Docket Number: EPA-HQ-OPP-2011-0920
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Dinotefuran Summary Document
Registration Review: Initial Docket
December 2011

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Case No. 7441

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12/14/2011

Date

TABLE OF CONTENTS

Please Note

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

1. Registration Review: Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Dinotefuran. December 13, 2011.

2. Dinotefuran: Human Health Assessment Scoping Document in Support of Registration Review. September 15, 2011.

3. Dinotefuran: Review of Human Incidents. July 26, 2011.

4. Dinotefuran (044312) Screening Level Usage Analysis (SLUA). February 4, 2011.

5. BEAD Chemical Profile for Registration Review: Dinotefuran (044312). July 20, 2011.

6. Appendix A: Food/Feed & Non-Food/Non-Feed Uses Considered in Registration Review Work Planning. May 23, 2011.

Additional supporting documents for dinotefuran may be found in the registration review docket EPA-HQ-OPP-2011-0920 located on the internet at www.regulations.gov.

I. PRELIMINARY WORK PLAN – Dinotefuran

Introduction:

The Food Quality Protection Act (FQPA) of 1996 mandated a registration review program. All pesticides sold or distributed in the United States generally must be registered by the Environmental Protection Agency (EPA or the Agency), 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 dinotefuran.

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.

Anticipated Risk Assessment and Data Needs:

The Agency anticipates requiring data for use in conducting a comprehensive ecological risk assessment, including an endangered species risk assessment, for all uses of dinotefuran. The Agency also anticipates requiring 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 (BMSB) 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 United States Fish and Wildlife Service and the National Marine Fisheries Service 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 anticipates 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)

- In an attempt to address protection of pollinators and other beneficial insects, EPA is anticipating requiring data to assess bees as a representative for all beneficial insects. In moving forward with addressing potential risk to these organisms, EPA will consider the recommendations of the Society of Environmental Toxicology and Chemistry (SETAC) Workshop on Pesticide Risk Assessment for Pollinators, and is working with its federal and state partners, industry, and academia to determine appropriate assessment methodology. For compounds, such as dinotefuran, which (1) show acute toxicity to bees and (2) have exposure routes for bees, EPA anticipates requiring toxicity and exposure studies to allow for evaluation of risks to pollinators. The registrant should consult with EPA on the conduct of these studies.

- 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 anticipated 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 does not anticipate requiring additional toxicity data in support of registration review. However, the Agency anticipates reevaluating toxicological endpoints (points of departure), uncertainty factors, and updating 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 previously been identified as a conditional requirement for the registration of dinotefuran dog and cat spot-on products. The Agency has reviewed draft protocols for conducting this study based on the use of dinotefuran spot-on products for dogs and cats. However, submission of the final study remains outstanding and, per the conditions of registration, is due January 26, 2013. This study is also needed for use in this registration review and will be included in the registration review DCI.

- The Agency anticipates revising 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 anticipates 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 anticipated risk assessment and data needs.

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

Registration Review for Dinotefuran – Projected Registration Review Timeline	
Activities	**Estimated Date**
Close Public Comment	2012 – February
Case Development	
Final Work Plan	2012 – May
Issue DCI	2013 – Jan. – March
Data Submission	2016 – Jan. – March
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

Guidance for Commenters:

The public is invited to comment on EPA's preliminary 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 dinotefuran.

Trade Irritants:

Through the registration review process, the Agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. Growers and other stakeholders are asked to comment on any trade irritant issues resulting from lack of MRLs or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern.

Water Quality:

Dinotefuran is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[1]. In addition, no Total Maximum Daily Loads (TMDL) have been developed for dinotefuran[2]. More information on impaired water bodies and TMDLs can be found on the Agency's website[3]. 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*[4] in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

[1] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885
[2] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES
[3] http://www.epa.gov/owow/tmdl/
[4] http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm

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. 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 dinotefuran, 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.

Additional Information:

Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining its risk assessments, including any species-specific ecological effects determinations. The Agency is interested in receiving 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 and reason for changes in use
4. median and 90th percentile reported use rates (lbs ai/1000 sq ft) from usage data – national, state, and county
5. application timing (date of first application and application intervals) by use site – national, state, and county
6. sub-county use site location data
7. usage/use information for non-agricultural uses, especially turf and ornamentals
8. directly acquired county-level usage data (not derived from state level data)
    a. maximum reported use rate (lbs ai/1000 sq ft) from usage data – county
    b. percent use site treated – county
    c. median and 90th percentile number of applications – county
    d. total pounds per year – county
    e. the year the pesticide was last used in the county/sub-county area
    f. the years in which the pesticide was applied in the county/sub-county area
9. typical application interval (days)
10. state or local use restrictions
11. information on invertebrate resistance to this insecticide

12. ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
13. monitoring data
14. additional usage information on the following registered sites: warehouses, commercial/industrial machinery, bathrooms, and garbage areas.

Next Steps:

After the 60-day comment period closes, the Agency will review and respond to any comments received in a timely manner, and then issue a Final Work Plan for dinotefuran.

II. FACT SHEET

Background Information:

- Registration review case number: 7441
- PC code: 044312
- CAS number: 165252-70-0
- Dinotefuran was first registered in the U.S. in 2004 and, therefore, was not subject to reregistration under FIFRA.
- Technical registrants: Mitsui Chemicals, Inc.; Valent Biosciences Corp.; ICR, Inc.
- There are currently thirty-seven FIFRA Section 3 product registrations (3 technical, 2 formulation intermediates, 2 manufacturing-use, and 30 end-use product registrations); and sixteen active Special Local Need (SLN) registrations under FIFRA Section 24(c).
- Permanent tolerances are established for residues of dinotefuran, including its metabolites and degradates (expressed as dinotefuran), in and/or on food and/or feed commodities under 40 CFR §180.603. Also, a time-limited tolerance for residues of dinotefuran in and/or on rice is established under 40 CFR §180.603, which is scheduled to expire on December 31, 2012.
- Pesticide Re-evaluation Division (PRD) Chemical Review Manager (CRM): Steven Snyderman, *snyderman.steven@epa.gov*.
- Registration Division (RD) Product Manager (PM): John Hebert, *hebert.john@epa.gov*.

Use & Usage Information: For additional details on label rates and use sites, refer to the following documents: *BEAD Chemical Profile for Registration Review: Dinotefuran*, July 20, 2011; *Dinotefuran Screening Level Usage Analysis (SLUA)*, February 4, 2011; and *Appendix A: Food/Feed & Non-Food/Non-Feed Uses Considered in Registration Review Work Planning*, May 23, 2011.

- Dinotefuran is a broad-spectrum, second generation neonicotinoid insecticide that is currently registered for agricultural use on the following food/feed commodities: brassica, cotton, leafy and fruiting vegetables, grapes, curcurbits, pineapple, potatoes, and nut trees. It is also registered for non-agricultural use in residential and commercial settings, which include: forest trees; ornamental plants (flowering and foliage plants, wood shrubs, vines and trees); ornamental lawns and turf; pets and pet premises; animal premises; domestic dwellings; picnic areas; transportation vehicles; food handling establishments; hospitals; and commercial, institutional, and industrial buildings. In addition, there are a number of SLN registrations, which are registered for use on turf, ornamentals, and vegetable transplants in enclosed structures.

- Dinotefuran is formulated as an intermediate, soluble concentrate, granular, soluble granule, bait, gel, and read-to-use (RTU) spray.

- Based on market pesticide usage data from 2006-2010, the annual total agricultural usage averaged approximately 4,000 pounds active ingredient (a.i.) over 30,000 acres for an

average of 0.1 lbs. a.i. application rate per acre. In comparison, the average application rate in lbs. a.i. per acre is 0.1 for wine grapes, 0.2 for cantaloupes, 0.1 for rice, and 0.2 for both watermelons and tomatoes. Non-agricultural usage data were not available from Agency data sources.

- From 2006-2010, the largest markets in terms of total pounds a.i. applied were wine grapes (35%), cantaloupes (17%), rice (12%), and watermelons and tomatoes (10% each). The highest total area treated (TAT) were wine grapes (41%), rice (19%), cantaloupes (11%), watermelons (7%), and tomatoes (6%). On average, the states with the most agricultural usage in terms of pounds a.i. applied were California (43%), Arizona (20%), Texas (18%), and Florida (13%).

Recent and Ongoing Actions:

- As a condition of registration for the dinotefuran dog and cat spot-on products, a fur dislodgeability study (GDLN 875.2300) is required and is due January 26, 2013. The Agency has reviewed draft protocols for conducting this study based on the use of spot-on products for dogs and cats; however, submission of the final study remains outstanding. Additionally, this study is needed in support of registration review.

- During the 2011 growing season, seven Section 18 emergency exemptions were granted to control Brown Marmorated Stink Bugs (BMSB) on stone and pome fruit in several states. The emergency exemptions were in effect from April 15 to October 15, 2011.

- On October 31, 2011, a Section 18 emergency exemption for use on rice to control stink bugs, expired and is no longer in effect.

- On September 30, 2011, EPA sent letters to registrants with pet spot-on pesticide products, informing them on how to make necessary label changes for their products. In the spring of 2009, EPA observed a significant increase in incident reports associated with pet spot-on products. EPA investigated this increase, received additional information on those incidents from the pet spot-on pesticide registrants, and conducted an intensive evaluation of the incidents and the pet spot-on products themselves. Examples of label changes EPA believes may be necessary for pet products include: repeating the words “dog” and “cat” throughout the label (as appropriate), including the word “only” with size and breed restrictions, adding “do not allow your dog (or cat) to ingest this product,” incorporating a large, clear picture of the appropriate animal in the weight range for the product as packaged on the front panel of the label, and placing the breed and weight restrictions on the vial itself. EPA expects registrants to submit revised labels addressing all changes described in its letter no later than six months from the receipt of the September 30, 2011 letter. For more information on EPA’s increased restrictions on pet spot-on products, please visit: http://www.epa.gov/pesticides/health/pets.htm

- On April 21, 2011, the Agency received a petition (Petition No. 1E7863) to establish tolerances on the following proposed commodities: low growing berry subgroup 13-07H, except strawberry; watercress; green onion subgroup 3-07B; bulb onion subgroup 3-07A; peach; tuberous and corn vegetable subgroup 1C; small fruit, vine climbing, subgroup 13-07F, except fuzzy kiwifruit; chives; and tea. For further details regarding this pending action, please refer to docket EPA-HQ-OPP-2011-0433.

Ecological Risk Assessment Status:

The key findings of the most recent ecological risk assessments for dinotefuran are summarized below. For a detailed discussion of the ecological risk assessment status, 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*, in the dinotefuran registration review docket EPA-HQ-OPP-2011-0920.

- The most 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 2004 assessment concluded that acute and chronic risk estimates to non-endangered and endangered aquatic and terrestrial organisms (mammals, birds, fish, invertebrates, plants) did not exceed the Agency's level of concern (LOC). The Agency acknowledged that dinotefuran is highly toxic to honey-bees but that the registered uses assessed were not associated with areas high in pollinating insects; and, therefore, not likely to result in exposure to pollinators at that time. Dinotefuran's degradates, DN (1-Methyl-3-(tetrahydro-3-furylmethyl) guanidinium dihydrogen) and MNG (1-Methyl-2-nitroguanidine), were found to be nontoxic to freshwater invertebrates (daphnids) and aquatic plants (green algae).

- The most recent ecological risk assessment in support of FIFRA Section 3 registrations was conducted in May of 2011, for forestry uses (Christmas trees, trees in plantations, reforestation nurseries, forests, and woodland areas). For all application types, except tree injection, the Agency cited the conclusions of its prior risk assessments; and concluded that the forestry uses did not exceed the Agency's LOC for acute risks to non-target terrestrial and aquatic species. In addition, chronic risks did not exceed the Agency's LOC for these taxa, with the exception of estuarine/marine fish and invertebrates (no chronic data were available and, therefore, risk could not be precluded).

- In previous assessments, risk to honey-bees had not been quantitatively assessed. However, given that dinotefuran is highly toxic to bees and is systemic in nature, the Agency identified potential concerns for the possibility of long-term exposure to bees from residues that remain in pollen and nectar of flowering crops. For the tree injection use, the Agency conducted a screening level analysis, which concluded that translocation of dinotefuran from the site of injection to edible parts of a tree may result in effects to birds, mammals, and terrestrial invertebrates. Potential risks to saltwater invertebrates

could not be precluded given the sensitivity of the mysid shrimp to relatively low concentrations of dinotefuran.

- Several ecological risk assessments were completed to assess Section 18 emergency exemptions. The most recent of which, was completed on June 16, 2011 for use on stone and pome fruit to control BMSB. The Agency concluded that there was potential risk to listed terrestrial invertebrates from acute and chronic exposure; and for commercially beneficial insects, all non-target listed terrestrial invertebrates and the organisms that prey on them. Risks to listed and non-listed estuarine/marine invertebrates from chronic exposure could not be precluded, and was thus assumed. Risks were below the Agency's LOC for: non-target birds, reptiles, terrestrial-phase amphibians, mammals, terrestrial plants, estuarine/marine and freshwater fish and invertebrates, and aquatic plants.

Human Health Risk Assessment Status:

The key findings of the most recent human health risk assessments for dinotefuran are summarized below. For a detailed discussion of the human health risk assessment status, please refer to the September 15, 2011 document, *Dinotefuran: Human-Health Assessment Scoping Document in Support of Registration Review*, in docket EPA-HQ-OPP-2011-0920.

- 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 exemption for use on pome and stone fruits to control the BMSB. 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.

Hazard Characterization:

- Available toxicity data indicate that the main target tissues are the nervous system and the spleen/thymus. Nervous system toxicity manifested as clinical signs and decreased motor activity seen after acute dosing (in both rats and rabbits) and increased motor activity seen after repeated dosing. These findings are consistent with effects on the nicotinic cholinergic nervous system. Decreased spleen and thymus weights were observed in all species tested, but no evidence of functional immunotoxicity was observed in recently submitted immunotoxicity (rat and mouse) studies.

- No adverse effects in fetuses were seen in the developmental toxicity studies. There was a qualitative increase in sensitivity in rat pups in the reproductive toxicity study.

- Dinotefuran is not considered to be mutagenic, and it has been characterized by EPA as "not likely" to be a human carcinogen.

- EPA selected toxicity endpoints based on the most sensitive effect, decreased thymus weight (chronic toxicity dog study). An additional 10X uncertainty factor (UF) was applied in the absence of a NOAEL in this study. This endpoint (decreased thymus

weight) has been subject to comprehensive reevaluation (2005 FIFRA Scientific Advisory Panel entitled, *A Comparison of the results of Studies on Pesticides from 1- or 2-year Dog Studies with dog studies of Shorter Duration*) and, as such, may not be appropriate for future dinotefuran risk assessments.

Dietary (Food and Drinking Water):

- In 2011, EPA conducted unrefined acute and partially refined chronic dietary (food and drinking water) exposure assessments for the general U.S. population and various subgroups. Acute and chronic dietary exposure estimates were below EPA's levels of concern for all population subgroups.

Residential:

- In 2011, residential handler and post-application exposure assessments were conducted for all currently registered uses of dinotefuran; risks were below the Agency's level of concern for all assessed uses.

Aggregate:

- In 2011, aggregate exposure assessments were performed for acute and chronic dietary exposure (food and drinking water), and residential intermediate-term exposure to children (from dermal and incidental oral exposures) and adults (from dermal and inhalation exposures). Risks were below the Agency's level of concern for all assessed uses.

Occupational:

- In 2011, occupational handler and post-application exposure assessments were conducted for all registered uses. Risks were below the Agency's level of concern for all assessed uses.

Human Studies:

- Past dinotefuran risk assessments rely in part on data from studies in which adult human subjects were intentionally exposed to a pesticide to determine their dermal and inhalation exposure. Many such studies, involving exposure to many different pesticides, comprise generic pesticide exposure databases such as the Pesticide Handlers Exposure Database (PHED) and the Agricultural Reentry Task Force (ARTF) Database. EPA has reviewed all the studies supporting these multi-pesticide generic exposure databases, and has found no clear and convincing evidence that the conduct of any of them was either fundamentally unethical or significantly deficient relative to the ethical standards prevailing at the time the research was conducted. All applicable requirements of EPA's Rule for the Protection of Human Subjects of Research (40 CFR Part 26) have been satisfied, and there is no regulatory barrier to continued reliance on these studies.

Cumulative:

- EPA has not yet determined whether or not dinotefuran shares a common mechanism of toxicity with any other chemical substances. If the Agency determines that new information on dinotefuran is available that could potentially affect a cumulative risk assessment and result in a risk of concern, the Agency will revisit the need for a cumulative assessment.

Incidents:

- A summary report listing reported human incidents for dinotefuran has been provided in the docket item entitled *Dinotefuran: Review of Human Incidents*, July 26, 2011. The Agency consulted the Office of Pesticide Programs (OPP) Incident Data Systems (IDS) for pesticide incident data on the active ingredient dinotefuran. In Aggregate IDS, from January 1, 2006 to June 13, 2011, 94 incidents involving dinotefuran were identified. Aggregate IDS only includes counts of incidents classified as "minor," "unknown," or "no effects," and no additional details about the incidents are provided. For the main IDS, from January 1, 2006 to June 13, 2011, three cases were reported for the single chemical dinotefuran (classified as moderate severity); and two incidents involving more than one chemical were reported. Based on the low frequency and severity of incident cases, there does not appear to be a concern at this time that would warrant further investigation. However, the Agency will continue to monitor the incident information for dinotefuran and will conduct additional analyses if needed.

- The Agency has conducted a preliminary review of the Ecological Incident Information System (EIIS), which is maintained by OPP, and the Avian Monitoring Information System (AIMS), which is maintained by the American Bird Conservancy. No incidents have been reported in which dinotefuran has been associated with some type of environmental effect.

Tolerances and International Harmonization:

- Tolerances are established for residues of dinotefuran under 40 CFR §180.603 for use on various food and feed crops. 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.

- A time-limited tolerance for residues of dinotefuran in and/or on rice is established under 40 CFR §180.603, which is scheduled to expire on December 31, 2012.

Data Call-In Status:

- No Data Call-Ins (DCIs) have previously been issued for dinotefuran.

Labels:

- Dinotefuran Section 3 product labels can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home

III. SUMMARY OF ANTICIPATED DATA GAPS – Dinotefuran

The table below summarizes all anticipated data needs for dinotefuran identified in Section I of this document (Preliminary Work Plan), the *Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Dinotefuran*, dated December 13, 2011, and the *Dinotefuran: Human-Health Assessment Scoping Document in Support of Registration Review*, dated September 15, 2011.

Table 1. Summary of Current Data Gaps for Dinotefuran

Guideline Number	Anticipated Data Requirement	Test Material	Study Duration[5]
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)[6]	TGAI	12
850.3040	Field Testing for Pollinators[7]	TEP	24
Non-Guideline (Special Study)	Pollinator Larval Toxicity Study[8]	TGAI	12
Non-Guideline (Special Study)	Laboratory Pollinator Chronic Feeding Study[8]	TGAI	12
Non-Guideline (Special Study)	Residues in Pollen and Nectar/Field Residue Analysis[8, 9]	TGAI; Degra.	36
875.2300	Fur Dislodgeability Study	TGAI	1/26/2013[10]

[5] Measured from receipt of DCI

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

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

[8] The anticipated DCI will provide that the registrant is to consult with the Agency prior to initiation of these studies and 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 has satisfied the anticipated Agency data requirements.

[9] 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.

[10] The Fur Dislodgeability Study, in addition to being a data gap for the registration review of dinotefuran is required as a condition of a previous dinotefuran registration. Conditions stipulated a due date of January 26, 2013 and the Agency still requires the study by this date.