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Imidacloprid Summary Document
Registration Review: Initial Docket
December 2008

Registration Review Case No. 7605
PC Code 129099

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Director
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Date: 12/11/08

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Please Note

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

1. EFED Preliminary Problem Formulation for the Registration Review of Imidacloprid (December, 2008)

2. HED Human Health Risk Scoping Document in Support of Registration Review of Imidacloprid (November, 2008)

3. Imidacloprid Screening Level Usage Analysis (SLUA) (March, 2008)

Additional supporting documents for imidacloprid may be found in the docket EPA-HQ-OPP-2008-0844, which may be found on the internet at www.regulations.gov.

I. Preliminary Work Plan

Introduction

The Food Quality Protection Act of 1996 mandated a registration review program. All pesticides distributed or sold in the United States generally must be registered by the EPA, based on scientific data showing that they will not cause unreasonable risks to human health, workers or the environment when used as directed on product labeling. The registration review program is intended to ensure 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. 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 the change occurs, products in the marketplace can be used safely. Information on this program is provided at the following website: http://www.epa.gov/oppsrrd1/registration_review/.

The Agency has begun to implement the registration review program and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. 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 is knows about the pesticide and what additional risk analyses and data or other 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 imidacloprid.

Imidacloprid is systemic neonicotinoid nitroguanidine insecticide used on food crops, ornamentals, turf, seed treatments, domestic pets, and structural pests. Imidacloprid's mode of toxic action is the disruption of the nervous system by acting as an inhibitor at nicotinic acetylcholine receptors. It was first registered for use in 1994, and as a result was not reviewed under the reregistration process.

Anticipated Risk Assessment and Data Needs

Ecological Risk:

- The most recent ecological risk assessment for all registered uses was conducted in October 2007. However, the Agency has not conducted a risk assessment that supports a complete endangered species determination for imidacloprid.

- An ecological risk assessment for all registered uses will be conducted as part of registration review including a risk assessment that supports a complete endangered species determination.

- In light of the current database and the high toxicity of imidacloprid to aquatic organisms and bees, the Agency anticipates needing the following data in order to conduct a

complete ecological risk assessment, including an endangered species assessment, for all uses:

- (GLN 835.4300) Aerobic aquatic soil metabolism study using TGAI imidacloprid.
- (GLN 850.3040) Field test for pollinators using TEP imidacloprid.
- (Special Study) Repeat dose field study for pollinators.
- (GLN 850.4100) Tier 1 seedling emergence study (Tier 1) using TEP imidacloprid.
- (GLN 850.4150) Tier 1 vegetative vigor study using TEP imidacloprid.
- (GLN 850.4400) Tier 1 aquatic plant growth study using TGAI imidacloprid.
- (Special Study) Seed leaching study using TEP imidacloprid.

- Data reviewed by EPA indicates that imidacloprid is highly toxic to honeybees on an acute exposure basis; however, there is uncertainty regarding the potential chronic effects of imidacloprid on the honeybee colony. As part of the Registration Review process, the Agency is requiring field-based data on imidacloprid to better understand its potential impact on pollinators. In addition, EPA will be working with Federal and State officials, (such as USDA and California Department of Pesticide Regulation), as well as the international community and other stake holders to develop data and to better understand the potential impact of neonicotinoid insecticides, such as imidacloprid, on pollinators using honeybees as a surrogate. EPA is committed to a comprehensive review of the all available data and information and to proceeding in a deliberate manner so that actions to protect pollinators are based on sound science. Please refer to the following web page for additional information: http://www.epa.gov/pesticides/about/intheworks/honeybee.htm.

- The planned ecological risk assessment will allow the Agency to determine whether imidacloprid's use has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitats. If the assessment indicates that imidacloprid "may affect" a listed species or its designated critical habitat, the assessment will be refined. The refined assessment will allow the Agency to determine whether use of imidacloprid is "likely to adversely affect" the species or critical habitat or "not likely to adversely affect" the species or critical habitat. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, whether those effects are likely or not likely, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Services (the Services), as appropriate.

- Please refer to, *EFED Problem Formulation for the Registration Review of Imidacloprid*, for a detailed discussion of the anticipated risk assessment needs.

Human Health Risk:

- The most recent HED human-health risk assessment was completed in May 2007, and reflects current registrations and uses of imidacloprid, current FQPA policies, and addresses susceptibility of infants and children, and aggregate exposures.

- Human health risk assessments for imidacloprid conducted in 2007, including dietary, occupational, non-occupational and aggregate, did not indicate any risks of concern.

- The imidacloprid residue chemistry database is sufficient to support the current registrations.

- The existing hazard data base for imidacloprid does not include any immunotoxicity data, and while traditional chronic and subchronic rodent studies provide useful information on certain immunological endpoints, they do not provide a full and integrated evaluation of the immune system. Therefore, an immunotoxicity study will be required.

- In addition, exposure data (a wood wipe/leaching study) will be required to reassess non-dietary exposure from residential post-application scenarios (i.e., hand-to-mouth exposure from treated lumber). Therefore, the Agency will need for the following data to revise the human health risk assessment for imidacloprid.
    - (GLN 870.7800) Immunotoxicity study using TGAI.
    - (Special Study) Post-application wood wipe and leaching study

- While the existing dietary exposure assessment could likely support Registration Review, new toxicity data may require that the dietary risk assessment be revised.

- Similar to the dietary exposure scenario for imidacloprid, the existing residential exposure scenario is likely to support Registration Review. However, receipt of a post-application wood-wipe/leaching study may require reassessment of certain post-application exposure scenarios.

- A new occupational assessment will be required to support registration review to assess additional scenarios not previously assessed.

- Since imidacloprid is used on domestic pets and has residential indoor uses, a companion animal risk assessment, including an analysis of pet incidents, will be part of the registration review of imidacloprid.

Timeline

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

Activities	Estimated Month/Year
Phase 1: Opening the Docket	
Open Public Comment Period for Imidacloprid Docket	2008– Dec.
Close Public Comment Period	2009– Mar.
Phase 2: Case Development	
Final Work Plan (FWP)	2009– May
Issue DCI	2010– Jan.-Mar.
Data Submission	2012– Jan.-Mar.
Preliminary Risk Assessment & Public Comment	2013– Jul.-Sep.
Close Public Comment Period	2013– Oct.-Dec.
Phase 3: Registration Review Decision	
Open Public Comment Period for Proposed Reg. Review Decision	2014– Jan.-Mar.
Close Public Comment Period	2014– Apr.-Jun
Final Decision and Begin Post-Decision Follow-up	2014– Jul-Sept.
Total	6 years

Guidance for Commenters

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

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. There are 161 permanent U.S. tolerances for imidacloprid and its metabolites and currently two FIFRA Section 18 emergency tolerances. The Codex Alimentarius Commission has established MRLs for residues of imidacloprid. Please refer to Attachment 2, *Imidacloprid Human Health Risk Scoping Document in Support of Reregistration Review*, for more information on MRLs.

Imidacloprid is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://oaspub.epa.gov/tmdl/waters_list.impairments?p_impid=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* (see: http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-

sop.pdf), in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

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 or unusually high exposure to imidacloprid, compared to the general population. Please comment if you are aware of any sub-populations that may have atypical or unusually high exposure compared to the general population.

Imidacloprid is very toxic to honey bees and other beneficial insects. Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining its ecological risk assessment, including any species-specific effects determinations. In addition, the Agency is interested in suggestions from stakeholders on ways to reduce honeybee exposure to imidacloprid.

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 in units related to mass per unit area of treatment zone
    e. frequency of application, application intervals, and maximum number of applications per season
    f. geographic limitations on use
2. use or potential use distribution (e.g., acreage and geographical distribution of relevant crops)
3. use history
4. median and 90th percentile reported use rates (lbs ai/acre) from usage data – national, state, and county
5. application timing (date of first application and application intervals) by crop – national, state, and county
6. sub-county crop location data
7. usage/use information for non-agricultural uses (e.g., forestry, residential, rights-of-way)
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. percent crop 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 interval (days)
10. state or local use restrictions

11. ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
12. monitoring data

Next Steps

After the 90-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 imidacloprid.

II. Fact Sheet

Background Information

- **Imidacloprid** is the only chemical involved in registration review case number 7065
- Imidacloprid PC Code: 129099 CAS#: 138261-41-3
- Technical Registrants:
  - Bayer CropScience LP (Company No. 264)
  - Laxness Corp. (Company No. 39967)
  - Albaugh Inc. (Company No. 42750)
  - Control Solutions Inc. (Company No. 53883)
  - United Phosphorus, Inc. (Company No. 70506)
  - NuFarm Inc. (Company No. 71368)
  - Rotam Ltd. (Company No. 81598)
  - Etigra LLC (Company No. 81959)
  - Sharda Worldwide Exports Pvt. Ltd. (Company No. 82633)
  - Ensystex III Inc. (Company No. 82957)
  - Amtide LLC (Company No.83851)
- Imidacloprid was first approved for use in a registered product in 1994.
- There are currently 397 FIFRA Section 3 Registrations, 12 of which are technicals and 38 FIFRA Section 24(c) special local need registrations for imidacloprid.
- Special Review and Reregistration Division Chemical Review Manager (CRM): Rusty Wasem wasem.russell@epa.gov
- Registration Division Product Manager (PM): Venus Eagle eagle.venus@epa.gov

Use & Usage Information

- Imidacloprid is systemic neonicotinic insecticide used to control soil insects, sucking insects, chewing insects, and termites.
- Imidacloprid is used on food, feed, seed, and for other non-food/non-feed uses.
- Imidacloprid is sold in the following formulations: dry flowable, dust, emulsifiable concentrate, soluble concentrate, granular, impregnated material, liquid, pelleted/tableted, plant spikes, ready to use liquid, water dispersible granule, and wettable powder.
- Residential uses of imidacloprid include the following uses: residential lawns, turf, golf courses, ornamental plantings, pets, and pre- and post construction uses as a termiticide and wood preservative.
- The greatest agricultural poundage of imidacloprid is used on corn, which only represents 1-2.5% of crop treated.
- Other primary use sites of imidacloprid include: lettuce, where 60-80% is treated with approximately 30,000 lbs a.i.; broccoli, where 35-55% is treated with approximately 9,000 lbs a.i.; apples, where 25-40% is treated with approximately 9,000 lbs a.i.; and, potatoes, where 35-40% is treated with approximately 50,000 lbs a.i..

(For additional details, please refer to the Attachment 3, Imidacloprid Screening Level Usage Analysis (SLUA))

Recent Actions

- In April 2007 and March 2006, drinking water exposure assessments for imidacloprid on proposed new uses were completed.
- In May 2007 and April 2006, EFED ecological risk assessments for proposed and registered uses were completed.
- In April 2007 and June 2006, HED human health risk assessments for proposed and registered uses were completed.

Ecological Risk Assessment Status

The following ecological outcomes are anticipated based on the data and risk assessments currently available. Please refer to Attachment 1, *EFED Problem Formulation for the Registration Review of Imidacloprid*, for a detailed discussion of the anticipated ecological risk assessment needs. A summary follows:

- Imidacloprid is environmentally persistent, thereby increasing the probability of exposure by non-target organisms.
- Imidacloprid has the potential to cause chronic risk to avian species and small mammals. A screening level ecological assessment indicates that imidacloprid may also pose an acute and chronic risk to both freshwater and estuarine/marine invertebrates. Secondary toxicity to fish is also possible through alteration in food chains based on invertebrates.
- EPA expects to require data to evaluate sublethal risks to bees and other beneficial insects. The Agency's risk assessment will consider indirect effects to plants that rely on bees for pollination and fish that feed on sensitive aquatic invertebrates.

Human Health Risk Status

The following human health outcomes are anticipated based on the data and risk assessments currently available. Please refer to Attachment 2, *Imidacloprid Human Health Assessment Scoping Document in Support of Registration Review*, for a detailed discussion of the anticipated risk assessment needs for human health. A summary follows:

Dietary (Food and Water)

- Use of imidacloprid was previously determined not to present acute or chronic dietary risks that present risk concerns to the Agency.

Residential

- All previously assessed residential handler and post-application exposures and risks do not present risk concerns to the Agency.

Aggregate

- A short-term aggregate risk assessment has been completed which combined dietary (food and drinking water) exposures, residential handler exposures, and residential post-application exposures. The short-term aggregate risk, which OPP believes is conservative enough to adequately cover the intermediate term exposures as well, does not present risk concerns to for the Agency. The Agency has not conducted a long-term aggregate risk assessed for

imidicloprid. However, since long-term exposure is possible due to the pet uses of imidacloprid, a long-term aggregate assessment will be conducted for registration review including adjustments to the dietary assessment.

- A cancer aggregate risk assessment has not been performed. OPP has classified imidacloprid as a "Group E" (no evidence of carcinogenicity to humans) and therefore does not require a cancer risk assessment.

Occupational

- All previously assessed occupational exposure scenarios that have been assessed adequately do not present risk concerns to the Agency. However, several additional occupational scenarios will be assessed in the registration review of imidacloprid.

Incidents

- Environmental Fate and Effects Division (EFED) incident database reports several incidents involving non-target organisms. One incident involved avian species, another involved aquatic invertebrates, and two incidents involved plants (specifically residential lawns). A brief discussion of these incidents can be found in Attachment 1, *EFED Problem Formulation for the Registration Review of Imidacloprid*.

- The OPP Incident Database System (IDS) was searched for human incidents involving imidacloprid. IDS includes reports of incidents from various sources, including mandatory Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) Section 6 (a)(2) reports from registrants, other federal and state health and environmental agencies and individual consumers. Since 2000, approximately 400 incidents involving imidacloprid have been reported. Please refer to *Updated Review of Imidacloprid Incident Reports* in the docket for additional detail on these incidents.

- A comprehensive review of human and ecological incident reports will be conducted during the registration review process.

Tolerances

- CFR §180.472 lists 161 tolerances for imidacloprid and its metabolites containing the 6-chloropyridinyl moiety.

Data Call-In (DCI) Status

- The Agency has not yet issued a DCI for imidacloprid.
- DCI(s) are expected to be issued for imidacloprid during the registration review process.

Labels

A list of registration numbers may be found in the docket and the labels for imidacloprid can then be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

II. Glossary of Terms and Abbreviations

ai	Active Ingredient
AR	Anticipated Residue
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DNT	Developmental Neurotoxicity
DWLOC	Drinking Water Level of Comparison
EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GENEEC	Tier I Surface Water Computer Model
IR	Index Reservoir
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOAEL	Lowest Observed Adverse Effect Level
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking submitted studies.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Ambient Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data

PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
Q_1*	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel
SF	Safety Factor
SLN	Special Local Need (Registrations Under Section 24©) of FIFRA)
TGAI	Technical Grade Active Ingredient
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WPS	Worker Protection Standard