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Supplemental Environmental Impact Statement for State of Washington Aquatic Plant and Algae Management

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4.3 EVALUATION OF PROCELLACOR™ (FLORPYRAUXIFEN-BENZYL)

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 (2-pyridinecarboxylic acid, 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-, phenylmethyl ester also known as Rinskor™; 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™ (florpyrauxifen-benzyl)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. Florpyrauxifen-benzyl 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 summer 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 late 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 florpyrauxifen-benzyl 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 florpyrauxifen-benzyl's (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 (florpyrauxifen-benzyl), 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°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 µg/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 and 2017). 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 cold water 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 using environmentally representative exposure concentrations. Test endpoints include acute mortality, growth, and other sublethal and behavioral endpoints (e.g. erratic swimming, on-bottom gilling, etc.) to evaluate more subtle toxicological effects potentially associated with Procellacor™. Preliminary results from this testing

indicate little to no effects associated with exposure to florpyrauxifen-benzyl, and a final report on this work will be forthcoming later in 2017.

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 µg 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

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.

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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