

APR 29 1999



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

**MEMORANDUM**

**SUBJECT:** Isoxaflutole: EFED's Response to Plant Field Studies Rebuttal  
DP Barcode D255262, D255259

**FROM:** Michael Davy, Agronomist  
Environmental Risk Branch II  
Environmental Fate and Effects Branch (7505C)

**Thru:** Betsy Grim, Acting Chief  
Environmental Risk Branch II  
Environmental Fate and Effects Branch (7505C)

**TO:** Joanne Miller, PM-23  
Dan Kenny, PMT-23  
Registration Division (H7506)

ERB II has reviewed the registrant's rebuttal of the protocols for the simulated and irrigation plant field studies science chapter for isoxaflutole. These studies were submitted under DP Barcode D255262 and D255259 for section 3 conditional registration of isoxaflutole.

The results of the review are as follows:

***Simulated Drift***

**I. EFED has requested that the field design consist of**

*Six replicates for each test dose and control should be provided. Each replicate should consist of a split plot. Each plot should have randomized allocation of treatments. There should be a 50 foot buffer inside each plot between the test and control plots. There should be at least 100 feet between adjacent plots. Each control should have metal flashing around the plot to protect from runoff from other treated plots. See the diagram for details.*

**Rhone-Poulenc (RP)**

- a. will increase the replicates from four to six,
- b. does feel the design is not feasible and a large amount of space will be needed,
- c. the use of the metal flashing is not feasible due to disruption of plots (i.e., removal of flashing) during every maintenance event and that runoff of treated soil can be

controlled by an adequate number of buffer rows between individual plots.

EFED

- a. is satisfied that six replicates will be used
- b. is willing to make the design much smaller provided that a method is made to prevent runoff from treated plots from going onto control plots and that the control plots are protected from any contamination from the treated plots.
- c. is willing to forgo the use of metal flashing if an alternative can be found to protect the control plots from runoff from the adjacent treated plot. EFED does not share the confidence of RP that a small number of buffer rows between the treated and control plots can prevent runoff from occurring on the control plot. Perhaps a shallow (4 inch) ditch surrounding the control plot and RP's proposed buffer strip of 40 feet will be sufficient to protect the control plot from runoff containing isoxaflutole residues. EFED is willing to forgo the 100 feet between plots.

## II. EFED has requested that

*At time of application, the control should be on the windward side of the treated plot. Rows are to be planted perpendicular to the wind so that shield guards can be more effective. See diagram for details.*

RP

- a. maintains that typical agronomic practices plant rows on field contours.
- b. alternating direction of rows within replicated plots or a field is not normal agronomic practice especially when the plots will be harvested for yield determinations.
- c. shielded sprayers will be specified and used in the protocol.

EFED

- a & b.. assumes that research plots would be on soil with a minimal slope so that contours would not be needed. If possible, rows should be in a direction that shield guards would be more effective in cutting down drift. During experimental trials, agronomic practices cannot always be used in all circumstances. EFED is more concerned that agronomic practices are followed as close as possible for planting, maintenance and weed, insect and disease control for the particular crops tested.
- c. is satisfied that shielded sprayers will be used.

## III. EFED has requested that

*Control plants should be protected from spray drift by white, plastic, and light gauge sheeting at time of application and for one hour after application. Shield guards should be used with test plants at application. For the spray, minimum volume of water and maximum PSI as allowed on label should be used. Care must be given to control plants in order to minimize injury from plastic sheeting. Shheeting should be anchored down with tubing on the edge of plot and with tubing raised in the middle to keep the sheeting off the plants. Plastic should not be reused.*

RP

- a. maintains that covering the controls are not practical with 3200 square feet and that the controls will be adequately separated from the treated plots. Furthermore, the practice is atypical for row crops.
- b. has said that applications will be made in early morning to minimize wind effects.

c. has indicated that the plot will be applied in 10 gallons per acre as specified on label using appropriate nozzles.

#### EFED

a. maintains that agronomic practices should be used in the planting and maintenance (including disease, weeds and insect control) of the crops. EFED also maintains that this is an experimental plot that cannot and should not be bound to every common agronomic practice. Without the protection of controls from possible contamination from the treated plots, this study would be scientifically invalid. EFED does not share the confidence of RP that RP proposed buffer zones will eliminate Isoxaflutole drift to the control plots. EFED also maintains that the use of the plastic sheeting is practical. b & c. is satisfied that applications will be made in early morning to minimize drift with 10 gallons of water per acre used with appropriate nozzles.

#### IV. EFED has requested

*A representative portion of the seed harvested (for yields) from each plot should be sent to a State seed lab where a 400 seed germination test should be conducted. The amount of seed sent to the lab should be given in the section below that deals with each specific crop. Each sample should be labeled to reflect the replicate and controls it came from. A chain of custody should be maintained for these samples. Results of the test including abnormal seedlings should be a part of the report.*

#### RP

a. requests justification for seed germination tests.  
b. has maintained that seedling emergence studies (MRID 44291501 and 43573242) demonstrated the EC<sub>25</sub> values.

#### EFED

a & b. looks at yield trials to be also a life-cycle study of the plant tested. As part of the life-cycle study, EFED's Plant Tech Team has requested that the viability of the seeds (embryo) be measured. EFED policy has always been that crops can represent non-target native/introduced species. Crops are usually tested because they are bred to be uniform, are more easily accessible and have standardized growth requirements. The seed germination test would provide viability data. These seed germination tests of the harvested seeds are different from the seedling emergence studies (MRID 44291501 and 43573242) in that the seed source and the endpoints measured are different. In the seedling emergence studies, the seed is from high quality crops that come from normal agricultural production. The seed from these studies comes from an experiment using a chemical that is phytotoxic to these crops. These studies are being done to determine if there are adverse impacts to the crop yield (reproductive life-cycle). EFED is aware that each State has a State seed lab that can test the seed under AOSA (Association of Official Seed Analysts) rules. An official test under AOSA rules calls for 400 seeds. EFED would compare the seed from the treated plots with the seed from the control plots.

V. EFED has requested

*Field history of past two years should be provided showing that no pesticide residues are on the field that may inhibit the growth of the crops tested.*

RP has indicated that field history is part of the GLP. EFED is satisfied.

VI. EFED has requested

*Under "Test System Maintenance", the protocol should first recommend the use of biological pest controls before using registered pesticides for that specific crop. Controls should also be maintained in same way as the test plots including use of pesticides.*

RP has indicated that a statement that biological pest control may be used will be added to the protocol. EFED is satisfied.

VII. EFED has requested

*During severe moisture stress of crops, irrigation should be used. The timing and methods of irrigation should be documented.*

RP has indicated that

- a. supplemental irrigation is available at most locations but not at all locations.
- b. some of the crops chosen by EPA for testing are not grown under nor adapted to irrigation.

EFED maintains that experimental trials should still be irrigated under severe moisture stress and that all of the crops selected can be and has been irrigated under experimental conditions.

VIII. EFED has requested

*After crops are harvested for yield, the roots should be dug up and visual observations noted of the roots as compared to the controls.*

RP says that roots are highly variable and the only reasonable measure of potential affects to measure is yield.

EFED says that development of root growth and shape are indicators of the plant's health. However, upon re-evaluation, EFED does not see the need to need to evaluate the roots.

IX. EFED has requested

*Twenty plants per replicate instead of 10 plants should be randomly measured for height weekly.*

RP has asked for 20 plants to be measured at maturity instead of weekly. EFED is satisfied.

X. EFED has requested

*The size of the plot should be large enough to harvest five 50-foot rows or more of the crops. At least four rows or 10 ten feet on each side of the crop should serve as border rows that are not to be part of the official yield. The front and back 10 feet should also not be part of the official yield harvest. A minimum of five 50-foot rows should be harvested for yield for each plot.*

RP has indicated that plot and sample size were based on the experiences of the researchers, normal agronomic practices (row spacing, etc.) of the growing region of the crop. Where possible, plot size will increase and larger areas sampled for yield determinations. Edge effects will be taken into consideration.

EFED finds RP's statements to be acceptable.

XI. EFED has requested

*The report should also include calculations made for spray volume, concentration in spray tank, and application of pounds per acre from a spray tank. The report should also show calculations of the yield into pounds per acre and bushels per acre.*

RP says that the report are under GLP and the information requested will be collected and reported. EFED is satisfied.

XII. EFED has requested

*On site weather station should record humidity, rainfall, temperature and wind speed and direction up to one month prior to application and during application on a daily basis. After application, all rainfall and temperature must be recorded.*

RP says that field researchers conducting the studies have weather stations on site. If one of the researchers must go off-site to conduct the study, rainfall and temperature data will be collected at that site and other data will be collected at nearest weather station. EFED is satisfied.

XIII. EFED has requested

*Map and layout of sites should show the direction of North.*

RP says that maps and layouts are provided as part of GLP. EFED notes that maps and layouts provided for plant survey did not show the north direction. EFED would like to see north displayed on maps and layouts.

XIV. EFED has requested

*At time of application, one sample per tank mix must be taken, frozen immediately, and analyzed as soon as possible for the parent isoxaflutole and the degradate RPA 202248.*

RP will take spray tank samples, handle them appropriately and have them analyzed. EFED is satisfied.

XV. For Rice, EFED has requested

*1. Eliminate treatments 6 weeks prior to emergence and add a treatment 2 weeks after emergence. 2. Timing of flooding and maintenance should be recorded. 3. The minimum size of the seed sample for each replicate and control that should go to the State seed lab is 50 gm.*

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RP

- a. will eliminate the six-week application timing
- b. does not understand the need for adding the 2 weeks after emergence treatment since within this growing region, corn emerges a week after planting and to apply isoxaflutole two weeks after emergence of corn would be considered a postemergence use and be consistent with the labeling of corn as pre-emergence.
- c. says that under GLP, timing of flooding and maintenance will be recorded.

EFED

- a. is satisfied with elimination of 6 week application timing.
- b. would want the 2 week after application timing to be used for the following reasons:
  1. corn can be planted after rice in south Louisiana,
  2. the rice is being sprayed and not the corn and this is an experimental study (not a normal agronomic practice),
  3. as noted earlier, the rice can also represent many non-target plants that are not crops,
- c. EFED is satisfied that timing of flooding and maintenance of field will be recorded.

XVI. For cotton, EFED has requested

*1. The application treatment six weeks prior to emergence can be eliminated. EFED recommends that treatment application 2 weeks after planting is added to show possible timing in Louisiana and Texas due to double crop. 2. The minimum size of the seed sample for each replicate and controls that should go to the State seed lab is 300 gm.*

RP

- a. will eliminate the six-week application timing
- b. does not understand the need for adding the 2 weeks after emergence treatment since within this growing region, corn emerges a week after planting and to apply isoxaflutole two weeks after emergence of corn would be considered a postemergence use and be consistent with the labeling of corn as pre-emergence.

EFED

- a. is satisfied with elimination of 6 week application timing.
- b. would want the 2 week after application timing to be used for the following reasons:
  1. the cotton is being sprayed and not the corn and this is an experimental study (not a normal agronomic practice),
  2. as noted earlier, the cotton can also represent many non-target plants that are not crops, and there are several species that have emerge 2 weeks after the corn.

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XVII. For soybean, EFED has requested

*1. Application treatment 14 days prior to emergence can be eliminated. EFED recommends that treatment application 14 days after planting is added to show possible timing in Texas due to double crop. 2. The minimum size of the seed sample for each replicate and controls that should go to the State seed lab is 500 gm.*

RP

- a. will eliminate the 14-days prior to emergence application timing
- b. does not understand the need for adding the 14 days after emergence treatment since within this growing region, corn emerges a week after planting and to apply isoxaflutole two weeks after emergence of corn would be considered a postemergence use and be consistent with the labeling of corn as pre-emergence.

EFED

- a. is satisfied with elimination of 14 days prior to emergence application timing.
- b. would want the 2 week after application timing to be used for the following reasons:
  1. the soybean is being sprayed and not the corn and this is an experimental study (not a normal agronomic practice),
  2. as noted earlier, the soybean can also represent many non-target plants that are not crops, and there are several species that have emerge 2 weeks after the corn.

XVIII. For sunflowers, EFED requests that

*The treatment 6 weeks prior to emergence can be eliminated. The treatment application 2 weeks after emergence should be added to reflect that, sunflowers can be planted two weeks after corn in Texas. The minimum size of the seed sample for each replicate and control that should go to the State seed lab is 100 gm.*

RP will eliminate the six weeks prior to emergence application timing, but does not understand the need for adding the 2 weeks after emergence treatment since within this growing region, corn emerges a week after planting and to apply isoxaflutole two weeks after emergence of corn would be considered a postemergence use and be consistent with the labeling of corn as pre-emergence.

EFED is satisfied with elimination of 6 weeks prior to emergence application timing. EFED also would want the 2 week after emergence application timing to be used for the following reasons: 1. the sunflowers is being sprayed and not the corn and this is an experimental study (not a normal agronomic practice), and 2. as noted earlier, the soybean can also represent many non-target plants that are not crops, and there are several species that have emerge 2 weeks after the corn.

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## *Irrigation Water Spiked With Isoxaflutole*

### I. EFED requests that

*Six replicates for each test dose and control should be provided. Each replicate should consist of a split plot. Each plot should have randomized allocation of treatments. There should be a 50-foot buffer inside each plot between the test and control plots. There should be at least 100 feet between adjacent plots. See diagram for details.*

#### RP

- a. agrees to have six replications
- b. does not feel the design is feasible and a large amount of space will be needed, and

#### EFED

- a. is satisfied that six replicates will be used
- b. is willing to make the design much smaller provided that a method is made to prevent runoff and spray drift from treated plots from going onto control plots and that the control plots are protected from any contamination from the treated plots.

### II. EFED requests that

*Control plants should be protected from spray drift by white, plastic, and light gauge sheeting over the control plants at time of application and for one hour after application. Care must be given to control plants in order to minimize injury to plants from plastic sheeting. Sheeting should be anchored down with tubing on edge of plots and with tubing raised in middle to keep sheeting off of plants. Do not reuse plastic for any other controls.*

#### RP

- a. maintains that covering the controls is not practical with 3200 square feet and that the controls will be adequately separated from the treated plots. Furthermore, the practice is atypical for row crops.
- b. has said that applications will be made when crops are in the reproductive stage of growth and will be 3-7 feet tall.

#### EFED

maintains that agronomic practices should be used in the planting and maintenance (including disease, weeds and insect control) of the crops. EFED also maintains that this is an experimental plot that cannot and should not be bound to every common agronomic practice. Without the protection of controls from possible contamination from the treated plots, this study would be scientifically invalid. EFED does not share the confidence of RP that RP-proposed buffer zones will eliminate isoxaflutole drift from irrigated water to the control plots. EFED also maintains that the use of the plastic sheeting is not impractical. EFED is willing to forgo the use of plastic if another way/rational can be found to protect the controls from drift from the spiked irrigation water.



### III. EFED requests that

*Metal vertical flashing placed into the soil should help protect control plants from treated water. These flashing should be at least 4 inches above the soil. If metal flashing are not used then levees should be used. In addition, there should be a shallow ditch (about 4 inches deep) that should channel the water away from the control plots. Care must be given to position the controls so that the prevailing winds should not carry moisture from the contaminated irrigation plots. The controls must be at least 50 feet away from the treated plots.*

RP says that the use of the metal flashing is not feasible and that standard agronomic practices could not be used due to disruption of plots (i.e. removal of flashing) during every maintenance event and that runoff of treated soil can be controlled by an adequate number of buffer rows between individual plots and the rate at which the irrigation water is applied.

EFED is willing to forgo the use of metal flashing if an alternative can be found to protect the control plots from runoff from the adjacent treated plot. EFED does not share the confidence of RP that a small number of buffer rows between the treated and control plots can prevent runoff from occurring on the control plot. Perhaps a shallow (4 inch) ditch surrounding the control plot and RP's proposed buffer strip of 40 feet will be sufficient to protect the control plot from runoff containing isoxaflutole residues. In addition, the metal flashing can be put around the control plots prior to the use of spiked irrigation water since the plants will be at a stage of growth in which further maintenance should be minimal due to the weed control by the crop's canopy.

### IV. EFED requests that

*A representative portion of the seed harvested (for yield) from each plot should be sent to a State seed lab where a 400 seed germination test be conducted. The amount of seed sent to the lab should be given in the section below that deals with each specific crop. Each sample should be labeled individually. A chain of custody should be maintained for these samples. Results of the test including abnormal seedlings should be a part of the report.*

#### RP

- a. requests justification for seed germination tests.
- b. has maintained that seedling emergence studies (MRID 44291501 and 43573242) demonstrated the  $EC_{25}$  values.

#### EFED

a & b. looks at yield trials to be also a life-cycle study of the plant tested. As part of the life-cycle study, EFED's Plant Tech Team has requested that the viability of the seeds (embryo) be measured. EFED policy has always been that crops can represent non-target native/introduced species. Crops are usually tested because they are bred to be uniform, are more easily accessible and have standardized growth requirements. The seed germination test would provide viability data. These seed germination tests of the harvested seeds are different from the seedling emergence studies (MRID 44291501 and 43573242) in that the seed source and the endpoints measured are different. In the seedling emergence studies, the seed is from high quality crops that come from normal agricultural production. The seed from these studies come from an experiment using a chemical that is phytotoxic to these crops. These studies are being done to determine if there are adverse impacts to the crop yield (reproductive life-cycle). EFED is aware

that each State has a State seed lab that can test the seed under AOSA (Association of Official Seed Analysts) rules. An official test under AOSA rules calls for 400 seeds. EFED would compare the seed from the treated plots with the seed from the control plots.

V. EFED requests that

*Field history of past two years should be provided showing no pesticide residues should be on field that may inhibit the growth of the crops tested.*

RP has indicated that field history is part of the GLP. EFED is satisfied.

VI. EFED requests that

*Under "Test System Maintenance", the protocol should first recommend the use of biological pest controls before using registered pesticides for that specific crop. Controls should also be maintained in same way as the test plots.*

RP has indicated that a statement that biological pest control may be used will be added to the protocol. EFED is satisfied.

VI. EFED requests that

*Twenty plants instead of 10 plants should be randomly measured for height weekly*

RP has asked for 20 plants to be measured at maturity instead of weekly. EFED is satisfied.

VII. EFED requests that

*The size of the plot should be large enough to harvest five 50-foot rows or more of the crops and to have at least 3 rows or 10 ten feet on each side of the crop to serve as border rows that are not to be part of the official yield. The front and back 10 feet should also not be part of the official yield harvest. A minimum of five 50-foot rows should be harvested for yield for each replicate.*

RP has indicated that plot and sample size were based on the experiences of the researchers, normal agronomic practices (row spacing, etc.) of the growing region of the crop. Where possible, plot size will increase and larger areas sampled for yield determinations. Edge effects will be taken into consideration. EFED finds RP's statements to be acceptable.

VIII. EFED requests that

*The report should also include calculations of these concentrations in the tanks and the amount of water applied on each plot on a per acre basis. This report should also show calculations of yield into pounds per acre and bushels per acre.*

RP says that the studies are under GLP and the requested information will be reported. EFED is satisfied.

IX. EFED requests that

*An on site weather station should record humidity, rainfall, temperature and wind speed and direction up to one month prior to application and during application on a daily basis. After application, all rainfall and temperature must be recorded.*

RP says that field researchers conducting the studies have weather stations on site. If one of the researchers must go off-site to conduct the study, rainfall and temperature data will be collected at that site and other data will be collected at nearest weather station. EFED is satisfied.

X. EFED requests that

*Map and layout of sites should show the North direction.*

RP says that maps and layouts are provided as part of GLP. EFED notes that maps and layouts provided for plant survey did not show the north direction. EFED would like to see north displayed on maps and layouts.

XI. EFED requests that

*At time of application, one sample per irrigation dose must be taken, frozen immediately, and analyzed as soon as possible for the parent isoxaflutole and the degradate RPA 202248.*

RP will take spray tank samples, handle them appropriately and have them analyzed. EFED is satisfied.

XII. EFED requests that

*Application should be with parent isoxaflutole only or parent isoxaflutole (at least 10%) and RPA 202248. The mixture reflects PRZM-EXAMS ratio at 21 days.*

RP has indicated that "the conditional registration agreement for Balance states that small plot irrigation studies will be conducted with RPA 202248. Protocols will continue to reflect this agreement".

EFED understands that RP's claims that phytotoxicity of isoxaflutole parent is equivalent to the primary degradate RPA 202248. The spiked irrigation concentrations should reflect more accurately the PRZM-EXAMS predictions of a mixture of the parent and the primary degradate. Furthermore, EFED has not received any phytotoxicity data on RPA 202248 by accepting RP's claim that the phytotoxicity of the primary degradate is equivalent to the parent. Therefore, EFED desires that the spiked irrigation water reflect the PRZM-EXAMS model but is willing to live with the spiked concentrations being RPA 202248.

If there are any questions, please do not hesitate to contact Mike Davy at 305-7081.

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