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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

July 13, 1999

MEMORANDUM

SUBJECT: EFED Response to Rhone Poulenc Bebuttal to EFED's Science Chapter for Isoxaflutole. DP Barcode D236564

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Thru: Pat Jennings, Acting Chief
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TO: Joanne Miller, PM-23
Registration Division (H7506)

ERB II has reviewed the registrant's rebuttal of the science chapter for isoxaflutole. This rebuttal was submitted under DP Barcode D236564 for section 3 registration of isoxaflutole. The results of the review are as follows:

Environmental Fate

In the second paragraph of p. 10, Rhone Poulenc states that the combination of the low use rate, the rapid dissipation of the parent compound in surface water, and the extremely small concentrations of the metabolites formed suggests that no toxicologically-significant residue of either metabolite would be present in the aquatic environment. As a basis for the statement, the registrant correctly cites the rapid degradation in the acceptable hydrolysis study for isoxoflutole. The registrant also correctly cites the aqueous photolysis study, where RPA 202248 and RPA 203328 were formed at <5% of applied.

However, based on the results of the same submitted, acceptable studies, EFED does not agree

with the conclusion of the registrant that the degradates are not likely to reach aquatic environments in significant amounts in proportion to what is applied. EFED notes that RPA 202248 was a significant degradate in the sterile hydrolysis study, where it did not degrade. Also, RPA 202248 only slowly degraded with calculated, extrapolated half-lives of 250-700 days in the non-sterile aerobic aquatic metabolism study. In addition, EFED notes that in most surface water, aqueous photolysis is not a significant route of dissipation because of the presence of suspended sediments and lack of mixing by depth.

The only identified pathway of degradation in soil is from parent isoxaflutole to RPA 202248, which degrades to RPA 203328. If rainfall closely follows application, parent isoxaflutole is expected to reach surface water, where it will form RPA 202248 rapidly. The relative amounts of each degradate in surface water will depend on the amount and timing of rainfall following application. Since the degradates are both persistent and mobile, isoxaflutole degradates are expected to reach surface water in significant amounts.

The registrant is proposing to lower the maximum application rate from 0.1875 to 0.14 lb ai/A. The impact of this reduction in use rates on EEC's from PRZM-EXAMS and SCI-GROW was addressed in DP Barcode D239344, dated 2/26/98. In the 2/26/98 memo, EFED addressed the change in application rate and different half-lives of RPA 202248 in aerobic soil. These application rates and half-lives were used in the computer modeling for surface water and groundwater.

The registrant is proposing ground water, surface water, and irrigated water advisory statements for the product label. The registrant is also proposing spray drift management advisory statements and a restriction from application by chemigation and aerial application techniques. EFED does not believe that these labeling restrictions will reduce the phytotoxic risk below our level of concern.

The registrant conducted PRZM-EXAMS modeling on parent isoxaflutole, RPA 202248, and RPA 203328 (MRID 43988201). The registrant is correct in noting that the values for parent isoxaflutole and RPA 202248 were very similar. However, the registrant and EFED did not achieve similar results when modeling the secondary degradate, RPA 203328. In the modeling, the registrant provided half-lives for RPA 203328 from hydrolysis. There was no scientific basis for hydrolytic degradation, since no RPA 203328 was formed in the study. The registrant also used "special cards" to calibrate the modeling to aerobic soil metabolism studies. This assumes that no further formation of RPA 203328 occurred from degradation of RPA 202248 after 40 days, when in fact, formation of RPA 203328 was continuing at a slower rate than degradation. This is not consistent with normal EFED modeling practices.

Groundwater

EFED does not agree that all the isoxaflutole residues will be completely degraded "prior to the autumn recharge period." If EFED uses the shorter half-life for RPA-202248 as

2

demonstrated by R.P. , there will continue to be concern from carryover and runoff phytotoxic effects since it is still likely to leach in some areas. Once the degradates are carried below the root zone, degradation will be slow or significantly retarded. EFED also concluded that residues of the terminal degradate RPA-203328 are very likely to carryover past the end of the growing season.

PATRIOT modeling was conducted using extremely shallow ground water and was meant to be used in a qualitative manner to compare the leaching potential with other herbicides. The modeling for each compound was conducted over a ten-year interval using actual meteorological data from nearby weather stations and is presented as an average annual loading. The PATRIOT modeling also assumes that most of the degradation is occurring in the upper soil horizon (the root zone) and no significant degradation occurs in the subsurface (deeper than approx. 46 cm).

The model is especially sensitive to the water input (rainfall and irrigation) and to compounds with half-lives less than one-year. It is not particularly sensitive to compounds with half-lives greater than one year, such as RPA-203328 with a calculated half-life of 977 days.

Regarding the half-life of RPA-202248, R.P. provided additional information resulting in revision of the half-life for the modeling from 186 days to 92 days.

Additional data provided early in the registration process resulted in revision of the half-life of RPA-203328 from "stable" to 977 days. R.P. has not adequately demonstrated that the calculated half-life for RPA-203328 of 977 days should be changed. There is a degree of uncertainty in this calculation however the half-life is so extreme, that even if it were modified significantly, it would not make much difference in regards to the modeling.

EFED does agree that the statement "hundreds of ppb" does **not** represent typical concentrations expected in ground water and that it should be much lower. R.P. presented estimations that the theoretical maximum concentration of isoxaflutole residues in a 5 ft. thick aquifer from application to a one hectare field would be 35 ppb. This did not account for any soil degradation and R.P. argues that dilution would be much greater than this resulting in even lower concentrations in ground water.

R.P. has provided data demonstrating that the phytotoxic concerns are with the degradate RPA-202248 and not RPA-203328. EFED's agrees and concerns for phytotoxicity have been focused onto RPA-202248. EFED's concerns for RPA-203328 have been modified to a general ground water quality issue.

Ecotoxicity

Avian Dietary Studies (71-2): **EFED and the registrant agree that avian dietary studies with RPA 203328 are not needed at this time.**

Avian Reproduction Studies (71-4): The registrant requests that the avian reproduction studies be waived because of 1) the low amounts of the RPA 202248 and RPA 203328 that will be in the terrestrial environment, 2) the pre-emergence use pattern would provide minimal amounts on avian food items, 3) the low acute toxicity that the metabolites have to the birds, 4) isoxaflutole was not shown to be teratogenic or a reproductive toxin in mammalian studies, and 5) it is not a bioaccumulator. EFED maintains that avian reproductive studies are needed to access avian chronic toxicity from the labeled use of isoxaflutole because 1) the metabolites are expected to be persistent in the environment, birds will be exposed to the metabolites through food items such as plants (directly or by drift), soil invertebrates, and water, 2) there is no correlation between avian acute and chronic toxicity since there are pesticides known to very toxic on a chronic basis while being practically nontoxic on an acute basis, and 3) HED has indicated that isoxaflutole is a developmental toxicant. **EFED again requests that the registrant conduct avian reproduction tests for RPA 202248 on the mallard and the bobwhite. The avian reproductive study using RPA 203328 is held in reserve pending the results of the RPA 202248.**

Two-Generation Rat Reproduction Study: The registrant has requested that the two-generation rat studies with the metabolites, RPA 202248 and RPA 203328 be waived because 1) no reproductive effects were observed in the parent isoxaflutole, 2) no effects were observed in a 28-day rat feeding study using RPA 203328, 3) parent isoxaflutole was not shown to be teratogenic or a reproductive toxin in mammalian studies, and 4) RPA 203328 was of no toxicological concern. EFED maintains that mammalian reproductive studies are needed on the metabolites because 1) the reasons cited for the avian reproductive studies above and 2) the rat reproductive studies evaluated by HED was done on the parent isoxaflutole and not on the metabolites. However, since the mammals tend to be less sensitive to pesticides than birds, **EFED will hold the two-generation rat studies on RPA 202248 and RPA 203328 in reserve pending the results of the avian reproductive studies.**

Mysid Shrimp Acute: **Rhone-Poulenc has agreed to conduct the acute mysid shrimp study on RPA 203328.**

Sheepshead Acute Studies: The registrant has requested that the sheepshead acute studies on RPA 202248 and RPA 203328 be waived because 1) the mysid is the most sensitive aquatic species tested and acute studies should be on the mysid and not on the sheepshead, 2) concentrations are not expected to be significant, and 3) that the combination of the low use rate, the rapid dissipation of the parent compound in surface water, and the extremely small concentrations of the metabolites formed suggests that no toxicologically-significant residue of either metabolite would be present in the aquatic environment.

EFED maintains that acute sheepshead toxicity studies are needed because 1) although mysid is the most sensitive species, EFED has no data on the metabolites' toxicity to estuarine fish to determine if chronic toxicity is needed, 2) the amount of concentrations is only needed to determine data requirements for aquatic chronic toxicity and not acute toxicity, and 3) RPA

202248 was a significant degradate in the sterile hydrolysis study and in the non-sterile aerobic aquatic metabolism study (t1/2=250-700 days). The only identified pathway of degradation in soil is from parent isoxaflutole to RPA 202248, which then degrades to RPA 203328. Therefore, significant concentrations of the degradates in proportion to the amount applied are expected to reach aquatic environments.

EFED maintains that acute testing of sheepshead fish (72-3) using RPA 202248 is needed for a data baseline and to decide if chronic toxicity studies are needed. Testing of sheepshead on RPA 203328 is reserved pending results of RPA 202248.

Aquatic and Terrestrial Plant Testing: All five species of the aquatic plant testing under 123-2 have been submitted for the parent isoxaflutole. There is no further need for additional 123-2 aquatic plant species (*Lemna gibba, Selenastrum capricornutum, Naviculla sp., Anabaena flos-aquae, Skeletonema costatum)* to be tested with the metabolites.

All of the terrestrial plant species have been acceptably tested using the parent isoxaflutole and RPA 203328.

If there are any questions, please do not hesitate to contact Mike Davy at 305-7081 for ecotoxicity, James Breithaupt for fate at 305-5925 and Ian Kennedy at 605-0206 for groundwater.

5