on the proposed uses. Florpyrauxifen-benzyl reaching water bodies by drift or applied directly to water (aquatic use) is expected to degrade rather quickly, forming into degradates that are structurally similar to the parent compound and are expected to have the same or lesser toxicity and similar hazard to florpyrauxifen-benzyl. Therefore, the degradates are not expected to cause any human health adverse effects and the EPA does not have any hazard concern for metabolites and/or degradates of florpyrauxifen-benzyl that may be found in food or drinking water.

Aggregate Exposure Assessment

Potential exposure to florpyrauxifen-benzyl residues in food (including fish and shellfish) could occur because florpyrauxifen-benzyl may be applied directly to growing rice and aquatic sites. These applications can also result in florpyrauxifen-benzyl reaching surface and groundwater, both of which can serve as sources of drinking water. There are no proposed uses in residential settings and there are no anticipated residential exposures.

Based on the lack of toxicity in the florpyrauxifen-benzyl toxicological database, the EPA has determined that a quantitative risk assessment is not needed at this time for dietary (food and drinking water), residential, aggregate, or cumulative exposure. Since no adverse toxicity is found in any of the available toxicological studies, and no toxicity endpoints and points of departure are established for risk assessment, no quantitative risk assessment was conducted. Therefore, the FQPA safety factor to protect infants and children is not necessary. The EPA concludes that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to florpyrauxifen-benzyl.

Occupational Exposure Assessment

Occupational handler and post-application short and intermediate term exposures to florpyrauxifen-benzyl may occur as a result of the proposed agricultural uses. Applicators might be exposed while handling the pesticide prior to application, mixing/loading the pesticide, and during application. Also, there is a potential for post-application exposure for workers re-entering treated fields.

No adverse effects were observed in the submitted toxicological studies for florpyrauxifen-benzyl regardless of the route of exposure; therefore, a quantitative occupational exposure assessment was not conducted. Thus, no quantitative occupational exposure assessments are

needed for the EPA to conclude with reasonable certainty that occupational exposures to florpyrauxifen-benzyl do not pose a significant human health risk. Technical florpyrauxifen-benzyl is of low acute toxicity by oral, dermal, and inhalation routes of exposure, since all acute studies were in the lowest toxicity category (Category IV). The acute studies showed that the four end-use products were also in toxicity Category IV except for the eye irritation study which was toxicity Category III for all end-use products. Based on the low acute toxicity, baseline personal protective equipment (PPE) is required which includes a long sleeved shirt, long pants, shoes, socks, protective eyewear, and waterproof gloves. The restricted entry interval (REI) is 12 hours.

Assessment of Ecological Risk

Environmental Fate

Florpyrauxifen-benzyl has a relatively low potential for volatility from water, moist soils, and dry surfaces, due to its low vapor pressure. Florpyrauxifen-benzyl shows low mobility in soils and readily binds to soil or sediment. The dominant routes of degradation of florpyrauxifen-benzyl are through aerobic aquatic metabolism and aqueous photolysis. When applied to rice, florpyrauxifen-benzyl is expected to reach paddy water and soil from labeled uses, but is expected to partition to the soil where it is strongly bound to sediment. The parent compound is expected to degrade via aerobic flooded soil metabolism (half-lives of 12 – 31 days), anaerobic soil metabolism (half-lives of 15 – 46 days), and aqueous photolysis (half-life of < 1 day). When applied directly to aquatic sites, florpyrauxifen-benzyl is expected to dissipate much more quickly, with rapid photolysis (<1 day) and aerobic aquatic metabolism (4-6 days) as the major routes of degradation.

The degradation of parent florpyrauxifen-benzyl results in the following major transformation products: XDE-848 acid, XDE-848 benzyl hydroxy, and XDE-848 hydroxy acid. These degrade more slowly than the parent compound, with half-lives ranging from 6.3 – 18 days for the acid, 6 – 14 days for the benzyl hydroxy, and 127-729 days for the hydroxy acid.

Exposures to florpyrauxifen-benzyl are expected through spray drift (from rice and foliar applications), direct contact with treated water (aquatic applications), or from runoff from treated areas (rice soil applications). Florpyrauxifen-benzyl and its degradates may reach surface waters due to run-off or release of paddy waters into receiving surface water bodies, or may move downstream after direct application to water. Thus, exposure to florpyrauxifen-benzyl and its degradates may occur to terrestrial organisms (from spray drift and runoff), and aquatic organisms (from direct exposure and downstream movement of treated water) from the proposed uses.

Ecological Hazard

Florpyrauxifen-benzyl is practically non-toxic on an acute basis to bird, mammals, and bees. Toxicity to fish and aquatic organisms was not observed, in most cases, at the highest levels tested, which approach the limit of solubility of the compound. Chronic toxicity to birds and mammals was not observed in the available data; however, chronic tests with the midge and mysid both showed toxicity at all levels tested. The parent compound as well as the three degradates demonstrate some toxicity to plants, however, the degradates show lower toxicity than the parent compound. For terrestrial plants, dicots are far more sensitive than monocots, and for aquatic plants, vascular plants are more sensitive than non-vascular species. Bioaccumulation data in fish showed low bioconcentration factors and rapid depuration, suggesting extensive metabolism of florpyrauxifen-benzyl. Metabolism data for mammals also demonstrates extensive metabolism, indicating bioaccumulation of florpyrauxifen-benzyl is unlikely. Additionally, florpyrauxifen-benzyl is relatively short lived in aquatic metabolism systems (2-6 days), which further limits its potential for bioaccumulation in the environment.

Ecological Risk Characterization

Ecological risk characterization integrates the results of the exposure analysis and ecotoxicity data to evaluate the likelihood of adverse ecological effects. The means of integrating the results of exposure and ecotoxicity data is called the quotient method. For this method, risk quotients (RQs) are calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic (RQ = Exposures/Toxicity). RQs are then compared to the EPA's levels of concern (LOCs). The LOCs are criteria used by the EPA to indicate potential risk to non-target organisms. The criteria indicate whether a pesticide, when used as directed, has the potential to cause adverse effects to non-target organisms.

The originally proposed labels for the aquatic use instructed the applicator to achieve a target water concentration of 150 ppb. Due to risk concerns to certain taxa at that rate, a lowered target concentration of 50 ppb was also assessed. This level, which is still efficacious for aquatic weed control, results in significantly lower exposure, and therefore risk, to non-target organisms and has been implemented on the proposed labels. Additional details for the comparison of the two rates and ecological risk characterization can be found in the document *"Florpyrauxifen-benzyl Environmental Fate and Ecological Risk Assessment for the Section 3 New Chemical Registration"* at http://www.regulations.gov, docket ID number EPA-HQ-OPP-2016-0560.

Risks to Aquatic Animals

Acute

For the proposed use on rice, acute risks to freshwater and estuarine/marine fish (which are also surrogates for aquatic-phase amphibians), and freshwater and estuarine/marine aquatic

invertebrates do not exceed the EPA's LOCs. For the proposed aquatic uses, the acute risks to freshwater and estuarine/marine fish and invertebrates (water column) slightly exceed the EPA's LOC (with RQs ranging from <0.56 to <3.7). However, acute toxicity was not observed at any level in the submitted studies, which were conducted up to the limit of solubility for florpyrauxifen-benzyl. Additionally, acute toxicity data for typical end-use products (TEP) and degradates show that the levels where toxicity was demonstrated are well above the levels of the chemicals in aquatic environments expected from the proposed use. Therefore, the potential for acute risk to fish and invertebrates from the proposed aquatic uses is expected to be low.

Chronic

Chronic RQs did not exceed the EPA's LOC for freshwater fish or freshwater invertebrates (water column) for either the rice or aquatic uses. Likewise, the chronic RQs did not exceed the LOC's for freshwater (benthic) invertebrates. For freshwater benthic invertebrates, the submitted study showed toxicity at all of the levels tested, resulting in uncertainty regarding what level of florpyrauxifen-benzyl residues in the environment would be below the threshold for toxicity. Using the lowest level tested in that study and comparing it to the expected environmental concentration of florpyrauxifen-benzyl, the RQ was below the LOC; however, risk to these organisms cannot be entirely precluded due to the uncertainty regarding what level of florpyrauxifen-benzyl would be non-toxic. Any potential toxicity of concern would be due to the parent compound and is likely to be short lived due to dissipation in the environment. Therefore, chronic risks of concern are not expected for these taxa.

Chronic risk potential to estuarine/marine invertebrates, both water-column and benthic, is also uncertain. There was toxicity observed at all levels of the submitted mysid chronic toxicity study, resulting in uncertainty regarding what level of florpyrauxifen-benzyl residues in the environment would be below the threshold for toxicity to these organisms. In the case of water-column estuarine/marine invertebrates, using the lowest level tested in that study and comparing it to the expected environmental concentration of florpyrauxifen-benzyl, the RQ was slightly above the LOC (>2.5). The marine/estuarine benthic RQ did not exceed the LOC; however, risk to these organisms cannot be entirely precluded due to the uncertainty regarding what level of florpyrauxifen-benzyl would be non-toxic. In addition, chronic risks to estuarine/marine fish could not be evaluated due to the lack of toxicity data for both the rice and aquatic uses. However, the proposed uses are not expected to result in significant residues of florpyrauxifen-benzyl or its degradates in saltwater/brackish water environments. Rice is not grown in salt or brackish water, and the proposed aquatic uses are for freshwater sites only. Additionally, the label specifically prohibits direct application to salt or brackish waters. The proposed rice use requires a 60-day pre-harvest interval (PHI), which means that the product cannot be applied within 60 days of rice harvest. Since the typical practice for rice cultivation in the eight states listed on the label is to hold flood water until very close to harvest, there will be a substantial built-in holding period between the time of the last application and when the paddy water is

released, allowing ample time for florpyrauxifen-benzyl to degrade into compounds that do not demonstrate toxicity to aquatic animals. The proposed aquatic uses are limited to slow-moving/quiescent waters, again allowing time for parent florpyrauxifen-benzyl to degrade. Furthermore, due to the likelihood that significant dilution will also occur, concentrations are not expected to reach estuarine/marine waters in concentrations high enough to reach levels of concern in estuarine/marine environments.

Risks to Terrestrial Animals

Florpyrauxifen-benzyl is considered "practically non-toxic" to bees, birds, reptiles, terrestrial-phase amphibians and mammals on an acute basis. The acute RQs for these species do not exceed the EPA's LOC. Additionally, chronic RQs for birds (which are also surrogates for reptiles and amphibians) and mammals also did not exceed the EPA's LOC. Therefore, EPA has no chronic risks of concern for terrestrial animals.

Risks to Plants

As would be expected for an herbicide, florpyrauxifen-benzyl is toxic to plants, and there are some risks of concern for both terrestrial and aquatic plant species. When assessing risk to non-target aquatic plants, the EPA used a Total Toxic Residues (TTR) approach, since the parent compound, as well as the major degradates, all demonstrate some level of toxicity to aquatic plants at environmentally relevant levels. The TTR approach assumes the parent and degradates have the same fate and toxicity characteristics. Although two of the most persistent degradates (benzyl hydroxyl and hydroxyl acid) are considered toxicologically relevant to aquatic plants based on the proposed uses, their toxicity to aquatic plants is several orders of magnitude less than the parent compound. Therefore, the resulting RQ derived from the TTR approach is considered a conservative (e.g., "worst case") approach. Actual RQs would be lower when considering differential toxicity of the parent and relevant degradates.

Aquatic Plants

When considering total toxic residues, the resulting RQs for non-target aquatic vascular plants are 410 for the rice use, and 3,090 for the aquatic use, which exceed the LOC. However, these are based on conservative assumptions, assuming exposure at the applied rate. For the rice use, the label prohibits applications within 60 days of harvest. As described above, since the flood water is held in the paddy until close to the time of harvest, there is ample time for the parent compound and the XDE-848 acid to degrade prior to release of the paddy water into receiving waters. Additionally, the labels prohibit application to ratoon crops, because these would have a shorter holding time prior to release of paddy water.

For aquatic uses, florpyrauxifen-benzyl would be at or below the target concentration of 50 ppb in the treatment area at the time of application. The label limits the treatments to slow-moving, quiescent waters, thus reducing potential exposure to non-target aquatic plants. Additionally, the most toxic components of the TTR (parent compound and acid degradate) degrade relatively rapidly (e.g., within days to a few weeks), further reducing the risk that would be expected downstream from the treated area. Other degradates degrade more slowly but are shown to be much less toxic.

Terrestrial Plants

When considering just the parent compound and the XDE-848 acid residues, exposure may occur from spray drift, runoff, either individually or in combination from the proposed rice or aquatic uses. Exposure could also potentially occur if treated water was used to irrigate crops or other plants. The maximum RQs for non-target terrestrial monocots ranged were 0.65 for parent, and 0.91 for the acid, which did not exceed the LOC. For dicots, maximum RQs were 29 for parent, and 12.6 for the acid, which do exceed the LOC. Though the RQ values range widely based on the type of plant exposed, the EPA assumes the highest risk scenario when determining mitigation measures in order to protect the most sensitive species. To reduce non-target terrestrial plant risk, label elements for both the rice and aquatic uses such as prohibiting use of treated water for irrigation and language to reduce the potential for spray drift have been added to the product labels. These are further explained in the "Mitigation and Labeling Requirements" section of the document.

Compost

Residues of other chemicals belonging to the synthetic auxin class of chemistry have been detected in finished compost derived from the composting of auxin-treated agricultural material, including plant material and manure. Due to the current uncertainty regarding the potential presence of florpyrauxifen-benzyl in compost, label mitigation has been proposed to remove this exposure pathway by restricting the use of treated plant material in compost. In addition, livestock will be restricted from drinking treated water so that residues do not potentially accumulate in manure that may be used for compost. The specific label requirements are further explained in the "Mitigation and Labeling Requirements" section of the document. The registrant may elect to conduct a compost residue study in the future to determine if the restrictions could be removed.

Tank Mixing Florpyrauxifen-benzyl

The EPA has developed an interim process to evaluate mixture effects on an active ingredient basis where the U.S. Patent and Trademark Office (PTO) granted a patent basis on the applicant showing that the combined effects of the mixture are synergistic (*i.e.*, the effect of a mixture of pesticides is greater than the sum of the individual effects). To ensure that mixture effects data that may be relevant to ecological risk assessments are considered, the Agency requested that

registrants of new chemicals submit mixture toxicity data provided to the U.S. PTO. The EPA provided criteria to assist registrants in identifying relevant data for submission.
Several patent claims of synergism for specific combinations of florpyrauxifen-benzyl with other herbicides including patent claims regarding use of the two active ingredients found in the florpyrauxifen-benzyl co-formulated products (cyhalofop and penoxsulam) have been identified. The registrant has submitted data on these co-formulated products to determine if synergy exists. The studies did not show substantially increased phytotoxicity to soybeans, the most sensitive crop, and therefore did not change the overall risk profile for florpyrauxifen-benzyl.
Several other patents involving florpyrauxifen-benzyl with other ingredients have been identified. EPA is currently evaluating the nature of these patent claims and any supporting data. The EPA is continuing its work to better understand the scope of the uncertainties for these specific combinations and to develop an approach that best manages the potential risks while still maintaining the important benefits derived from tank mixing. While evaluation of these patents are still in progress, the EPA has placed a restriction on the end-use product labels that prohibits tank mixing with those active ingredients for which a patent has been approved at the time of registration. If the EPA determines that sufficient data do not exist to support true synergistic effects with a particular active ingredient, that active ingredient may be removed from the list of restricted tank mix combinations. The specific label requirements are further explained in the "Mitigation and Labeling Requirements" section of the document.

Benefits

A fundamental problem facing U.S. agriculture is the spread of herbicide-resistant weeds causing growers to experience yield and economic losses due to weeds developing resistance. This has become important as it is a significant financial, production, and pest management issue. Weed management in rice is essential for economical rice production because weeds reduce yields by competing with rice for nutrients, light, and moisture. Infestations can also interfere with harvest and reduce the quality of grain. Rice is a major field crop in the Southern United states, especially in Arkansas, Louisiana, Mississippi, Missouri, and Texas. These states produced over 75% of the total U.S. rice crop in 2012. Arkansas alone produced almost 9.7 billion pounds of rice in 2012, nearly half of the total U.S. production. The value of sales of rice in these five state was over $2 billion (in 2012) more than two-thirds of the total value of rice in the U.S. ($~3 billion). Rice production is adversely impacted by weed infestations and many resources go into weed management. In Arkansas, weed control costs from 2006 to 2012 averaged nearly $69 per acre. Barnyardgrass competes (or outcompetes) rice for nitrogen, sunlight, space, and moisture. Yield reduction of rice due to season-long weed infestation are well-known. If uncontrolled, heavy infestation of weeds impact yields by as much as 82% for red rice weed and 70% for barnyardgrass. Managing barnyardgrass, as well as other weeds, has become more difficult in recent years as several weed species have developed resistance to commonly used herbicide chemistries.

Florpyrauxifen-benzyl is expected to be a valuable tool in combating the proliferation of resistant weed populations that are causing yield and economic losses for rice farmers in the southern states of Arkansas, Florida, Louisiana, Mississippi, Missouri, South Carolina, Tennessee and Texas. It will provide a much needed control of weeds including barnyardgrass and other weeds which are significant for rice producers.

New chemicals, such as florpyrauxifen-benzyl, can be helpful in pest management and resistance-management programs as an additional resource for weed control, especially where current treatments are less successful. Florpyrauxifen-benzyl is expected to be an important tool to manage weed species that have developed resistance to commonly used herbicides for weed control in rice production. For example, barnyardgrass has known resistance to alternative active ingredients, such as propanil and quincolorac, but is effectively controlled by florpyrauxifen-benzyl. Florpyrauxifen-benzyl's mechanism of action (MOA) involves a preference for a different binding site protein compared to other Group 4 herbicides. This could be a benefit in managing weeds that have developed resistance to other synthetic auxin herbicides which bind more strongly to other binding site proteins. In addition, florpyrauxifen-benzyl has a wide application window (from the 2 leaf stage up to 60 days prior to harvest), and can be applied in place of herbicides that might currently have resistant weed populations. Thus, this new active ingredient is expected to be an additional tool which could potentially be used in place of other available herbicides where resistance has developed. However, resistance management is advised to maintain efficacy since weeds can develop resistance to this active ingredient as they have to many herbicides. In addition, florpyrauxifen-benzyl will be an effective tool for spot and wide area treatments for control of problematic aquatic weeds. It will provide an additional tool to manage resistant aquatic weed species and a tool to restore aquatic habitat.

Resistance management for weeds in aquatic systems differs considerably from terrestrial herbicide resistance management. Options are limited, as there are only 14 registered aquatic herbicides in the United States. Florpyrauxifen-benzyl is expected to be an effective tool for spot and wide area treatments to quickly control problematic invasive aquatic weeds such as hydrilla, Eurasian watermilfoil, and crested floating heart. Florpyrauxifen-benzyl also provides an additional tool to manage herbicide-resistant aquatic weeds and restore aquatic habitat in ecosystems that have been compromised by invasive species. Aquatic weeds often require significant resources for control, as invasive species can interfere with use of water, increase the risk of flooding, and result in conditions that threaten public health (e.g. harmful algal blooms that produce cyanotoxins).

For invasive weed control, as an auxin herbicide (WSSA Group 4), florpyrauxifen-benzyl will provide a new effective mechanism of action (MOA) for the particularly problematic invasive weed hydrilla *(Hydrilla verticillata)*. There are multiple aquatic herbicides labeled for hydrilla

control in the United States: endothall (WSSA Group undefined), diquat (WSSA Group 22), flumioxazin (Group 14), copper products (WSSA Group not defined), fluridone (WSSA Group 12), penoxsulam (WSSA Group 2), bispyribac-sodium (WSSA Group 2), imazamox (WSSA Group 2), and topramezone (WSSA Group 28). None of these herbicides belong to WSSA Group 4. Therefore, florpyrauxifen-benzyl demonstrates an alternate MOA for the invasive aquatic weed hydrilla and could play an important role in an integrated pest management (IPM) program.

Controlling hydrilla is especially problematic because it has shown resistance to the widely used herbicides fluridone and endothall. Hydrilla reproduces efficiently, out competes native plants, reduces habitat for aquatic wildlife and fish and can obstruct water flow resulting in clogged irrigation systems and flooding. Hydrilla, particularly when very dense and expansive, is very disruptive to native environments and can threaten native species by reducing the level of dissolved oxygen, preventing sunlight penetration, and limiting nutrients for use by other native organisms. In addition to suppressing native plants, hydrilla, can also limit water flow and cause flooding, increase extinction rate of rare, threatened and endangered species, disrupt hydropower generation, provide habitat for insect-borne disease vectors, degrade water quality, reduce species diversity, change sediment chemistry, and interfere with recreational activities such as boating, fishing, and swimming. The economic impacts of controlling hydrilla (mechanical, biocontrol, and/or chemical control) can be substantial. For example, the cost of hydrilla control in Florida over a seven-year period from 2008-2015 were estimated at $66 million. Non-chemical means of control are often ineffective when used alone or prohibitively expensive. For example, mechanical control and suction control of hydrilla can cost as much as $1,000 per acre and $25,000 per acre, respectively. In addition, mechanical control methods are known to cause breakage in many invasive aquatic weeds and send viable fragments downstream where they take root and establish new populations. There is documented resistance to both fluridone and endothall in hydrilla species and florpyrauxifen-benzyl will provide a new MOA for control of this resistant species. Hydrilla has also been documented as hosting *Aetokthonos hydrillicola,* a cyanobacterium that is believed to produce a neurotoxin responsible for avian vacuolar myelinopathy (AVM). AVM is a neurological disease which impacts waterfowl in the southeastern U.S., including bald eagles. Florpyrauxifen-benzyl also provides excellent control of the troublesome watermilfoil species. Florpyrauxifen-benzyl is expected to be a helpful resource for hydrilla weed control and other troublesome weeds and provide an additional tool in resistance-management programs.

Florpyrauxifen-benzyl will also offer flexibility in use to meet the need for spot/partial treatment. The alternatives such as fluridone, penoxsulam, and topramezone require 2 to 4 months to provide target plant control while florpyrauxifen-benzyl provides control in several days to a few weeks.

Florpyrauxifen-benzyl is a new reduced risk pesticide based on lower risks to human health when compared to registered alternatives. The toxicity profile for florpyrauxifen-benzyl identifies no risks of concern to human health from any route of exposure and may provide a better alternative to older chemistries that require higher levels of risk mitigation practices in order to reduce exposure. For instance, several alternatives to florpyrauxifen-benzyl (diquat, endothall, triclopyr, imazapyr, and 2,4-D) have drinking water or recreational use restrictions. There are no restrictions on the use of water treated with florpyrauxifen-benzyl for recreational purposed including swimming and fishing and no drinking water restrictions. The lack of drinking water and recreational use restrictions will allow applicators more flexibility in planning their integrated weed management program.

With respect to non-target risks, florpyrauxifen-benzyl has no risk concerns for non-target wildlife and is considered "practically non-toxic" to bees, birds, reptiles, amphibians, and mammals. Overall, the EPA expects that there may be meaningful benefits for florpyrauxifen-benzyl for controlling difficult weeds in rice and aquatic systems and also helping to reduce weed resistance.

Public Comments

The proposed regulatory decision was published on June 28, 2017, remained open for 30 days, and closed on July 28, 2017. The Agency received a total of forty comments in that period. Thirty-eight of the forty comments were in support of the registration of florpyrauxifen-benzyl and agreed with the Agency's benefits assessment of florpyrauxifen-benzyl. A portion of those comments included concerns over the proposed restriction of tank mixing florpyrauxifen-benzyl products with other registered pesticides for applications to rice, and concerns over the proposed restriction of irrigating with water treated with florpyrauxifen-benzyl for aquatic plant management. The Agency's rationale for these restrictions can be found in the sections of this document "Tank Mixing Florpyrauxifen-benzyl" and "Mitigation and Labeling Requirements – Irrigating Crops," respectively. The comments opposing the registration highlighted the lack of an endangered species assessment and formal consultation under Section 7 of the Endangered Species Act and expressed concerns with EPA's assessment of the toxicity of pesticide mixtures.

The EPA acknowledges the comments Center for Biological Diversity (CBD) submitted regarding the duty to consult with the U.S. Fish and Wildlife Service (FWS) and National Marine Fisheries Service (NMFS) in regard to risk to endangered species, including the potential drift of residues, common mechanisms of toxicity, the use of Bulletins Live! and the concerns of water quality conditions and critical habitat. These considerations are encompassed in the extensive efforts and resource investments the EPA is focusing to assess impacts to listed species as part of the EPA's registration review program for currently registered pesticides. The EPA believes that, as a general matter, older chemistries present a greater degree of risk to listed

species than newest chemistries coming to market, including florpyrauxifen-benzyl, since registration standards have increased over time. Therefore, it is environmentally preferable in most circumstances for the EPA to focus resources to assess the impacts of existing pesticides sooner in the process than newer pesticides that have been held to higher standards to meet current registration requirements such as new guideline studies to assess risk to additional species and through assessment of new exposure pathways. Furthermore, florpyrauxifen-benzyl was granted reduced risk status for both of the proposed uses. The determination was based on the lack of human health risk, lower hazard to human health compared to leading market alternatives, and its efficacy against certain highly invasive weeds such as hydrilla which are not adequately suppressed and/or controlled by the alternatives. Controlling hydrilla is especially problematic because it has shown resistance to the widely used herbicides fluridone and endothall. Hydrilla reproduces efficiently, out competes native plants, reduces habitat for aquatic wildlife and fish and can obstruct water flow resulting in clogged irrigation systems and flooding. Hydrilla, particularly when very dense and expansive, is very disruptive to native environments and can threaten native species. The determination concluded that florpyrauxifen-benzyl will be an important tool for integrated pest management programs for the labeled uses. In addition, florpyrauxifen-benzyl exhibits low acute ecological risk to mammals, reptiles, amphibians, bees, and birds and shows lower acute ecological risks then many of the alternatives. As a result, the EPA does not believe the environment or the public would be best served by delaying the registration of florpyrauxifen-benzyl to complete consultation. Focusing the EPA' s, and the Services' (the FWS's and the NMFS's) limited resources on completing a consultation on the effects of florpyrauxifen-benzyl would by necessity come at the expense of putting more resources into evaluating – and consequently, regulating, where appropriate - what the EPA believes to be more toxic compounds, that, among other things, pose greater risk, to endangered species than does florpyrauxifen-benzyl.

It is important to understand that the development of the Interim Approaches does not by its terms suggest that existing or recently developed risk assessments using the criteria articulated in OPP's 2004 Overview document (http://www.epa.gov/espp/consultation/ecorisk-overview.pdf) are necessarily "under-protective." The Interim Approaches are intended to identify interim thresholds for interagency review as the Agencies jointly work to implement the recommendations of the National Academy of Sciences (NAS) on certain specific registration review actions. The Agencies have made no determination that these thresholds are necessary to prevent take and preclude likely jeopardy and, in any case, the Interim Approaches do not establish legally binding thresholds for consultation under the Services ' implementing regulations. As the EPA and the Services work through the initial actions that are being reviewed under the Interim Approach, the EPA will determine whether these thresholds should be modified before they are extended more broadly to additional regulatory actions. The details of the joint Interim Approaches are contained in the white paper *Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the*

National Academy of Sciences April/2013 Report, dated November 1, 2013, available at http://www.epa.gov/espp/2013 /nas.html. With respect to the evaluation of florpyrauxifen-benzyl specifically, it is important to understand that under any internal or interagency review, the ecological risk evaluation will continue to rely on the body of information used in the current EPA ecological assessment.

For the reasons explained above, the EPA is not consulting with the Services on the issuance of the florpyrauxifen-benzyl registration. However, the EPA is currently working to prioritize its consultation activities with the Services and will evaluate the appropriate timing and scope of consultation on florpyrauxifen-benzyl in connection with those efforts. In addition, to the extent the EPA receives new information indicating that florpyrauxifen-benzyl may pose a greater risk to listed species than indicated by the existing scientific database for this pesticide, the EPA will re-evaluate the terms of registration and determine whether additional use restrictions to protect listed species are necessary.

The EPA also acknowledges the comments CBD submitted regarding the assessment of the toxicity of pesticide mixtures. The EPA has traditionally viewed tank mixes to have an additive effect, meaning the combined effect of two chemicals is predictable based on the known toxicity of both compounds; no specific interactions occur. Therefore, as long as the applicator/handler follows the most restrictive use directions for all chemical partners in the tank mix, there are no unidentified or additional risks with use of tank mixes. However, as a result of chemical companies making claims of synergism with unique combinations of chemicals for patent and licensing purposes, the topic of synergy and multiple stressors has introduced uncertainty in assessing risk with tank-mix combinations. The EPA has developed an interim process to evaluate mixture effects on an active ingredient basis where the U.S. Patent and Trademark Office (PTO) granted a patent basis on the applicant showing that the combined effects of the mixture are synergistic (*i.e.,* the effect of a mixture of pesticides is greater than the sum of the individual effects). Several patent claims of synergism for specific combinations of florpyrauxifen-benzyl with other herbicides have been identified. While evaluation of these patents are still in progress, the EPA is requiring a restriction on the end-use product labels that prohibits tank mixing with those active ingredients for which a patent has been approved at the time of registration. If the EPA determines that sufficient data do not exist to support true synergistic effects with a particular active ingredient, that active ingredient may be removed from the list of restricted tank mix combinations. Further details are outlined in the "Tank Mixing Florpyrauxifen-benzyl" section of this document.

Regulatory Rationale

In accordance with FIFRA, the EPA only registers a pesticide when it determines that it will not cause unreasonable adverse effects on humans or the environment, taking into account the

economic, social, and environmental costs and benefits of the use of the pesticide. Under FIFRA, the EPA is charged with balancing the uncertainties and risks posed by a pesticide against its benefits. The EPA must determine if the benefits in light of its use outweigh the risks in order for the EPA to register a pesticide.

The database submitted to support the assessment of human health, and environmental fate and ecological risk outlined in 40 CFR part 158 is adequate to support the risk determinations for us of florpyrauxifen-benzyl. There are no risk estimates of concern for human health. Florpyrauxifen-benzyl is not likely to result in direct risk of concern to non-target terrestrial animals, including insects, birds, reptiles, terrestrial-phase amphibians, and mammals, nor to aquatic animals including amphibians, fish, and invertebrates. As expected of an herbicide, florpyrauxifen-benzyl may pose a risk of concern to terrestrial and aquatic vascular and non-vascular plants. Label language, as outlined in the "Mitigation and Labeling Requirements" section of the document, will reduce any potential risk to non-target terrestrial and aquatic plants.

It should be noted that florpyrauxifen-benzyl was granted Reduced Risk status for both the rice and aquatic uses based on reduced risk to human health when compared to registered alternatives. The Office of Pesticide Program's Conventional Reduced Risk Pesticide Program expedites the review and regulatory decision-making process of conventional pesticides that pose less risk to human health and the environment than existing conventional alternatives. In addition, florpyrauxifen-benzyl demonstrates an alternate mode of action to control hydrilla, and should play an important role in integrated pest management (IPM). Introduction of an alternate mode of action should also help to prolong the effectiveness of existing reduced risk chemistries when introduced into resistance management strategies with these chemicals.

Florpyrauxifen-benzyl is expected to be a valuable tool in combating the proliferation of resistant weed populations that are causing yield and economic losses for rice producers. It will provide a much needed control of weeds including barnyardgrass and other weeds which are significant for producers. In addition, florpyrauxifen-benzyl will be an effective tool for spot and wide area treatments for control of problematic aquatic weeds. It will provide an additional tool to manage resistant aquatic weed species and a tool to restore aquatic habitat. Florpyrauxifen-benzyl will improve control of economically detrimental aquatic weed species, control of resistant species, and increase flexibility in integrated weed management plans as well as reduce the economic impact of controlling invasive hydrilla and protecting native species.

After weighing the risks against the benefits of the registered use, the EPA finds that, when the mitigation measures are implemented, the potential risks that may remain are minimal, while the benefits are potentially significant. Therefore, the EPA concludes that the benefits outweigh the risks and registering these uses will not generally cause unreasonable adverse effects on human health or the environment. Therefore, the EPA proposes to grant the registration of

florpyrauxifen-benzyl for use on rice in Arkansas, Florida, Louisiana, Mississippi, Missouri, South Carolina, Tennessee and Texas and for aquatic uses intended for management of freshwater aquatic vegetation in slow-moving/quiescent waters with little or no continuous outflow in ponds, lakes, reservoirs, freshwater marshes, wetlands, bayous, drainage ditches, and non-irrigation canals, including shoreline and riparian areas in or adjacent to these sites, as well as for management of invasive freshwater aquatic vegetation in slow-moving/quiescent areas of rivers (coves, oxbows, or similar sites). The available data and scientific assessments as well as the overall considerations for benefits for weed management in rice and the specified aquatic uses support a registration under FIFRA Section 3(c)(5).

Mitigation and Labeling Requirements

For Occupational Handlers

The required personal protective equipment (PPE) is a long sleeved shirt and long pants, socks, shoes, protective eyewear, and waterproof gloves. The restricted entry interval (REI) is 12 hours.

Potential for Contamination of Compost

With the current uncertainty that exists regarding the potential for adverse effects to non-target plants exposed to compost containing residues of florpyrauxifen-benzyl, the following label restrictions will be included until additional information is provided to address this uncertainty:

- Do not compost any plant material from treated area.
- To minimize potential exposure in compost, do not allow livestock to drink treated water.

The inclusion of this language on the label is intended to prevent potential contamination of compost by restricting the use of plant material treated with florpyrauxifen-benzyl or manure with florpyrauxifen-benzyl residues to be used as compost inputs.

Irrigating crops

No data have been provided to account for potential residues on irrigated crops resulting from the use of water from treated irrigation ditches and channels. With the current uncertainty that exists regarding the potential for adverse effects to non-target plants exposed to residues from treated irrigation water, the EPA proposed the following label restriction until additional information is provided to address this uncertainty:

- Do not use treated water for any form of irrigation.

Potential for exposure to non-target plants downstream for the aquatic use:
In order to minimize the risk of exposure to non-target plants downstream, the aquatic use sites will be limited to:

- Slow moving/quiescent waters with little or no continuous outflow.
- Only invasive weeds may be treated in moving water which is limited to slow-moving/quiescent areas of rivers (coves, oxbows, or similar sites).

Potential for exposure to marine/estuarine invertebrates downstream for the aquatic use:
In order to minimize the risk of exposure to marine/estuarine invertebrates downstream, the aquatic use label will include the following restriction:

- Do not apply to salt/brackish water.

Potential for exposure to non-target plants downstream from release of patty water:
In order to minimize the risk of exposure to non-target plants downstream from release of patty water for the rice use, the following restrictions are proposed:

- Do not apply to ratoon rice.
- Do not apply within 60 days of rice harvest.

Tank-mixing Restrictions

- DO NOT TANK MIX ANY PESTICIDE PRODUCT WITH THIS PRODUCT without first referring to the following website for the specific product: www.3206kmix.com; www.3301tankmix.com; www.3480tankmix.com; or www.3565tankmix.com. This website contains a list of active ingredients that are currently prohibited from use in tank mixture with this product. Only use products in tank mixture with this product that: 1) are registered for the intended use site, application method and timing; 2) are not prohibited for tank mixing by the label of the tank mix product; and 3) do not contain one of the prohibited active ingredients listed on www.3206kmix.com; www.3301tankmix.com; www.3480tankmix.com; or www.3565tankmix.com website.
- Applicators and other handlers (mixers) must access the website within one week prior to application in order to comply with the most up-to-date information on tank mix partners.
- Do not exceed specified application rates for respective products or maximum allowable application rates for any active ingredient in the tank mix.
- Read carefully and follow all applicable use directions, precautions, and limitations on the respective product labels. It is the pesticide user's responsibility to ensure that all products in the mixtures are registered for the intended use. Users must follow the most

restrictive directions for use and precautionary statements of each product in the tank mixture.
- Always perform a (jar) test to ensure the compatibility of products to be used in tank mixture.

Potential for Off-site Transport via Spray Drift

In order to minimize the risks of spray drift, language is included on the label that is intended to reduce off-site transport, thereby reducing the potential for exposure to non-target plants. This includes minimum droplet size restrictions of coarse or coarser droplet category per S-572 ASABE standard, application pressures less than 30 psi, maximum wind speed restriction of 10 mph with a minimum wind speed of 2 mph, maximum boom heights of 36 inches for ground application and 10 feet for aerial application, and extensive Spray Drift Management language. Additional labeling is required to reduce risk to non-target plants through drift as follows:

Susceptible Plants

- Do not apply under circumstances where spray drift may occur to food, forage, or other plantings. Spray drift may damage or render crops unfit for sale, use or consumption. Small amounts of spray drift that may not be visible may injure susceptible broadleaf plants.
- Before making an application, please refer to your state's sensitive crop registry (if available) to identify any commercial specialty or certified organic crops that may be located nearby.
- Do not apply when wind is blowing toward adjacent cotton, carrots, soybeans, corn, grain sorghum, wheat, grapes, tobacco, vegetable crops, flowers, ornamental shrubs or trees, or other desirable broadleaf plants.

International Harmonization

Maximum Residue Limits (MRLs) have not been established by Codex for florpyrauxifen-benzyl for the commodities affected by this action. However, tolerances are being established on rice, freshwater fish and shellfish for international trade purposes.

Regulatory Decision

The database submitted to support the assessments of human health risk and environmental fate and ecological risk is adequate to support use of florpyrauxifen-benzyl on rice and use in aquatic vegetation management. Considering the assessed risk to human health and the environment, the EPA concludes that florpyrauxifen-benzyl meets the regulatory standard under FIFRA. The EPA is concluding that, in consideration of the approaches and mitigation described above, the risks are not unreasonable when considered in conjunction with the benefits of a new chemical and

new mode of action for control of hydrilla in freshwater aquatic weed control management. Therefore, the EPA granting an unconditional registration of florpyrauxifen-benzyl under Section 3(c)(5).

The EPA is registering the following five products:

Rinskor™ Technical

- 94.6% florpyrauxifen-benzyl
- Only for formulation into an herbicide for use on rice and freshwater aquatic use sites

GF-3301

- 26.5% florpyrauxifen-benzyl
- Only for use on rice in AR, FL, LA, MS, MO, SC, TN, and TX and for freshwater aquatic use sites

GF-3206

- 2.7% florpyrauxifen-benzyl
- Only for use on rice in in AR, FL, LA, MS, MO, SC, TN, and TX

GF-3565

- 1.3% florpyrauxifen-benzyl
- 2.1% penoxsulam
- Only for use on rice in in AR, FL, LA, MS, MO, SC, TN, and TX

GF-3480

- 2.13% florpyrauxifen-benzyl
- 10.64% cyhalofop-butyl
- Only for use on rice in in AR, FL, LA, MS, MO, SC, TN, and TX

4.3 EVALUATION OF RINSKOR (PROCELLACOR™)

NOTE: GEI Consultants, Inc. executed a confidential non-disclosure agreement with SePRO Corporation to obtain and review proprietary studies and data. SePRO is working in partnership with Dow AgroSciences to develop this technology for aquatic weed control. In the absence of peer-reviewed journal articles or other scientific literature, these studies—many of which were performed in support of EPA's Office of Pesticide Programs (OPP) registration requirements—were used to prepare the evaluation of the candidate aquatic herbicide.

4.3.1 Registration Status

PROCELLACOR™ (Procellacor™) Aquatic Herbicide (active ingredient Rinskor™, or 2-pyridinecarboxylic acid, 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-, phenylmethyl ester; common name: florpyrauxifen-benzyl) has not yet been registered nationally by the EPA or in Washington State by the WSDA under 15.58 Revised Code of Washington (RCW). This SEIS provides technical, environmental, and other information required by Ecology to determine whether to add Procellacor™ to existing water quality NPDES permits, which will allow this herbicide to be discharged to the waters of the State as allowed under the Clean Water Act.

Procellacor™ (as the aquatic use of Rinksor)was granted Reduced Risk status by EPA under the Pesticide Registration Improvement Act (PRIA) Version 3 (https://www.epa.gov/pria-fees/pria-overview-and-history#pria3) in early 2016 (Denny, Breaux, 2016; also see notification letter at Attachment A) because of its promising environmental and toxicological profiles in comparison to currently registered herbicides utilized for partial treatment of hydrilla, invasive watermilfoils, and other noxious plant species. EPA concluded that the overall profile appeared more favorable when compared to the registered alternatives for the proposed use patterns for these noxious species, and that the reduction in risk pertaining to human health was the driving factor in this determination. As discussed later in the document, Procellacor™ shows excellent selectivity with few or limited impacts to native aquatic plants such as aquatic grasses, bulrush, cattail, pondweeds, naiads, and tapegrass. In its review, EPA also noted that the overall profile for the herbicide appears favorable when compared to currently registered alternative herbicides (e.g. 2,4-D, endothall, triclopyr) for this aquatic use pattern. Procellacor™ represents an alternative mode of chemical action which is more environmentally favorable than currently registered aquatic herbicides. Procellacor™ would be expected to offer improvements in IPM for control of noxious aquatic weeds. The alternative mode of action should also help to prolong the effectiveness of many aquatic herbicide solutions by offering a new rotation or combination alternative as part of herbicide resistance management strategies.

The new candidate aquatic herbicide is under expedited review from EPA under the PRIA per the Reduced Risk status designation discussed above, with an anticipated registration date of April 2017. As part of the review, EPA's OPP is also currently conducting human health and ecological risk assessments with an expected date of release in spring 2017. This SEIS document relies on information currently available at this time, much of which necessarily is limited to data provided by Dow AgroSciences and SePRO Corporation in developing and testing the herbicide. It can be revised with more updated information following the release of EPA review information as well as other peer-reviewed literature expected to be released later in 2017. Dow AgroSciences has also concurrently applied to EPA for

registration of the Rinskor active ingredient for weed control in rice paddies. The initial Procellacor™ formulation is expected to be a 300 g TGAI/L suspension concentrate. Control of hydrilla and invasive watermilfoils can be achieved at in-water spot/partial treatment rates of 10 to 50 µg a.i./L with Procellacor™, as opposed to rates of 1,000 to 5,000 µg a.i./L for endothall, 2,4-D, and triclopyr (Getsinger 2016, Beets and Netherland 2017a *in review*, Netherland et al 2017 *in prep*).

This analysis considers Procellacor™'s mode of action, efficacy, and range of in-water treatment concentrations required to achieve control across different water exchange / exposure scenarios. The review discusses results of mesocosm and other field studies conducted in partial site and whole pond treatments, described in more detail below.

To help expedite development and future adoption of the technology, SePRO has been working with numerous partners and collaborators to conduct experimental applications to confirm field efficacy on a variety of target aquatic vegetation, as well as to document non-target effects or impacts. As an unregistered product that does not have a federal experimental use permit, EPA guidelines require that field testing be limited to one acre or less of application per target pest species and that uses of water potentially affected by this application such as swimming, fishing, and irrigation be restricted. The discussion below provides a summary of the herbicides' physical properties, mammalian and ecotoxicological information, environmental fate, and other requirements for EPA registration. Most of these studies have been conducted by Dow AgroSciences and SePRO Corporation in fulfillment of EPA's OPP pesticide registration requirements under FIFRA (as represented by Heilman 2016). As noted above, few peer-reviewed publications have yet been released, although more are expected later in 2017 and beyond.

4.3.2 Description

Procellacor™ is the aquatic trade name for use of a new active ingredient (Rinskor), which is one chemistry in a novel class of herbicides known as the arylpicolinates. The primary end-use formulation anticipated for in-water application at time of registration is a 300 g active ingredient/liter suspension concentrate, but other aquatic use formulations are being considered for registration shortly after the initial EPA decision.

Aquatic herbicides are grouped by contact (controls plant shoots only) vs. systemic (controls entire plant), and by aqueous concentration and exposure time (CET) requirements. In general, contact products are quicker acting with shorter CET requirements, while systemic herbicides are slower acting with longer CET requirements. In light of this, Procellacor™ is quick-acting, has relatively short CET requirements, is systemic, and requires low application rates compared to other currently registered herbicides. Moreover, it has shown short persistence in both water and sediment relative to currently registered herbicides such as endothall, 2,4-D, and triclopyr, is species-selective, and has minimal non-target effects to both plant and animal species. Its effective chemical mode of action and high selectivity for aquatic invasive and noxious plants provides a significant impetus for its development and eventual registration. Procellacor™ has demonstrated this selective, systemic activity with relatively short CET requirements on several major aquatic weed species, including hydrilla and invasive watermilfoils. Netherland and Richardson (2016) and Richardson *et al*. (2016) investigated the sensitivity of numerous aquatic plant species to the compound, and provided verification of Procellacor™'s activity on key

invasives and greater tolerance by the majority of native aquatic plants tested to date. Additional government and university research has documented high activity and different selectivity patterns relative to possible impacts to non-target aquatic vegetation compared to other currently registered, well-documented herbicides such as triclopyr, endothall, and/or 2,4-D (Beets and Netherland 2017a *in review*, Beets and Netherland 2017b *in prep*, Haug and Richardson 2017 *in prep*).

4.3.2.1 Environmental Characteristics: Product Use and Chemistry

Procellacor™ shows excellent activity on several major US aquatic weeds including hydrilla (*H. verticillata*) and multiple problematic watermilfoils (*Myriophyllum spp.)*, including Eurasian (EWM) and hybrid Eurasian (*M. spicatum X M. sibiricum*), parrotsfeather (*M. aquaticum*), and variable-leaf milfoil (*M. heterophyllum*). Procellacor™ provides a new systemic mode of action for hydrilla control and a new class of auxin-mimic herbicide chemistry for selective management of invasive watermilfoils. It also has in-water or foliar herbicidal activity on a number of noxious emergent and floating aquatic plants such as water hyacinth and invasive floating hearts (*Nymphoides spp*.). Procellacor™ has low application rates (50 µg/L or less) for systemic activity with short CET requirements (12 – 72 hours depending on rate and target weed) allowing for spot and/or partial in-water applications. For such treatments, Procellacor™ provides selective control with several hundred times less herbicide use versus current in-water, spot treatment herbicides such as endothall (5,000 µg/L maximum use rate for dipotassium salt form) and 2,4-D (4,000 µg/L maximum use rate). Procellacor™ also appears to show high selectivity with few impacts to native aquatic plants such as aquatic grasses, bulrush, cattail, pondweeds, naiads, and tapegrass (see discussion on selectivity below).

Procellacor™ is effective in controlling hydrilla, and offers a new pattern of selectivity for removing hydrilla from mixed aquatic-plant communities. The strong activity of this new alternative mode of action supports its development for selective hydrilla control. Mesocosm studies summarized by Heilman (2016) and in preparation or under active review for peer-reviewed publication have shown that control of standing biomass of hydrilla and EWM can be achieved in two to three weeks, with high activity even on 2,4-D and triclopyr-tolerant stands of hybrid EWM (Beets and Netherland 2017a *in review*, Netherland et al. 2017 *in prep*). Multiple small-scale laboratory screening studies were conducted to support both target weed activity and regulatory consideration of potential effects of Procellacor™ on non-target aquatic vegetation. The test plant EC_{50} response (herbicide concentration having 50% effect) to static exposures of Procellacor™ was determined for 12 different plant species: the general EC_{50} range was approximately 0.11 µg/L to greater than 81 µg/L (Netherland and Richardson, 2016; Richardson *et al*., 2016). Similar small-scale comparative efficacy testing of Procellacor™ vs. 2,4-D and triclopyr on multiple invasive watermilfoils confirms orders of magnitude greater activity with Procellacor™ versus the older auxin herbicides, including activity on hybrid EWM with documented tolerance to the older herbicides (Beets and Netherland 2017b *in prep*). These findings are promising for Procellacor™, as they support significantly lower herbicide application rates combined with a favorable environmental profile, discussed in more detail below.

4.3.2.2 Environmental Mobility and Transport

Procellacor™/Rinskor is known to have low water solubility (laboratory assay of TGAI: 10 to 15 µg/L at pH 5 to 9, 20^{o}C), low volatility (vapor pressure approx. 10^{-7} mm Hg), with moderately high partition

coefficients (log K_{ow} values of approximately 5.4 to 5.5), which describe an environmental profile of low solubility and relatively high affinity for sorption to organic substrates.

The environmental fate of the herbicide in soil and water has been characterized as part of the registration package and is well understood. The parent compound is not persistent and degrades via a number of pathways including photolysis, aerobic soil degradation, aerobic aquatic degradation, and/or hydrolysis to a number of hydroxyl, benzyl-ester, and acid metabolites. In aerobic soil, Procellacor™ degrades moderately quickly, with half-lives ranging from 2.5 to 34 days, with an average of 15 days. Anaerobic soil metabolism studies also show relatively rapid degradation rates, with half-lives ranging from 7 to 15 days, and an average of 9.8 days. The herbicide is short-lived, with half-lives ranging from 4 to 6 days and 2 days, respectively, in aerobic and anaerobic aquatic environments, and in total water-sediment systems such as mesocosms. These half-lives are consistently rapid compared to other currently registered herbicides such as 2,4-D, triclopyr, and endothall. Degradation in surface water is accelerated when exposed to sunlight, with a reported photolytic half- life in laboratory testing of 0.07 days.

In two outdoor aquatic dissipation studies, as summarized by Heilman (2016), the SC formulation of the herbicide was directly injected into outdoor ponds at nominal rates of 50 and 150 µg/L as the active ingredient. Water phase dissipation half-lives of 3.0 – 4.9 days were observed, which indicates that the material does not persist in the aquatic environment. With conditions similar to wetland and marsh habitat, results from another field dissipation study in rice paddies that incorporated appropriate water management practices for both wet-seeded and dry-seeded rice (also reported by Heilman 2016) resulted in aquatic-phase half-lives ranging from 0.15 to 0.79 days, and soil phase half-lives ranging from 0.0037 to 8.1 days These results do not indicate a tendency to persist in the aquatic environment. The herbicide can be classified as generally immobile based on soil log K_{oc} values in the order of 10^{-5}, and suggest that the potential for off-site transport is minimal. This is consistent with numerous observations that Procellacor™ undergoes rapid degradation in the soil and aqueous environments via a number of degradation mechanisms, summarized above.

4.3.2.3 Field Surveys and Investigations

A human health and ecological risk assessment is currently being conducted by EPA Office of Pesticide Programs. Results of this assessment are expected to be released during spring of 2017 (Denny, 2016), and these conclusions will either support or refute data already collected for Procellacor™. There are no preliminary findings to report, but based on the current understanding of available environmental fate, chemistry, toxicological, and other data, there is little to no cause for concern to human health or ecotoxicity for acute, chronic, or subchronic exposures to Procellacor™ formulations.

4.3.2.4 Bioconcentration and Bioaccumulation

A fish bioconcentration factor study and magnitude of residue studies for clam, crayfish, catfish, and bluegill support that, as anticipated from its physical chemistry and organic affinity, Procellacor™/Rinskor will temporarily bioaccumulate but is rapidly depurated and/or metabolized within freshwater organisms within 1 – 3 days after exposure to high concentrations (150 µg/L or higher). Based on these findings and the low acute and chronic toxicity to a wide variety of receptor organisms, summarized below, bioconcentration or bioaccumulation are not expected to be of concern for the

Procellacor™ aquatic use. EPA's forthcoming human health and ecological risk assessment will include exposure scenarios that will help to further clarify and refine the understanding of bioconcentration or bioaccumulation potential for Procellacor™.

4.3.2.5 Toxicological Profile

Mammalian and Human Toxicity

Extensive mammalian toxicity testing of Procellacor™ has been conducted by the proposed registrant, and results have shown little evidence of acute or chronic toxicity. Acute mammalian toxicity testing for Procellacor™ showed very low acute toxicity by oral or dermal routes (LD_{50} values greater than 5,000 mg/kg). Acute toxicity is also reported low via the inhalation route of exposure (LC_{50} value greater than 5.2 mg/L). Procellacor™ is reported not to be an irritant to eyes or skin and only demonstrated a weak dermal sensitization potential in a mouse local lymph node assay (EC_3 of 19.1%).

Absorption, distribution, metabolism, and elimination profiles have been developed for Procellacor™. In summary, Procellacor™ has demonstrated rapid absorption (T_{max} of 2 hours), with higher absorption rates at lower doses (36 to 42% of the administered dose), rapid hydrolysis, and rapid elimination via the feces (51 to 101%) and urine (8 to 42%) during the first 24 hours following administration to laboratory mammals. In general, the lower doses tested would be more representative of levels potentially encountered by people, mammals, or other organisms.

Based on laboratory testing, Procellacor™ is not genotoxic, and there was no treatment-related toxicity even up to the highest doses tested in the acute, short-term, two generation reproduction or developmental toxicity studies or in the acute or subchronic neurotoxicity studies. Chronic administration of the herbicide did not show any carcinogenicity potential and did not cause any adverse effects in mice, rats or dogs, at the highest doses tested. In summary, studies conducted in support of EPA registration indicate there is little or no concern for acute, short term, subchronic or chronic dietary risk to humans from Procellacor™ applications. Tests have shown no evidence of genotoxicity/carcinogenicity, immunotoxicity, neurotoxicity, subchronic or chronic toxicity, reproductive or developmental toxicity, and only showed evidence of low acute toxicity.

Several studies conducted on both mice and rats, over the course of 1-2 years have indicated no treatment-related (post-necropsy) clinical observations or gross histopathological lesions. An 18-month mouse study was conducted, and no chronic toxicity, carcinogenicity, or other adverse effects were observed, even in those male and female mice receiving the highest doses tested. A 1-year dog study is also ongoing; similar to the above mammalian toxicity tests, no treatment-related toxicity or pathology has yet been observed during this study. Reproductive, developmental, and endocrine toxicity (immunotoxicity) has also been tested, and results of all these tests showed no evidence of toxicity. Although no specific human testing has been conducted for Procellacor™, based on extensive laboratory testing on mammalian species, little to no acute or chronic toxicity would be expected in association with environmental exposures.

General Ecotoxicity

Procellacor™ has undergone extensive ecotoxicological testing and has been shown to be nearly non-toxic to birds in acute oral, dietary, and reproduction studies. Similar to the mammalian testing

summarized above, no toxicity was observed for avian, fish, or other species exposed to the herbicide in acute and long-term studies, with endpoints set at the highest concentration tested, which are well above those actually released as part of label-specified application of Procellacor™. As would be expected for an herbicide, toxicity has been observed to certain sensitive terrestrial and aquatic plants (see plant discussion below).

As noted above, the TGAI of Procellacor™ exhibits low water solubility, and in laboratory aquatic ecotoxicity studies, the highest concentration of TGAI that could be dissolved in the test water (or functional solubility) was approximately 40-60 µg/L in freshwater. The acute and/or chronic endpoints for freshwater fish and invertebrates are generally at, or above, the limit of functional solubility. Additional evaluations indicate a lack of toxicity of the aquatic end-use product (greater functional solubility than the TGAI) and metabolites up to several orders of magnitude above the typical in-water use rates of Procellacor™ (50 µg/L or less).

Fish Ecotoxicity

A variety of fish tests have been conducted in cold and warm water fish species using the TGAI as well as the end-use formulation and various metabolites. Acute toxicity results using rainbow trout (*O. mykiss*, a standard cold water fish testing species) indicated LC_{50} values of greater than 49 µg/L, and greater than 41 µg/L for fathead minnow (*P. promelas*, a standard warm water species). The pure TGAI would not be expected to be released into the environment, and comparable acute ecotoxicity testing was performed for carp using an end-use formulation for Procellacor™. Results indicate an LC_{50} value of greater than 1,900 ug/L for carp (*C. carpio*), indicating much lower acute toxicity potential. A marine toxicity test was identified, where sheepshead minnows (*C. variegatus*) were tested for acute toxicity, and a LC_{50} value of greater than 40 µg/L was produced, which is comparable to freshwater species tested for acute toxicity. This value is indicative of slight acute toxicity potential if environmental concentrations were to be present at these levels, which is unlikely. Comparable acute ecotoxicity testing using various Procellacor™ metabolites indicated LC_{50} values uniformly greater than 1,000 µg/L, indicating a minimal potential for acute toxicity from metabolites. Salmonid toxicity data also indicated no overt toxicity to juvenile rainbow trout at limit of solubility for both the TGAI and end-use formulation at the maximum application rate (40 µg/L). If fish were to occupy a plant-infested littoral zone that was treated by Procellacor™, no toxic exposure would be expected to occur, as toxicity thresholds would not be exceeded by the concentrations predicted to be allowed for use by the FIFRA label.

Fish toxicity testing, in addition to that summarized above, has been planned and is currently under way for sensitive and ESA-listed aquatic species and habitat considerations in the Pacific Northwest, as reported by Grue (2016). The emphasis for this aquatic toxicity testing is on salmonid species (Chinook salmon, bull trout, coho salmon, etc.), which are the most frequently listed and probably the most representative fish species in the Northwest under ESA. The most commonly accepted surrogate fish test species for salmonids is the coldwater salmonid rainbow trout (*O. mykiss*), but to help alleviate additional uncertainty, this additional testing will use age- and species- appropriate salmon species, and is intended to replicate pre-registration toxicity tests with trout. Test endpoints will include acute mortality, growth, and other sublethal endpoints (e.g. erratic swimming, on-bottom gilling, etc.) to evaluate more subtle toxicological effects potentially associated with Procellacor™.

This testing will screen comparable treatments to the trout testing (0, 40 and 80 µg/L Procellacor™, with the latter being well in excess of anticipated maximum labeled use rate). Testing will follow standard guidelines (ASTM, 2002; EPA, 1996) as did the earlier testing (e.g. Breaux, 2015), to ensure comparability. Results from this additional testing are expected to become available by late spring 2017, and will be useful in expanding our understanding of the toxicological properties of Procellacor™ when used in salmon-bearing waters.

Avian Toxicity

As noted above, Procellacor™ has been shown to be of low acute and chronic toxicity to birds as shown in a series of acute oral, dietary, and reproduction studies (Breaux, 2015). Little to no toxicity was observed for avian species exposed to the herbicide in both acute and longer-term chronic studies, with the highest test concentrations exceeded expected labeled rates, a common practice in laboratory toxicology. Bird testing was conducted to include standard test species including mallard duck (*A. platyrhynchos*), the passerine (songbird) species zebra finch (*T. guttata*), and bobwhite quail (*C. virginianus*). Tests involved oral administration for acute and chronic testing and reproductive studies, eggshell thinning, life cycle testing, and other endpoints. In summary, acute oral testing using bobwhite quail and zebra finch yielded LD_{50} values of greater than 2,250 mg/kg-day for both species. Two five-day acute dietary tests were also conducted, which both yielded LC_{50} values of greater than 5,620 mg/kg-day. Subchronic reproductive tests were also conducted for bobwhite quail and mallard ducks both yielded NOEC values of 1,000 mg/kg in the feed. All of these results are highly indicative of little to no toxicity to each of the avian species tested.

No amphibian or reptile toxicity testing was required by EPA Office of Pesticide Programs registration requirements, or conducted as part of the testing regimen for Procellacor™. EPA guidelines generally assert that avian testing is an adequate surrogate for amphibian or reptile testing, and invertebrate and mammalian test results are available as well to support projection of minimal toxicity of Procellacor™ to amphibians or reptiles.

Invertebrate Ecotoxicity

Acute and chronic testing of Procellacor™ with honey bees, the only insect species tested, has indicated no evidence of ecotoxicity to this species (Breaux, 2015). Concerning aquatic invertebrates, acute testing was performed for both the daphnid *D. magna* and the midge *Chironomus* sp. Tests were conducted using both the TGAI and end-use formulation for Procellacor™, as well as various metabolites. Acute toxicity results for the TGAI using *D. magna* indicated LC_{50} values of greater than 62 µg/L, and greater than 60 µg/L for *Chironomus.* This is generally consistent with acute toxicity testing conducted for the freshwater amphipod *Gammarus* sp., for which a NOEC value of 42 µg/L was developed. These results are indicative of little to no acute toxicity to these species. Comparable acute ecotoxicity testing was performed for *D. magna* using a Procellacor™ end-use formulation, and results indicated an LC_{50} value of greater than 80,000 µg/L, also indicating negligible acute toxicity potential. Acute ecotoxicity testing using various metabolites of the herbicide indicated LC_{50} values uniformly greater than 980 µg/L, with most values exceeding 10,000 µg/L, indicating little to no potential for acute toxicity for the metabolites.

Life cycle testing was also completed for a freshwater (*D. magna*) for both the TGAI and metabolites, and results showed a Lowest Observable Adverse Effect Concentration (LOAEC) and an NOAEC of 38

µg/L (both endpoints) showing low toxicity potential for the TGAI in an artificial scenario of static exposure using a renewal protocol design. The spot/partial use pattern of the herbicide and instability of TGAI under natural conditions project to a lack of chronic exposure to aquatic fauna. Comparable testing with metabolites showed LOAEC/NOAEC values both exceeding 25,000 µg/L, indicating negligible levels of toxicity for metabolites. Whole sediment testing using the TGAI for a freshwater invertebrate (chironomid midge) was also conducted for acute (10 day) and chronic (28 day) duration. The chronic test spiked water overlying sediments to a target concentration as the means to initiate exposure. Results of the whole sediment testing indicated an acute 10-day LOAEC of 10.5 mg ai/kg sediment and 28-day NOEC level of 78.5 µg/L (overlying water target concentration), which would generally be indicative of very low to negligible aquatic ecotoxicity.

Additionally, acute screening was recently performed by North Carolina State University (Principal Investigator: Dr. Greg Cope, cited as Buczek *et al.* 2017) on the juvenile life stage of a representative freshwater mussel (*L. siliquoidea*) with the TGAI, a primary metabolite (acid metabolite), and two TEP / formulations (the SC above and a 25 g/L EC formulation). The study showed no toxicity to juvenile mussels in any test with formulated results showing No Effect Concentrations (NOEC) that were 25 – 50 times greater than anticipated maximum application rate for the new herbicide (Cope *et al.* 2017 *in prep*).

Although the proposed registration for Procellacor™ in Washington State will be for freshwater application, it is possible that Procellacor™ would be applied near marine or estuarine habitats for weed control. Acute toxicity testing, using TGAI, conducted on the eastern oyster (*C. gigas*) produced an NOEC of greater than 24 µg ai/L and a comparable NOEC value for mysid shrimp (*M. bahia*) of greater than 26 ug ai/L, both the highest rates tested due to solubility limits with assays. Comparable NOEC values developed for primary aquatic end-use formulation were greater than 1,100 and 1,350 µg/L as formulated product (>289 and >362 µg/L as active ingredient), respectively, for the oyster and shrimp.

Marine invertebrate life cycle testing was conducted using the TGAI on a mysid shrimp) and a chronic NOAEC of 7.8 µg/L (LOAEC of 13 µg/L) was developed, which is potentially indicative of chronic toxicity to marine or estuarine invertebrates if these sustained concentrations were attained in environmental settings. Acute NOECs for oyster and mysids tested with the TGAI were set at the highest mean measured rate of tested material. There were no adverse effects noted in those studies. There are potential unknowns with possible effects with acute exposures to concentrations greater than 24-26 µg/L, but range finding-finding toxicity testing demonstrated that this range of concentrations were the highest limits to maintain solubility of TGAI in the assays.

In practice, due to rapid degradation of the TGAI in the field, rapid dilution from spot applications (main use pattern), and not labelling for estuarine and marine sites will mitigate any chance of acute exposures to marine invertebrates above the range of mid-20 µg/L. Chronic toxicity results for mysid shrimp do suggest possible chronic effects at 7.8 µg/L, with extended exposures to the TGAI. Again, however, the use pattern is not intended for estuarine/marine application with the initial labelling. The use pattern in freshwater is spot/partial treatments with negligible chance of sustained TGAI concentrations migrating downstream to estuarine habitat even if the freshwater site was in close proximity to an estuarine area. In general, the labeled freshwater use for spot/partial applications (high dilution potential) to control noxious freshwater aquatic plants and the rapid degradation of the TGAI

suggest minimal risk to marine and estuarine invertebrates following application to a nearby freshwater site. Metabolite testing with marine species yielded NOECs of greater than 25,000 µg/L, indicating negligible toxicity.

Data Gaps

No data gaps have been identified for the basic environmental profile, including environmental fate, product chemistry, toxicology and ecotoxicology, and field studies required by EPA for pesticide registration. However, a number of recent trials are currently in review (e.g., Beets and Netherland 2017a) or in preparation for publication (e.g. Beets and Netherland, 2017b, Netherland *et al.* 2017, Haug *et al.* 2017). These, along with the continued use of Procellacor™ under a variety of plant management scenarios, will add valuable information that can be incorporated into the product labels, improved treatment profiles and potentially required mitigation measures.

4.3.3 Environmental and Human Health Impacts

4.3.3.1 Earth

Soil and Sediments

Procellacor™ has moderately high measured K_{ow} and K_{oc} partition coefficients, with log K_{ow} and K_{oc} values of approximately 5.4 to 5.5, or about 10^{-5}, which supports low solubility and demonstrates a relatively high affinity for sorption to organically enriched substrates such as soils or sediments. However, as noted above, in aerobic soil Procellacor™ degrades quickly, with half-lives ranging from 2.5 to 34 days, with an average of 15 days. Anaerobic soil metabolism studies are similar, showing relatively rapid degradation rates with half-lives ranging from 7 to 15 days, and an average of 9.8 days. This rapid degradation in the soil and sediment environment strongly suggests low persistence in these media. Due to the low acute and chronic toxicity described below, low to negligible impacts are expected in soils and sediments adjoining Procellacor™ treatment areas. The herbicide can be classified as largely immobile based on soil log K_{oc} values in the order of 10^{-5}, and that potential for off-site transport would be minimal.

Agriculture

At anticipated use concentrations, irrigation or flooding of crops with water treated with Procellacor™ are not expected to damage crops or non-target wild plants, except under scenarios not addressed in the forthcoming EPA label.

Terrestrial Land Use

At anticipated use concentrations, water reentry or swimming in water treated with Procellacor™ is not expected to cause dermal, eye, or other irritation or toxicity to human or wildlife species.

4.3.3.2 Water

Surface Water and Runoff

Procellacor™ is known to have low water solubility (about 15 µg/L in lab testing) and the parent compound is not persistent and is known to quickly degrade via a number of well-established pathways.

As discussed above, the herbicide is short lived in aerobic and anaerobic aquatic environments in a total water-sediment system. When exposed to direct sunlight, degradation in surface water is even more accelerated, with a reported photolytic half-life as little as 0.1 days.

The two outdoor aquatic dissipation studies summarized above further support this rapid dissipation and low impact. Both studies show that when Procellacor™ was directly injected into outdoor freshwater ponds at nominal rates of 50 and 150 µg/L, very rapid water-phase dissipation half-lives (3 to 4.9 days) were observed. These characteristics strongly suggest that the potential for off-site transport or mobility is minimal. As noted above, Procellacor™ undergoes rapid degradation in both soil and aqueous-phase environments via a number of degradation mechanisms.

No use for aquatic vegetation management in marine or estuarine water using Procellacor™ will be labeled at this time in Washington State (Heilman, 2016).

No specific studies or exposure scenarios were identified where drift or runoff were specifically investigated, but the forthcoming EPA risk assessment for Procellacor™ is expected to address these scenarios. For drift, the low vapor pressure (approximately 10^{-7} mm Hg) indicates that the material is not prone to volatilize following application, thus minimizing drift potential, and the low water solubility, low acute and chronic toxicity, along with minimal potential for persistence suggest that potential hazards associated with surface water runoff would be minimal.

Groundwater and Public Water Supplies

Few studies have yet been completed for groundwater, but based on known environmental properties concerning mobility, solubility, and persistence, Procellacor™ is not expected to be associated with potential environmental impacts or problems in groundwater.

In laboratory aquatic ecotoxicity studies, the highest concentration of TGAI that could be dissolved in the test water (or functional solubility) was approximately 40-60 µg/L in freshwater and 20-40 µg/L in saltwater. This is due to the low water solubility of the active ingredient and limits the range for which these toxicity tests can be conducted. This finding suggests that the water chemistry of Procellacor™ would limit potential environmental impacts to groundwater or surface water.

Impacts to public water supplies are expected to be low to negligible based on the low solubility, low persistence, and low acute and chronic toxicity of Procellacor™. Section 4.3.4 discusses possible measures or best management practices (BMPs) that could be used to further reduce potential impacts to public water supplies. The Ecology permit has mitigation that requires permittees to obtain an approval letter for this treatment prior to obtaining coverage under the permit.

4.3.3.3 Wetlands

The habitat and aquatic structure found in rice paddies is similar to those in a wetland and marsh environments, making the studies reported by Heilman (2016a) and Netherland and Richardson (2016) important tools for this analysis. The wetland and marsh study, discussed above in Section 4.3.2.2., incorporated appropriate water management practices for both wet-seeded and dry-seeded rice, and reported rapid aquatic-phase half-lives ranging from 0.15 to 0.79 days, and soil phase half-lives were also rapid, ranging from less than 0.01 to 8.1 days.

4.3.3.4 Plants

Algae

Limited ecotoxicity testing using a growth endpoint was conducted for two species of freshwater algae, including a diatom and green algae. These tests showed EC_{50} values using the TGAI of greater than 40 and 34 µg/L, respectively (solubility limit of assays). These results indicate that Procellacor™ is generally not toxic to green algae, freshwater diatoms, or blue-green algae at the anticipated label rate. Metabolite testing showed little toxicity to these algae, with no EC_{50} value less than 450 µg/L. Comparable growth testing was also conducted using the end-use formulation for aquatic algal plant growth, and results showed an EC_{50} greater than 1,800 µg/L (480 µg/L as active), with a NOAEC of 420 µg/L of formulation (111 µg/L as active), again showing a lack of toxicity to algae within anticipated label use rates. A comparable test of the TGAI was performed for cyanobacteria (blue-green algae), and results showed an EC_{50} of greater than 45 µg/L, with a calculated NOAEC value of 23.3 µg/L, showing little evidence of toxicity for any of these species.

Higher Plants and Crops

Procellacor™ is known to have strong herbicidal activity on key target aquatic invasive species, and testing shows that many native plants are able to tolerate Procellacor™ at exposure rates greater than what is necessary to control key target invasives. Data collection is still underway for specific toxicity to non-target plant species. Initial results of a 2016 collaborative mesocosm study conducted in Texas, for which results will be formally available later in 2017 indicate favorable selectivity by Procellacor™ of multiple invasive watermilfoils in the presence of representative submersed aquatic native plants (Netherland *et al.* 2017 *in prep*). Aquatic native plants challenged in this study included tapegrass, Illinois pondweed, American pondweed, waterweed, and water stargrass. Using aboveground biomass as a response endpoint, no significant treatment effects were observed with tapegrass or American/Illinois pondweed. Similarly, no statistically significant treatment effects were observed with stargrass, although injuries were observed at higher rates and exposures, although it was much more tolerant than the two target milfoil species. Other mesocosm studies have shown similar responses in white water lily with other non-target species including Robbins pondweed, American pondweed, and multiple bladderwort species showing little or no discernible impact. Richardson *et al*. (2016) and Haug and Richardson (2017 *in prep*) report that Procellacor™ provides a new potential for selectivity for removing hydrilla from mixed aquatic-plant communities. They recommend that further research should be conducted to further characterize observed patterns of selectivity.

4.3.3.5 Habitat

Impacts to critical habitat for aquatic plant or animal species are expected to be minimal, and may benefit critical habitat overall by supporting plant selectivity. Procellacor™ is generally of a low order or acute and chronic toxicity to plants and animals and generally does not persist in the environment. Due to its documented selectivity, Procellacor™ would allow many native non-target plants to thrive and thus enhance quality habitat. Removing noxious aquatic plants creates open spaces in the littoral zone that may be recolonized by not only native plants but other invasive plant species.

For example, when left unchecked, dense stands of unwanted weeds such as watermilfoil, parrotsfeather, hydrilla, or numerous other noxious plant species can negatively impact critical salmonid or other habitat used at all life stages, as well as habitats to a wide variety of plant and animal species, including vulnerable life stages. Stands of invasive weeds can reduce water flow and circulation, thus impeding navigation for migrant salmonids. Such stands can also provide ambush cover for predatory species such as bass, which prey on critical juvenile and other salmonid life stages. Moreover, noxious plants may outcompete native plant species, thus reducing overall biodiversity and reducing overall habitat quality. Dense stands may also be conducive to creating warmer water (through reduced circulation and dissolved oxygen sags), and could become subject to wide fluctuations in water quality (e.g. temperature, dissolved oxygen (DO)) on a diurnal/seasonal basis.

4.3.4 Mitigation

4.3.4.1 Use Restrictions

Procellacor™ should only be used for the control of aquatic plants in accordance with label specifications. No data gaps have been identified for the basic environmental profile required by EPA for pesticide registration, although continued use of Procellacor™ under a variety of plant management scenarios will add valuable information that can be incorporated into improved treatment profiles and possible mitigation measures. For potential future irrigation with Procellacor™-treated water, final EPA labeling will include guidance on appropriate water use. Such restrictions can be refined once the human health and ecological risk assessment currently being conducted by EPA are released in spring 2017. The proposed label language is expected to reflect fewer application-related restrictions than other herbicides. Lower levels of personal protective equipment (PPE) for workers will be required, which is consistent with lower use rates, lower water use restrictions, and minimal effects to crops or other non-target species.

4.3.4.2 Swimming and Skiing

Recreation activities such as swimming, water skiing and boating are expected to be unaffected by applications or treatments using Procellacor™ herbicide formulations.

4.3.4.3 Irrigation, Drinking and other Domestic Water Uses

As a mitigation measure for experimental purposes, irrigation has been and will continue to be restricted until the herbicide has dissipated. In addition, Ecology's Aquatic Plant and Algae permit provides specific mitigation measures for irrigation water and water rights. Following registration, however, no water use restrictions are anticipated for the product use label except for some forms of irrigation. Any such restrictions will be specified on the final label language in collaboration with EPA. Procellacor™ is not expected to have any restrictions for watering turf. Before irrigation use on potentially sensitive crops or other plants, the final label language is anticipated to require concentrations to be analytically verified to less than 1 µg/L. Restrictions on irrigation use on sensitive plants may alternatively or additionally include times of post-application restrictions, depending on use rates and scale/locations of application. These options are currently being reviewed with EPA.

Drinking water is not expected to be affected by Procellacor™ applications.

4.3.4.4 Fisheries and Fish Consumption

Neither fisheries nor human fish consumption are expected to be affected by application of Procellacor™ herbicides. If there is potential to impact listed salmonid species (e.g. salmon, steelhead, bull trout, etc.) Ecology would enforce a fish timing window that would be protective of those species. Guidance for such timing windows are found at: http://www.ecy.wa.gov/programs/wq/pesticides/final_pesticide_permits/aquatic_plants/permitdocs/wdfwtiming.pdf.

4.3.4.5 Endangered Species

Data are limited for specific listed threatened or endangered species under the ESA, however, a number of carefully designed and relevant laboratory toxicity tests for endangered species are currently under way, as discussed above. These tests will increase available testing data and enhance our understanding of how to more effectively protect non-target listed and vulnerable species, with particular emphasis on ESA-listed salmonid species such as salmon species, steelhead, and bull trout.

4.3.4.6 Wetlands or Non-Target Plants

Ecology's APAM permit outlines specific restrictions on what can be treated in wetlands. For example, in identified wetlands, the APAM specifies that the permittee "may treat only *high use areas* to provide for safe *recreation* (e.g., *defined swimming corridors*) and boating (e.g., *defined navigation channels*) in *identified and/or emergent wetlands.* The permittee must also limit the treated area to protect native wetland vegetation. However, final mitigation measures and best management practices concerning potential effects to beneficial or desirable wetland plant species will be developed in conjunction with testing on higher plants, some of which may occur in wetlands.

In general, effects to wetlands are anticipated to be minimal. Toxicity to fish, invertebrates, wildlife, and non-target plants would not generally be expected, and persistence (and thus food chain effects) would also be minimal. No specific toxicity testing was required or conducted for amphibians or reptiles which are ubiquitous in wetlands, but test results from invertebrate, avian, mammalian and other test species would be expected to serve as representative surrogate species for amphibians and reptiles.

Regarding potential impacts to rare or endangered plants occurring in wetlands, Ecology uses the Washington Department of Natural Resources (WDNR) Natural Heritage Site guidelines to determine if rare plants are likely to occur in the treatment area. If rare plants may be present at the treatment site, Ecology would require a field survey, and if such plants are found mitigation would be required.

4.3.4.7 Post-treatment Monitoring

EPA, Ecology, and other agencies routinely require both short- and long-term post-treatment monitoring for the purpose of evaluating non-target effects from herbicides such as Procellacor™. For Ecology, this post-treatment monitoring would be required under the permit, and would be a permit condition requiring monitoring to determine potential non-target impacts. These requirements will be incorporated into both label and permit, as appropriate, in conjunction with pesticide registration prior to application.

4.3.5 References

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