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OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

December 10, 2004

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MEMORANDUM

SUBJECT: RESPONSE TO PUBLIC COMMENTS. The Health Effects Division's Response to Comments on EPA's HED Chapter of the Fluazifop-P-Butyl Tolerance Reregistration Eligibility Decision Document (09/29/04). PC Code: 122809. Case# 2285. DP Barcode D310696.

FROM: Diana Locke, Ph.D.
Toxicologist
Reregistration Branch II
Health Effects Division (7509C)

THRU: Alan Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division (7509C)

TO: Margaret Rice, Chief
Reregistration Branch II
Special Review and Reregistration Division (7508W)

The attached document titled, *"HED's Response to Comments for Fluazifop-P-butyl,"* was generated in the Phase 3 period of the Proposed Public Participation Process (FR Notice 03/15/00) to address comments submitted by the registrant, Syngenta, to the Agency following the completion of *Fluazifop-P-butyl: HED Chapter of the Tolerance Reassessment Eligibility Document (TRED). PC Code: 122809, Case # 2285, DP Barcode: D299490. September 29, 2004.* The Agency solicited these comments from the registrants as part of procedures to ensure transparency and public participation in reregistration eligibility decision-making. The Agency specifically solicited comments on errors in the original risk assessment, "such as those that are mathematical, computational, or typographical" rather than comments pertaining to "matters of policy, interpretation, or applicability of data." A revised risk assessment (*Fluazifop-P-butyl:*

Revised HED Chapter of the Tolerance Reassessment Eligibility Document (TRED). PC Code: 122809, Case # 2285, DP Barcode: D291903. December 10, 2004) has also been generated that accounts for errors of the first type as submitted by the registrants, and does not address comments of the second type. We believe that this revised assessment is suitable now for public review and comment. The attached document is the Agency's Health Effects Division's (HED) response to those comments. This response includes input from Sherrie Kinard (Residue Chemistry and Dietary Assessment), David Anderson (Toxicology), Margarita Collantes (Occupational and Residential Exposure), Jerry Blondell (Incident Data), and Diana Locke (Risk Assessment).

cc: Carmen Rodia
Debbie Edwards
Jeff Herndon
William Hazel

TABLE OF CONTENTS

I. Introduction . . . . . Page 4 of 10

II. Risk Assessment/HED Chapter . . . . . Page 4 of 10

III. Dietary Risk Assessment . . . . . Page 4 of 10

IV. Residue Chemistry . . . . . Page 5 of 10

V. Metabolism . . . . . Page 7 of 10

VI. Toxicology . . . . . Page 7 of 10

VII. Incident Data . . . . . Page 9 of 10

VIII. Residential/Non-occupational Exposure . . . . . Page 9 of 10

December 10, 2004

HED'S RESPONSE TO COMMENTS FOR FLUAZIFOP-P-BUTYL

I. Introduction

The following is HED's response to comments on the TRED document for fluazifop-P-butyl, generated in response to the comments submitted to the Agency by Syngenta in Phase 2 of the Proposed Public Participation Process. Some of the responses serve as clarification or a restatement of Agency policies and guidance and it is hoped that this will provide a greater understanding of the Agency's position and procedures on these matters. During Phase 1, the HED TRED document on fluazifop-P-butyl was sent to the registrants for error review.

Several issues related to the environmental fate of fluazifop-P-butyl and the generation of drinking water estimates, were raised in the comments and will be addressed in separate documents by the Ecological Fate and Effects Division (EFED).

II. Risk Assessment/HED Chapter

Errors and omissions have been corrected and are reflected in the revised HED chapter, "Fluazifop-P-butyl: Revised HED Chapter of the Tolerance Reassessment Eligibility Document (TRED). PC Code: 122809, Case # 2285, DP Barcode: D291903. December 10, 2004." The details of the corrections can be found in the discipline-specific sections below.

III. Dietary Risk Assessment

Page 4 of "Fluazifop-P-butyl: Acute and Chronic Dietary Exposure Assessments for the Tolerance Reassessment Eligibility Decision (TRED) Document. Sherrie L. Kinard, Chemist, September 29, 2004 DP Barcode: D291906." The footnote of Table 1 has a calculation error (0.003+0.019)/0.0885 = 0.25 (not 0.13).

This was corrected in the dietary assessment.

Page 2 and Page 9, the fourth sentence of the second paragraph reads: "This assessment concludes that for all supported registered commodities, the acute dietary risk estimates are below the Agency's level of concern (<100 % aPAD) for the U.S. population (<2 % aPAD) and all population subgroups at the 95th exposure percentile."

Should be corrected to read: "This assessment concludes that for all supported registered commodities, the acute dietary risk estimates are below the Agency's level of concern (<100 %aPAD) for the Females, 13-49 years old, (<2 % aPAD) and all population subgroups at the 95th exposure percentile, since the US population was not evaluated for acute exposure."

The assessment reads, "Dietary risk estimates are provided for the only population subgroup with an acute dietary endpoint, females 13-49 years of age. This assessment concludes that for all supported registered commodities, the acute dietary risk estimates are below the Agency's level of concern (<100 %aPAD) for females 13-49 years of age (<2 % aPAD) at the 95th exposure percentile." and "This assessment also concludes that for all commodities, the chronic dietary risk estimates are below the Agency's level of concern (<100 % cPAD) for the U.S. population (30% cPAD) and all population subgroups." on page 2. On page 9 the assessment reads, "This assessment concludes that for all supported registered commodities, the acute dietary risk estimates are below the Agency's level of concern (<100 %aPAD) for females 13-49 years of age (<2 % aPAD) at the 95th exposure percentile." and "The chronic assessment concludes that for all supported commodities, the chronic dietary risk estimates are below the Agency's level of concern (<100 %cPAD) for the U.S. population (30% cPAD) and all population subgroups.."

IV. Residue Chemistry

The following comments and responses are specific to the "Fluazifop-P-butyl: TRED - Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decisions. Residue Chemistry Considerations. Case No. 2285. Sherrie L. Kinard, Chemist, August 11, 2004. PC Code: 122809."

The pages of the document need to have page numbers added to them. Please also check the table of contents and include the correct page numbers. Also note that on pages 28, 29, 41, and 42, the following is included: "x/x/04."

The document has page numbers and a Table of Contents with those numbers and page links. The date should read 10/13/04 instead of "x/x/04". This error was corrected.

Page 5 and Page 14, 860.1340 Residue Analytical Methods. No radiovalidation data are available for the enforcement methods; radiovalidation studies should be conducted in conjunction with the required plant and animal metabolism studies. In addition, the registrant must submit a regulatory method for poultry eggs.

Syngenta would like to point out that with respect to the enforcement methods for animal tissues, radiovalidation was reported in studies previously reviewed by the EPA. In the cow feeding study report MRID 00093843 the radiovalidation was reported in section 3.3.1. It stated that the acetonitrile: acetone: hexane 1: 1: 1 v/v used to extract both milk and tissue samples extracted greater than 95% of the total radioactive residue from the milk and greater than 95% of the radioactivity from cow liver. In the hen feeding study report MRID 00093845 the radiovalidation was reported in sections 2.3 and 3.3.1. It stated that the chloroform: methanol 1:1 v/v used to extract egg samples extracted 100% of the radioactivity from eggs. The extraction solvent of chloroform: methanol 1:1 v/v used to extract the chicken tissue samples was shown to extract 95% of the radioactivity from cow liver. The hydrolysis conditions used in the methods cleaved >90% of the lipophilic ester conjugates in bovine milk and hen egg yolk from the radiolabeled

studies. Please note that the two reports mentioned above (MRID's 00093843 and 00093845) are not cited directly in the bibliography starting on page 36 of the Residue Chemistry review, but the Phase 3 summaries of these reports are included in the bibliography as MRID's 92067044, 92067042, 92067043, and 92068021.

These studies were only summarized and determined to be eligible for review; but were not yet reviewed. These studies are currently under review. Once the data are reviewed, the data requirement will be updated accordingly.

With respect to the requirement for submission of a regulatory method for eggs, an egg analytical method is listed in the bibliography on page 40 of the review, i.e. 92068040: Atreya, N. (1990) ICI Americas Inc. Phase 3 Summary of MRID 0093845. The Determination of Residues of Fluazifop-butyl (PP009): Fluazifop and Conjugate Esters of Fluazifop in Eggs and Chicken Tissue: Plant Protection Division Residue Analytical Method (PPRAM) No. 58. Prepared by ICI Agrochemicals.

These studies were only summarized and determined to be eligible for review; but have not yet been reviewed. These studies are currently under review. Once the data are reviewed, the data requirement will be updated accordingly.

Please also note that there appears to be an error in the assignment of MRID # 00093845. It is currently assigned to two different reports, as listed in the Phase 3 summaries on page 38 (under MRID 92067044) and page 40 (under MRID 92068040) of the bibliography.

These studies are currently under review, and once reviewed, the dual MRID number issue will be looked into.

Page 16: It was noted that results for residues in muscle were not presented; it was not clear whether the data were simply not included in the summary document or muscle samples were not analyzed.

Data are reported for adductor, pectoral, and cardiac muscle in report MRID 00093843. It appears that the Phase Reviews that are cited in the bibliography did not include this data (see MRID's, 92067042, 92067043, and 92068021 of the Residue Chemistry Review bibliography).

These studies were only summarized and determined to be eligible for review; however, have not yet been reviewed. These studies are currently under review. Once the data are reviewed, the data requirement will be updated accordingly.

Page 22, 1st sentence (started on page 21), reads, "Additional field trial studies need to be conducted in Regions 5 (1 trial), 11 (1 trial), and 16 (2 trials) along with additional storage stability data to determine the true length of stable frozen storage for fluazifop residues." Syngenta believes that Region 16 should be listed as Region 10.

The data requirement should read, "Additional field trial studies need to be conducted in Regions 5 (1 trial), 11 (1 trial), and 10 (2 trials) along with additional storage stability data to determine the true length of stable frozen storage for fluazifop residues." This error was corrected.

Page 23, last paragraph, reads, "The reregistration requirements for confined accumulation in rotational crops are not satisfied. The qualitative nature of the residue in rotational crops is not understood. New confined rotational crop studies must be submitted. The confined rotational crop study has been determined to be inadequate to satisfy data requirements."

Syngenta will be submitting a recent study to fulfill the requirements (report Bramley, Leahey and Skidmore (1994) Fluazifop-P-Butyl : Confined Crop Rotation Report No. RJ 1457B).

V. Metabolism

The following comment and response are specific to the Fluazifop-P-butyl. Report of the Metabolism Assessment Review Committee. Sherrie L. Kinard, Chemist, July 8, 2004 DP Barcode: 298939.

In reference to all MARC document comments, no changes will be made to this document since it demonstrates what was looked at and used to make residue of concern decisions in that particular meeting.

VI. Toxicology

The following comments and responses are specific to the HED chapter (September 29, 2004).

Page 16, second to last paragraph reads, "Metabolism - Rat, dog, human with fluazifop-butyl and comparative in the rat with fluazifop-butyl and fluazifop-P-butyl." Please include "Hamster study with fluazifop-P-butyl."

The comment is accepted and the HED chapter has been corrected to read: "Metabolism - Rat, dog and human with fluazifop-butyl and comparative in the rat with fluazifop-butyl and fluazifop-P-butyl and in the hamster with fluazifop-P-butyl."

Page 22, Table 4.1b, second study MRID No. 46158401. In the results section the Dev NOAEL and LOAEL must be exchanged, NOAEL = 1 mg/kg/d and LOAEL = 20 mg/kg/d.

The comment is accepted and was corrected to: Developmental NOAEL = 1 mg/kg/day. LOAEL = 20 mg/kg/day based on dose related delayed ossification in skull bones, cervical arches and centrum in fetuses and litters and delayed ossification in the manus and pes.

Page 23, Table 4.1b, reproductive and fertility effects. In the result section the reproductive NOAEL in males should be 0.74 and not 7.4 mg/kg/day.

The comment is accepted and was corrected to: Reproductive NOAEL = M/F 0.74/0.88 mg/kg/day.

Page 32, last paragraph: statistical value should be p<0.05 rather than 0.5.

The comment is accepted and was corrected from 0.5 to p<0.05

Page 33, 5th paragraph, 2nd sentence reads "However, the study authors acknowledged the incidence of delayed ossification in the hyoid bone, thoracic and vertebral centra were decreased at 5 and 10 mg/kg/day as well as 200 mg/kg/day." Please change to read, "However, the study authors acknowledged the incidence of delayed ossification in the hyoid bone, thoracic and vertebral centra ***was increased*** *at 5 and 10 mg/kg/day as well as 200 mg/kg/day."*

The comment is accepted and was corrected from "were decreased" to "was increased."

The following comments and responses are specific to ***ATTACHMENT 1*** *of the HED chapter (September 29, 2004).*

Page 50: last paragraph reads: "However, male (-79 g to -123g versus 101 in control males) and female (-9 g to -24 g versus -24g in control females) rats lost body weight between week 81-85 and the end of the study." Please correct to read: "However, male (-79 g to -123g versus ***-101*** *in control males) and female (-9 g to -24 g versus -24g in control females) rats lost body weight between week 81-85 and the end of the study." (i.e. add the negative sign).*

The comment is accepted and was corrected from "101 in control males" to "-101 in control males."

Page 54, Table 4.4, 5th row, 2nd and 3rd column, Chronic RfD and cPAD are written as "0.008." These should be 0.0074 mg/kg/d.

The comment is accepted and was corrected from "0.008" to "0.0074."

Page 74: 2nd and 3rd columns for Mutagenicity study requirements are not filled in.

The columns have been filled in and all data requirements are satisfied.

Page 75, second to last paragraph, first sentence reads, "At necropsy in the 2000 ppm group, slight relative liver weights (97%) and kidney weights (11%) were statistically significantly increased in males and in females absolute (9%) and relative liver weight (10%) were increased." Please correct to read, "At necropsy in the 2000 ppm group, slight relative liver weights ***(48%)*** *and kidney weights (11%) were statistically significantly increased in males and in females absolute (9%) and relative liver weight (10%) were increased."*

The comment is accepted and was corrected from "97%" to "48%." The number at the HDT of

the report was blurred in the copy available to the Agency (MRID# 00093820). The correction was verified from the absolute weight liver weight and body weight data.

Page 76, 3rd to last paragraph, 1st sentence reads, "In a 90-day oral toxicity study (MRID 46158402) PP005 (95.5% fluazifop-butyl and 93% [R] a.i. fluazifop-P-butyl batch/lot #P12) was administered to 20 Alpk/AP Wistar rats/sex/group in the diet at dose levels of 0, 10, 100 or 2000 ppm (equivalent to 0, 0.5, 5 or 100 mg/kg bw/day)." Please change to read, "In a 90-day oral toxicity study (MRID 46158402), ***fluazifop-P-butyl (95.5% purity for batch P12 and 93.8% purity for batch P8)*** *was administered to...." (fluazifop-P-butyl was the only test substance in this study).*

Batch P12 was be corrected according to MRID# 46158202: The sentence now reads "In a 90-day oral toxicity study (MRID 46158402]), fluazifop-P-butyl (batch/lot #P12; 95.9% [RS, mixture] and 93% [R, isomer], and batch/lot #P8; 93.8% [RS, mixture] and 92% [R isomer]) was administered to 20 Alpk/AP Wistar rats/sex/group in the diet at dose levels of 0, 10,100 or 2000 ppm (equivalent to 0, 0.5, 5, or 100 mg/kg bw/day)."

Syngenta provided a number of comments on ***"Fluazifop-butyl/Fluazifop-P-butyl - Report of the Hazard Identification Assessment Review Committee."*** *David G Anderson, June 14, 2004. TXR NO. 0052611, PC Code: 122805/122809.*

HIARC documents are no longer being generated by the OPP/HED and all corrections and revisions that are pertinent to the HED risk assessment chapter have been made and are reflected in the revised HED chapter.

VII. Incident Data

On page 3 of "Review of Fluazifop Butyl Incident Reports. Jerome Blondell, Ph.D., March 10, 2004. DP Barcode D299665" the first sentence (Incident 7340-27), reads, "A pesticide incident occurred in 1998, when an individual reported a rash that was not considered not to be related to exposure. No further information on the disposition of the case was reported." Please check if the word "not" underlined above was unintentionally added to this sentence.

The inclusion of the word "not" is correct.

VIII. Residential/Non-occupational Exposure

The following comments and responses are specific to the HED chapter (September 29, 2004).

Page 64. Table 6.3.1.1: The values (dermal and inhalation doses) for scenarios 3 and 4 were reversed.

These values have been corrected in the revised HED chapter (December 10, 2004) and are reflected in the revised exposure chapter (November 29, 2004).

Pages 66 - 69. Tables 6.3.1.2a,b, and c: Cite maximum application rates of 0.09 lb ai/A for selective weed control (Ornamec by PBI Gordon Corp, EPA Reg No. 2217-728) for residential turfgrass and golf courses by lawn care operators, and 0.98 lb ai/A for lawn renovation (Grass and Weed Killer by Chemsico, EPA Reg NO. 9688-106).

Although Syngenta submitted a revised lower rate of 0.075 lb ai/A in their closure memo, the Agency has not received official revised labels for these products specifying the lower rate. Until the Agency receives the revised labels, the residential risk assessment will determine risk based on the worst case scenario resulting from the highest application rates available to the public. However, the residential risk assessment was modified to include exposure risk resulting from the lower application rate of 0.075 lb ai/A. Tables 6.3, 6.3.1.2a, b, and c reflect these changes.