Shaughnessy No.: 128201
Date Out of EAB: APR 4 1988

To: Robert Taylor
Product Manager PM #25
Registration Division (TS-767)

From: Emil Regelman, Supervisory Chemist
Environmental Chemistry Review Section #3
Exposure Assessment Branch/HED (TS-769C)

Thru: Paul F. Schuda, Chief
Exposure Assessment Branch/HED (TS-769C)

Attached, please find the EAB review of...

Reg./File # : 352-UUR

Chemical Name: DPX-Y6202 (Quizalofop Ethyl)

Type Product : Herbicide

Product Name : ASSURE

Company Name : E.I. du Pont de Nemours and Co.

Purpose : Expedited review of Du Pont's response to EAB's reviews dated 12/18/87 and 1/5/88.

Action Code: 111 EAB #(s): 80591

Date Received: 3/21/88 Total Reviewing Time: 3 days

Date Completed: 4/1/88

Monitoring Study Requested: _____

Monitoring Study Volunteered: _____

Deferrals to: ___ Ecological Effects Branch

___ Residue Chemistry Branch

___ Toxicology Branch

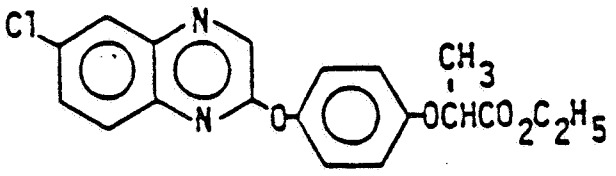
1. CHEMICAL:

chemical name: Ethyl 2-[4-(6-chloroquinoxalin-2-yloxy) phenoxy] propanoate

common name: Quizalofop Ethyl, DPX-Y6202

trade name: ASSURE

structure:



physical/chemical properties:

molecular formula:	$C_{19}H_{17}ClN_2O_4$
molecular weight:	372.5
physical state:	white, crystalline solid
melting point:	91.7-92.1°C
vapor pressure:	3×10^{-7} mm Hg at 20°C

2. TEST MATERIAL:

Not applicable. No studies were submitted.

3. STUDY/ACTION TYPE:

Expedited review of Du Pont's response to EAB's conclusions about recently submitted studies.

4. STUDY IDENTIFICATION:

"Du Pont Responses to Review of Residue Chemistry and Exposure Branch Questions." Submitted by Tony E. Catka of Du Pont. Received by EPA on March 7, 1988.

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5. REVIEWED BY:

Dana Spatz
Chemist, ECRS #3
EAB/HED/OPP

Date: APR 1 1988

6. APPROVED BY:

Emil Regelman
Supervisory Chemist, ECRS #3
EAB/HED/OPP

Date: APR 4 1988

7. CONCLUSIONS:

Confined Accumulation in Rotational Crops:

EAB's conclusions concerning the Confined Accumulation in Rotational Crops study, (Accession # 402423-02, reviewed on 12-18-87), were as follows:

"The accumulation in rotational crops study requirement is partially fulfilled by this submission. The question that still must be answered is what happens to the other end of the ether upon cleavage; 2-[(4-hydroxyphenyl)oxy] propanoic acid, for example. Since only the quinoxaline ring was labeled, one cannot determine the fate of the other end of the molecule upon cleavage of the ether linkage."

Du Pont's response to the conclusions was that because the quinoxaline-labeled study was performed at 2x the proposed maximum use rate and that "no accumulation of radioactivity occurred in harvested crops versus the initial concentration in the soil (0.098 ppm) at the time of planting..., low levels of residues of [^{14}C-phenyl]DPX-Y6202 would be anticipated to be present in soil after a 120 day preplant period.

EAB's response to Du Pont is that it may be true that low levels of residues of [^{14}C-phenyl]DPX-Y6202 will be found but, this theory must be proven and thus data must be generated with the phenyl-labeled material in a confined accumulation study.

Du Pont also states in their response that because the major metabolites from phenyl-labeled DPX-Y6202 soil metabolism studies are DPX-Y6202 Acid and Phenol 4, (2-[(4-hydroxyphenyl)oxy] propanoic acid), and that Phenol 4 was found to comprise only 18% at 4 months on soil treated with

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4x the use rate, then at the proposed use rate in a confined accumulation study, Phenol 4 would be available for uptake in very small and insignificant amounts.

EAB's response is, however, that soil metabolism studies cannot be used to predict the outcome of a confined accumulation study. Both studies are designed to give very specific information that the other study cannot produce. The main purpose of a confined accumulation study is to determine what residues are accumulated in plants so that in a field accumulation study, it is known what residues to analyze for.

Aerobic Soil Metabolism:

EAB's conclusions concerning the Aerobic Soil Metabolism study requirement were as follows:

"Because the quinoxaline moiety and phenyl moiety are separated upon cleavage of the ether linkage, both moieties must be labeled in all studies employing radiolabeling techniques. Therefore, since the aerobic soil metabolism study was done with only the phenyl group labeled, this study must also be performed with the radiolabel on the quinoxaline ring in order to satisfy the requirements for registration."

Du Pont's response to these conclusions was that a quinoxaline-labeled aerobic soil metabolism study (accession # 255760, reviewed on 4-10-85), was submitted and that deficiencies in this experiment were responded to by them on 9-10-85.

The reason why the study was originally rejected by EAB was because of very poor correlation coefficients for the data, suggesting inadequate recovery procedures. The reviewer (Emil Regelman), suggested that the registrant try fitting the data to a biphasic degradation scheme.

Du Pont suggests that EAB's hypothesis is correct, but has not supplied the necessary data to confirm this. Therefore, DuPont must perform a short quinoxaline-labeled study with frequent sampling within the first week and attempt to fit the data to a biphasic curve. If the correlation coefficients are acceptable, then this study will be deemed acceptable and the aerobic soil metabolism study requirement will be fulfilled.

Anaerobic Aquatic Metabolism:

EAB's conclusions concerning the Anaerobic Aquatic Metabolism

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study (accession #073548), were as follows:

"It does not appear that an effort was made to identify all the residues greater than 0.01 ppm in the Anaerobic Aquatic Soil Metabolism study. The analytical technique used (TLC) was not of sufficient sensitivity to identify metabolites 1, 2, and 3. These unknown metabolites were present at levels >0.01 ppm. Other, more highly sensitive, techniques should have been employed in an attempt to identify these degradates.

Du Pont's response to these conclusions was that the study was done at 1.0 ppm (4x the maximum use rate), and hence, the unidentified metabolites would be present at less than 0.01 ppm at the maximum use rate.

However, the Pesticide Assessment Guidelines, Subdivision N, specifically state that the "test substance should be applied at a rate sufficient to permit measuring the disappearance of the parent compound and identification of major degradates." Unknown metabolites were present at levels sufficient enough to identify but, were not identified.

This study must be repeated. All metabolites present at levels greater than 10% of applied must be identified.

TLC as an Analytical Technique:

TLC cannot be used as a technique for making positive identifications of residues. It can only appropriately be used as a method for making tentative identifications. Other methods such as GC-Mass Spectrometry must be used where conclusive identification is necessary.

Field Soil Dissipation:

EAB's conclusions concerning the Field Soil Dissipation study (accession #403360-01), were as follows:

"A major metabolite of DPX-Y6202, Phenol 4, (2-[(4-hydroxyphenyl)oxy] propanoic acid), was not included in the study as a degradate that should have been identified and quantitated by soil analyses. The Aerobic Soil Metabolism of [Phenyl-^{14}C(U)]DPX-Y6202 study (Cadwgan and McFetridge, 1985), indicated that in Flanagan silt loam soil treated at 0.1 ppm, Phenol 4 levels were 26% of applied ^{14}C by week 2, and that in soil treated at 1 ppm, Phenol 4 levels were 30% by week 5. This information establishes the prevalence of Phenol 4 and, as such, suggests that this degradate be included in the list of degradates being analyzed for in the

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dissipation/mobility studies."

Du Pont's response to these conclusions was that "Phenol 4 would not be present at detectable levels in the cold field soil dissipation with detection limits of 0.05 ppm." This statement was based on the fact that "no HO-Phenol 2 was detected in the cold field soil dissipation study...and that HO-Phenol 2 was present at greater or equivalent levels to Phenol 4 in soil metabolism studies of DPX-Y6202."

However, EAB cannot accept this reasoning as proof of the fate of Phenol 4. Actual measurements of the residues in the field must be provided.

Secondly, Du Pont feels these results were confirmed by the data in the ^{14}C-DPX-Y6202 Field Soil Dissipation study which showed a maximum of 0.02 ppm of Phenol 4.

However, the radiolabeled Field Soil Dissipation study was rejected by EAB for numerous reasons. The study (accession #073771, reviewed on 2-11-87), cannot be used even to provide supplemental information because in the phenyl-labeled portion of the study, the following problems are noted:

a. Poor recoveries- Only 88.5% of the total [^{14}C] was recovered on Day 0 and the recoveries continued to decline to 32.8% by month 16.

b. Only one soil was tested. Note that EAB requirements call for at least 2 soils.

c. The application rate (3.5 oz ai/acre), was below the maximum application rate stated on the product label (4 oz ai/acre).

The Field Soil Dissipation study requirement remains unfulfilled.

8. RECOMMENDATIONS:

See Conclusions above.

9. BACKGROUND:

Most of EAB's concerns explained in this review were relayed to Du Pont in a meeting with them on March 23, 1988. This expedited review serves as EAB's written response.

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10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

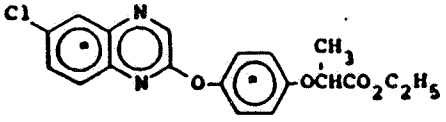
Not applicable. No studies were submitted.

11. COMPLETION OF ONE-LINER:

Not applicable.

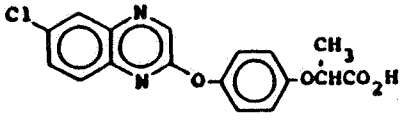
12. CBI APPENDIX:

Not applicable.



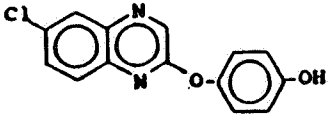
DPX-Y6202

Ethyl 2-[4-(6-chloroquinoxalin-2-yloxy)phenoxy]propanoate



"DPX-Y6202 Acid"

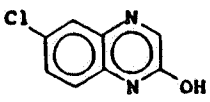
2-[4-(6-chloroquinoxalin-2-yloxy)phenoxy]propanoic acid



"Phenol 1"

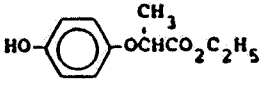
4-(6-chloroquinoxalin-2-yloxy)phenol

* (uniformly labeled on either the quinoxaline-phenyl or phenyl ring)



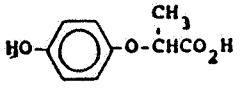
"Phenol 2"

6-chloroquinoxalin-2-ol



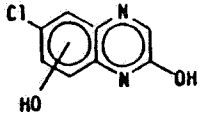
"Phenol 3"

ethyl-2-[(4-hydroxy phenyl)oxy]propanate



"Phenol 4"

2-[(4-hydroxyphenyl)oxy]propanoic acid



Hydroxy-Phenol 2

Hydroxylated 6-chloroquinoxaline-2-ol

Figure 1. CHEMICAL STRUCTURES AND NAMES FOR DPX-Y6202 AND POTENTIAL DECOMPOSITION PRODUCTS.