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MEMORANDUM

SUBJECT: Review of Data Requested to Support Registration of Azoxystrobin (ICIA5504) Use on Grapes, Bananas, Tomatoes, Peanuts, Peaches, Wheat, and Turf.

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This memo summarizes the EFED position for food and turf uses of azoxystrobin. There were some outstanding data requirements for the turf uses which the registrant addressed with the submission of additional data. These additional data have been reviewed and are summarized below Attachments.

The main concern that EFED has in granting a registration for the food uses of azoxystrobin is the lack of field dissipation data in the wheat and peanut/peach production areas of the U.S. . These crops occupy vast acreages in this country and represent a potentially large input of azoxystrobin. Additionally, there are two outstanding ecological effects studies: (1) a bobwhite quail reproduction study (71-4a) to replace an invalid study; and (2) a mysid shrimp chronic toxicity study (72-4b) triggered by acute toxicity and estimated aquatic exposure levels. The registration, if granted, should be conditional until these data are submitted and reviewed.

EFED will provide a preliminary water resource assessment to HED for use in dietary risk assessment.

Azoxystrobin was shown to be practically non-toxic to birds, mammals and bees, but highly toxic to freshwater fish, freshwater invertebrates, and marine/estuarine fish.

The main concern that EFED has in granting a registration for the food uses of azoxystrobin is the lack of field dissipation data in the wheat and peanut/peach production areas of the U.S. These crops occupy vast acreages in this country and represent a potentially large input of azoxystrobin. The registration, if granted, should be conditional until these field data are submitted and reviewed.

Status of Environmental Fate Data Requirements and Water Resource Assessment

The registrant has submitted acceptable additional information to upgrade the photodegradation in water (161-2) and aerobic/anaerobic soil metabolism (162-1) data requirements for azoxystrobin. The field dissipation (164-1) data requirement, however, cannot be upgraded because clarification is needed on the length of storage period in the storage stability study (MRID 44150903). Additionally, the registrant has requested new uses on bananas, grapes, peanuts, peaches, wheat, and tomatoes. Since wheat, peanuts, and peaches are crops with large production acreages, additional field dissipation studies are needed in the Great Plains and southeastern regions of the United States. EFED has conducted a preliminary screen of the field studies in California, Mississippi, Florida and Europe (MRID 44058709, 44058710, 44058711, 44058712, 44058713) and these studies may provide information to support registration for grapes, tomatoes, and turf. The European field studies (44182001 - 44182012) may provide supplemental information on the dissipation of ICIA5504. These studies, however, cannot substitute for field dissipation in the United States because of geographical differences.

We have begun to conduct a preliminary water resource assessment for HED to use in evaluating the risk for drinking water. Early results indicate that the highest exposure is roughly 38 to 39 µg/L from surface water, based on 56 day average from GENEEC runs on multiple crops. Groundwater concentrations are almost certainly less.

Ecological Effects Summary

The available acute toxicity data on the TGAI indicate that azoxystrobin is practically nontoxic to birds (LD50> 2000 mg/kg; LC50 >5200 ppm), mammals (LD50> 5000 mg/kg) and bees (LD50 >200 µg/bee). Azoxystrobin is very highly toxic to estuarine/marine invertebrates (EC50 = 56 ppb). It is highly toxic to freshwater fish (LC50 = 470 ppb), freshwater invertebrates (EC50 = 259 ppb), and estuarine/marine fish (LC50 = 670 ppb). Plant studies indicated that the most sensitive species was carrot (EC25 = 0.59 lb ai/acre) and the most sensitive aquatic species was an algae (EC50 = 0.1 ppm).

Two studies are outstanding: (1) a bobwhite quail reproduction study (71-4a) to replace an invalid study; and (2) a mysid shrimp chronic toxicity study (72-4b) triggered by acute toxicity and estimated aquatic exposure levels. Because the acute bobwhite and mallard data and the mallard reproductive data indicate no adverse acute or chronic effects to birds, the value of this study is "low". The value of the mysid shrimp chronic toxicity study is also considered "low". Although peanuts, tomatoes, and pecans are grown in coastal counties and applications to these crops may contaminate the estuarine/marine waters, acreages of these crops are low in coastal areas. Therefore, EEB recommends that both the bobwhite quail reproductive study and the mysid chronic toxicity study be submitted as a condition of registration.

ATTACHMENT: REVIEW OF ADDITIONAL ENVIRONMENTAL FATE DATA

Photodedegradation in Water (161-3)

The aqueous photolysis study (MRID 43678173) in conjunction with additional data (MRID 44150904) fulfills the photodegradation in water (161-2) data requirement for ICIA5504.

The registrant (Zeneca) submitted clear photocopies of phosphoimages from two dimensional TLC chromatography (MRID 44150904). See attachment.

Aerobic/Anaerobic Soil Metabolism (162-1)

The aerobic soil metabolism study (MRID 43678175) in conjunction with additional data (MRID 44046801) fulfills aerobic soil metabolism (162-1) and anaerobic soil metabolism (162-2) data requirements.

Additional information on the concentration of ICIA5504 transformation products is shown below.

Aerobic Soil Metabolism

Compound 2 in the United Kingdom soils had a maximum concentration of 12 to 20% of applied at 62 days, 9.5 to 15.2% of applied at 120 days posttreatment, and then declined to 1.4 to 5.5% at 365 days posttreatment. The maximum concentration of Compound 2 in the Visalia soil was 28% of applied at 365 days posttreatment. No degradation of Compound 2 was observed in the Visalia soil.

Compound 3 had a maximum concentration 1.5% of applied at 30 days posttreatment in the Hyde soil, 1.1% of applied at 62 days posttreatment in the 18 Acre soil, and 3.1% of applied at 120 days posttreatment in the Visalia soil. The concentration of compound 3 in test soils declined to 0.3 to 1.5% of applied at 365 days posttreatment.

Compound 28 in the Visalia soil had a maximum concentration of 2.6% of applied at 120 days posttreatment. No clear degradation pattern of Compound 28 was observed in the Visalia soil. In the United Kingdom soils, the concentration of Compound 28 was less than 1% of applied.

Compound 36 in the Hyde Farm soil had a maximum concentration of 1.8% of applied at 181 days posttreatment and then declined to 1.2 of applied at 365 days posttreatment. In the 18 Acres soil, Compound 36 had a maximum concentration of 2.8% of applied at 120 days posttreatment and then declined to 0.6% of applied at 365 days posttreatment. The maximum concentration of Compound 36 in the Visalia soil was 2.4% of applied at 365 days posttreatment. No degradation of Compound 36 was observed in the Visalia soil.

Unidentified bands/spots were also detected (cumulative 0.8 to 11.6% of applied) on the TLC plates. The registrant stated the unidentified radioactivity within a designated TLC band did not exceed 5% of the applied or extracted radioactivity.

No degradation of Compound 36 was observed in the Visalia soil.

Anaerobic Soil Metabolism

Compound 2 was detected in the surface water and soil extracts. In the water-soil system, the maximum, concentration of Compound 2 was 60 to 68 % of applied at 181 days posttreatment and declined to 46 to 54% of applied at 360 days posttreatment. The concentration of Compound 2 in surface water ranged from 19 to 21% of applied at 181 days posttreatment and declined to 11 to 17% of applied at 360 days posttreatment. The concentration of Compound 2 in soil extracts ranged from 39 to 48% of applied at 181 days posttreatment and declined to 35% at 360 days.

Compound 3 in the water-soil systems had a maximum concentration of 0.1 to 0.6 % applied.

Compound 28 in the total soil-water system had a maximum concentration of 1.8 to 4.2% of applied at 62 days posttreatment and declined to 1.5 to 2.6% of applied at 360 days posttreatment. This degradate was predominately detected in soil extracts.

Compound 36 in the soil-water systems had a maximum concentration of 0.7 to 1.1 % of applied at 360 days posttreatment.

Unidentified bands/spots were also detected (cumulative < 8.3 of applied) on the TLC plates. (Reviewer Note: The registrant did not provide secondary confirmation of identification. The registrant also did not provide any information on the number of separate compound on the unidentified TLC spots or baseline.)

Terrestrial Field Dissipation Studies (164-1)

California Field Dissipation Studies (MRID 34678184 and 43678185)

Additional data were submitted to clarify the USDA soil taxonomic classification, to provide pan evaporation data, to indicate the handling of grass clipping, and to indicate the analytical limits of detection and quantification (MRID 44150904,44150905, 44150906, 44150907, 44150910).

1. EFED requested clarification of the USDA soil taxonomy of the soil at the test site because of the presence of a high seasonal water table. The test soil was reported as a Foster soil series or Aquic Haploxeroll. The registrant stated the Foster soil series designation is based on a 1939 soil survey. A more current USDA soil classification indicates the soil on the test site is mapped as a Norad A soil series or Cumulic Haploxeroll (MRID 44150904). This soil is well drained and has variable water table depth (25 to 60 feet).

2. EFED requested pan evaporation data to establish a field water balance. The registrant submitted average annual Class A pan evaporation data for Fresno, CA from 1960 to 1994. The estimated cumulative annual pan evaporation is 106 inches from May, 1993 to September, 1994. Since the amount of water evaporation (106 inches of water) exceeds the amounts of cumulative rainfall and irrigation (32.17 and 78.63 inches of water), EFED believes that leaching of ICIA5504 and its transformation products may not be a major route of dissipation because of a moisture deficit (27 and 74 inches of water) during the study.

2. Analytical limits of detection (LOD) and quantification (LOQ) for the field study MRID 43678184.

Compound	LOQ	LOD HPLC	LOD GC/MS
	mg/kg		
ICIA5504	0.02	0.005	0.002
R230310	0.02	0.005	0.002
R234886	0.02	0.005	0.002
R401553	0.01	-----	
R402173	0.01		

3. The registrant did not remove grass clippings from the turf test plots. EFED notes that removal of grass clippings was not a route of dissipation for ICIA5504 and its transformation products in the field study.

Florida Field Dissipation Studies (MRID 43678186)

Additional data was submitted to provide pan evaporation data, to indicate the handling of grass clippings, and to indicate the analytical limits of detection and quantification (MRID 44150908, 44150909, 44151401).

1. EFED requested clarification of the USDA soil taxonomy of the soil at the test site because of the presence of a high seasonal water table. Based on USDA soil taxonomy, the soil association at the test site was identified as a Leon-St. John-Delray soil association. These soils have an aquic soil moisture regime or a seasonally high water table. The registrant did not provide an explanation of the presence of seasonally high water table.

2. EFED requested pan evaporation data to establish a field water balance. The registrant submitted 35 year average annual Class A pan evaporation data for Lisbon, Florida from 1960 to 1994. The estimated cumulative annual pan evaporation is 82.94 inches of water from May, 1993 to September, 1994. Since the cumulative rainfall and irrigation amounts exceed the cumulative amount of evaporated water, ERCB notes that adequate moisture was available to promote the leaching of ICIA5504 and its transformation products under the study conditions.

3. Analytical limits of detection (LOD) and quantification (LOQ) are shown below.

Compound	LOQ	HPLC-LOD	HPLC-MS-MS-LOQ
	mg/kg		
ICIA5504	0.02	0.005	0.002
R230310	0.02	0.005	0.002
R234886	0.02	0.005	0.003

Compound	LOQ	GC-MS-LOD
	mg/kg	
R401553	0.01	0.002
R402173	0.01	0.002

4. The registrant did not remove grass clippings from the turf test plots. EFED notes that removal of grass clippings was not a route of dissipation for ICIA5504 and its transformation products in the field study.

Storage Stability Studies (MRID 4378184, 43678185, and 43678186)

GENERAL: The registrant submitted interim storage stability data for ICIA5504, R230310, R234886, R401553 or R402173. ERCB notes the registrant did not provide a complete description of material and methods.

The storage stability studies (MRID 44150902 and 44150903) provide upgradable information on the stability of ICIA5504, R230310, R234886, R401553, and R402173. Since the soil samples in field dissipation studies (MRID 34678184, 43678185, and 43678184) were stored frozen for 24 months, ERCB believes that additional data are needed to support the storage stability of R4015504 and R402173. Submission of this additional storage stability data would upgrade the field dissipation studies.

Additional studies were submitted to address storage stability of ICIA5504 residues during frozen storage (MRID 44150902). Duplicate samples of each test soil were amended with ICIA5504, R230310, or R234886 at a concentrations of 0.01 mg/kg. Amended soil samples were incubated for 24 months at <-15°C in the dark. Samples were taken at 0, 91-125 days, 175-188 days, 363-380 days, and 730-741 days posttreatment. Residue concentrations were determined using ZENECA Agrochemical Residue Analytical Method (SOP RAM/257). There was no apparent degradation during the 24 month storage period. ERCB notes these are interim data from a 36 month storage stability study.

Duplicate samples of each test soil were amended with R401553 or R402173 at a concentrations of 0.01 mg/kg (MRID 44150903). Amended soil samples were incubated for 12 months at <-15°C in the dark. Samples were taken at 0, 89-91, 190-194 days, and 378-382 days posttreatment. Residue concentrations were determined using ZENECA Agrochemical Residue Analytical Method (SOP RAM/269). There was no apparent degradation of R401553 and R402173 during a 12 month frozen storage period. ERCB notes the registrant stated R401553 and R402173 were stable during a 24 month storage stability period. However, the submitted data can only support a 12 month storage period. ERCB notes these are interim data from a 36 month storage stability study.

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Additional Field Dissipation Studies For Turf and Other Uses (MRID 44058709,44058710,44058711,44058712,44058713)

A preliminary screen of the additional field studies shows that they may potentially provide acceptable information to support registration on grapes, tomatoes, and turf. Several European studies conducted in the major grape and cereal production regions may provide supplemental information on the dissipation of ICIA5504. These studies, however, cannot substitute for field dissipation in the United States because of geographical differences.

Foliar Dissipation Studies

GENERAL: EFED requested ancillary data on foliar dissipation of ICIA5504 to assess the contribution of foliar-dissipation to overall field dissipation processes. Foliar dissipation is not a guideline study under Subdivision N, EFED appreciates the registrant submission of foliar field dissipation data because such data assists in elucidating the major routes of dissipation of ICIA5504.

The foliar dissipation studies (MRID 44150911 and 44058708) provide ancillary data on the dissipation rate of ICIA5504 from cereal and grape foliage. These data should not be used as ancillary data in the environmental fate assessment without further clarification of residue sampling and analysis procedures. In particular, the studies do not provide any direct evidence on the fate of foliar applied residues through wash-off onto soil surface, photo-degradation on the leaf surface, or binding into the leaf cuticle. All data interpretations are suggestive because direct measurement of degradation products on leaf surfaces and soil residue data were not presented. EFED appreciates the registrant submission of foliar field dissipation data. Such data assists in elucidating the major routes of dissipation of ICIA5504.

Azoxystrobin had a foliar dissipation half-life of 7 to 29 days (average=14 days) for fresh wheat foliage, 6 to 13 days (average=10 days) for dry wheat foliage, 9 to 14 days (average=11 days) for fresh barley foliage, and 7 to 11 days (average=8 days) for dry barley foliage. Foliar wash-off did not appear to be a major route dissipation because there was little correlation between rainfall amount and residue decline.

Summary of Residue Decline Data on Cereal Forage in Germany (MRID 44150911)

The study is a summary of field foliar dissipation studies on cereal crops (*e.g.*, barley and wheat) in France and Germany. Azoxystrobin (ICIA5504), formulated as 25SC and 50WP, was foliar-spray at cumulative rates of 516 to 850 grams/ha (1.14 to 1.87 lbs a.i./A). Three spray applications were conducted at approximately one-third the cumulative rate. Whole plants (minus roots) were harvested at immediately after the last application to 53 days posttreatment. The sampling size (or number of plants sampled) was not reported. Azoxystrobin was analyzed in the foliage using an unidentified analytical method. Dry weight of the moist foliage was estimated using a regression equation. First-order foliar dissipation half-lives were estimated on both a fresh and dry weight basis.

Azoxystrobin had a foliar dissipation half-life of 7 to 29 days (average=14 days) for fresh wheat foliage, 6 to 13 days (average=10 days) for dry wheat foliage, 9 to 14 days (average=11 days) for fresh barley foliage, and 7 to 11 days (average=8 days) for dry barley foliage. Foliar wash-off did not appear to be a major route dissipation because there was little correlation between rainfall amount and residue decline.

Dislodgeable Residues of ICIA5504 80WG on Grape Forage (California 1995) (MRID 44058708)

Azoxystrobin, formulated as 80WP, was sprayed onto Thompson seedless grapes in Visalia, CA. Six foliar applications of azoxystrobin, at 0.25 lbs/A, were accomplished using a U boom sprayer equipped with 8 nozzles at spray volumes of 47 to 73 gallons/A. Applications were made at 1-to-5 inch shoot growth, 21, 59, 133, 147, 169 days after the first application. Leaf samples were taken immediately after the 3rd, 4th, and 6th applications. Additional samples were taken at 3, 7, 14, and 21 days after the last application to establish a foliar dissipation rate. Leaf samples were further subsampled using forty 2.5 cm diameter leaf discs. Azoxystrobin residues were sequentially extracted from leaf samples using 2% Aerosol solution (dilute soap). Extractable azoxystrobin residues were analyzed using Zeneca Standard Operating Procedure RAM 243/03. The limit of quantification (LOQ) was 0.01 $\mu g/ml$ (or 0.006 $\mu g/cm^2$ of leaf area).

Dislodgeable ICIA5504 residues on grape leaves had a half-life of 18 days. The maximum average azoxystrobin concentrations was 0.65 $\mu g/cm^2$ (CV=24%) after the 6th application and then declined to 0.28 $\mu g/cm^2$ (CV=2.0%).

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