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Dinotefuran Final Work Plan
Registration Review
June 2012

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Case No. 7441

Approved By:

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Date

Introduction:

This is the Environmental Protection Agency's (EPA or the Agency) *Final Work Plan* (FWP) for the registration review of dinotefuran. The FWP includes the expected registration review timeline. The FWP also addresses any public comments received on the *Preliminary Work Plan* (PWP) in the *Summary Document*, which was posted in the dinotefuran registration review docket (EPA-HQ-OPP-2011-0920). The *Summary Document*, dated December 14, 2011, provided information on what EPA knows about the pesticide and what additional risk analyses and data or information the Agency believes are needed to make a registration review decision.

The Agency's implementation of the registration review program requires review of each registered pesticide every 15 years to determine whether it continues to meet the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) standard for registration. Changes in science, public policy, and pesticide use practices occur over time. 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 that statutory standard. The public phase of registration review begins when the initial docket is opened for each case. Information on this program is provided at http://www.epa.gov/oppsrrd1/registration_review/.

Dinotefuran is a broad-spectrum, second generation neonicotinoid insecticide that is currently registered for agricultural use on a variety of food and feed commodities, including: brassica; leafy and fruiting vegetables; grapes; curcurbits; pineapple; and nut trees. It is also registered for non-agricultural use in residential and commercial settings, including: forest trees; ornamentals (plants, lawns and turf); pets and pet premises; and commercial, institutional, and industrial buildings. Dinotefuran was first registered for use in the United States in 2004 and, therefore, was not subject to reregistration under FIFRA. There are currently thirty-seven FIFRA Section 3 product registrations, and sixteen Section 24(c) Special Local Need (SLN) registrations for use on turf, ornamental, and vegetable transplants in enclosed structures.

Updates Since the Summary Document was Issued:

As mentioned in the dinotefuran PWP, a fur dislodgeability study (Guideline 875.2300) was previously required as a condition of registration for dinotefuran dog and cat spot-on products (due January 26, 2013). In addition, this study is required in support of registration review. After the dinotefuran PWP was issued, a fur dislodgeability study was submitted to the Agency and is currently in review. EPA expects to finish its review of this study prior to issuance of the registration review data call-in (DCI). Once the study has been reviewed and classified, EPA will determine whether or not it should be included in the registration review DCI.

Comments Received on the Preliminary Work Plan:

The dinotefuran docket was open for a 60-day comment period, beginning December 21, 2011 and closing February 21, 2012. During the 60-day comment period, one public comment was received regarding dinotefuran. This comment is addressed below and did not result in changes to the work plan, data requirements, or timeline as described in the dinotefuran *Summary Document* and PWP. Three comments relevant to another neonicotinoid registration review

case, clothianidin, were inadvertently posted to the dinotefuran docket and are not addressed in this FWP. For further information regarding these comments and the Agency's response, refer to the clothianidin docket (EPA-HQ-OPP-2011-0865).

Comment:
Jeff Durand of Durand Farms in St. Martinville, Louisiana commented that dinotefuran is very important to southern Louisiana's rice crop for controlling rice stinkbugs. In his comments, Mr. Durand noted the following: (1) dinotefuran was very effective in controlling rice stinkbugs on their 2011 rice crop; (2) he did not observe injury to crawfish which were harvested from his ponds located close to the dinotefuran-treated rice crops; and, (3) he believes that dinotefuran will play a significant part in managing pest resistance because it is a different class of chemistry and can be rotated with pyrethroids, in some areas.

Agency Response:
The Agency thanks Mr. Durand for his comment and will consider this information during registration review.

Risk Assessment and Data Needs:

The Agency will require data for use in conducting a comprehensive ecological risk assessment, including an endangered species risk assessment, for all uses of dinotefuran. The Agency will also require data for use in conducting an updated human health risk assessment for registration review. A summary of the issues relevant to the registration review of dinotefuran is given below.

Ecological Risk:

- The most recent comprehensive ecological risk assessment for dinotefuran was completed in 2004 in support of its initial registration for use on leafy vegetables, turf grasses, and various residential uses. All subsequent ecological risk assessments have relied on the conclusions of this assessment.

- The most recent ecological risk assessment in support of FIFRA Section 3 registrations was completed on May 3, 2011 for forestry uses (Christmas trees, trees in plantations, reforestation nurseries, forests, and woodland areas). In June 2011, an ecological risk assessment was completed in support of FIFRA Section 18 emergency exemptions for use on commercial pome and stone fruit to control the brown marmorated stink bug during the 2011 growing season; these Section 18 exemptions expired on October 15, 2011.

- The Agency has not conducted a risk assessment that supports a complete endangered species determination for dinotefuran. The ecological risk assessment planned during registration review will allow the Agency to determine whether dinotefuran 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 U.S. Fish and Wildlife Service and/or National Marine Fisheries Service (the Services), as appropriate.

- On January 19, 2011, the Center for Biological Diversity and the Pesticide Action Network North America filed a lawsuit in the United States District Court for the Northern District of California, against the Environmental Protection Agency (EPA) for allegedly failing to undergo consultation with the Services regarding the effects of over 350 pesticides, including dinotefuran, on over 200 endangered and threatened species throughout the United States (Center for Biological Diversity, et al. v. EPA, et al., No. C 11-00293 (N.D.Cal.).

- The Agency is requiring the following data for use in conducting a comprehensive ecological risk assessment, including an endangered species assessment, for the registration review of dinotefuran:

    - GDLN 835.4400 – Anaerobic Aquatic Metabolism
    - GDLN 850.1350 – Estuarine/Marine Invertebrates – Life Cycle Test (mysid)
    - GDLN 850.2100 – Acute Avian Oral Toxicity (passerine)
    - GDLN 850.3040 – Field Testing for Pollinators
    - Non-GDLN – Pollinator Larval Toxicity Study (Special Study)
    - Non-GDLN – Laboratory Pollinator Chronic Feeding Study (Special Study)
    - Non-GDLN – Residues in Pollen and Nectar/Field Residue Analysis (Special Study)

- The EPA is aware of registrant-submitted studies and other open literature studies regarding the potential effects of neonicotinoid insecticides on insect pollinators and specifically on honey bees. The Agency is also aware of concerns regarding the potential association between the use of neonicotinoids and honey bee losses characterized as Colony Collapse Disorder (CCD) and the broader phenomenon of declining honey bee health globally. While a number of factors (*e.g.*, nutrition, habitat loss, disease, parasites, bee management practices, and pesticides) have been hypothesized, no single factor has yet to be identified as the "cause" of declines.

  As part of the review process, EPA examines the effects of chemicals on bees based on both laboratory and when appropriate, field studies to determine whether individual bees and entire bee colonies may be affected by the use of a compound and to support risk mitigation decisions. EPA is currently revising its process for assessing pesticide risks to bees to reflect advancements in the state of the science that underlie bee exposure and effects assessments. Interim guidance (USEPA 2011[1]) on factors to consider when evaluating exposure and effects to bees is available to ecological risk assessors. In 2012, EPA will present to a FIFRA Scientific Advisory Panel (SAP) a proposed process for

[1] USEPA. 2011. Pesticides: Science and Policy. Interim Guidance on Honey Bee Data Requirements. http://www.epa.gov/pesticides/science/efed/policy_guidance/team_authors/terrestrial_biology_tech_team/honeybee_data_interim_guidance.htm

quantifying risks to honeybees and identifying exposure and effect studies needed to inform that process. Based on input from the SAP, EPA will incorporate its revised assessment process to quantify risks to bees in a similar manner as that used to evaluate risks to other taxa.

As EPA's understanding of the science evolves, its need for data and its evaluation of those data will evolve as well. Therefore, as with all taxa, EPA reserves the right to require additional data it deems necessary to inform its understanding of potential ecological risks and support its associated risk management decisions. Additional data requirements for pollinators may extend beyond those identified in problem formulations and preliminary work plans written in support of the registration review process.

- The Agency has also identified additional information needs (i.e., independent laboratory validation, purity of test compounds, missing study information) regarding several existing studies, which are described in "Appendix C" of the Problem Formulation; and, is interested in receiving information to supplement these existing data. This information, though not considered data gaps, will be useful in refining potential ecological risks and reducing the use of default assumptions for the registration review of dinotefuran.

- Please refer to the December 13, 2011 document, *Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Dinotefuran*, located in docket EPA-HQ-OPP-2011-0920 for a detailed discussion of the risk assessment and data needs.

Human Health Risk:

- The most recent human health risk assessment for dietary, residential and aggregate exposure of dinotefuran was conducted in May of 2011 in support of the FIFRA Section 18 emergency exemptions for use on pome and stone fruits. The most recent human health risk assessment for occupational exposure (in support of FIFRA Section 3 registrations) was conducted in February 2011 for forestry uses.

- The existing human health toxicity database is sufficient and the Agency will not require additional toxicity data in support of registration review. However, the Agency will re-evaluate toxicological endpoints (points of departure) and uncertainty factors, and update the human health toxicity profile at the time of the risk assessment, as needed.

- During registration review, a revised dietary (food and drinking water) risk assessment may be needed to incorporate refined estimated drinking water concentrations (EDWCs), updated food residues and Pesticide Data Program (PDP) data, and any changes to toxicological points of departure or uncertainty factors.

- The residential and occupational exposure databases for dinotefuran are adequate with the exception of the following study, which is needed for use in this registration review.

This study will be used to assess exposure of dinotefuran to humans handling pets treated with spot-on products.

- GDLN 875.2300 - Fur Dislodgeability

This study has been identified previously as a conditional requirement for the registration of dinotefuran dog and cat spot-on products.

- The Agency will revise residential and occupational handler and post-application risk assessments using standards and exposure and/or risk assessment policies/procedures that are in place at the time of the risk assessment, including any changes to the points of departure or the uncertainty factors.

- The Agency will be revising the aggregate risk assessment using standards and exposure and/or risk assessment policies/procedures that are in place at the time of the risk assessment; including any changes to the points of departure or the uncertainty factors; and potential changes to dietary exposure estimates from food and/or drinking water (e.g., updated EDWCs).

- Residential and occupational bystander inhalation exposure may occur as a result of dinotefuran aerial applications and/or off-site transport (e.g., spray drift or volatilization). The Agency is examining its policies and procedures regarding inhalation risk assessment, and will re-evaluate the need for residential and occupational bystander risk assessments based on current Agency policy at the time of the risk assessment.

- The tolerance expression in 40 CFR §180.603 has been reviewed to ensure that it appropriately covers the metabolites and degradates of dinotefuran and that it specifies the residues to be measured for each commodity.

- There are no established or proposed international Codex, Canadian, or Mexican MRLs for dinotefuran. However, should MRLs be established, the Agency will work to harmonize tolerances/MRLs, where possible, in key export markets during registration review.

- Please refer to *Dinotefuran. Human Health Scoping Document in Support of Registration Review*, September 15, 2011, located in the docket, for a detailed discussion of the risk assessment and data needs for human health.

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, subchronic 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 dinotefuran, 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 section 408(p), dinotefuran 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 section 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. Dinotefuran is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Accordingly, as part of registration review, EPA will issue future EDSP orders/data call-ins, requiring the submission of EDSP screening assays for dinotefuran. For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

Timeline:

EPA has created the following estimated timeline for the completion of the dinotefuran registration review.

Registration Review for Dinotefuran – Projected Registration Review Timeline	
Activities	**Estimated Date**
Opening the Docket	
Open Docket and Public Comment Period	2011 – December
Close Public Comment	2012 – February
Case Development	
Final Work Plan	2012 – June
Issue DCI	2013 – Jan. – March
Data Submission	2016 – Jan. – March

Registration Review for Dinotefuran – Projected Registration Review Timeline	
Activities	**Estimated Date**
Open Public Comment Period for Draft Risk Assessments	2017 – July – Sept.
Close Public Comment Period	2017 – Oct. – Dec.
Registration Review Decision	
Open Public Comment Period for Proposed Registration Review Decision	2018 – Jan. – March
Close Public Comment Period	2018 – April – June
Registration Review Decision and Begin Post-Decision Follow-up	2018
Total (years)	7

Next Steps:

The Agency will require ecological effects and human health studies through a DCI, which is expected to be issued in early 2013. This new information will be used to conduct risk assessments for all registered uses of dinotefuran.

Summary of Data Needs – Dinotefuran:

The table below summarizes the data needs for dinotefuran. For additional discussion of the data needs, see the *Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Dinotefuran,* December 13, 2011, and *Dinotefuran. Human Health Scoping Document in Support of Registration Review,* December 15, 2011.

Table 1. Data Needs for Dinotefuran Registration Review

Guideline Number	Data Requirement	Test Material	Estimated Timeframe (Months from receipt of DCI)
835.4400	Anaerobic Aquatic Metabolism	TGAI	24
850.1350	Estuarine/marine Invertebrates – Life Cycle (mysid species)	TGAI	12
850.2100	Avian Oral Toxicity (passerine species)[2]	TGAI	12
850.3040	Field Testing for Pollinators[3]	TEP	24
Non-Guideline (Special Study)	Pollinator Larval Toxicity Study[4]	TGAI	12
Non-Guideline (Special Study)	Laboratory Pollinator Chronic Feeding Study[4]	TGAI	12
Non-Guideline (Special Study)	Residues in Pollen and Nectar/Field Residue Analysis[4, 5]	TGAI	36
875.2300	Fur Dislodgeability	TGAI	January 26, 2013 (In review)[6]

[2] The DCI will require the submission of a study protocol for review and approval by the Agency prior to study initiation.

[3] The DCI will require that the test crop be one on which bees will actively forage for both nectar and pollen (e.g., cotton, melon, alfalfa).

[4] The DCI will require the submission of a study protocol for review and approval by the Agency prior to study initiation. The registrant should not assume that any California Department of Pesticide Regulation data have satisfied the Agency data requirements.

[5] The Agency recommends residue studies of leaves, fruit, seeds, wax, sap, as well as blooming, pollen-shedding, and nectar producing parts (*i.e.*, flowers and, if present, extra floral nectarines) on pollinator-attractive crops on which the compound is registered for use.

[6] In addition to being a data requirement for the registration review of dinotefuran, GLN 875.2300, fur dislodgeability is required as a condition of registration for dinotefuran dog and cat spot-on products. Conditions stipulate a due date of January 26, 2013 and the Agency still requires the study by this date. This study was recently submitted to the Agency and is currently in review. Once the study has been fully reviewed and classified, EPA will determine whether or not it should be included in the registration review DCI.