

Docket Number EPA-HQ-OPP-2009-0842
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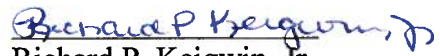


**Cyphenothrin Summary Document
Registration Review: Initial Docket
December 2009**

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Case # 7412

Approved By:


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12-16-09
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TABLE OF CONTENTS

	Page #
I. Preliminary Work Plan (PWP)	4
II. Fact Sheet	11

This Preliminary Work Plan and Fact Sheet summarize the Environmental Protection Agency's current position based on the following documents:

1. Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking water Assessments for Cyphenothrin, September 24, 2009
2. Cyphenothrin. Human Health Assessment Scoping Document in Support of Registration Review, August 20, 2009
3. Food/Feed & Non-Food/Non-Feed Uses Considered in Registration Review Work Planning – Cyphenothrin (129013), December 22, 2008
4. Updated Review of Cyphenothrin Incident Reports, June 4, 2009

Additional supporting documents for the registration review of cyphenothrin are located in docket EPA-HQ-OPP-2009-0842 at www.regulations.gov.

I. PRELIMINARY WORK PLAN – Cyphenothrin

Introduction:

The Food Quality Protection Act of 1996 mandated a registration review program. All pesticides distributed or sold in the United States (U.S.) generally must be registered by the Environmental Protection Agency (EPA), based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided at: http://www.epa.gov/oppsrrd1/registration_review/.

The Agency is implementing the registration review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The Agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this initial comment period, the Agency will develop and commit to a final work plan and schedule for the registration review of cyphenothrin.

Cyphenothrin (Case #7412) is a systemic pyrethroid ester insecticide used indoors in household/domestic dwellings, storage areas, pet living quarters, ships, processing plants, on horses and dogs; and outdoors on external doorways, window cracks and under porches. Cyphenothrin is registered as a liquid, squeeze-on product for insect control on dogs and horses; as a total release aerosol and fogger for insect control in indoor residential and commercial settings; and as an aerosol spray for crack and crevice spot treatments around doorways, windows, and under porches. Target insects include spiders, ticks, fleas, beetles, ants, flies, midges, yellow jackets, small flying insects, cockroaches; and other pests in domestic, public health and industrial situations. Since cyphenothrin was first registered in 1991, it was not subject to a Reregistration Eligibility Decision.

Anticipated Risk Assessment and Data Needs

The Agency anticipates conducting a comprehensive ecological risk assessment, including an endangered species risk assessment, for all uses of cyphenothrin. The Agency also anticipates reviewing toxicological studies required as part of registration review and reevaluating the

cyphenothrin endpoints selected for human health risk assessment as necessary. An updated occupational exposure risk assessment may be necessary if toxicological endpoints are revised for inhalation and dermal toxicity. In addition, the Agency anticipates performing a quantitative residential exposure assessment for all registered uses.

Ecological Risk:

- The Agency has not previously conducted an ecological risk assessment for cyphenothrin because its use was considered limited to the indoors. However, Agency policy has changed since the last cyphenothrin registration was granted. Current Agency policy dictates an assessment of potential ecological pesticide exposure from washoff of treated pets and runoff from outdoor spot treatments. Therefore, a complete ecological risk assessment for all cyphenothrin uses is planned during registration review.
- The ecological risk assessment planned during registration review will allow the Agency to examine whether cyphenothrin's current use has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, the Agency will consult with the FWS and/or National Marine Fisheries Service (the Services), as appropriate.
- The Agency anticipates needing the following data in order to conduct a complete ecological risk assessment, including an endangered species assessment for cyphenothrin:
 - GLDN 850.1300– Aquatic Invertebrate Life Cycle (freshwater)
 - GLDN 850.1400 – Fish Early Life-Stage (freshwater)
 - GLDN 850.1735 – Whole Sediment: Acute Freshwater Invertebrates
 - GLDN 850.2100 – Avian Acute Oral Toxicity
 - GLDN 850.2300 – Avian Reproduction
 - GLDN 850.3020 – Honeybee Acute Contact Toxicity
 - GLDN 850.4150 – Vegetative Vigor
 - GLDN 835.2120 – Hydrolysis
 - GLDN 835.2240 – Photodegradation in Water
 - GLDN 835.4100 – Aerobic Soil Metabolism
 - GLDNs 835.1230 and 835.1240 – Leaching and Adsorption/Desorption
- Please refer to *Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking water Assessments for Cyphenothrin*, September 24, 2009, for a more detailed discussion of the anticipated ecological risk assessment needs.

Human Health Risk:

- The most recent human health risk assessment for cyphenothrin was completed in 2006 to support a new use – squeeze-on spot treatment for dogs.
- The cyphenothrin toxicity database is not complete. EPA anticipates requiring the following guideline studies to reevaluate toxicological endpoints for cyphenothrin:
 - GDLN 870.3250 – 90-Day Dermal Toxicity Study in Rats
 - GDLN 870.3700 – Developmental Toxicity Study in Rats
 - GDLN 870.3700 – Developmental Toxicity Study in Rabbits
 - GDLN 870.6200 – Acute Neurotoxicity Study
 - GDLN 870.6200 – Subchronic Neurotoxicity Study
 - GDLN 870.6300 – Developmental Neurotoxicity Studyⁱ
 - GDLN 870.7800 – Immunotoxicity Study
- Based on the Agency’s review of existing pyrethroid data, EPA has come to the conclusion that the DNT is not a particularly sensitive study for comparing the sensitivity of young and adult animals to pyrethroids. EPA has recently determined that, as an alternative to the generation and submission of a new DNT study, pyrethroid registrants may instead choose to cite to the six previously submitted DNT studies for pyrethroid pesticides. The Agency is also investigating the need for additional experimentation, specific to the mode of action and pharmacokinetic characteristics of pyrethroids, to evaluate the potential for increased susceptibility of young organisms. The Agency will make a decision regarding the need for an FQPA or other database uncertainty/safety factors following receipt of the remaining required toxicity data, and following a final determination of the potential for increased susceptibility of infants and children to pyrethroid pesticides based on the results of all available data.
- Based upon the limited nature of the registered outdoor uses of cyphenothrin, the Agency does not anticipate conducting a drinking water assessment for cyphenothrin.
- The Agency has no plans to conduct a dietary assessment because there are no registered food uses, and dietary exposure is not expected.
- HED is currently revising the Residential Standard Operating Procedures (SOPs) for treated pets and indoor settings. The Agency anticipates conducting a new quantitative residential exposure assessment, which incorporates the revised SOPs and all cyphenothrin uses.
- The Agency does not anticipate conducting an aggregate assessment because dietary exposure from food and water is not expected.
- The Agency does not anticipate conducting an occupational health risk assessment unless endpoints are updated for dermal and inhalation toxicity.

- Please refer to *Cyphenothrin. Human Health Assessment Scoping Document in Support of Registration Review*, August 20, 2009, available in the docket, for a detailed discussion of the anticipated human health risk assessment and data needs for cyphenothrin.

Other Data Needs:

- GLDN 830.7050 UV/Visible Light Absorption – this study is a new data requirement under 40 CFR part 158 (Product Chemistry Data Requirements) for registration of a pesticide (food and non-food uses). The Agency anticipates requiring this study to obtain basic information about the compound's identity/composition and the wavelengths at which the compound may be susceptible to photochemical degradation.

Endocrine Disruptor Screening Program

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (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 quantitative relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA is issuing test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Cyphenothrin is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP orders/data call-ins for all Registration Review cases, including those for which EPA has already opened a Registration Review docket for a pesticide active ingredient.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: <http://www.epa.gov/endo/>.

Timeline:

The Agency has created the following estimated timeline for the completion of the cyphenothrin registration review.

Registration Review for Cyphenothrin – Projected Registration Review Timeline	
Activities	Estimated Year/Month
Opening the Docket	
Open Docket and Public Comment Period	December 2009
Close Public Comment	February 2010
Case Development	
Issue Final Work Plan (FWP)	May 2010
Issue Data Call-in (DCI)	January – March 2011
Data Submission	January – March 2015
Open Public Comment Period for Preliminary Risk Assessments	July – September 2016
Close Public Comment Period	October - December 2016
Registration Review Decision	
Open Public Comment Period for Proposed Registration Review Decision	January – March 2017
Close Public Comment Period	April - June 2017
Final Registration Review Decision & Begin Post-Decision Follow-up	2017
Total (years)	8¹

¹ If the registrants choose to cite the six previously submitted DNT studies for pyrethroid pesticides, as explained above, rather than conducting a DNT study with cyphenothrin, this time estimate will likely be shortened by approximately two years.

Guidance for Commenters:

The public is invited to comment on EPA's preliminary registration review work plan and rationale. The Agency will carefully consider all comments, as well as any additional information or data provided in a timely manner, prior to issuing a final work plan for the cyphenothrin case.

- 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. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to cyphenothrin compared to the general population. Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure, compared to the general population.

- Cyphenothrin is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885. In addition, no Total Maximum Daily Loads (TMDL) have been developed for cyphenothrin based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES. More information on impaired water bodies and TMDLs can be found at <http://www.epa.gov/owow/tmdl/>. The Agency invites submission of water quality data for this pesticide. To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process* (see: <http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-sop.pdf>), in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

- Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining the ecological risk assessment, including any species-specific effects determinations. The Agency is interested in obtaining the following information:
 1. Confirmation on the following label information.
 - a. sites of application
 - b. formulations
 - c. application methods and equipment
 - d. maximum application rates
 - e. frequency of application, application intervals, and maximum number of applications per season and per year
 - f. geographic limitations on use
 2. Use or potential use distribution (e.g. geographical distribution of relevant uses).

3. Use history.
4. Median and 90th percentile reported use rates (lb/animal, lb/ft³) from usage data – national, state and county.
5. Application timing (date of first application and application intervals) by use – national, state, and county.
6. Usage/use information for non-agricultural uses.
7. Directly acquired county-level usage data (not derived from state level data).
 - a. maximum reported use rate (lb/A, gal/A, ppb/A) from usage data – county
 - b. median and 90th percentile number of applications – county
 - c. total pounds per year – county
 - d. the year the pesticide was last used in the county/sub-county area
 - e. the years in which the pesticide was applied in the county/sub-county area
8. Typical application interval (days).
9. State or local use restrictions.
10. Ecological incidents specific to cyphenothrin (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency.
11. Monitoring data.
12. Honeybee toxicity data.

Next Steps:

After the 60-day comment period closes, the Agency will consider and respond to any comments received in a timely manner and then expects to issue a Final Work Plan in the spring of 2010 for cyphenothrin.

II. FACT SHEET

Background Information:

- Cyphenothrin registration review case number: 7412
- Cyphenothrin PC Code: 129013; CAS # 39515-40-7
- Cyphenothrin was first registered in the United States in 1991.
- Technical registrant: Sumitomo Chemical America, Inc.
- There are 15 FIFRA Section 3 active product registrations including one technical registration.
- Pesticide Re-evaluation Division Contact: Joy Schnackenbeck (schnackenbeck.joy@epa.gov)
- Registration Division Contact: Olga Odiott (odiott.olga@epa.gov)

Use and Usage Information: (For additional details, please refer to *Food/Feed & Non-Food/Non-Feed Uses Considered in Registration Review Work Planning – Cyphenothrin (129013)*, December 22, 2008, in the cyphenothrin docket).

- Cyphenothrin is a pyrethroid insecticide used to control insects on pets, and in and around residential and commercial settings.
- Cyphenothrin is used to control a variety of insects including fleas, ticks, ants, beetles, crickets, cockroaches, mosquitoes, spiders, flies, midges, water bugs, moths, yellow jackets, and other insects in domestic, public health and industrial situations.
- Cyphenothrin is formulated as a liquid.
- Cyphenothrin can be applied by sprayer, fumigation or fogger.

Recent Actions:

- In 2006, EPA approved cyphenothrin use on domestic pets (dogs and puppies).

Ecological Risk Assessment Status

- The following summarizes ecological effects data from registrant-submitted studies, and data available from open literature. The Agency has not previously conducted an ecological risk assessment that integrates environmental exposure and ecological effects. Please refer to *Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking water Assessments for Cyphenothrin*, September 24, 2009 located in the docket, for a detailed discussion of what is currently known about the environmental fate and ecological effects associated with cyphenothrin.

- Technical cyphenothrin is classified as very highly toxic on an acute basis to fish, aquatic-phase amphibians, and aquatic invertebrates. Toxicity to aquatic organisms from chronic cyphenothrin exposure has not been evaluated.
- Cyphenothrin is practically nontoxic on a subacute dietary exposure basis to birds, terrestrial-phase amphibians and reptiles from dietary exposure; however, no data are available evaluating acute oral exposure. Chronic exposure to birds, terrestrial-phase amphibians and reptiles has not been evaluated for cyphenothrin.
- Cyphenothrin is moderately toxic to mammals on an acute oral exposure basis. Limited information is available regarding the effects of chronic exposure to mammals.
- No data are available on the potential effects of cyphenothrin exposure on honeybees.
- No data are available to evaluate toxicity of cyphenothrin to terrestrial and aquatic plants.

Human Health Risk Assessment Status

- The following are key findings of the human health risk assessments conducted to support cyphenothrin registered uses. Please refer to *Cyphenothrin. Human Health Assessment Scoping Document in Support of Registration Review*, August 20, 2009 located in the docket for a detailed discussion of the human health risk assessment status.

Hazard Characterization:

- Cyphenothrin is a pyrethroid chemical with a neurotoxic mode of action. Historically, EPA has required that a developmental neurotoxicity study (DNT) be submitted for this class of chemicals. Given the similarity of certain results across all these studies, EPA has concluded that, when considered together, these studies provide sufficient information for EPA to determine that the conclusions are applicable to all pyrethroids. EPA will therefore consider citation of all of the six studies as a substitute for generating a single new study for cyphenothrin.
- Cyphenothrin has moderate acute toxicity via the oral route of exposure, and low or mild acute toxicity via the inhalation and dermal routes of exposure. Cyphenothrin is not irritating to the skin or the eye and is not a skin sensitizer.
- Cyphenothrin is classified as a group E carcinogen “evidence of non-carcinogenicity for humans.” This classification is based on the lack evidence of carcinogenicity in mice and rats in two carcinogenicity studies.
- In the most recent human health risk assessment for cyphenothrin, an additional 10x database uncertainty factor was retained for all potentially exposed populations because of the lack of acceptable developmental studies.

Dietary:

- A dietary risk assessment has not been conducted because there are no registered food uses of cyphenothrin and dietary exposure from cyphenothrin in food and drinking water is not expected.

Residential and Recreational:

- Cyphenothrin residential use is likely to result in short-term exposure (< 30 days). The worst case scenario, toddler post-application exposures to treated companion animals from playing on floors after fogger treatment and from space spray applications, did not result in risks of concern. However, chemical-specific exposure data for cyphenothrin is lacking, and uncertainties remain.

Aggregate:

- An aggregate exposure assessment is not required for cyphenothrin in registration review because there are no registered food uses and exposure from drinking water is not expected.

Occupational:

Handlers:

- The most recent occupational assessment evaluating short- and intermediate-term exposure to occupational handlers applying cyphenothrin did not demonstrate risks of concern.

Post-application:

- A post-application occupational risk assessment has not been performed because the Agency believes post-application exposure is minimal.

Cumulative:

- Cyphenothrin is a member of the pyrethroid class of insecticides. This class also includes permethrin, cypermethrin, cyfluthrin, fluvalinate, bifenthrin, fenpropathrin, and lambda-cyhalothrin, among others. EPA developed a draft science policy document on the proposed common mechanism of toxicity for naturally-occurring pyrethrins and synthetic pyrethroids (Proposed common mechanism grouping for the pyrethrins and pyrethroids, draft, May 19, 2009; <http://www.regulations.gov/search/Regs/home.html#documentDetail?R=09000064809a62df>). This document was supported by the FIFRA Scientific Advisory Panel (SAP). Upon finalization of this draft science policy, the pyrethroids will be subject to cumulative risk assessment under the FQPA. Research is on-going by EPA's Office of Research and Development (ORD) to make improvements to the SHEDS probabilistic exposure model, which is important for the pyrethroid cumulative risk assessment. EPA ORD is also

developing physiologically-based pharmacokinetic models for several pyrethroids. The status of both of these research modeling efforts will be reviewed by the FIFRA SAP in July, 2010. For information regarding EPA's efforts to evaluate the risk to pyrethroids, <http://www.epa.gov/oppsrrd1/reevaluation/pyrethroids-pyrethrins.html>.

Incidents

- In July 2009, a preliminary review of the Ecological Incident Information System Database revealed that there have been no cyphenothrin ecological incidents reported to the Agency between 2000 and 2009.
- There have been several reported pet incidents involving the use of cyphenothrin pet treatments on dogs. From January 2006 to November 2009, there were 149 reported mortalities, 367 major reported incidents, 13,455 moderate reported incidents and 32,713 minor reported incidents. From all reported pesticide related pet incidents, cyphenothrin products account for 10% of the total reported pet mortalities, 13% of all major incidents, 54% of all moderate incidents, and 65% of all minor incidents. Some of these incidents resulted from cyphenothrin products co-formulated with pyriproxifen, and it is unclear whether one active ingredient or the other, or an emergent effect from the formulation is responsible for these incidents.
- On June 4, 2009, an updated review of cyphenothrin human incident reports was prepared by consulting the OPP Incident Data System (IDS). In the United States from 2002 to the present, 27 incidents were reported for the single chemical, cyphenothrin. Many of these incidents were described as dermal and ocular irritation, shortness of breath, and dizziness.

Tolerances and International Harmonization

- There are no established U.S. tolerances or MRLs for Mexico, Canada and Codex associated with cyphenothrin.

Data Call-In & Conditional Registration Status

- There have been no issued data call-ins associated with cyphenothrin.
- As part of the registration process for the liquid squeeze on product for pets, a petting/stroke study to provide chemical-specific exposure data following application to pets was required as a condition of registration. Although a protocol for this study was submitted, the Agency concluded the study involved intentional human dosing with a pesticide. The Agency is postponing development of chemical specific data for cyphenothrin pending evaluation of the revised Residential SOPs, and the identification of additional data needs for evaluation exposure associated with pesticides used on pets.

Labels

- Active Section 3 labels for cyphenothrin can be obtained from the Pesticide Product Label System (PPLS) website: <http://oaspub.epa.gov/pestlabl/ppls.home>.
-