Chlormequat Chloride

Interim Registration Review Decision
Case Number 7069

March 2022

Approved by: _____

Mary Elissa Reaves, Ph.D.
Director
Pesticide Re-evaluation Division

Date: 3/21/2022

Table of Contents

I. INTRODUCTION

This document is the Environmental Protection Agency's (EPA or the Agency) Interim Registration Review Decision (ID) for chlormequat chloride (PC Code 018101, case 7069). In a registration review decision under the Federal Insecticide, Fungicide, Rodenticide Act (FIFRA), the Agency determines whether a pesticide continues to meet FIFRA's registration standard.[1] Where appropriate, the Agency may issue an interim registration review decision before completing a registration review.[2] Among other things, the Interim Registration Review Decision may determine that new risk mitigation measures are necessary, lay out interim risk mitigation measures, identify data or information required to complete the review, and include schedules for submitting the required data, conducting the revised risk assessment and completing the registration review.[3] For more information on chlormequat chloride, see EPA's public docket (EPA-HQ-OPP-2015-0816) at www.regulations.gov.

FIFRA[4] mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States must be registered by EPA based on scientific data showing that they will not cause unreasonable risks to human health or to the environment when used as directed on product labeling. In 2006, the Agency began implementing the registration review program. EPA will review each registered pesticide every 15 years. Through the registration review program, the Agency intends to verify that all registered pesticides continue to meet the FIFRA registration standard as the ability to assess and reduce risk evolves and as policies and practices change. By periodically re-evaluating pesticides as science, public policy, and pesticide-use practices change, the Agency ensures that, when used according to label specifications, pesticide products in the marketplace do not present unreasonable adverse effects. For more information on the registration review program, see http://www.epa.gov/pesticide-reevaluation.

The Agency is issuing an ID for chlormequat chloride so that it can (1) move forward with aspects of the registration review that are complete and (2) implement interim risk mitigation. EPA is currently working with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (the Services) to improve the consultation process for federally threatened and endangered (listed) species and their designated critical habitat for pesticides under the Endangered Species Act (ESA).[5] The Agency has not yet fully evaluated chlormequat chloride's risks to federally listed species and their designated critical habitat. However, EPA will complete its listed-species assessment and any necessary consultation with the Services before completing the chlormequat chloride registration review. Before completing registration review, EPA will also complete endocrine screening for chlormequat chloride under the Federal Food, Drug, and Cosmetic Act (FFDCA).[6] For more information on the listed-species assessment and the endocrine screening for the chlormequat chloride registration review, see Appendices B and C.

This document is organized in five sections:

[1] Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) § 3(g), 7 U.S.C. § 136a(g); 40 C.F.R. § 155.57.
[2] 40 C.F.R. §§ 155.56, 155.58.
[3] 40 C.F.R. § 155.56.
[4] As amended by the Food Quality Protection Act (FQPA) of 1996, Pub. L. No. 104-170, 110 Stat. 1489.
[5] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.
[6] Federal Food, Drug, and Cosmetic Act (FFDCA) § 408(p), 21 U.S.C. § 346a(p).

- *Introduction* (summarizing milestones in the registration review case and responding to public comments on the Proposed Interim Decision [PID]);
- *Use and Usage* (discussing how and where chlormequat chloride is used);
- *Scientific Assessments* (summarizing EPA's human health risk, ecological risk, and benefits assessments);
- *Interim Registration Review Decision* (presenting EPA's interim decision, regulatory rationale, and any mitigation measures to address risks of concern); and
- *Next Steps and Timeline* (discussing how and when EPA intends to complete this registration review).

A. Updates to the Proposed Interim Decision

In October 2021, EPA published the PID for chlormequat chloride. The PID did not propose any labeling changes. The Agency has made two changes from the PID in this ID. The Agency is increasing the restricted entry interval (REI) from 12 hours to 24 hours in accordance with the Worker Protection Standard (WPS). The Agency is also updating the personal protected equipment (PPE) and gloves statement currently on the chlormequat chloride label, to be consistent with Chapter 10 of the Label Review Manual (See Section IV.A). This ID finalizes the Agency's risk mitigation and draft supporting documents (*Chlormequat Chloride: Draft Human Health Risk Assessment for Registration Review* and *Chlormequat Chloride: Draft Ecological Risk Assessment for Registration Review*), which are available in EPA's public docket (EPA-HQ-OPP-2015-0816).

B. Summary of Chlormequat Chloride Registration Review

On November 3, 2016, the Agency formally initiated registration review for chlormequat chloride with the opening of the registration review docket for the case.[7] The following summary highlights the docket opening and other significant milestones that have occurred thus far during the registration review of chlormequat chloride:

- November 2016 – EPA posted the *Chlormequat Chloride Preliminary Work Plan* (PWP) (September 11, 2016), *Chlormequat Chloride Human Health Assessment Scoping Document in Support of Registration Review* (July 14, 2016), and *Registration Review: Preliminary Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments for Chlormequat Chloride* (August 8, 2016) to the public docket for a 60-day public comment period.

- August 2017 – EPA posted the *Chlormequat Chloride Final Work Plan* (FWP) (June 18, 2017) to the public docket. The Agency received 4 comments on the PWP. In the FWP, EPA removed several environmental fate and ecotoxicity requirements. The Agency removed the soil photolysis study after reconsidering the use pattern and exposure assessment modeling needs. The Agency removed the aerobic aquatic and aerobic soil

[7] 40 C.F.R. § 155.50

metabolism studies on the basis that additional data would not likely impact quantified risk. The Agency removed the anaerobic aquatic metabolism study because open literature data indicated that chlormequat chloride is stable to biodegradation in anaerobic environments. EPA removed the freshwater fish full life cycle and fish bioconcentration requirements since chlormequat does not meet the criteria specified in the Code of Federal Regulations (40 CFR Section 158). The Agency determined that the fish early life stage study was more useful for risk assessment than the fish full life cycle study. These changes in data needs had a slight impact on the registration review schedule, delaying the anticipated timeline by 3-4 months.

- February 2019 – EPA issued a generic data call-in (GDCI) for chlormequat chloride to obtain data needed to conduct the registration review risk assessments (GDCI-018101-1625). The registrants submitted all required data; however, the GDCI is not satisfied due to the need for additional vegetative vigor data. Test concentrations in the submitted vegetative vigor study were not low enough to cover all potential exposures resulting in a non-definitive, no-observed adverse effect concentration (NOAEC). See Section III. B. for more details.

- July 2021 – EPA posted *Chlormequat Chloride: Draft Human Health Risk Assessment for Registration Review* (March 16, 2021) and *Chlormequat Chloride: Draft Ecological Risk Assessment for Registration Review* (March 26, 2021) for a 60-day public comment period. The Agency received 2 comments from 2 commenters. The comments did not change the risk assessments or registration review timeline for chlormequat chloride.

- October 2021 – EPA posted the *Chlormequat Chloride Proposed Interim Decision for Registration Review* (September 27, 2021) for a 60-day public comment period. The Agency received 2 comments from 2 commenters. The Agency has summarized and responded to these comments in Section I.B., below. The comments did not change the risk assessments or registration review timeline for chlormequat chloride. Along with the PID, EPA posted the following documents to the public docket:
    - *Response to Comments on the Draft Ecological Risk Assessment of Chlormequat Chloride in Support of Registration Review* (August 30, 2021)

- March 2022 – EPA completed this *Chlormequat Chloride Interim Registration Review Decision*. Along with the ID, EPA plans to post the following documents to the public docket:
    - *EFED Response to Comments on the Proposed Interim Registration Review Decision for Chlormequat Chloride (Case Number 7069)* (March 4, 2022)
    - *HED Response to Public Comments on the Proposed Interim Registration Review Decision for Chlormequat Chloride.* (March 8, 2022)

C. Summary of Public Comments on the Proposed Interim Decision and Agency Responses

During the 60-day public-comment period for the *Chlormequat Chloride Proposed Interim Registration Review Decision* (which opened on October 22, 2021, and closed on December 21,

2021), the Agency received 2 public comments. Comments were submitted by the United States Department of Agriculture and the Center for Food Safety. The Agency has summarized and responded to all substantive comments below. The Agency thanks all commenters for participating and has considered all comments in developing this ID.

Comments Submitted by the United States Department of Agriculture (Docket ID: EPA-HQ-OPP-2015-0816-0029)

Comment: The United States Department of Agriculture (USDA) supported EPA's human health risk assessment, which found no dietary, residential, aggregate, occupational, or non-occupational spray drift risks of concern. USDA further supported EPA's determination that the current label language and spray drift management measures significantly limit environmental exposures and are sufficient to mitigate the risks identified in the ecological risk assessment. USDA agreed with EPA's conclusion that the current use patterns of chlormequat chloride do not present risks of concern and consequently do not require any additional mitigation measures.

EPA Response: The Agency appreciates USDA's support of the PID and associated risk assessments.

Comments Submitted by the Center for Food Safety (Docket ID: EPA-HQ-OPP-2015-0816-0030)

Comments Pertaining to Human Health Risk: The Center for Food Safety (CFS) generally opposed the mitigation proposed in the PID, citing several human health concerns associated with both the current registered uses and the pending applications for new uses of chlormequat chloride.

CFS expressed concern regarding the reproductive toxicity of chlormequat chloride, citing European studies and asserting that the EPA has not properly screened chlormequat chloride for its endocrine disruption potential. CFS cited neurotoxicity concerns, noting that EPA needs to require both a sub-chronic (90-day) neurotoxicity study and a developmental neurotoxicity study. CFS claimed that current safety thresholds may not be protective enough with regard to co-exposure, particularly exposure alongside anti-androgenic compounds.

European food detection data and statistics were included in the comments; CFS indicated that EPA should consider the potential short-term consumer risks identified by the European Union (EU).

CFS claimed that the tolerances proposed by the registrant (Taminco, LLC) would increase exposure risk by encouraging sub-par agricultural practices.

EPA Response: The Agency thanks CFS for its comments. EPA reviewed the reproductive toxicity database, including developmental toxicity studies in rats and rabbits and a two-generation reproduction study in rats and concluded that there is no evidence of increased susceptibility/sensitivity of pre- or postnatal animals following exposure to chlormequat chloride in rats or rabbits. In the rat two-generation reproduction study, evidence of reproductive and

offspring toxicity was observed, but these effects occurred at the same doses causing parental toxicity. The endpoints chosen for risk assessment are protective and exposure estimates are unlikely to underestimate risk for chlormequat chloride. In addition, after a full review of the open literature, no studies were identified that contained relevant information that would impact the human health risk assessment for registration review. EPA selected the most sensitive endpoints relevant for all risk assessment scenarios from the existing hazard database.

Although a sub-chronic neurotoxicity study is not available, evidence of potential neurotoxicity was observed in the acute neurotoxicity, developmental rat, two-generation reproduction, sub-chronic inhalation, and chronic dog studies. Based on a weight-of-evidence (WOE) approach, the EPA has concluded that the sub-chronic neurotoxicity and developmental neurotoxicity studies are not required at this time because adequate information is available to assess neurotoxicity.[8]

There are no dietary risks of concern from the current uses. Chlormequat chloride is not currently approved for use on crops grown in the United States intended for animal or human consumption. Current use is restricted to containerized ornamentals. There are pending Pesticide Registration Improve Extension Act (PRIA) applications for new uses on wheat, triticale, barley, oats, and grasses grown for seed, but these have not yet been approved. The aggregate risk assessment for chlormequat chloride includes exposure from food and drinking water sources only as there are no residential uses. Consequently, the consumption estimates coupled with tolerance level residues for the acute dietary assessment, average field trial values for the chronic dietary assessment, and assuming 100% crop treated values indicate that there is adequate protection of the consumer, including infants, children, adults, and seniors, from dietary residues of chlormequat chloride.

Chlormequat chloride is applied to cereal grains at various growth stages and a range of pre-harvest intervals depending on the country the pesticide is registered. Using pesticide residue data from Europe and Denmark would not be appropriate to assess dietary risk in the U.S. due to the different use patterns registered. Previously, chlormequat chloride could be applied to cereal grains once at growth stage 32 (at 1.2 lbs. ai/A) or at growth stage 37 to 39 (at 1.3 lbs. ai/A). The current label includes a split application of 0.63 lb ai/A between growth stage 12 and growth stage 30, followed by a second application of 0.63 lb ai/A between growth stage 31-39. There is no anticipated exposure from food based on applications made at higher rates or later growth stages. Based on the registered uses, the dietary risk estimates are not of concern for the general U.S. population and all population subgroups.

For more detailed responses to CFS's comments, please see *HED Response to Public Comments on the Proposed Interim Registration Review Decision for Chlormequat Chloride,* which is available in the public docket.

Comments Pertaining to Ecological Risk: CFS cited the persistence of chlormequat chloride as a concern in relation to ecological exposure and the potential for build-up in soil and water over time. CFS purported that chlormequat chloride has a comparatively slower degradation process,

[8] US Environmental Protection Agency/Office of Pesticide Programs. (2016). *Chlormequat chloride: Summary of Hazard and Science Policy Council (HASPOC) Meeting of December 10, 2015: Recommendation on the Requirement for Acute Neurotoxicity and Subchronic Neurotoxicity Studies*. Gallager, S.

which should have been considered by EPA when the risks to birds and mammals were assessed for the risk assessments. CFS stated that risks to mammals and birds are amplified by several orders of magnitude due to reproductive effects at very low doses across multiple species.

CFS expressed concerns relating to terrestrial invertebrate risk, particularly the chronic risk quotients (RQs) associated with honey bee (*Apis mellifera*) larvae, where the adverse effect was a 15% reduction in adult emergence, which would have colony-survival impacts. CFS suggested that chlormequat chloride's persistence and systemic nature would enable translocation of residues to pollen and nectar. CFS cited bee data from the Czech Republic which showed that chlormequat was by the most frequently detected pesticide in honeybee hives that exhibited signs of poisoning. Persistence in soil was cited as a potential concern for ground-dwelling bees and other soil organisms and CFS urged EPA to require data on ground-dwelling bees and fully assess effects on soil organisms.

EPA Response: Chlormequat chloride is persistent in soil and the degradation/transformation of the compound is likely to be slower in aquatic systems than in soil. Therefore, chlormequat chloride has the potential to accumulate in the environment over time in the event that the compound reaches waterbodies/aquatic environments where it is expected to persist. However, current outdoor use of chlormequat chloride is limited to containerized ornamentals with application via backpack sprayer and mechanically pressurized handguns. Backpack sprayer applications are considered controlled and directed, off-site transport resulting from this application is not considered a major exposure pathway in terms of leaching and runoff. There is a limited exposure pathway for aquatic risk.

The risk assessment for birds and mammals and other terrestrial vertebrates utilized a default 35-day foliar dissipation value based on work conducted by Willis and McDowell 1987.[9] Chlormequat chloride is highly soluble in water and is susceptible to both leaching and runoff. Therefore, the extent to which the compound would remain on foliar surfaces is uncertain. Also, there is uncertainty in extrapolating spot treatments to a per acre basis and it is likely that such extrapolated application rates are conservative.

EPA acknowledges that risk quotients (RQs) for terrestrial invertebrates exceed the chronic risk level of concern (LOC=1.0) for both adult and larval bees; however, RQ values are based on extrapolated application rates from spot treatments. Also, the extent to which *Apis* and non-*Apis* bees may forage on horticultural/ornamental plants is uncertain given hybridization efforts which may reduce attractiveness to pollinators. With respect to social bees, there is also uncertainty regarding the extent to which effects detected in laboratory-based studies of individual bees translate to colony-level effects. CFS cited a study from the Czech Republic to demonstrate the extent to which chlormequat chloride residues are detected in bee-related matrices; however, EPA does not have an understanding of how chlormequat is used in the Czech Republic and how those conditions relate to use in the U.S. Based on data collected in the U.S., chlormequat

[9] Willis, G.H., and L. L. McDowell. Pesticide Persistence on Foliage. Reviews of Environmental Contamination and Toxicology 100: 23 – 73.

chloride has not been detected in national-level surveys of honey bee colonies.[10,11] The EPA currently does not have a developed method to assess risk specific to ground-dwelling bees. EPA acknowledges the persistence of chlormequat chloride in soil; however, the compound is expected to be mobile and subject to both runoff and leaching. Therefore, its presence in the soil profile may change with time depending on soil type and the extent of precipitation.

Depending on the availability of data, risk assessments may include an evaluation of potential for adverse effects on soil invertebrates, particularly for compounds for which there is evidence of bioaccumulation. However, chlormequat chloride is not expected to bioaccumulate and EPA is not aware of toxicity data on soil invertebrates for this compound. EPA does not have a defined process for consistently and reliably estimating risk to soil life.

For more detailed responses to CFS's comments, please see the *EFED Response to Comments on the Proposed Interim Registration Review Decision for Chlormequat Chloride (Case Number 7069*), which is available in the public docket.

Comments Pertaining to Endangered Species Risk Assessment: CFS commented on the EPA's duty under the Endangered Species Act (ESA) to complete endangered species risk assessment and consult with the Services on the registration review of chlormequat chloride. CFS asked EPA to refrain from issuing an interim registration review decision prior to a full threatened and endangered species assessment.

EPA Response: EPA has reviewed CFS's comments and is addressing many of the concerns about listed species by collaborating with the Services and USDA to improve the consultation process for listed species and pesticides.[12] For more information on this ongoing collaboration, see Appendix B. EPA intends to address endocrine-disruption and listed-species concerns specific to chlormequat chloride when developing its final registration review decision. For more information on endocrine disruption, see Appendix C.

II. USE AND USAGE

Chlormequat chloride [(2-chloroethyl) trimethylammonium chloride] is a plant growth regulator (PGR) that belongs to the quaternary ammonium class of chemicals. It was first registered in 1962. There are currently four FIFRA Section 3 active product registrations and one FIFRA Section 5 active experimental use permit. Chlormequat chloride is registered for use on ornamental plants and is formulated as a soluble concentrate/liquid. Chlormequat chloride may be applied to containerized ornamentals produced for resale and grown in greenhouses (indoors), nurseries (outdoors), and shade houses (outdoors). Application methods of chlormequat chloride are backpack sprayers and manually or mechanically pressurized handguns. There are no

[10] Ostiguy, N., F. A. Drummond, K. Aronstein, B. Eitzer, J. D. Ellis, M. Spivak and W. S. Sheppard. 2019. Honey Bee Exposure to Pesticides: A Four-Year Nationwide Study. Insects 10 (13) doi:10.3390/insects10010013
[11] Mullin CA, Frazier M, Frazier JL, Ashcraft S, Simonds R, et al. 2010. High Levels of Miticides and Agrochemicals in North American Apiaries: Implications for Honey Bee Health. PLoS ONE 5(3): e9754. doi:10.1371/journal.pone.0009754
[12] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.

registered residential or food uses for chlormequat chloride. Chlormequat chloride is registered for conventional pesticidal use only and has no antimicrobial or biopesticidal uses.

The amount of chlormequat chloride used annually is unknown because there are no recent nationally representative surveys of pesticide usage on ornamentals. Please see the *BEAD Chemical Profile for Registration Review: Chlormequat Chloride (018101)* in EPA's public docket (EPA-HQ-OPP-2015-0816) for more information.

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

The Agency has summarized the 2021 *Chlormequat Chloride Draft Human Health Risk Assessment for Registration Review* below. The Agency used the most current science policies and risk assessment methodologies to prepare this risk assessment in support of the registration review of chlormequat chloride. For additional details on the 2021 human health risk assessment, see EPA's public docket (EPA-HQ-OPP-2015-0816). The human health risk assessment was amended to update occupational handler risks due to revised inhalation endpoints. See the *Chlormequat Chloride Addendum to the Human Health Draft Risk Assessment for Registration Review* in the public docket for more information.

1. Risk Summary and Characterization

There are no risks of concern for dietary and occupational exposure. There are no registered residential uses, so residential risk was not calculated. The aggregate assessment is equivalent to the dietary exposure and risk estimates, which were not of concern. There are no data deficiencies.

Dietary (Food + Water) Risks

The unrefined acute and chronic dietary risk estimates were below the level of concern (LOC) for the general U.S. population and all population subgroups. Acute dietary risk estimates are equal to 18% of the acute population adjusted dose (aPAD) for the general US population, which is below the Agency's level of concern of 100% for dietary risk. Infants <1 year old were the most highly exposed population subgroup at 52% of the aPAD.

Chronic dietary risk estimates are equal to 18% of the chronic population-adjusted dose (cPAD) for the general U.S. population, which is below the Agency's level of concern of 100%. Children 1-2 years old were the most highly exposed population subgroup, at 72% of the cPAD.

Chlormequat chloride is not likely to be a human carcinogen; therefore, a cancer dietary risk assessment is not required.

Residential Risks

There are no registered residential uses for chlormequat chloride, nor are the registered uses expected to result in the potential for residential exposures. Therefore, residential exposure and risks were not assessed.

Aggregate Risks

In an aggregate assessment, EPA considers the combined pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. The Agency sums the exposures from these sources and compares the aggregate risk to quantitative estimates of hazard. EPA considers the route and duration of exposure when assessing aggregate risks. For chlormequat chloride, aggregate exposures are equivalent to dietary exposure estimates because there are no residential exposures. Aggregate risk estimates are equivalent to dietary risk estimates and are not of concern.

Non-occupational Spray Drift Risks

Non-occupational spray drift exposure was not assessed because the registered uses are not applied in a manner which could result in potential spray drift. Applicators are directed to apply chlormequat using only handheld equipment, and outdoor use is restricted to containerized ornamentals only.

Non-Occupational Bystander Post-Application Inhalation Risks

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its FIFRA Scientific Advisory Panel (SAP) in December 2009 and received the SAP's final report on March 2, 2010 (EPA-HQ-OPP-2009-0687-0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (EPA-HQ-OPP-2014-0219). In addition to this screen, the Agency has developed a preliminary bystander volatilization inhalation exposure assessment for chlormequat chloride utilizing the currently available inhalation toxicity and air monitoring data.

A quantitative residential post-application inhalation exposure assessment was not performed because there are no residential uses for chlormequat chloride. An inhalation exposure assessment was conducted for occupational handlers and this exposure scenario is considered protective of potential post-application inhalation exposure. Since there are no occupational handler inhalation risks of concern, there are no bystander post-application inhalation risks of concern.

Cumulative Risks

EPA has not made a common-mechanism-of-toxicity-to-humans finding for chlormequat chloride and any other substance. Chlormequat chloride does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has not assumed that chlormequat chloride has a common mechanism of toxicity with other substances.

Occupational Handler Risks

Based on the registered use sites, the Agency assessed the potential for occupational exposure. Short- and immediate-term occupational handler exposure is associated with handler activities, such as mixing, loading, and applying. The short- and immediate-term inhalation risk estimates for occupational handlers are not of concern [*i.e*., margins of exposure (MOEs) are > the LOC of 100] at baseline attire (*i.e*., long sleeved shirt, long pants, shoes and socks, no respirator). The MOEs range from 640 to 300,000. Occupational handler dermal exposures were not assessed since a dermal endpoint was not selected for chlormequat chloride due to the lack of adverse effects attributable to a single dose.

Occupational Post-Application Risks

Occupational post-application dermal and inhalation exposures are not expected for chlormequat chloride. Occupational post-application dermal exposure was not quantitatively assessed due to the lack of adverse effects attributable to a single dose. Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for chlormequat chloride at this time. Although a quantitative post-application inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for handlers (*i.e*., treaters, *etc*.). This handler exposure scenario is considered protective of any potential low-level post-application inhalation exposure that could result from these types of applications. Since occupational handler inhalation risks were not of concern, occupational post-application inhalation risks are not expected to be of concern.

Currently, labels list an REI of 12 hours. In accordance with the WPS, chlormequat chloride is an acute toxicity category II chemical, which requires a 24-hr REI.

2. Human Incidents and Epidemiology

The Agency reviewed chlormequat chloride incidents reported to the Incident Data System (IDS) and the National Institute for Occupational Safety & Health (NIOSH) Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides. As of the Agency's most recent search in 2020, IDS did not show any incidents related to chlormequat chloride reported to Main IDS and Aggregate IDS from January 1, 2016 to November 12, 2020.

The Agricultural Health Study (AHS) is a federally funded study that evaluates associations between pesticide exposure and cancer/other health outcomes. Chlormequat chloride is not included in the AHS.

EPA's incident review for chlormequat chloride does not indicate that additional analyses of incidents are warranted at this time.

3. Tolerances

The tolerance expression for chlormequat chloride described in Title 40 of the Code of Federal Regulations (40 CFR §180.698) reflects current guidance and does not need to be updated as a part of Registration Review. However, the Agency intends to update the tolerances for residues

in barley grain, wheat grain, and livestock commodities to make them consistent with the Organization for Economic Co-Operation and Development (OECD) rounding classes. See section IV.C of this document for more information.

4. Human Health Data Needs

The human health database for chlormequat chloride is considered complete. The Agency does not anticipate any further data needs for chlormequat chloride.

B. Ecological Risks

The Agency has summarized the 2021 *Chlormequat Chloride Draft Ecological Risk Assessment for Registration Review* below. The Agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of chlormequat chloride.[13] For additional details on the 2021 ecological risk assessment, see EPA's public docket (EPA-HQ-OPP-2015-0816).

The EPA is currently working with its federal partners and other stakeholders to improve the consultation process for federally-listed species and their designated critical habitats. The Agency has not yet fully evaluated chlormequat chloride's risks to listed species. However, EPA will complete its listed-species assessment and any necessary consultation with the Services before completing the chlormequat chloride registration review. See Appendix B for more details. As such, potential risks for non-listed species only are described below.

1. Risk Summary and Characterization

Terrestrial Risks

Potential risks of concern were identified for mammals, birds (which serve as surrogates for reptiles and terrestrial-phase amphibians), honey bees (which serve as surrogates for solitary and social *Apis* and non-*Apis* bees) and terrestrial plants. Risk to terrestrial vertebrates was assessed based on 9 applications of both the maximum single label application rate of 3.7 lbs ai/A and the maximum extrapolated (to a per-acre basis) spot treatment application rate of 8.24 lbs ai/A, following a re-application interval of 5 days in nurseries. Since birds serve as surrogates for reptiles and terrestrial-phase amphibians, concerns regarding acute and chronic risk to birds apply to these taxa as well.

Mammals

Both dose-based and dietary-based RQs were calculated for mammals. Dietary-based RQs are calculated by directly comparing the concentration of an administered pesticide to a relevant

[13] The 2021 ERA only addresses potential risks to species not listed under the Endangered Species Act. EPA is working with its federal partners and other stakeholders to implement a Revised Method (EPA-HQ-OPP-2019-0185-0054) for assessing potential risk to federally listed species and their designated critical habitats. The Agency will complete chlormequat chloride's listed-species assessment once EPA has fully implemented the scientific methods necessary to complete listed species' risk assessments. For more details, see Appendix B.

toxicity endpoint. Dietary-based RQs do not account for the fact that smaller sized animals need to consume more food relative to their body weight than larger animals or that differential amounts of food are consumed depending on water content and nutritive value of the food. Dose-based RQs account for these factors. For mammals, dose-based RQs (<0.1-11) exceed the acute risk LOC of 0.5 for all-sized mammals feeding on short grass, tall grass, broadleaf plants and arthropods based on the maximum extrapolated rate of 8.24 lbs ai/A. For chronic risk, dose-based RQs (0.4-62) and dietary-based RQs (0.4 – 7.2) exceed the chronic risk LOC of 1 for all-sized mammals foraging on short grass, tall grass, broadleaf plants, fruit/pods and arthropods. Chronic risk estimates for mammals are based on a no-observed adverse effect level (NOAEL) above which there were 9% reductions in growth (weight) and 34% reductions in reproduction (mean litter size) at the lowest observed adverse effect level (LOAEL).

Based on the maximum single label application rate of 3.7 lbs ai/A, dose-based RQs (<0.1-4.9) exceed the acute risk LOC for all-sized mammals feeding on short grass, tall grass, broadleaf plants and arthropods. Chronic dose-based RQs (0.2-28) exceed the chronic risk LOC for all-sized mammals foraging on short grass, tall grass, broadleaf plants and arthropods. Chronic dietary-based RQs (0.2-3.2) exceed the chronic risk LOC for short grass, tall grass, broadleaf plants and arthropods.

Despite these exceedances, the Agency has determined that the opportunity for chronic exposure from this use profile may be limited for currently registered products. The majority of the uses are indoor-only (*e.g.*, greenhouses), with outdoor use restricted to containerized plants in nurseries and shadehouses. Outdoor nurseries and shadehouses tend to be heavily managed areas in which extraneous plants are minimized to limit the extent to which forage/habitat is available for animals. In addition, applications to containerized outdoor ornamentals occur using targeted methods such as handheld and backpack sprayers. Risks of concern to mammals are limited to the site of application and adjacent areas.

Birds, Reptiles, and Terrestrial-Phase Amphibians

Based on the maximum extrapolated rate of 8.24 lbs ai/A, the acute risk LOC of 0.5 is exceeded by both dietary- and dose-based RQs for birds feeding on short grass, tall grass, broadleaf plants and arthropods. Acute dose-based RQs range from <0.1 to 33, and acute dietary-based RQs range from <0.2 to <3.9. Chronic dietary-based RQs (2-32) exceed the chronic risk LOC for birds feeding on all food types assessed.

Based on the maximum single label application rate of 3.7 lbs ai/A, acute dose-based RQs (<0.1-15) exceed the acute risk LOC for birds feeding on short grass, tall grass, broadleaf plants, fruit/pods and arthropods; acute dietary-based RQs (0.1-1.7) exceed the acute risk LOC for birds feeding on short grass, tall grass, and arthropods. For chronic risk at a single application of 3.7 lbs ai/A, dietary-based RQs (0.9-14) exceed the chronic risk LOC for birds feeding on short grass, tall grass, broadleaf plants and arthropods. Using the lowest-observed adverse effect concentration (LOAEC) to calculate the RQ instead of the no-observed adverse effect concentration (NOAEC) still results in chronic risk LOC exceedances for birds. The LOAEC is based on a 5% reduction in survival (*i.e.*, the ratio of 14-day hatchlings to number hatched).

Despite these exceedances, the Agency has determined that the opportunity for chronic exposure due to the use profile may be limited for currently registered products. The majority of the uses are indoor-only (*e.g.*, greenhouses), with outdoor use restricted to containerized plants in nurseries and shadehouses. Outdoor nurseries and shadehouses tend to be heavily managed areas in which extraneous plants are minimized to limit the extent to which forage/habitat is available for animals. In addition, applications to containerized outdoor ornamentals occur using targeted methods such as handheld and backpack sprayers. Risks of concern to birds are limited to the site of application and adjacent areas.

Terrestrial Invertebrates

For adult honey bees, RQs for contact and oral exposure are below the acute risk LOC of 0.4. Because the acute contact LD_{50} value (lethal dose at which 50% of the test population dies) is non-definitive and higher than the highest dose tested, and about 10 times higher than the Estimated Environmental Concentrations (EECs), the likelihood of adverse effects on adult bees from acute contact exposure as a result of current uses is expected to be low. Since the acute oral LD_{50} values are non-definitive and higher than the highest dose tested, and about 100 times higher than the EEC based on the maximum extrapolated application rate of 8.24 lbs ai/A, the likelihood of adverse effects on either adult or larval bees from acute oral exposure as a result of current uses of chlormequat chloride is also expected to be low.

At the extrapolated single application rate of 8.24 lbs ai/A, the chronic RQ (4.1) for adult honey bees exceeds the chronic risk LOC of 1 based on a NOAEL of 64 µg a.i./bee/day above which there was a 41% increase in adult bee mortality at the LOAEL of 139 µg a.i./bee/day. The chronic RQ (45) for larval honey bees also exceeds the chronic risk LOC of 1.0 based on a NOAEL of 2.5 µg a.i./bee/day above which there was a 15% reduction in adult emergence at the LOAEL of 8.3 µg a.i./bee/day. Even at the maximum single label rate of 3.7 lbs ai/A, chronic RQ values for adults and larvae are 1.9 and 20, respectively, and exceed the chronic risk LOC. Therefore, there is a potential for adverse effects on both larval and adult honey bees from chronic exposure to chlormequat chloride on the treated area.

There is a potential for chronic risk to both larval and adult honey bees from exposure to chlormequat chloride in the nursery or shadehouse. Since honey bees serve as surrogates for solitary and social non-*Apis* bees, these risk concerns extend to these species of bees. The extent to which bees may be able to access plants in shadehouses (which are partially enclosed) and greenhouses (which are fully enclosed) may be limited; however, containerized plants in outdoor nurseries with unrestricted access could serve as a route of exposure for bees.

Terrestrial Plants

Based on the most sensitive monocotyledonous (monocot) and dicotyledonous (dicot) terrestrial plant species tested and an extrapolated application rate of 8.24 lbs ai/A, RQs exceed the LOC of 1 for risk to terrestrial plants in semi-aquatic areas with non-definitive RQ values of <2.6 and <2.5 for monocots and dicots, respectively. However, based on the most sensitive monocots and dicots and an application rate of 3.7 lbs ai/A, RQs (<1.1) only exceed the LOC of 1 for risk to dicot terrestrial plants in semi-aquatic areas. It should be noted that these RQs are calculated

using EECs based on residues from off-site exposure via spray drift and/or run-off to non-target plants found near application sites.

Because exposure to non-target terrestrial plants in nurseries and shadehouses via spray drift and/or run-off is likely to be limited by the controlled spraying of targeted plants in containers, these RQs may be overestimating risk to terrestrial plants. The Agency has determined that there is minimal risk of concern for terrestrial plants due to the controlled application methods for currently registered products.

Aquatic Risks

The aquatic exposures associated with the use of chlormequat chloride were estimated using standard modeling scenarios for nursery use. When EECs are compared to the measured toxicity endpoints for chlormequat chloride, RQs do not exceed either the acute or chronic risk to non-listed species LOC of 0.5 and 1, respectively, for aquatic vertebrates and invertebrates. Risk to sediment-dwelling invertebrates was not assessed because the octanol-water partition coefficient (K_{ow}) and organic-carbon normalized soil-water distribution coefficient (K_{oc}) values are below threshold values for these parameters, indicating that sediment exposure is not a primary pathway of concern. For aquatic plants, risk estimates are below the LOC of 1.

Based on this assessment, the Agency has determined that there are no aquatic risks of concern.

2. Ecological Incidents

EPA reviewed chlormequat chloride incidents reported to the Incident Data System (IDS). As of EPA's latest search on January 25, 2021, IDS did not show any incidents reported. Incidents may have occurred due to chlormequat chloride exposures but may not have been reported due to various factors. Therefore, the lack of incident reports does not necessarily indicate the absence of incidents. EPA's incident review for chlormequat chloride does not indicate that additional analyses of incidents are warranted at this time.

3. Ecological and Environmental Fate Data Needs

The ecological and environmental fate database is considered incomplete for the currently registered uses of chlormequat chloride. One ecological effects data gap remains: A vegetative vigor study with a typical end-use product (TEP) tested on sunflower at concentrations of ≤0.21 lbs a.i./A. A new vegetative vigor study would be used to determine a definitive toxicity endpoint for terrestrial plants, complete endangered species analysis, and fully assess the effect of the TEP on terrestrial plants.

Apart from the above data, the Agency does not anticipate any further data needs for currently registered uses of chlormequat chloride. Based on the results of the Tier 1 pollinator studies and chlormequat chloride's currently registered use patterns and application rates, no additional higher tiered pollinator data are needed at this time.

C. Benefits Assessment

Plant growth regulators are beneficial for use in nurseries and greenhouses due to their ability to alter plant growth in a way that makes the plant more marketable. Plant height is one of the most important aspects in greenhouse crop production and chemical control can be a highly useful tool in managing plant height especially where growers are managing large varieties of genera, species and cultivars in the same greenhouse environment.[14] Chlormequat chloride is a growth retardant that inhibits stem elongation by interfering with gibberellic acid biosynthesis.[14] Plants treated with this product tend to be sturdier and more compact, which may enhance the aesthetic appeal as well as provide greater durability during postproduction shipping. Chlormequat chloride can also accelerate flowering in some ornamental plants (*e.g.*, seed geranium cultivars) when applied between two and five weeks after germination making the plants more marketable and reducing the time the plants need to develop before being marketable.[15]

IV. INTERIM REGISTRATION REVIEW DECISION

A. Risk Mitigation and Regulatory Rationale

The Agency has reviewed the risks and benefits associated with the registered uses of chlormequat chloride in developing this Interim Registration Review Decision. In its human health risk assessment, EPA has determined that there are no dietary, residential, aggregate, occupational, or non-occupational spray drift risks of concern. However, the Agency is correcting the REI to be consistent with the WPS and updating the PPE and glove statements in accordance with Chapter 10 of the EPA's Label Review Manual.

In its ecological risk assessment, EPA identified potential risks to non-target terrestrial plants; potential acute and chronic risks to mammals, birds, reptiles, and terrestrial-phase amphibians; and potential chronic risks to terrestrial invertebrates. Potential risks to nontarget organisms are spatially limited to the application site and adjacent areas based on the registered uses and application methods.

EPA has also considered the benefits of chlormequat chloride. Chlormequat chloride is used in nursery and greenhouse production for its ability to ensure production of a shorter and thicker stem that makes plants more marketable and easier to transport. In addition, chlormequat can accelerate flowering in some ornamental plants reducing the time the plants need to develop before being marketable.

EPA has concluded that the benefits outweigh the potential risks of concern to nontarget organisms. The Agency has determined that the current label language and spray drift management measures are sufficient in mitigating the spatially-limited risks identified in the risk assessments.

---

[14] Currey, C.J. and R.G. Lopez. Undated. Applying plant growth retardants for height control. Commercial Greenhouse and Nursery Production. Purdue Extension HO-248-W https://www.extension.purdue.edu/extmedia/ho/ho-248-w.pdf

[15] Runkle, E. 2014. Using chlormequat chloride with success. Michigan State Extension. https://www.canr.msu.edu/uploads/resources/pdfs/using-chlormequat-chloride.pdf

Revised REI

The current end-use label (EPA reg. no. 62097-21) lists a 12-hour REI. However, chlormequat chloride is classified as acute toxicity category II via the oral and dermal routes of exposure which requires a 24-hour REI. The Agency is revising the REI to 24 hours in accordance with the WPS. This change is unlikely to impact users. Users of chlormequat chloride can adapt to the longer REI with little difficulty, as the longer REI is unlikely to significantly interfere with important activities in greenhouses and shadehouses. In addition, chlormequat chloride is often recommended to be tank mixed with daminozide and this plant growth regulator already requires a 24-hour REI.[14,15]

Updated PPE and Gloves Statement

The current end-use label contains outdated PPE and glove instructions. The current PPE statement instructs the user to "follow the instructions for Category C on an EPA chemical-resistance category selection chart." The current glove statement instructs workers to use "chemical-resistant gloves made of any waterproof material." These instructions are unclear. In accordance with current labeling guidance, registrants are to specify the specific types of chemical-resistant materials and appropriate glove types on the label.

The Agency is updating the PPE and gloves statement currently on the chlormequat chloride label, consistent with Chapter 10 of the Label Review Manual.[16] In particular, EPA is removing any references to specific categories in EPA's chemical-resistance category selection chart and specifying the appropriate types of glove and PPE materials.[17] This clarification does not fundamentally change the PPE that workers currently must use.

B. Environmental Justice

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. Throughout the registration review process, EPA has sought to include all communities and persons across the Nation, including minority, low-income, and indigenous populations who may be disproportionately overburdened by the use of chlormequat chloride. The Agency has reviewed the risks and benefits associated with the registered uses of chlormequat chloride in developing this Interim Registration Review Decision. For example, one community which may experience disproportionate exposure is workers in greenhouses/nurseries. However, in its human health risk assessment, EPA has determined that there are no dietary, residential, aggregate, occupational, or non-occupational spray drift risks of concern.

The Agency sought information during the public comment periods throughout registration review on any other groups or segments of the population who, as a result of their location or other factors, may have atypical and unusually high exposure to chlormequat chloride compared

[16] Label Review Manual, https://www.epa.gov/pesticide-registration/label-review-manual.
[17] For specific label language, see Appendix A.

to the general population or who may otherwise be disproportionately affected by the use of chlormequat chloride as a pesticide. EPA did not receive any comments concerning environmental justice.

C. Tolerance Actions

The Agency expects to use its FFDCA authority to propose modification of the tolerances for chlormequat chloride as summarized in Table 1, below. EPA intends to update the tolerance for residues in barley, wheat grain, ruminant, egg, poultry meat byproduct, and livestock commodities to be consistent with the Organization for Economic Co-Operation and Development (OECD) rounding classes.

Table 1: Summary of Anticipated Tolerance Actions

Chlormequat chloride 40 CFR § 180.698: Summary of Anticipated Tolerance Actions			
Commodity	**Established Tolerance (ppm)[1]**	**Anticipated Tolerance (ppm)[2]**	**Comments**
40 C.F.R. § 180.698			
Barley, grain	2.0	2	
Cattle, meat byproduct	0.50	0.5	
Cattle, meat	0.20	0.2	
Egg	0.10	0.1	
Goat, meat byproduct	0.50	0.5	
Goat, meat	0.20	0.2	
Hog, meat byproduct	0.50	0.5	
Hog, meat	0.20	0.2	Harmonization with Canada
Milk	0.50	0.5	
Oat, grain	40	no change anticipated	Based on OECD rounding class practice
Poultry, meat byproduct	0.10	0.1	
Poultry, meat	0.04	no change anticipated	
Sheep, meat byproduct	0.50	0.5	
Sheep, meat	0.20	0.2	
Wheat, grain	3.0	3	

CFR=Code of Federal Regulations; OECD=Organization for Economic Cooperation and Development; ppm=parts per million (equivalent to mg/kg).
[1] There are no current U.S. registrations for these commodities.
[2] EPA anticipates harmonization with Codex maximum residue limits (MRLs) for imported uses on cereal grains and livestock commodities. EPA anticipates tolerances only on meat and meat byproduct which will cover the liver and kidney tissues.

There are established Codex, European, and Canadian maximum residue limits (MRLs) for the imported uses. EPA has harmonized with the Codex MRLs on cereal grains and livestock commodities. Canadian MRLs are established for residues in/on wheat grain only at 1 ppm. Also, there are established Codex MRLs for residues of chlormequat chloride in/on oat grains at 4 parts per million (ppm; equivalent to mg/kg). Canada has established an MRL for residues in/on oat grain at 40 ppm. The barley and wheat grain tolerance value should be revised based on

the OECD rounding class practice. Also, EPA anticipates updating the ruminant, egg, and poultry meat byproduct tolerances according to current rounding class practices.

D. Interim Registration Review Decision

The Agency is issuing this ID in accordance with 40 C.F.R. §§ 155.56 and 155.58. The Agency has made the following interim decision: (1) apart from vegetative vigor data already required in GDCI-018101-1625, no additional data are required at this time for the current uses of chlormequat chloride; and (2) EPA has determined that the current uses of chlormequat chloride meet the registration standard with the REI change and updates to the PPE and glove statement noted in section IV.A, pending the completion of endocrine-disruptor and listed-species reviews.

The Agency conducted detailed draft human health and ecological risk assessments. No risks of concern were identified for human health, and the ecological risks identified are limited to treated areas and adjacent areas based on the current use patterns.

EPA also determined that continuing to register the current uses of chlormequat chloride provides benefits to growers in terms of sturdier, and more compact ornamental plants which may enhance aesthetic appeal, as well as provide greater durability during post-production shipping.

During registration review, EPA considers whether a pesticide registration "continues to satisfy the FIFRA standard for registration."[18] EPA states that the currently registered uses of chlormequat chloride meet the FIFRA registration standard with changes to the REI and updates to the PPE and glove statement as noted in section IV.A.

EPA also determines that there is no human dietary risk from the currently registered uses of chlormequat chloride that is inconsistent with the FFDCA safety standard. Taking into consideration the available information on toxicity and exposure, EPA assessed chlormequat chloride's potential aggregate risks, including dietary (food and water) and non-occupational residential exposures, and found no risks exceeding the Agency's levels of concern.[19]

EPA concludes that there is a reasonable certainty that no harm will result from aggregate exposure to chlormequat chloride, including all anticipated dietary exposures and all other exposures for which there is reliable information. Therefore, chlormequat chloride's residues do not present human dietary risk and EPA intends to modify existing tolerances only as a means of harmonizing with Canada based on the OECD rounding class practices, and EPA's analysis indicates that such tolerance modifications would also be safe.

---

[18] 40 C.F.R. § 155.40(a); 7 U.S.C. § 136a(c)(5); *see also* 7 U.S.C. §§ 136(bb) (defining "unreasonable adverse effects on the environment" as encompassing both "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" [FIFRA's risk-benefit standard] **and** "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]").

[19] https://www.regulations.gov/document/EPA-HQ-OPP-2015-0816-0019

In this ID, the Agency is not making any human health or environmental safety findings associated with the Endocrine Disruptor Screening Program (EDSP) screening of chlormequat chloride. The Agency will complete a listed-species assessment and any necessary Endangered Species Act (ESA) Section 7 consultation with the Services and make an EDSP determination before issuing a final registration review decision for chlormequat chloride. For more information, see Appendices B and C.

E. Data Requirements

EPA does not anticipate calling in additional data for chlormequat chloride's registration review at this time. The Agency will work with the technical registrant to ensure fulfillment of the vegetative vigor study guideline requirement (Guideline Number 850.4150) already required in GDCI-018101-1625.

V. NEXT STEPS AND TIMELINE

A. Interim Registration Review Decision

A Federal Register Notice will announce the availability of this chlormequat chloride ID. A final registration review decision for chlormequat chloride will only be made after EPA completes (1) an endangered species determination and any necessary consultation with the Services, and (2) an EDSP determination.

B. Implementation of Mitigation Measures

Registrants must submit a cover letter, a completed Application for Registration (EPA form 8570-1) and electronic copies of the amended product labels within 60 days after the announcement of this ID in the Federal Register. Two copies for each label must be submitted, a clean copy and an annotated copy with changes. In order for the application to be processed, registrants must include the following statement on the Application for Registration (EPA form 8570-1):

"I certify that this amendment satisfies the requirements of the *Chlormequat Chloride Interim Registration Review Decision* and EPA regulations at 40 C.F.R. Section 152.44, and no other changes have been made to the labeling of this product. I understand that it is a violation of 18 U.S.C. Section 1001 to willfully make any false statement to EPA. I further understand that if this amendment is found not to satisfy the requirements of the chlormequat chloride Interim Registration Review Decision and 40 C.F.R. Section 152.44, this product may be in violation of FIFRA and may be subject to regulatory and/or enforcement action and penalties under FIFRA."

Within the required timeframe, registrants must submit the required documents to the Registration Review section of EPA's Pesticide Submission Portal (PSP), which can be accessed through EPA's Central Data Exchange (CDX) at https://cdx.epa.gov/. Registrants may instead send paper copies of their amended product labels, with an application for a fast-track, Agency-initiated non-PRIA label amendment to Rachel Stephenson at the following address, so long as

the labels and application are submitted within the required timeframe:

VIA US Mail

USEPA Office of Pesticide Programs
Pesticide Re-evaluation Division
Mail Code 7508M
1200 Pennsylvania Ave NW
Washington, DC 20460-0001

Appendix A: Labeling Changes for Chlormequat Chloride Products

Description	Label Language for Chlormequat Chloride Products	Placement on Label
	End Use Products	
Updated Personal Protective Equipment and Gloves Statement	Update the PPE and glove statement to be consistent with Chapter 10 of the Label Review Manual. In particular, remove reference to specific categories in EPA's chemical-resistance category selection chart and list the appropriate chemical-resistant materials and glove types to use.	In the Personal Protective Equipment (PPE) within the Precautionary Statements and Agricultural Use Requirements, if applicable
Updated Restricted Entry Interval	Update the REI to 24 hours to be consistent with the WPS. Remove reference to the 12-hour REI on all labels.	In the Agricultural Use Requirements box

Appendix B: Listed-Species Assessment

In 2015, EPA, along with the Services—the Fish and Wildlife Service (FWS) and the National Marine Fisheries Service (NMFS)—and the United States Department of Agriculture (USDA) released their joint Interim Approaches for assessing risks to listed species from pesticides. The agencies jointly developed these Interim Approaches in response to the 2013 National Academy of Sciences' recommendations that discussed specific scientific and technical issues related to the development of pesticide risk assessments conducted on listed species. Since that time, the agencies have been continuing to work to improve the consultation process.

EPA initially conducted biological evaluations (BEs) using the interim method on three pilot chemicals representing the first nationwide pesticide consultations (final pilot BEs for chlorpyrifos, malathion, and diazinon were completed in January 2017). These initial pilot consultations were envisioned as the start of an iterative process. Later that year, NMFS issued a final biological opinion for these three pesticides. In 2019, EPA requested to reinitiate formal consultation with NMFS on malathion, chlorpyrifos and diazinon to consider new information that was not available when NMFS issued its 2017 biological opinion. EPA recently received a draft revised biological opinion on these pesticides from NMFS and posted it for public comment.[20] In February 2022, EPA also received a final malathion biological opinion[21] from FWS, which the Agency plans to implement according to the 18-month timeframe specified in the opinion.

After receiving input from the Services and USDA on proposed revisions to the pilot interim method and after consideration of public comments received, EPA released an updated *Revised Method for National Level Listed Species Biological Evaluations of Conventional Pesticides* ("Revised Method") in March 2020.[22] During the same timeframe, EPA also released draft BEs for carbaryl and methomyl, which were the first to be conducted using the Revised Method. To date, EPA has used the Revised Method to complete final BEs for carbaryl, methomyl, atrazine, simazine, and glyphosate.

The 2018 Farm Bill established a FIFRA Interagency Working Group (IWG) to recommend improvements to the ESA section 7 consultation process for FIFRA actions and to increase opportunities for stakeholder input. This group is led by EPA and includes representatives from NMFS, FWS, USDA, and the Council on Environmental Quality (CEQ). The IWG outlines its recommendations and progress on implementing those recommendations in reports to Congress.[23] The agencies continue to work collaboratively, consistent with Congress's intent in creating the IWG.

In January 2022, EPA announced a policy[24] to evaluate potential effects of new conventional pesticide active ingredients to listed species and their designated critical habitat and initiate

[20] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions
[21] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions
[22] https://www.regulations.gov/document?D=EPA-HQ-OPP-2019-0185-0084
[23] https://www.epa.gov/endangered-species/reports-congress-improving-consultation-process-under-endangered-species-act
[24] https://www.epa.gov/newsreleases/epa-announces-endangered-species-act-protection-policy-new-pesticides

consultation with the Services, as appropriate, before registering these new pesticides. Before the Agency registers new uses of pesticides for use on pesticide-tolerant crops, EPA will also continue to make effects determinations. If these determinations are likely to adversely affect determinations, the Agency will not register the use unless it can predict that registering the new use will not jeopardize listed species or adversely modify their designated critical habitats. EPA will also initiate consultation with the Services as appropriate.

Appendix C: Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, sub-chronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision for chlormequat chloride, the EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA § 408(p), chlormequat chloride is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA § 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The Agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013,[25] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. Chlormequat chloride does not appear on either of the lists. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, visit EPA website.[26]

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

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