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Emamectin Benzoate
Summary Document
Registration Review: Initial Docket
June 2011

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Case # 7607

Approved By:

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Date

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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 the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Emamectin Benzoate*. June 23, 2011.

2. *Emamectin Benzoate. Human Health Assessment Scoping Document in Support of Registration Review*. June 16, 2011.

3. *Emamectin Benzoate: Review of Human Incidents.* March 1, 2011.

4. *Emamectin Benzoate California Department of Pesticide Regulation Usage Data*. July 14, 2010.

5. *Emamectin Benzoate Screening Level Usage Analysis (SLUA).* July 29, 2010.

6. *PRD Appendix A: Food/Feed & Non-Food/Non-Feed Uses Considered in Registration Review Work Planning. Emamectin Benzoate*. October 26, 2010.

Supporting documents for the registration review of emamectin benzoate are located in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov.

I. PRELIMINARY WORK PLAN

Introduction

The Food Quality Protection Act (FQPA) 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 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 emamectin benzoate.

Emamectin benzoate is an insecticide and miticide currently registered for agricultural use on tree nuts and a variety of vegetable crops. Emamectin benzoate also has registered non-agricultural use on ornamental nonbearing trees as a tree injection for borers and for commercial industrial indoor sites as a ready-to-use cockroach bait. There are currently no residential uses or uses expected to result in direct residential exposure. Emamectin benzoate was first registered in the U.S. in 1999; therefore, it was not subject to the reregistration requirements of FIFRA.

Anticipated Risk Assessment and Data Needs

The Agency anticipates conducting comprehensive human health and ecological risk assessments, including an endangered species risk assessment, for all uses of emamectin benzoate. The Agency anticipates needing data for use in conducting these assessments. Below is a summary of the issues relevant to the registration review of emamectin benzoate and a list of the anticipated data requirements.

Ecological Risk:

- The most recent ecological risk assessments for emamectin benzoate were conducted in 1998 in support of the first registration of this chemical, in 2005 in support of its use on pome fruit, and in 2010 in support of the request for expansion of tree species for the tree injection use to control arthropod pests.

- The Agency anticipates conducting an updated environmental fate and ecological risk assessment for emamectin benzoate, including an endangered species assessment, during registration review. The new assessment will incorporate the most up-to-date modeling methodologies, updated toxicological endpoints, and any new data submitted and determined to be adequate.

- The Agency has not conducted a risk assessment that supports a complete endangered species determination for emamectin benzoate. The ecological risk assessment planned during registration review will allow the Agency to determine whether emamectin benzoate's 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 (USFWS) and/or National Marine Fisheries Service (NMFS) (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 EPA for allegedly failing to undergo consultation with the USFWS and the NMFS regarding the effects of over 350 pesticides, including emamectin benzoate, on over 200 endangered and threatened species throughout the U.S. (Center for Biological Diversity, et al. v. EPA, et al., No. C 11-00293 (N.D.Cal.).

- The environmental fate database for emamectin benzoate is currently considered complete; however, data gaps exist in the ecological toxicity database. The Agency anticipates needing the following data for use in conducting a complete ecological risk assessment, including an endangered species assessment, for emamectin benzoate:

  <u>Ecological Toxicity – Aquatic Data</u>
  - Non-Guideline Study – Special Study – Chronic Sediment Toxicity
    - Test Method 100.4: *Hyalella azteca* 42-d Test for Measuring the Effects of Sediment Associated Contaminants on Survival, Growth, and Reproduction in USEPA 2000 Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates EPA 600/R-99/064

- Test Method 100.5: Life cycle Test for Measuring for Measuring the Effects of Sediment-associated Contaminants on *Chironomus dilutus* (formerly known as *C. tentans*) in USEPA 2000 Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates EPA 600/R-99/064
- *Leptocheirus plumulosus* in USEPA 2001 Method for Assessing the Chronic Toxicity of Marine and Estuarine Sediment-associated Contaminants with the Amphipod *Leptocheirus plumulosus* EPA 600/R-01/020

- Guideline No. 850.1075 – Fish Acute Toxicity Test, Freshwater (bluegill sunfish, *Lepomis macrochirus*)

<u>Ecological Toxicity – Terrestrial Data</u>

- Guideline No. 850.2100 – Avian Acute Oral Toxicity (passerine species)
- Guideline No. 850.4100 – Nontarget Area Phytotoxicity Tier II, Seedling Emergence (with TEP)[1]
- Guideline No. 850.4150 – Nontarget Area Phytotoxicity Tier II, Vegetative Vigor (with TEP)[2]
- Non-Guideline Study – Special Study – Acute Oral Honeybee
- Non-Guideline Study – Special Study – Magnitude of Residues Study: Field Residue Analysis of Edible Parts of Trees/Plants (Whole Flowers, Leaves, Fruit, Seeds, Pollen, and Nectar [from flowers and, if present, extrafloral nectarines])

- The Agency seeks additional information, particularly use and usage information, for use in conducting a refined, complete ecological risk assessment, including an endangered species assessment for emamectin benzoate. For further details, see the "Guidance for Commenters" section below.

- Please refer to *Registration Review – Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Emamectin Benzoate*, dated June 23, 2011, located in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov, for a more detailed discussion of the anticipated ecological risk assessment and data needs.

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[1] A Tier II study is expected to be required. The DCI expected to be issued will provide that a Tier I plant study may be conducted in lieu of a Tier II study with the understanding that any adverse effects observed by the Tier I study would necessitate conduct and submission of a Tier II study as well. The purpose of a Tier II study is to establish both a definitive No Observed Adverse Effect Concentration (NOAEC), or alternatively, a concentration at which there is a 5% observed inhibition effect (IC_{05}) to be used in a risk assessment and effects determination for endangered or threatened species (listed species), and a definitive IC_{25} (concentration at which there is a 25% observed inhibition effect) for assessing risk to non-listed nontarget plants. If any adverse effects are observed in a Tier I study and neither a definitive NOAEC nor a definitive IC_{05} value is available, then the Agency may have to presume in its effects determination, that Emamectin benzoate "may affect" and is "likely to adversely affect" listed plant species

[2] See footntote 1.

Human Health Risk:

- The most recent human health risk assessments were conducted in 2005 in support of the use of emamectin benzoate on pome fruit and in 2008 in support of the uses of emamectin benzoate on tree nuts and pistachios, as an injection treatment for ornamental/nonbearing trees, and an occupational assessment for the use as a cockroach bait.

- During registration review, the endpoints, doses, and safety factors used in the most recent human health risk assessments will be revisited based on current policy as well as to incorporate any new data received and determined to be adequate.

- The Agency anticipates conducting updated dietary, aggregate, and occupational exposure risk assessments to include any changes in toxicological endpoints, doses, and procedures for dermal and inhalation risk assessment.

- Based on current registered use patterns of emamectin benzoate and the current toxicological points of departure, the Agency does not anticipate conducting an updated drinking water exposure risk assessment at this time. If, in the future, any new uses are requested or if there is any reason for re-evaluation of the points of departure, a revised dietary (food + water) risk assessment may be needed.

- Currently, there are no registered uses for emamectin benzoate that would result in residential exposure. As such, risks from residential exposures have not been considered in previous assessments nor would they be considered at this time. However, residential bystander inhalation exposures resulting from off-site transport (e.g., spray drift or volatilization) may occur as a result of applications of emamectin benzoate. The Agency is in the process of examining its policies and refining the methods used to complete residential exposure assessments. Therefore, the potential need for a bystander inhalation risk assessment for emamectin benzoate will be examined during registration review.

- During registration review, the Agency anticipates conducting a quantitative occupational postapplication inhalation exposure and risk assessment based on updated doses, endpoints, and procedures for inhalation risk assessment.

- The tolerance expression in 40 CFR §180.505 will be reviewed during registration review to ensure that it appropriately covers the metabolites and degradates of emamectin benzoate and that it specifies the residues to be measured in each commodity. Any proposed revisions likely would be to the chemical description rather than the individual tolerance level(s).

- The toxicity database for emamectin benzoate is complete except for the following studies, which the Agency anticipates requiring for use in conducting an updated human health risk assessment:

  Toxicology Data
  - Guideline No. 870.3465 – 28-Day Inhalation Toxicity
  - Guideline No. 870.7800 – Immunotoxicity

- Please refer to *Emamectin Benzoate. Human Health Assessment Scoping Document in Support of Registration Review*¸ dated June 16, 2011, available in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov, for a detailed discussion of the anticipated human health 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. EPA selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database in 2003 and reviewed the data again in 2008 as part of the most recent emamectin benzoate registration decision. However, as required by FFDCA section 408(p), emamectin benzoate 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. Emamectin benzoate 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 emamectin benzoate. 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

The projected timeline for the completion of the emamectin benzoate registration review is presented in Table 1.

Table 1. Projected Emamectin Benzoate Registration Review Timeline

Activity	Estimated Date
Opening the Docket	
Open Docket and Open Public Comment Period	2011 – June
Close Public Comment Period	2011 – August
Case Development	
Develop Final Work Plan (FWP)	2011 – November
Issue Data Call-In (DCI)	2012 – July – Sept.
Data Submission	2014 – July – Sept.
Develop Preliminary Risk Assessments and Open Public Comment Period	2015 – Jan. – March
Close Public Comment Period	2016 – April – June
Registration Review Decision	
Develop Proposed Registration Review Decision and Open Public Comment Period	2016 – July – Sept.
Close Public Comment Period	2016 – Oct. – Dec.
Issue Registration Review Decision and Begin Post-Decision Follow-up	2017
Total (years)	6

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 the emamectin benzoate case.

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 Maximum Residue Limits (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.

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 emamectin benzoate 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.

Water Quality

Emamectin benzoate is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[3]. In addition, no Total Maximum Daily Loads (TMDLs) have been developed for emamectin benzoate[4]. More information on impaired water bodies and TMDLs can be found at the Agency's website[5]. 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*[6] in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

Other Information

Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining risk assessments, including any species-specific ecological effects determinations, for emamectin benzoate. The Agency is interested in receiving the following information:

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

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*. acreage and geographical distribution of relevant uses/use sites)
3. Use history
4. Median and 90th percentile reported use rates (lbs ai/acre, lbs ai/1000 sq. ft.) from usage data – national, state and county
5. Application timing (date of first application and application intervals) by use – national, state, and county
6. Sub-county use site location data
7. Usage/use information for non-agricultural uses on ornamental nonbearing trees as a tree injection for borers and in commercial industrial indoor sites as a ready-to-use cockroach bait; and information on effective alternatives
8. Directly acquired county-level usage data (not derived from state level data)
    a. maximum reported use rate (lbs ai/acre) 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
9. Typical application interval (days)
10. State or local use restrictions
11. Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian, mammalian mortalities, and bee or beneficial insect mortalities) not already reported to the Agency
12. Monitoring data

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 the registration review of emamectin benzoate. The Agency expects to issue a Final Work Plan for emamectin benzoate in November 2011.

II. FACT SHEET

Background Information

- Registration Review Case Number: 7607.
- Pesticide Chemical (PC) Code: 122806.
- Chemical Abstracts Service (CAS) Numbers:
  - Emamectin: 119791-41-2 (formerly 123997-28-4).
  - Emamectin benzoate: 155569-91-8 (formerly 137512-74-4 and 179607-18-2).
- Emamectin benzoate was first registered in the U.S. in 1999.
- Emamectin benzoate was not subject to reregistration; therefore, there is no Reregistration Eligibility Decision (RED) for emamectin benzoate.
- Currently, the technical registrant for emamectin benzoate is Syngenta Crop Protection, LLC.
- Currently, there are seven Section 3 registrations for emamectin benzoate, including two technical products, one manufacturing use product (MUP), and five end-use products (EUPs).
- U.S. tolerances for emamectin benzoate currently range from 0.002 ppm to 0.2 ppm [40 CFR §180.505].
- Pesticide Re-evaluation Division (PRD) Contact: Katherine St. Clair (stclair.katherine@epa.gov).
- Registration Division (RD) Contact: Tom Harris (harris.thomas@epa.gov).

Use and Usage Information

For additional details, please refer to *Emamectin Benzoate California Department of Pesticide Regulation Usage Data*, dated July 14, 2010; *Emamectin Benzoate Screening Level Usage Analysis (SLUA)*, dated July 29, 2010; and *PRD Appendix A: Food/Feed & Non-Food/Non-Feed Uses Considered in Registration Review Work Planning. Emamectin Benzoate (122806).*, dated October 26, 2010; located in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov.

- Emamectin benzoate is currently registered for agricultural uses to control insects on a variety of tree nut and vegetable crops.

- Registered non-agricultural use sites for emamectin benzoate include ornamental nonbearing trees as a tree injection for borers to control arthropod pests as well as commercial industrial indoor sites as a ready-to-use cockroach bait.

  All emamectin benzoate EUPs are Restricted Use pesticides (for retail sale to and use only by certified applicators or persons under their direct supervision, and only for those uses covered by the certified applicator's certification), except for one ready-to-use cockroach bait product for commercial industrial indoor use.

- Emamectin benzoate formulation types include soluble granular products for use on various terrestrial food/feed crops, emulsifiable concentrates for use on cotton and tobacco and for tree injection, and ready-to-use gels for use as a cockroach bait,.

- Emamectin benzoate application methods for terrestrial crops include multiple foliar sprays using ground equipment, aircraft, or airblast equipment (for orchards).

- Agricultural usage of emamectin benzoate is mainly on apples, broccoli, cabbage, cauliflower, celery, lettuce, pears, peppers, and tomatoes, and it fluctuates from year to year. According to July 2010 screening level estimates of the agricultural uses of emamectin benzoate in the U.S., the largest agricultural use is on apples, with approximately 1,000 pounds of ai used annually in 2010, an average of 10 percent of the crop treated, and a maximum of 20 percent of the crop treated. Screening level estimates do not include non-agricultural uses.

Recent and Pending Actions

- There were 12 Section 24c Special Local Need (SLN) registrations for emamectin benzoate which were voluntarily cancelled by the registrant on March 12, 2010.

- The Agency approved a request for expansion of the emamectin benzoate tree injection use to a variety of trees and pests in 2011.

Ecological Risk Assessment Status

The following are key findings from the most recent ecological risk assessments regarding the environmental fate, ecological effects and risks of emamectin benzoate. Please refer to *Registration Review – Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Emamectin Benzoate,* dated June 23, 2011, located in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov, for a detailed discussion.

- The most recent ecological risk assessments for emamectin benzoate were conducted in 1998 in support of the first registration of this chemical, in 2005 in support of its use on pome fruit, and in 2010 in support of the request for expansion of tree species for the tree injection use to control arthropod pests.

Ecological Effects:

- Based on toxicity data and other information gathered to date, the acute risks of concern from the use of emamectin benzoate are primarily related to direct effects on terrestrial birds, mammals, terrestrial invertebrates (acute contact basis), freshwater and saltwater fish, and freshwater and saltwater invertebrates.

- Based on toxicity data and other information gathered to date, the chronic risks of concern from the use of emamectin benzoate are primarily related to direct effects on mammals, freshwater and saltwater fish, and freshwater and saltwater invertebrates.

- There are potential risks to nonvascular plants from the use of emamectin benzoate. Potential risks to listed and non-listed species of non-target terrestrial plants have not been quantitatively assessed because there is no acceptable data available to assess risk to these taxa.

Human Health Risk Assessment Status

The following are key findings from the human health risk assessments conducted for emamectin benzoate registered uses. Please refer to *Emamectin Benzoate. Human Health Assessment Scoping Document in Support of Registration Review*¸ dated June 16, 2011, located in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov, for a detailed discussion of the human health risk assessment status.

- The most recent human health risk assessments were conducted in 2005 in support of the use of emamectin benzoate on pome fruit and in 2008 in support of the uses of emamectin benzoate on tree nuts and pistachios, as an injection treatment for ornamental/nonbearing trees, and an occupational assessment for the proposed commercial use as a cockroach bait.

Hazard Characterization:

- The acute toxicity of technical grade emamectin benzoate is low to moderate via the oral, dermal, and inhalation routes of exposure, depending on the test substance. It is a severe eye irritant, but not a skin irritant. It is not a skin sensitizer.

- Emamectin benzoate has been classified as "not likely to be carcinogenic in humans." There is no mutagenicity concern for emamectin benzoate based on the available data.

Summary of Risks:

Dietary (Food and Drinking Water)

- Acute and chronic non-cancer dietary (food and drinking water) risk estimates for emamectin benzoate were below the Agency's level of concern for the general U.S. population and all population subgroups. Emamectin benzoate was classified as "not likely to be carcinogenic to humans." Therefore, a cancer dietary risk assessment was not conducted for emamectin benzoate.

Residential

- Emamectin benzoate is not registered for use in residential settings and there is currently no risk concern for residential exposure.

Aggregate

- Since a residential risk assessment was not conducted for emamectin benzoate, acute and chronic aggregate risks were equivalent to acute and chronic dietary (food and drinking water) risks and were below the Agency's level of concern.

Occupational

- All occupational handler dermal and inhalation exposures and risks were previously assessed based on current Agency policies. All scenarios resulted in dermal and inhalation exposure risk estimates below the Agency's level of concern based on use of the personal protective equipment (PPE) required by the product label.

- All occupational postapplication dermal exposures and risks have been previously assessed based on current Agency policies. All scenarios resulted in dermal exposure risk estimates below the Agency's level of concern.

Cumulative

- The Agency has not determined whether emamectin benzoate shares a common mechanism of toxicity with other chemical substances. If, in the future, EPA obtains new data suggesting that emamectin benzoate shares a common mechanism of toxicity with other chemical substances, the Agency will revisit the need for a cumulative risk assessment.

Human Studies

- Past emamectin benzoate 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 (40 CFR Part 26) have been satisfied, and there is no regulatory barrier to continued reliance on these studies.

Incidents

Ecological Incidents:

- The Agency reviewed the Ecological Incident Information System (EIIS), which is maintained by the EPA Office of Pesticide Programs (OPP), and the Avian Monitoring System (AIMS), which is maintained by the American Bird Conservancy, for ecological incident reports associated with the use of emamectin benzoate in the U.S. There were no reported ecological incidents associated with the use of emamectin benzoate. A review of the OPP Aggregate Incident Report database also yielded no ecological incident reports for emamectin benzoate.

- Although no incidents have been reported to the Agency, the absence of reported incidents should not be construed as the absence of incidents.

Human Health Incidents:

- The Agency reviewed the OPP Incident Data System (IDS) for human health pesticide incident data associated with the use of emamectin benzoate in the U.S. to identify potential patterns on the frequency of health effects attributed to emamectin benzoate exposure. The IDS aggregate summaries from January 1, 2002 to February 1, 2011 include two minor cases reported for emamectin benzoate. There were no incidents reported to the IDS resulting in higher severity outcomes from January 1, 2002 to February 1, 2011.

- Based on the low frequency and low severity of incident cases reported in the OPP IDS, there does not appear to be a concern at this time that would warrant further investigation

of emamectin benzoate human health incidents in the preliminary risk assessment phase of registration review. However, the Agency anticipates continuing to monitor the incident information and including additional analysis in the registration review risk assessment if a concern is triggered.

Tolerances and International Harmonization

- U.S. tolerances for emamectin benzoate are established for residues of emamectin benzoate and its metabolites in or on the crop and livestock commodities listed in 40 CFR §180.505.

- A table listing the differences between U.S. tolerances and Canadian, Mexican, and CODEX Maximum Residue Limits (MRLs) for emamectin benzoate is included in the *Emamectin Benzoate. Human Health Assessment Scoping Document in Support of Registration Review*¸ dated June 16, 2011, available in docket EPA-HQ-OPP-2011-0483 at www.regulations.gov. Currently, there are no harmonization issues with Canada, CODEX, or Mexico. During registration review, if any Codex MRLs have been established, the Agency anticipates harmonizing the U.S. tolerances with the Codex MRLs when the data warrant harmonization.

Data Call-Ins

- No DCIs have been issued for emamectin benzoate.

Labels

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

III. SUMMARY OF DATA GAPS

A summary of the anticipated data needs for the emamectin benzoate registration review is presented in Table 2.

Table 2. Summary of Anticipated Data Needs for Emamectin Benzoate

Guideline Number	Anticipated Data Requirement	Test Material	Study Duration
Non-Guideline	Special Study – Chronic Sediment Toxicity Test Method 100.4: *Hyalella azteca* 42-d Test for Measuring the Effects of Sediment Associated Contaminants on Survival, Growth, and Reproduction in USEPA 2000 Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates EPA 600/R-99/064	TGAI	24
Non-Guideline	Special Study – Chronic Sediment Toxicity Test Method 100.5: Life cycle Test for Measuring for Measuring the Effects of Sediment-associated Contaminants on *Chironomus dilutus* (formerly known as *C. tentans*) in USEPA 2000 Methods for Measuring the Toxicity and Bioaccumulation of Sediment-associated Contaminants with Freshwater Invertebrates EPA 600/R-99/064	TGAI	24
Non-Guideline	Special Study – Chronic Sediment Toxicity *Leptocheirus plumulosus* in USEPA 2001 Method for Assessing the Chronic Toxicity of Marine and Estuarine Sediment-associated Contaminants with the Amphipod *Leptocheirus plumulosus* EPA 600/R-01/020	TGAI	24
850.1075	Fish Acute Toxicity Test, Freshwater (bluegill sunfish, *Lepomis macrochirus*)	TGAI, TEP	12
850.2100	Avian Acute Oral Toxicity (passerine species)	TGAI	12
850.4100	Nontarget Area Phytotoxicity Tier II, Seedling Emergence[7]	TEP	12
850.4150	Nontarget Area Phytotoxicity Tier II, Vegetative Vigor[8]	TEP	12
Non-Guideline	Special Study – Acute Oral Honeybee	TGAI	12

[7] A Tier II study is expected to be required. The DCI expected to be issued will provide that a Tier I plant study may be conducted in lieu of a Tier II study with the understanding that any adverse effects observed by the Tier I study would necessitate conduct and submission of a Tier II study as well. The purpose of a Tier II study is to establish both a definitive No Observed Adverse Effect Concentration (NOAEC), or alternatively, a concentration at which there is a 5% observed inhibition effect (IC_{05}) to be used in a risk assessment and effects determination for endangered or threatened species (listed species), and a definitive IC_{25} (concentration at which there is a 25% observed inhibition effect) for assessing risk to non-listed nontarget plants. If any adverse effects are observed in a Tier I study and neither a definitive NOAEC nor a definitive IC_{05} value is available, then the Agency may have to presume in its effects determination, that Emamectin benzoate "may affect" and is "likely to adversely affect" listed plant species.

[8] See footnote 7.

Guideline Number	Anticipated Data Requirement	Test Material	Study Duration
Non-Guideline	Special Study – Magnitude of Residues Study: Field Residue Analysis of Edible Parts of Trees/Plants (Whole Flowers, Leaves, Fruit, Seeds, Pollen, and Nectar [from flowers and, if present, extrafloral nectarines])	TEP	24
870.3465	28-Day Inhalation Toxicity	TGAI	12
870.7800	Immunotoxicity	TGAI	12