Indole-3-Butyric Acid
Final Work Plan

Registration Review Case 2330
Docket Number EPA-HQ-OPP-2010-0608

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Registration Review Case Number: 2330

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TABLE OF CONTENTS

Indole-3-Butyric Acid (Case Number 2330) Registration Review Team

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I. INTRODUCTION

This Environmental Protection Agency (EPA or the Agency) document is the Final Work Plan for indole-3-butyric acid (IBA), and includes the expected registration review timeline. The Final Work Plan is intended to address any public comments received concerning the Preliminary Work Plan in the Summary Document, which was posted in IBA's registration review docket (EPA-HQ-OPP-2010-0608) on September 29, 2010, as well as other comments concerning the initial docket postings. In the Summary Document, EPA provided information on the Agency's current knowledge of the pesticide and the additional risk analyses and data or information it believes are needed to make a registration review decision.

The Agency is implementing the Registration Review program and will review each registered pesticide every 15 years to determine whether it continues to meet the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) standard for registration. Changes in science, public policy, and pesticide use practices will occur over time. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet that statutory standard. The public phase of registration review begins when the initial docket is opened for each case. Information on this program is provided at: http://www.epa.gov/oppsrrd1/registration_review/.

IBA is a plant growth regulator (PGR), registered for use to promote and accelerate root growth of plant clippings, reduce transplant shock, promote growth development of flowers and fruit, and increase crop yields. Historically, the Agency has classified IBA as a synthetic plant hormone that is structurally related to the naturally-occurring plant growth hormone, indole-3-acetic acid (IAA) (EPA, 1992); however, recent information indicates that IBA occurs naturally in a variety of plant species (EPA, 2010; EPA, 2011). IBA is metabolized into IAA in the human body and IAA is a common metabolite in tryptophan (an amino acid) metabolism in humans (EPA, 1992).

Pesticide products containing IBA were first registered in 1960 for use on ornamental plant cuttings and transplants to promote root growth and to reduce transplantation shock. In 1990, IBA was registered for use on fruit and vegetable crops, field crops, and ornamental turf, to promote growth development of flowers and fruit, and to increase crop yields. In 1992, the Agency published a Reregistration Eligibility Document (RED) and a RED Fact Sheet for IBA. The current exemption from the requirement of a tolerance for residues of IBA and IAA in or on all food commodities was established in 1999 (listed under the auxins group at 40 CFR 180.1158).

Currently, there are a total of 68 EPA registered products containing IBA as their active ingredient (a.i.). Of these, five are registered as technical grade active ingredients/manufacturing-use products (TGAI/MPs), 26 are end-use products (EPs) containing IBA as their sole a.i., and 37 are EPs containing IBA as well as other a.i.s. Registered products with IBA as their only a.i. are used to regulate plant growth on food and ornamental crops. Application methods include dipping to stimulate root growth and foliar spraying to enhance yields. Products containing IBA and additional active ingredients are also labeled for use as root stimulators and yield enhancers, but can also act in accordance with other ais as fungicides, insecticides, and herbicides. Please refer to the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608) for a more detailed discussion.

II. RESPONSES TO COMMENTS

During the 60 day comment period, which closed on November 29, 2010, the Agency received no comments on the Preliminary Work Plan for IBA associated with Registration Review Docket EPA-HQ-OPP-2010-0608.

III. RISK ASSESSMENT AND DATA NEEDS

Product Chemistry

All product chemistry data requirements for IBA have been satisfied. In the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608), the Agency considered the stability to normal and elevated temperatures, metals, and metal ions data requirement (OCSPP Guideline 830.6313) as a data gap. After further review, the Agency finds that this data requirement has been fulfilled by public literature submitted in support of a technical grade active ingredient IBA product (EPA, 2006).

Assessment of these product chemistry data shows that they continue to meet the standard for registration under FIFRA, as amended by the FQPA. No further product chemistry data are required. Please refer to the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608) for a more detailed discussion of the product chemistry.

Human Health Risk Assessment

Based on the available information, the Agency does not foresee the need for new data or a new human health risk assessment. At this time, the labels for the currently registered EPs include the appropriate signal word and precautionary statements, including appropriate personal protection equipment (PPE) requirements. In addition, based on extremely low exposures to those people involved in the use of products that contain IBA and due to the negligible dietary exposures expected from the use of IBA on food and feed crops, human exposure to pesticidal residues of IBA from registered uses is expected to be minimal. The Agency has concluded that unreasonable adverse effects should not result to the U.S. population, including infants and children, from aggregate exposure to residues of IBA, when the registered products are used according to their labels.

All human health data requirements, per 40 CFR 158.2050, have been fulfilled for IBA. Please refer to the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608) for a more detailed discussion of the human health risk assessment.

Environmental Fate and Ecological Risk Assessment

1. Effects on Nontarget Organisms

In the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608), the Agency considered the nontarget insect (OCSPP Guideline 880.4350) data requirement a data gap and indicated that it would further investigate this data requirement and determine whether it can be addressed without the need for a Data Call In (DCI) notice.

The Agency has determined that there is adequate information in the scientific literature to indicate that IBA is practically nontoxic to insects. Nontarget insect toxicity data on a similar chemical, 2,4-dichlorophenoxyacetic acid (2,4-D) will be used to support the data requirement. While IBA is a naturally-occurring plant auxin, 2,4-D is a synthetic auxin and is considered to be more biologically potent than IBA (EPA, 2011). According to the available nontarget insect data in the Agency's ECOTOX database (2011), 2,4-D is considered to be practically nontoxic to honeybees (*Apis mellifera*). These data are summarized in Table 1.0 below.

Table 1.0. Summary of Nontarget Insect Toxicity for 2,4-D (Surrogate for IBA)

Test	Results	Classification	Source
880.4350 Nontarget Insect Testing (*Apis mellifera*)	LD_{10} = 66.3-80.0 LD_{10} = 98.9-119.4 µg/bee LD_{50} = 113.3-117.0 µg/bee LD_{50} = 147.2-151.9 µg/bee LD_{50} > 18.13 µg/org	Practically nontoxic	EPA ECOTOX Database, 2011

IBA is expected to be practically nontoxic to insects. The chemical occurs naturally in a variety of plants, has a nontoxic mode of action, is used in relatively low concentrations and is expected to degrade rapidly in the environment.

With the above information for the nontarget insect data requirement and the nontarget information for the other applicable nontarget data requirements listed in the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608), all nontarget toxicity data requirements for IBA have been fulfilled and meet the standard for registration required under FIFRA, as amended by FQPA. Based on the available information for IBA, the Agency does not foresee the need for additional ecotoxicity data or a new risk assessment. Please refer to the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608) and the EPA Memorandum from A. Gonzales through R. Jones to C. Walsh (EPA, 2011) for a more detailed discussion of the nontarget organism data.

2. Ecological Risk Assessment

Although a quantifiable nontarget organism risk assessment has not been conducted for mammals, birds, insects, or plants, no toxicological concern has been identified and the data available to the Agency indicate that IBA is practically nontoxic to these organisms. Based on the a.i.'s lack of toxicity, nontoxic mode of action, natural occurrence in the environment, current use patterns, expected rapid degradation in the environment, and relatively low concentrations in pesticide products, the Agency believes that a nontarget organism risk assessment is not necessary for terrestrial organisms – mammals, birds, insects or plants. The Agency did conduct risk assessments for aquatic organisms because available data indicate that IBA is slightly toxic to these organisms. These risk assessments are discussed below.

Using the Agency's Generic Estimated Environmental Concentration model (GENEEC) version 2.0 (EPA, 2001), estimated environmental concentrations (EECs) were calculated to assess potential aquatic organism exposure to IBA. Risk quotients (RQs) were calculated using the hazard and EEC data and were determined to be significantly less than the Agency's level of concern (LOC), RQ $\geq$ 0.05, for threatened and endangered aquatic organism species. This information is summarized in Table 2.0 below.

Table 2.0. Determination of Risk Quotients (RQs) for Aquatic Organisms for IBA

Species	LC_{50}	Peak EEC (ppb)	RQ
Aquatic vertebrates: Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} = 90.5 mg/L	12.23	0.00014
Aquatic invertebrates: Water flea (*Daphnia magna*)	48 hr LC_{50} = 55 mg/L	12.23	0.00022

Due to the RQs being significantly lower than the Agency's LOCs for endangered and threatened aquatic organism species, along with the lack of toxicological concern for mammals, birds, insects, and plants, the Agency has determined that there are no risk concerns for all nontarget organisms. Please refer to the Summary Document posted in the initial docket (EPA-HQ-OPP-2010-0608) and the EPA memorandum from A. Gonzales through R. Jones to C. Walsh (EPA, 2011) for a more detailed discussion of the ecological risk assessment.

3. Endangered Species Assessment

Based on IBA's minimal toxicity to terrestrial and aquatic organisms, nontoxic mode of action, natural occurrence in the environment, current use patterns, expected rapid degradation in the environment, and low concentrations in pesticide products, the Agency has concluded that no endangered or threatened species will be affected if products containing IBA are used according to label instructions. Therefore, the Agency has made a "No Effect" (NE) finding for endangered or threatened aquatic or terrestrial organisms, or their designated critical habitats, as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Marine Fisheries Service (NMFS).

IV. ENDOCRINE DISRUPTORS

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 reregistration decision, 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), indole-3-butyric acid 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. indole-3-butyric acid 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 indole-3-butyric acid. 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/.

V. ESTIMATED TIMELINE

EPA has created the following estimated timeline for completion of IBA's registration review case.

Activities	Estimated Month/Year
Phase 1: Opening the docket	
Open Public Comment Period for IBA	September 2010
Close Public Comment Period	November 2010
Phase 2: Case Development	
Final Work Plan (FWP)	March 2011
Phase 3: Registration Review Decision	
Open Public Comment Period for Proposed Reg. Review Final Decision	September 2011
Close Public Comment Period	November 2011
Publish Final Decision and Begin Post-Decision Follow-up	March 2012
*Estimated Total (months)	18 months

* This schedule is subject to revision should unforeseen issues arise during the registration review process.

VI. NEXT STEPS

EPA expects to issue a Proposed Registration Review Final Decision for public comment in September, 2011.

VII. REFERENCES

ECOTOX. 2011. ECOTOX Database for 2,4-dichlorophenoxyacetic acid. January 13, 2011. http://cfpub.epa.gov/ecotox/

EPA. 1992. Reregistration Eligibility Document (RED) and R.E.D. Fact Sheet for Indole-3-Butyric Acid. U.S. Environmental Protection Agency Office of Pesticide Programs. August 1992.
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EPA. 2010. Memorandum from Angela L. Gonzales to Colin G. Walsh. Preliminary Nontarget Organism Risk Assessment for the Registration Review of Indole-3-Butyric Acid. U.S. Environmental Protection Agency Office of Pesticide Programs. August 18, 2010.

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