Registration Decision for the New Active Ingredient

(2S)-5-Oxopyrrolidine-2-carboxylic Acid (L-PCA)

A plant growth regulator for use on agricultural crops, turf, and ornamental plants and as a seed treatment.

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Approved by:

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1. Introduction

This document announces that the Environmental Protection Agency (EPA) has completed its initial evaluation of the new biochemical active ingredient (AI), (2S)-5-oxopyrrolidine-2-carboxylic Acid (L-PCA), for use as a plant growth regulator (PGR) and has concluded that it meets the regulatory and safety standards under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA). EPA's assessment of L-PCA also included consideration of a public participation process, which allowed for a 15-day comment period. No comments were received.

L-PCA is derived from L-glutamic acid (a Federally registered PGR compound) via an intramolecular condensation reaction and is naturally found in mammalian tissues. As a PGR, L-PCA has a non-toxic mode of action and can enhance upregulation of the glutamine synthesis pathway. L-PCA has a long history of use in consumer cosmetic products (as a skin condition agent i.e., humectant), and some use as a dietary supplement to improve memory function. There are two forms of L-PCA: an acid and a salt. EPA is registering the acid form as a new active ingredient; however, there is an expectation that the end-use product (EP) formulations will be applied as buffered (salt) forms since unbuffered solutions will not be effective as a plant growth regulator and would likely destroy the plant due to the acidity of L-PCA. When applied to plants in its salt (buffered) form, L-PCA does not harm the plant and is intended to increase growth, increase nodulation and provide greater fresh plant weight. It is also used as a seed priming agent. Both the acid and the salt versions release a common moiety that is the pesticidal active component and serves as the basis for risk assessment and tolerance regulation.

As a biopesticide PGR, the EP, VLS 2002-03 is intended to be applied (in salt form) to agricultural crops, turf, and ornamental plants at an application rate of 6-12 fl oz/Acre via hand-held equipment, such as backpack sprayers or as a commercial seed treatment at 0.01-0.04 fl oz per 100 lbs. of seed.[1] Sufficient water volume is used to obtain thorough uniform coverage of all plant surfaces. Personal Protective Equipment (PPE) requirements for all mixers, loaders, applicators and other handlers include long-sleeved shirt and long pants, waterproof gloves, shoes plus socks, and protective eyewear.

After reviewing all submitted data, EPA has concluded that there is reasonable certainty of no harm from residues of L-PCA and that its use on all food commodities will cause no unreasonable adverse effects to human health or the environment. Therefore, the Agency is granting unconditional registration of two products: a Manufacturing-Use Product (MP)/technical grade of the active ingredient (TGAI), (2S)-5-Oxopyrrolidine-2-carboxylic Acid (L-PCA) Technical (EPA File Symbol: 73771-RE); and an End-Use Product (EP), VLS 2002-03 (EPA File Symbol: 73771-R. Relatedly, on August 10, 2023, the Agency published a final rule to amend 40 CFR 180.1404 to establish a tolerance exemption for residues of L-PCA in or on all food commodities (https://www.federalregister.gov/documents/2023/08/10/2023-17135/2s-5-oxopyrrolidine-2-carboxylic-acid-l-pca-exemption-from-the-requirement-of-a-tolerance).

[1] End-use products containing L-PCA as their active ingredient can only be applied via handheld sprayer or seed treatment (to reduce ecological exposure to non-target vegetation). The registered products will bear pesticide product labeling which explicitly states that all other application methods are prohibited.

2. Background

L-PCA was classified as a biochemical pesticide by the Agency's Biochemical Classification Committee (BCC) on July 3, 2017, due to its natural occurrence, history of exposure to humans and the environment, and non-toxic mode of action to the target pest(s).

On February 9, 2018, EPA received applications from Exponent, on behalf of Verdesian Life Sciences U.S., LLC, for the registration of three pesticide products, an MP and two EPs (one of which has since been withdrawn by the applicant), containing the new biochemical active ingredient L-PCA and a petition [8F8663] to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for residues of L-PCA when used as a plant growth regulator on agricultural crops, turf, and ornamental plants, in accordance with label directions and good agricultural practices. Exponent provided a combination of guideline studies, data waiver requests, and scientific rationales supported by information from the open scientific literature to address product chemistry, human health, and ecological toxicity data requirements.

In the Federal Register of May 17, 2018, EPA published a Notice of Receipt (NOR) that announced receipt of three new product applications: one MP and two EPs, containing the new active ingredient, L-PCA. Since the publication of the NOR, the applicant has withdrawn one of the EP applications. One MP and one EP remain. No comments were received in response to the NOR. In the Federal Register of May 18, 2018, EPA published a Notice of Filing (NOF) that announced a request to establish an exemption from the requirement of a tolerance in 40 CFR part 180 for residues of L-PCA, when used as a plant growth regulator on agricultural crops, turf, and ornamental plants, in accordance with label directions and good agricultural practices. No substantive comments were received in response to this Notice of Filing. The Final Rule formally establishing the exemption from the requirement of a tolerance for L-PCA was published in the Federal Register on August 10, 2023.

3. Evaluation

In evaluating a pesticide registration application, EPA assesses a variety of studies to determine the likelihood of adverse effects (i.e., risk) from exposures associated with the use of the pesticide product. Risk assessments are developed to evaluate how the active ingredient might affect a range of non-target organisms, including humans and terrestrial and aquatic wildlife (plants and animals). Based on these assessments, EPA evaluates and approves language for each pesticide label to ensure the directions for use and safety measures are appropriate to mitigate any potential risk. In this way, the pesticide's label helps to communicate essential limitations and mitigations that are necessary for public and environmental safety. In fact, the pesticide law has a provision that indicates it is a violation to use a pesticide in a way that conflicts with the label.

3.1 Assessment of Risk to Human Health

To assess risks to human health from the use of biochemical pesticides, EPA evaluates the potential toxicity of a product, and the likelihood, amount, and types of exposure users and

bystanders are likely to experience. In conducting a risk assessment, EPA must consider: (1) the hazards of a substance and (2) the human exposure to that substance as a consequence of use, either directly or indirectly. EPA uses this combined information to assess and characterize the risk(s) and predict the probability, nature, and magnitude of the adverse health effects that may occur from the use of the substance in the manner described.

On the toxicity side for biochemical pesticides, EPA typically requires a range of Tier I data: acute toxicity data (acute oral toxicity, acute inhalation toxicity, acute dermal toxicity); irritation tests (primary eye irritation, primary dermal irritation, and dermal sensitization); subchronic testing (90-day oral, 90-day dermal, and 90-day inhalation); mutagenicity testing (bacterial reverse mutation test and in vitro mammalian cell assay) and developmental toxicity testing (prenatal development). Tiers II and III testing are triggered only when there is indication, usually through lower tier testing, that a biochemical pesticide has unusual characteristics, such as subchronic toxicity, or is suspected or known to be a carcinogen.

3.1.1 Toxicological Data/Information

Adequate mammalian toxicology data/information are available to support a food-use registration of L-PCA on all food commodities or processed foods. All toxicology data requirements for L-PCA have been satisfied and a dietary risk assessment is available in the regulatory docket (search for "EPA-HQ-OPP-2018-0145" at http://www.regulations.gov). In summary, based on the results of the available acute toxicity studies, L-PCA has a low acute toxicity profile and is classified as Toxicity Category IV for acute inhalation and Toxicity Category III for acute oral and dermal toxicity. L-PCA has a low pH (2) and is likely corrosive. Therefore, waiver requests were granted for the primary dermal irritation and primary eye irritation data requirements. The available data suggest it is not a skin sensitizer. The EP will carry the signal word "CAUTION" and the MP will carry the signal word "DANGER."

In conducting its hazard assessment for L-PCA, EPA relied on the following data and information to satisfy the data requirements: 1) guideline Bacterial Reverse Mutation; and 2) non-guideline study and data waivers supported by information from the open scientific literature in lieu of guideline studies for the 90-day inhalation toxicity and 90-day dermal toxicity data requirements. No adverse effects at doses relevant to risk assessment have been identified in the available data.

In the case of the subchronic 90-day oral and prenatal developmental data requirements, studies from the open literature were determined to be acceptable. In the case of subchronic 90-day inhalation, 90-day dermal, and genotoxicity data requirements, EPA reviewed the data waivers and granted them based on a weight of evidence (WOE) approach due to the reasons listed below.

90-day oral toxicity

Studies from the open scientific literature on the sodium salt analog, Na-PCA, were submitted to satisfy the 90-day oral toxicity data requirement for L-PCA. The Na-PCA toxicity database is

considered appropriate for use in L-PCA risk assessment when EP formulations are buffered. This is because buffered L-PCA behaves similarly to Na-PCA. There is comparable acute toxicity between the EP formulations and Na-PCA. Further, both L-PCA and Na-PCA are naturally occurring and are products of human metabolism. Using a WOE approach, these studies allowed EPA to establish a no-observed-adverse-effect-level (NOAEL) of 849 mg/kg/day for subchronic oral toxicity for L-PCA in buffered end-use products.

Prenatal developmental toxicity

For developmental toxicity, a non-guideline 1-generation reproduction toxicity screening study was submitted on Na-PCA in lieu of a developmental toxicity study. The study showed no treatment-related effects on offspring body weights, body weight gains or on post-implantation losses, mean litter size, numbers of live and dead pups born, sex ratio, or the birth or survival indices. No gross or microscopic pathology of the reproductive tract was seen, and reproductive performance was not affected by treatment. The NOAEL is 1000 mg/kg/day (the limit dose level). While this study is not a guideline developmental toxicity study, EPA has determined that the screening study is acceptable to satisfy the prenatal developmental toxicity data requirement at this time for the specified products. This decision is based on the fact that no observable toxicity was produced at the limit dose level in this study and an effect would not be expected from structurally related compounds.

90-day inhalation toxicity

A waiver request to satisfy the 90-day inhalation toxicity data requirement was accepted by EPA on April 17, 2020, for L-PCA when used in EPs formulated with a buffer that raises the pH. The waiver was acceptable based upon the following: 1) physical and chemical properties of the buffered formulations of L-PCA are similar to those of Na-PCA; 2) use of the oral NOAEL (849 mg/kg/day) from the subchronic toxicity study on Na-PCA, and a dermal absorption factor of 100% to evaluate occupational risks resulted in margins of exposure (MOEs) greater than the level of concern (LOC) of 100 (10X for interspecies extrapolation and 10X for intraspecies variation). The occupational handler MOEs ranged from 1,500 to greater than 470,000 and the occupational post-application MOEs ranged from 1,500 to 190,000. These MOEs are more than 10X the LOC. Use of an oral endpoint to assess dermal and inhalation exposure is supported by the near complete absorption of L-PCA via the oral route of exposure; and 3) while technical L-PCA is severely irritating/corrosive to the eyes and skin and demonstrated some clinical signs indicative of respiratory irritation, no irritation was observed in studies conducted using the buffered end-use products. Occupational exposure via the inhalation route will be to the buffered products, not the technical material.

90-day dermal toxicity

A waiver request to satisfy the 90-day dermal toxicity data requirement was accepted by EPA on April 17, 2020, for L-PCA when used in EPs formulated with a buffer that raises the pH. The waiver was acceptable based upon the following: 1) physical and chemical properties of the buffered formulations of L-PCA are similar to those of Na-PCA; 2) use of the oral NOAEL (849 mg/kg/day) from the subchronic toxicity study on Na-PCA, and a dermal absorption factor of

100% to evaluate occupational risks resulted in MOEs greater than the LOC of 100 (10X for interspecies extrapolation and 10X for intraspecies variation). The occupational handler MOEs ranged from 1,500 to greater than 470,000 and the occupational post-application MOEs ranged from 1,500 to 190,000. These MOEs are more than 10X the LOC. The use of an oral endpoint to assess dermal and inhalation exposure is supported by the near complete absorption of L-PCA via the oral route of exposure; and 3) while technical L-PCA is severely irritating/corrosive to the eyes and skin, no acute dermal toxicity or eye or skin irritation was observed in studies conducted using the buffered end-use products. Occupational exposure via the dermal route will be to the buffered products, not the technical material.

Bacterial reverse mutation and in vitro *mammalian cell toxicity*

An acceptable guideline study on L-PCA was submitted for the Bacterial Reverse Mutation test and a waiver request was granted for the *in vitro* Mammalian Cell Assay requirement based upon the lack of mutagenicity in the *in vitro* Bacterial Reverse Mutation assay and the lack of genotoxic effects observed in the Na-PCA database. Overall, the active ingredient was determined to be non-mutagenic.

3.1.2 Dietary and Occupational Exposure and Risks

Dietary and Drinking Water Exposure and Risk Characterization: As part of its qualitative risk assessment for L-PCA, the Agency considered the potential for dietary exposure to residues of the chemical. EPA concludes that dietary (food and drinking water) exposures are possible. However, no toxicological endpoint of concern was identified for L-PCA, and therefore, a quantitative assessment of dietary exposure is not necessary. Dietary risk is not of a concern.

Residential (Non-occupational) Exposure and Risk Characterization: As there are no residential uses for lysate of L-PCA, a residential exposure and risk assessment is not necessary at this time.

Occupational Exposure and Risk Characterization: Occupational handler exposure and post-application exposure to L-PCA may occur when the EP is applied via backpack spray and seed treatment, but the risk related to exposure is not of concern. Application of the EP via aerial spray and ground applications (groundboom and airblast) are not allowed since spray drift is a potential source of exposure to L-PCA for those nearby applications.[1] However, even in the event of spray applications, occupational exposure to the active ingredient will not be of concern based on the low toxicity of the active ingredient and the PPE requirements for all mixers, loaders, applicators, and other handlers which will mitigate dermal and inhalation exposure.

3.1.3 Cumulative Risk

The EPA has not made a common mechanism of toxicity finding for L-PCA and any other substances, and this biopesticide does not appear to produce a toxic metabolite produced by other substances. Therefore, the EPA has not assumed that L-PCA has a common mechanism of toxicity with other substances.

3.1.4 Human Health Conclusions

EPA has determined that L-PCA and salts of L-PCA release a single common moiety that is the pesticidal active component and serves as the basis for risk assessment and pesticide regulation, and the active ingredient is best expressed as L-PCA. The toxicological database is complete for biopesticide risk assessment for the approved uses of L-PCA as a plant growth regulator and Data demonstrates that L-PCA is of low oral, dermal, and acute toxicity, and no adverse subchronic effects have been identified for any route of exposure. Any potential occupational exposures to individuals handling L-PCA for these uses are expected to be negligible. Furthermore, EPA does not expect dietary (food and drinking water) or other non-occupational risks of concern from use of L-PCA as an active ingredient for food use in buffered end-use products. EPA concludes that the use of L-PCA in buffered end-use products will not result in unreasonable adverse effects to humans and that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of L-PCA.

Determination of Safety for U.S. Population, Infants, and Children U.S. Population:

For all the reasons discussed above, EPA concluded that there is reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of L-PCA. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

Infants and Children:

With particular regard to infants and children, FFDCA section 408(b)(2)(C) provides that, in establishing or modifying a tolerance or tolerance exemption for a pesticide chemical residue, EPA shall assess risk considering the available information about consumption patterns among infants and children, special susceptibility of infants and children to pesticide chemical residues, and the cumulative effects on infants and children of the residues and other substances with a common mechanism of toxicity and ensure there is a reasonable certainty of no harm to infants and children from aggregate exposure to the pesticide chemical residue. In addition, FFDCA section 408(b)(2)(C) requires that, in the case of threshold effects, EPA apply an additional tenfold (10X) margin of safety for infants and children to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure, unless EPA determines, based on reliable data, that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the Food Quality Protection Act (FQPA) Safety Factor. In applying this provision, EPA either retains the default value of 10X or uses a different safety factor when reliable data available to EPA support the choice of a different factor. An FQPA safety factor is not required for L-PCA at this time as no dietary endpoints have been identified based on the lack of human-relevant adverse effects, including toxicity and allergenicity of L-PCA.

At this time, the database of studies required to support the hazard assessment to human health is complete. For more information on the human health hazard assessment of L-PCA, see the supporting documentation provided in the associated regulatory docket (search for “EPA-HQ-

OPP-2018-0145" at http://www.regulations.gov).

3.2 Assessment of Ecological Exposure and Risk

To assess ecological risks from the use of biochemical pesticides, EPA evaluates the likely environmental impacts as a result of exposure of the chemical to plants and animals in the environment and whether that exposure will cause harm or ecological effects. EPA uses this combined information and considers the overall toxicity to characterize the risk(s) in order to identify what levels may cause harmful effects on the plants and animals of concern that may occur from the use of the substance in the manner described.

On the toxicity side, EPA initially requires that a wide range of studies including Tier I testing be done on the following non-target organisms: mammalian (acute, sub-chronic, prenatal developmental, and mutagenicity), birds (acute oral and dietary), fish (acute freshwater fish and aquatic invertebrates), plants, and insects. Testing is organized in a tiered structure, where Tier I studies test worst-case exposure scenarios and higher tiers (Tiers II and III) generally encompass definitive risk determinations and longer-term greenhouse or field testing. Higher tier testing is implemented only when unacceptable effects are seen at the Tier I screening level. From study data, EPA formulates risk quotients (RQs) to characterize the risk to non-target species. An RQ is the quotient of the estimated environmental exposure (EEC) and the toxicological endpoint of interest.

The database of studies required to support the hazard assessment of L-PCA to the environment is complete. A combination of guideline studies demonstrate that L-PCA demonstrate a lack of effects to birds, mammals, terrestrial insects, fish, and aquatic invertebrates, as well as lack of exposure from the approved application methods. Therefore, the Agency has determined there is a reasonable expectation of no discernible direct or indirect effects to organisms in these groups. While toxicity was identified for both terrestrial and aquatic plants, the Agency has also determined that there is a reasonable expectation of no discernible effects to terrestrial and aquatic plants due to lack of exposure that results from the permitted application methods of handheld sprayer or seed treatment.[1] L-PCA also quickly degrades in the environment so any incidental exposure would be transitory and not at sufficient levels to impact non-target organisms. Therefore, the EPA makes a "no effect" determination for direct and indirect effects to federally threatened and endangered ('listed') species and their designated critical habitats for the approved uses of L-PCA.

For more information on the environmental hazard assessment of L-PCA, please see the supporting documentation provided in the associated regulatory docket (search for "EPA-HQ-OPP-2018-0145" at http://www.regulations.gov).

3.2.1 Terrestrial Animals and Plants

I. Birds, Mammals and Non-Target Insect Testing

Two avian toxicity studies were submitted with L-PCA. The acute toxicity test resulted in two mortalities at a limit dose of 2000 mg/kg bw (milligrams per kilogram bodyweight per day). The

unexplained mortality in a limit test classified this study as unacceptable and did not meet the requirement for OPPT 850.2100 guideline. Despite the unacceptable classification, this study suggests that the LD_{50} is likely to be greater than the limit dose used. An additional avian dietary study was also submitted. This study was classified as acceptable and indicated that L-PCA is practically non-toxic to birds and did not result in any adverse effects at a concentration of 5000 mg/kg-bw supporting the inference that the LD_{50} is likely to be higher than the limit dose. Because of this, an additional acute study is not needed for this risk assessment. T-REX was run using the LD_{50} of 2000 mg/kg bw and an LC_{50} of 5000 mg/kg bw. The RQs were all less than or equal to 0.1, the level of concern for listed species. The EECs for birds were highly conservative, using the default foliar half-life of 35 days. L-PCA rapidly degrades in the field and the foliar half-life of L-PCA is likely to be much quicker than the default foliar half-life. The rapid degradation of L-PCA combined with the lack of toxicity observed in the dietary toxicity study, suggests the adverse impacts to birds from the approved spray or seed treatment uses are not likely.

Similarly, L-PCA is also classified as practically non-toxic to mammals. All RQs were below the non-listed and listed species LOC of 0.5 and 0.1, respectively. Therefore, adverse effects to mammals are not anticipated.

In regard to non-target insects, L-PCA was classified as practically non-toxic to honeybees with acute contact and oral LD_{50} values of >103.5 and > 99.8 µg a.i./bee, respectively (MRID 50435521). While L-PCA is applied to bee-attractive crops through hand-held applications, it rapidly degrades in the environment. RQs were calculated using the BeeREX V1.0 (2015) model for spray applications at a rate of 0.225 lb a.i./A. The acute contact RQ is <0.01 and well below the non-listed and listed species LOC of 0.4 and 0.05 respectively. Given rapid degradation in the field, and the lack of toxicity of L-PCA to bees from both contact and oral exposure identified in toxicity tests, risks of concern to honeybees is not anticipated.

II. Non-Target Plants

The submitted studies for both vegetative vigor and seedling emergence were both conducted at the highest application rate of 0.225 lb a.i./A. In the vegetative vigor study (MRID 50435523), adverse effects were equivalent to an IC_{25} effect level for only one of the six species tested. The vegetative vigor study demonstrated statistically significant decreases in both weight and height for pea. Plant weight decreased 12% and 26 % when exposed to TGAI and formulated product, respectively, while plant height decreased 18% when exposed to the formulated product. There were not any effects seen in the other five plant species tested.

The seedling emergence study (MRID 50435522) was conducted with both TGAI and formulated product. Four of six species of plants were adversely affected. For lettuce and pea, seedling emergence decreased 53% and 44%, respectively, when exposed to TGAI and 73% and 66% when exposed to formulated product. Plant height decreased 13% and 22% in the treatments with TGAI and formulated product, respectively, while plant weight decreased 9% and 5% respectively for cucumber. Increases in both seedling emergence and plant weight were observed in cabbage.

The EP label directs the user to apply as a seed treatment (using commercial seed treatment equipment), which will have a localized and transitory affect to the treated seed, and as hand-held sprayer applications during the seedling stages of growth, which will minimize drift away from the target plant. Given the lack of exposure that results from the permitted application methods of handheld sprayer and seed treatment, effects are not anticipated to non-target plants. Therefore, risks of concern to non-target plants is not expected given that the application methods minimize exposure.

3.2.2 Aquatic Organisms

I. Freshwater Fish and Aquatic Invertebrates

L-PCA is applied as a seed treatment or with hand-held equipment, such as backpack sprayers, which will limit drift to aquatic environments. Additionally, L-PCA degrades rapidly in aquatic environments. In both semi-static toxicity studies, the concentration of L-PCA decreased below the limit of quantitation within 24 hours, suggesting transient exposure in aquatic environments. L-PCA is classified as practically non-toxic to rainbow trout and *Daphnia* with LC_{50} >100 ppm and 94.14 ppm, respectively (MRID 50435518 and 50435517). Exposure to aquatic environments is not expected as a result of hand-held applications and seed treatments since neither are expected to drift or runoff the area of application. The lack of exposure and the fact that L-PCA is practically non-toxic to fish and aquatic invertebrates suggests that there will be no effects to fish and aquatic invertebrates.

II. Aquatic Non-Target Plants

L-PCA is applied as a seed treatment or with hand-held equipment, such as backpack sprayers, which will limit drift to aquatic environments. Two aquatic non-target plant studies were submitted for a non-vascular and a vascular plant. The EC_{50} and NOAEC for *Pseudokirchneriella subcapitata* was 2.8 mg/L and 0.66 mg/L respectively (MRID 50435525). The EC_{50} and NOAEC for *Lemna gibba* was >3.4 mg/L and 0.46 mg/L respectively (MRID 50435524). Like the fish and invertebrate tests, the concentrations in these tests decreased below the limit of quantitation within 24 hours and the endpoints represent the time weighted averages over the course of the experiment. The results of these tests are consistent with the adverse effects observed in the terrestrial plant studies. Exposure to aquatic environments is not expected as a result of hand-held applications and seed treatments since neither are expected to drift or runoff the area of application. Additionally, the aquatic toxicity studies demonstrated that L-PCA decreased to below the limit of quantitation within 24 hours. The combination of a lack of deposition or runoff and rapid degradation of L-PCA in the aquatic studies suggests that aquatic exposure would not occur from the approved uses. Therefore, aquatic plants are not expected to be affected by the approved uses of L-PCA.

3.2.3 Endangered Species Conclusion

Based on a lack of effects to birds, mammals, terrestrial insects, fish and aquatic invertebrates, as well as lack of exposure, the Agency has determined there is a reasonable expectation of no discernible direct or indirect effects to organisms in these groups. While adverse effects were

identified for both terrestrial and aquatic plants in ecotoxicity studies, the Agency has also determined that there is a reasonable expectation of no discernible effects to terrestrial and aquatic plants due to lack of exposure to non-target plants both on the field and off the field that results from use as a seed treatment and directed application using handheld sprayers. L-PCA also quickly degrades in the environment so any incidental exposure would be transitory and not at sufficient levels to impact non-target organisms. Therefore, the EPA has made a "no effect" determination for direct and indirect effects to federally threatened and endangered ('listed') species and their designated critical habitats for the labeled uses of L-PCA and has concluded that consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service under ESA § 7(a)(2) is not required.

4. Benefits

L-PCA is a plant growth regulator with a low toxicity profile when applied in salt form (such as via buffered end-use products), making it an attractive alternative to conventional plant regulators and a valuable addition to the pesticide tool kit.

5. Public Comments

In the Federal Register of May 17, 2018 (83 FR 22972), EPA published a Notice of Receipt (NOR) that announced receipt of three new product applications containing the new active ingredient, L-PCA: (2S)-5-Oxopyrrolidine-2-carboxylic Acid (L-PCA) Technical (EPA File Symbol: 73771-RE), VLS 2002-03 (EPA File Symbol: 73771-RG) and VLS-2002-03-0.10 (EPA File Symbol: 73771-RU). No comments were received in response to the NOR.

In the Federal Register of May 18, 2018 (83 FR 23247), EPA published a Notice of Filing (NOF) that announced a request to establish an exemption from the requirement of a tolerance in 40 CFR part 180 for residues of L-PCA, when used as a plant growth regulator on agricultural crops, turf, and ornamental plants, in accordance with label directions and good agricultural practices. No substantive comments were received in response to this NOF.

Because the pesticide products contain a new active ingredient, L-PCA, EPA has completed a 15-day public comment period. EPA took this action in accordance with a policy, first implemented in October 2009, designed to provide a more meaningful opportunity for the public to participate in major registration actions. No comments were received.

6. Regulatory Decision

The L-PCA database is considered to be complete with regard to human health and environmental fate and ecological data requirements and supports a pesticidal food use. In considering the hazard assessment to human health and the environment, the Agency concludes that L-PCA meets the regulatory standard under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). Therefore, the EPA is granting the unconditional registration of L-PCA as a new active ingredient under Section 3(c)(5) of FIFRA. Moreover, the Agency has published a Final Rule formally establishing the exemption from the requirement of a tolerance for L-PCA was published in the Federal Register on August 10, 2023.

7. Registration Requirements

The EPA is registering the following products:

(2S)-5-Oxopyrrolidine-2-carboxylic Acid (L-PCA) Technical

- 99.1% L-PCA
- This product may be used for formulation into end-use products for use on crops, forestry, nursery, ornamental and seed treatment as plant growth regulator.

VLS 2002-03

- 25 % L-PCA
- For use on various field crops, on turf, ornamental plants, and as a seed treatment for alfalfa, canola, cereals (barley, rice, rye, and wheat), corn, cotton, soybeans, and sugar beets.

8. Supporting Documents

The risk assessments supporting this decision and the draft product labels for the two products to be registered can be found in the associated regulatory docket (search for "EPA-HQ-OPP-2018-0145" at http://www.regulations.gov).

9. Future Data Requirements

Should the formulation of the end-use products or the application methods described in 'Section 7' of this document change in the future, or if new products are proposed containing L-PCA, additional data may be required, and new risk assessments may need to be performed.