Shaughnessy Number: 109301

Date out of EFGWB: 11/30/90

To: George LaRocca/Adam Hayward
Product Manager 15
Registration Division (H7505C)

From: Henry Nelson, Acting Section Head
Environmental Fate Review Section #3
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

Thru: Hank Jacoby, Chief
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

Attached, please find the EFGWB review of...

Reg./File #: 352-515

Chemical Name: Fenvalerate

Type Product: insecticide

Product Name: Asana XL 0.66% EC

Company Name: E.I DuPont de Nemours

Purpose: submission of field dissipation and fish bioaccumulation studies

Date Received: 6/18/90 (90-0636), 10/4/90 (91-0024)

Action Code: 331

EFGWB#(s): 90-0636, 91-0024

Total Reviewing Time (decimal days): 6.5

Deferrals to: ___Ecological Effects Branch, EFED

___Science Integration and Policy Staff, EFED

___Non-Dietary Exposure Branch, HED

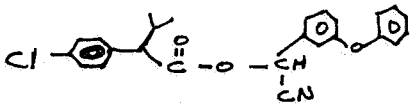
___Dietary Exposure Branch, HED

___Toxicology Branch

ebc

1. CHEMICAL:

chemical name: (S)-cyano(3-phenoxyphenyl)methyl-(S)-4-chloro-α(1-methylethyl)benzeneacetate
common name: fenvalerate (racemic mixture), esfenvalerate (S,S-isomer)
trade name: Pydrin® (racemic mixture), Asana® (S,S-isomer)
structure:



CAS #: 51630-38-1
Shaughnessy #: 109301

2. TEST MATERIAL: n.a.

3. STUDY/ACTION TYPE:

submission of field dissipation and fish bioaccumulation data on active isomer instead of racemic mixture

4. STUDY IDENTIFICATION:

EFGWB 90-0636
Schneiders, G.E. **Field Soil Dissipation Studies with Asana® and Pydrin® Insecticides**. dated 11/10/89. performed by Shell Development Company, Modesto, CA, and E.I. DuPont de Nemours & Co. Inc., Wilmington, DE. project ID AMR-1555-89. Submitted by E.I. DuPont de Nemours & Co., Inc. received by EPA 6/11/90, under MRID# 415203-01.

EFGWB 91-0024
Lee, P.W. **Bioaccumulation of Fenvalerate in Fish**. dated 8/23/90. performed by performed by Shell Development Company, Modesto, CA; Sumitomo Chemical Co. Ltd., Takarazuka, Japan; and E.I. DuPont de Nemours & Co. Inc., Wilmington, DE. project ID AMR-1827-90. Submitted by E.I. DuPont de Nemours & Co., Inc. received by EPA 9/25/90, under MRID# 416377-01.

5. REVIEWED BY:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 2
Organization: EFGWB/EFED/OPP

E. B. Conerly 11/30/90

6. APPROVED BY:

Typed Name: Henry Nelson
Title: Acting Section Head, Review Section 3
Organization: EFGWB/EFED/OPP

H Nelson 11/30/90

7. CONCLUSIONS:

The applicant has not demonstrated that the S,S-isomer is similar in environmental behavior to the racemic mixture. The necessity for this information was noted in JHJ 2/4/86.

ebc

The field dissipation study is not acceptable to fulfill data requirements due to several deficiencies. Since the deficiencies cannot be repaired, a new study is required. It does appear to be consistent with other information which indicates relatively low persistence and mobility.

The fish bioaccumulation study is not acceptable to fulfill data requirements. Since the deficiencies cannot be repaired, a new study is required. Based on the submitted study, esfenvalerate could possibly bioaccumulate.

8. RECOMMENDATIONS:

The applicant should submit information demonstrating that the S,S-isomer does in fact behave similarly to the racemic mixture. This will include soil photolysis, field dissipation, fish and rotational crop accumulation studies.

Since neither study discussed in this review is acceptable, the applicant should initiate new studies as soon as possible.

In the field dissipation study, particular attention should be given to confirmation of application rates, and the necessity to demonstrate that esfenvalerate is no more persistent than the racemic mixture. The applicant may want to consider a bare-ground study.

In the fish bioaccumulation study, the test animal should be one of the options mentioned in the Guidelines (Subpart N) or an acceptable justification presented for the use of another species. Special care should be taken that a steady state exists in the exposure tank during the entire experimental period.

9. BACKGROUND:

Data requirements which have not been fulfilled for the racemic mixture are the following:

HYDROLYSIS -- An acceptable hydrolysis study is required.[1]

FISH BIOACCUMULATION -- a study on fish bioaccumulation is discussed below.

The applicant wishes to use data developed in studies on the racemic mixture (25% each of four isomers) to support registration of the S,S-isomer, now isolated in a relatively pure form. Chemical processes can be expected to occur at similar rates for all isomers, but biologically-mediated processes may be similar for the four isomers or different for each individual isomer. There is little data to

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[1] Apparently in error, the hydrolysis data requirement was previously declared fulfilled, and the EFGWB one-liner states that fenvalerate is stable to hydrolysis. Examination of file material shows that there is no review of an acceptable hydrolysis study in EFGWB files. Based on results of two unacceptable hydrolysis studies and the dark control of an acceptable aqueous photolysis tudy, fenvalerate is subject to hydrolysis, not stable. The error seems to have occurred when EFGWB summarized Dynamac reviews referenced below. The review of one study says that fenvalerate is stable up to 93.5 hours, and then states that the study is not acceptable because it was discontinued too soon. EFGWB did not incorporate the second statement in its summary. A second study at elevated temperature was not acceptable for several reasons -- organic solvent in the mixture, incorrect pH.

indicate which is true in this case. In one aerobic soil metabolism study (reviewed by JHJ 2/4/86), the not too surprising result is that *in silt loam* the S,S-isomer does not persist any longer (75 days) when isolated than when it is present as a part of a racemic mixture (95 days). The review also references another review reporting a study showing that the $t_{\frac{1}{2}}$ of the racemic mixture is 65 days in sandy loam and 8 months in loam. Relative degradation rates of the various isomers are not given. The same review notes that field dissipation studies are necessary, and further notes the need to demonstrate by submission of data that the behavior of the S,S-isomer is similar (*or at least no more adverse than*) the racemic mixture.

The status of environmental fate data requirements to support registration of the S,S-isomer and the racemic mixture is given below (taken from Dynamac reviews of 3/18/86 and 3/9/88 except as noted). Studies were performed using the racemic mixture unless otherwise stated.

CHEMICAL PROCESSES

hydrolysis -- **NOT SATISFIED** for racemic mixture or S,S-isomer. Available information on the racemic mixture suggests a $t_{\frac{1}{2}}$ of ca. 14 days @ pH 5.

photolysis in water -- satisfied for racemic mixture and S,S-isomer by data on the racemic mixture -- half-life of 6 days at pH 5 vs a dark control with (hydrolytic) half-life of 13.8 days

leaching/adsorption/desorption -- satisfied for racemic mixture and S,S-isomer by data on the racemic mixture -- aged and unaged *via column leaching studies* -- immobile in sand, sandy loam, loam, and silt loam; 88% was found in the top 3 cm after leaching with 20 cm of water

PROCESSES WITH A BIOLOGICAL COMPONENT

soil photodegradation -- satisfied for the racemic mixture, **NOT SATISFIED** for the S,S-isomer -- half-life of phenoxyphenyl labelled compound was 14-28 days on sandy loam soil; more than 50% of chlorophenyl material was undegraded after 28 days -- under natural light, 53% was undegraded, and under artifical light, 60% was undegraded.

aerobic soil metabolism -- satisfied for the racemic mixture and the S,S-isomer -- **THE S,S-ISOMER WAS TESTED** -- $t_{\frac{1}{2}}$s of 65 days to more than 1 year in a variety of soils were reported for the racemic mixture. A study was submitted and accepted (JMJ 2/4/86) which demonstrates that in a silt loam soil the isolated S,S-isomer degrades with a half-life of 75 days. When followed as part of the racemic mixture, this same isomer has a half-life of 95 days under otherwise similar conditions.

anaerobic soil metabolism -- satisfied for the racemic mixture, **NOT SATISFIED** for the S,S-isomer -- rates for the racemic mixture were similar to aerobic metabolism

terrestrial field dissipation -- declared satisfied in 1979 for the racemic mixture, **NOT SATISFIED** for the S,S-isomer, as discussed below -- $t_{\frac{1}{2}}$ 25 days in sandy loam (AZ), 34 days in clay loam (OK), 54 days in silt loam (LA), and 54 days in sandy loam (AL). A newly submitted study is reviewed in an attached DER.

confined accumulation in rotational crops -- satisfied for the racemic mixture, **NOT SATISFIED** for the S,S-isomer -- residue from the racemic mixture detected at levels up to 0.061 ppm

field accumulation in rotational crops -- satisfied for the racemic mixture, **NOT SATISFIED** for the S,S-isomer -- no residues from the racemic mixture (lod 0.01 ppm)

fish bioaccumulation -- **NOT SATISFIED** for either the racemic mixture or the S,S-isomer -- a newly submitted study is discussed below

Fenvalerate degrades *via* a number of pathways (see summary below). Fenvalerate and its degradation products were not mobile in a variety of soils. The combination of lability and lack of mobility indicate that fenvalerate is not likely to contaminate ground-water.

half-lives:

hydrolysis ("semi-valid" data) --	$t_{1/2}$	13.8 days pH 5
aqueous photolysis --	$t_{1/2}$	6 days pH 5
soil photolysis --	$t_{1/2}$	14 - 28 days in sandy loam
aerobic soil metabolism --	$t_{1/2}$	65 - 365 days
anaerobic soil metabolism --	$t_{1/2}$	similar to aerobic
terrestrial field dissipation --	$t_{1/2}$	25 - 54 days

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES: see DERs

11. COMPLETION OF ONE-LINER:

12. CBI APPENDIX: attached to DERs

DATA EVALUATION REVIEW

I. Study Type: terrestrial field dissipation

II. Citation:

Schneiders, G.E. Field Soil Dissipation Studies with Asana® and Pydrin® Insecticides. dated 11/10/89. performed by Shell Development Company, Modesto, CA, and E.I. DuPont de Nemours & Co. Inc., Wilmington, DE. project ID AMR-1555-89. Submitted by E.I. DuPont de Nemours & Co., Inc. received EPA 6/11/90, under MRID# 415203-01.

III. Reviewer:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 3
Organization: EFGWB/EFED/OPP

E.B. Conerly 11/30/90

IV. Conclusions:

This study is not acceptable to fulfill this data requirement:

1) Although the study does suggest that soil build-up may not be a problem in this type of application [*i.e. foliar application to cotton plants*], it failed to answer the key question -- whether soil dissipation of Asana® is similar to that of Pydrin®. There are no data reported on Asana® since soil levels were below the limit of detection [this is probably a level of *quantitation*] at the first sampling time, per the applicant.

2) The study protocol was somewhat biased against detection of the S,S-isomer relative to the racemic mixture. To apply the same amounts of active ingredient in both cases, the dosage of Pydrin® should have been four times that of Asana®. Instead, the total material applied was approximately 5 to 12-fold more for Pydrin® as compared to Asana® [1.25 to 3 times as much active ingredient].

3) Because no bare-ground control was reported, it is impossible to confirm application rates. Although a bare-ground study is not an absolute requirement, it may offer a technically more feasible way of attaining soil concentrations which are measurable than would a new study similar to this one.

4) In this study, both Pydrin® and Asana® were applied to foliage, and not to soil. Soil was sampled only after the course of applications was completed, and intermediate concentrations of parent and degradates in soil are not known. Therefore, even for Pydrin®, the patterns of disappearance of fenvalerate and appearance and disappearance of degradates during the multiple applications of a growing season were not elucidated. It appears, however, that the field $t_{\frac{1}{2}}$ *after application is discontinued* is ca 1 - 3 months for the racemic mixture. As stated above, a course of multiple maximum applications of Asana® to foliage resulted in soil concentrations below the analytical method limit of detectability when examined immediately after the last treatment.

V. Materials and Methods:

General protocol -- The dissipation of fenvalerate residues in soil under field conditions was examined at seven sites. Soil characteristics at all sites are attached. Asana® (the active isomer) was applied to young cotton plants at three locations (Donna, TX [*sandy clay loam*]; Yuma, AZ [*sandy clay loam*]; and Montgomery, AL [*sandy clay loam*], ranging from 7 to 11 applications at 0.0375 to 0.05 lb/A (0.2625 to 0.55 lb/A total). Pydrin® (the racemic mixture) was applied similarly to young cotton plants at four locations (Hobart, OK [*clay loam*]; Bastrop, LA [*Gallion silt loam*]; Shorter, AL [*sandy loam*], and Maricopa, AZ [*sandy loam*], using 15 applications at 0.2 lb/A (3.0 lb/A total, ≈ 0.75 lb/A S,S-isomer). These application rates exceeded the maximum label use direction for both insecticides. Control[1] and treated soil samples were frozen immediately after collection and kept frozen until analyzed.

test material -- Asana® (1.9 EC), and Pydrin® (2.4 EC)

analytical method -- electron capture gas chromatography, minimum detection concentration = 0.01 ppm

analytical validity -- overall recoveries in the 0.05 to 0.5 ppm range were from 83 to 124%, and at the 0.1 ppm level were 104 to 110%. No degradation during storage took place over 588 days.

VI. Study Author's Results and/or Conclusions:

1) Fenvalerate did not persist. Fenvalerate residues degraded rapidly under actual field use conditions. Dissipation half-lives for Pydrin® ranged from 22 to 75 days depending on soil and weather conditions. Fenvalerate residues were below the quantitation limit of 0.01 ppm in the soil 30 - 90 days after multiple Asana® applications.

2) Fenvalerate metabolites did not build up. Significant concentrations of the major fenvalerate metabolites were not observed.

3) Neither fenvalerate nor its degradates leached. No significant concentrations of fenvalerate or its soil degradates were detected below the 0 - 3 inch depth.

4) Meaningful estimation of the field dissipation rate of [Es]fenvalerate applied as Asana® was not possible, because, even though it was applied at the maximum label rate, residues immediately following the last application were negligible (≤ 0.06 ppm). As stated above, the data clearly showed that the amount of total residue in the soil after extensive use is minimal, and well below the quantitation limit of 0.01 ppm by 30 - 90 days after the last application.

VII. Reviewer's Comments:

1) These data appear to be in general agreement with results from lab studies, i.e. fenvalerate does not seem to be persistent or mobile. However, the material was applied to plants, not to the soil. At an application rate of 0.2 lb/A (0.2 ppm for a 3-inch soil layer) Pydrin®

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[1] No control fields were described in the report, although this text implies that controls were performed.

repeated 15 times (a total of 30 ppm in a 3" soil layer), soil samples taken the day of the last treatment all showed less than 1 ppm present. Since a bare-ground application was not included, it is impossible to confirm application rates for this study. Further, because soils were only sampled after the last application, not throughout the experimental period, the pattern of disappearance of parent and appearance and disappearance of degradates has not been elucidated. Asana® was applied in lesser amounts (**0.265 to 0.55 lb/A total material** vs **3.0 lb/A total material** (0.75 lb/A S,S-isomer equivalent) in the racemic mixture), and was not detected at any sampling time.

2) The pH of all soils used to test Asana® is distinctly basic. One of the soils used to test Pydrin® is basic, and the other three are neutral or acid. This difference is of unknown significance.

VIII. CBI Information Addendum: attached

FENVALERATE Sh # 109301

Page_____ is not included in this copy.

Pages 9 through 17 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

DATA EVALUATION REVIEW

I. Study Type: fish bioaccumulation

II. Citation:

Lee, P.W. Bioaccumulation of Fenvalerate in Fish. dated 8/23/90. performed by Shell Development Company, Modesto, CA; Sumitomo Chemical Co. Ltd., Takarazuka, Japan; and E.I. DuPont de Nemours & Co. Inc., Wilmington, DE. project ID AMR-1827-90. Submitted by E.I. DuPont de Nemours & Co., Inc. received EPA 9/25/90, under MRID# 416377-01.

III. Reviewer:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 3
Organization: EFGWB/EFED/OPP

E.B. Conerly 11/30/90

IV. Conclusions:

The main study does not satisfy data requirements:

1) The system was probably not at a steady state during a significant portion of the study period.[1] This makes interpretation of the data questionable at best.

2) The test animal in the flow-through study was the carp, which is perhaps not the best representative of fish consumed for food in the United States.

It does provide the supplemental information that esfenvalerate may have the tendency to bioaccumulate.

The supplementary studies on rainbow trout and catfish were not done under flow-through conditions, and therefore are not acceptable to provide even supplemental information.

V. Materials and Methods:

general protocol

A dynamic flow-through study at 0.1 ppb[2] was conducted to determine the accumulation potential of ^{14}C-phenoxyphenyl-fenvalerate residues in

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[1] This may indicate one or more of the following:

that the aquarium is overloaded with fish which, in turn, are metabolizing a significant amount of compound -- this is the most likely explanation
that there is a problem with the apparatus
that the compound is degrading through chemical processes or microbial metabolism

Under proper conditions in a flow-through system, fish and/or microbes should not have a significant effect on the concentration of test compound.

[2] Water solubility reported as "< 2 ppb".

carp.[3] The concentration in the water and in the fish tissues were monitored throughout the 28-day exposure period and the 14-day depuration period. Only this study is discussed in detail below.

Additional studies examined the fate and bioaccumulation potential of rainbow trout and catfish under semi-flowthrough [*sic* - EBC] and static (sediment) test conditions. The rainbow trout were not exposed in a flow-through system, but were transferred to freshly treated water every three or four days [*sic* --EBC]. Catfish were exposed in a system containing water and treated soil (sediment) at two different levels (0.01 ppm and 1.0 ppm) of esfenvalerate.

test material -- ^{14}C-chlorophenyl-fenvalerate, 142 µCi/mg, radiochemical purity >99% by TLC radioautography

sampling schedule -- 1, 3, 5, 10, 15, 20, 30, 35 days during exposure; 1, 3, 9, 19, and 33 days during depuration

extraction and purification -- homogenized in acetone, extracted with acetone, then methanol. Acetone and methanol extracts were separately concentrated *in vacuo*. Residues were dissolved in ethyl acetate or methanol, and analyzed for total radioactivity by LSC. Extracts were subjected to TLC. Compounds were tentatively identified by co-chromatography with unlabelled standards. 4'-OH-fenvalerate-glucuronide and 4'-OH-phenoxybenzoic acid-sulfate were purified by preparative TLC, hydrolyzed enzymatically, and analyzed using TLC cochromatography against 4'-OH-fenvalerate and 4'-OH-phenoxybenzoic acid.

analytical methods

LSC -- total radioactivity fish extracts and combusted extracted tissue

TLC -- silica gel plates; two dimensional development in hexane/ethyl acetate/acetic acid (10/4/1) followed by toluene/ethyl formate/formic acid (5/7/1)

VI. Study Author's Results and/or Conclusions:

main study (carp)

1) No abnormality or mortality during the study was observed.

2) Calculated bioconcentration factors (BCFs) for total ^{14}C-residues from 28 days exposure were 2090, 5350, and 1500 respectively for whole fish, viscera, and carcass (meat) [*sic* -EBC].

3) Most residues were associated with viscera (head, skin, etc.).

4) The depuration half-life for residues was approximately 8 days.

5) Undegraded fenvalerate was the major component detected in the water and fish tissues.

6) Conjugated and free products of 4'-OH-fenvalerate, and 4'-OH-phenoxybenzoic acid were the major metabolites identified.

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[3] The reported acute toxicity (LC_{50} at 96 hrs) is 2.68 µg/l (2.68 ppb) -- this appears to exceed the water solubility of the compound.

supplementary studies

rainbow trout

1) Total residues were ca. 0.04 - 0.09 ppm in whole fish.
2) More than 80% of the residue was esfenvalerate.
3) BCFs ranged from 100 to 393 for whole fish.

catfish

1) Residues were undetectable in the fish exposed to the 0.01 ppm treated soil.
2) BCFs for the 1.0 ppm exposure were from 48 to 118 for whole fish. The highest BCF was at day 15, and decreased to an apparent plateau of ca 70 for the last three samplings.

VII. Reviewer's Comments:

main study

1) The system was probably not at a steady state:
   a) The concentration of esfenvalerate in the water was highly variable (SD ca. 33%). It went down markedly right after addition of the fish and took several days to recover. This may indicate that the quantity of fish added was sufficient to overload the system.
   b) "Up to 60%" of the total radioactivity was esfenvalerate. The applicant stated that esfenvalerate disappeared, and other compounds were generated, due to biological degradation. Other compounds which were present were phenoxybenzoic acid, 4'-OH-phenoxybenzoic acid, 4'-OH-fenvalerate, and other polar conjugates. The nature of the products would indeed tend to argue against chemical degradation, and suggest that metabolic activity (of microbes, or even of the fish themselves) was responsible.

2) Bioconcentration factors for the carp are relatively high, and depuration is relatively slow, indicating a tendency to bioaccumulate. Another way of stating the depuration rate is that ca. 25% of the accumulated residues would remain after 16 days (two half-lives). This is a matter for concern.

3) The test animals were carp (study performed in Japan by Sumitomo). The suitability of this species in this study is questionable. Carp is not commonly consumed for human food in this country, to the best of this reviewer's knowledge. [Whether it is used for pet food is not known.]

supplementary studies

rainbow trout

1) The fish apparently had not reached a steady state of accumulation, since the BCF did not reach a plateau.
2) This is neither a static nor a flow-through study, and therefore difficult to interpret.

catfish

1) This is a static study, and of little use in fulfilling EFGWB data requirements.
2) Two values are reported for day 21. The applicant should clarify whether this is correct or a typographical error.

VIII. CBI Information Addendum: attached

FENVALERATE Sh # 109301

Page_____ is not included in this copy.

Pages 21 through 30 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

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