

DP Barcode: D192427
D192760

Shaughnessy No.: 118202
Date Out of EFGWB:

TO: Richard Mountfort
Product Manager # 10
Registration Division (7505C)

FROM: Mah Shamim, Ph.D. *M. Shamim* NOV 02 1993
Acting Section Chief, Review Section #2
Environmental Fate and Groundwater Branch (7507C)

THROUGH: Henry Jacoby, Chief
Environmental Fate and Groundwater Branch
Environmental Fate and Effects Division (7507C)

Attached, please find the EFGWB review of:

Reg./File #(s) : 062719-EUP-EL; 062719-EUU; 062719-EUG.

Common Name : Hexaflumuron.

Chemical Name : DE-473.

Product Name : Hexaflumuron Termite Bait (NAF-46).

Company Name : DowElanco.

Purpose : Application for EUP for testing of termite bait stakes;
Review of four environmental fate studies submitted in
support of New Chemical Screen.

Action Code: 115 EFGWB #: 93-0825 Total review time: 5.0 days
Action Code: 700 EFGWB #: 93-0850 Total review time: 2.0 days

EFGWB Guideline/MRID/Status Summary Table: The review in this package contains...

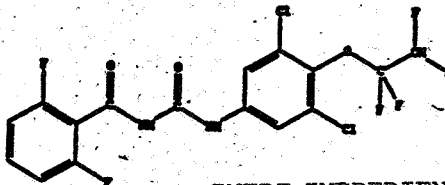
161-1	42648526	Y	162-4		164-4		166-1
161-2			163-1	42648527-A,-B,-C	P	164-5	166-2
161-3			163-2			165-1	166-3
161-4			163-3			165-2	167-1
162-1	42695901	S	164-1			165-3	167-2
162-2	42695901	P	164-2			165-4	201-1
	Request for EUP for bait tests in 21 states	Y	164-3			165-5	202-1

Y = Acceptable (Study satisfied the Guideline)/Concur P = Partial (Study partially satisfied the Guideline, but additional information is still needed)
S = Supplemental (Study provided useful information, but Guideline was not satisfied) N = Unacceptable (Study was rejected)/Non-Concur

1. CHEMICAL:

Common Name: Hexaflumuron.
Chemical Name: 1-(3,5-Dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl)-3-(2,6-difluorobenzoyl)urea.
CAS No.: 86479-06-3.
Trade Name: NAF-46 (formulated termite bait); DE-473 (technical).

Chemical Structure:



INERT INGREDIENT INFORMATION IS NOT INCLUDED

Formulation: Bait stakes (0.1 g of ai/100 g [REDACTED])

Physical/Chemical Properties of Active Ingredient:

Molecular Formula: $C_{16}H_8N_2O_3F_6Cl_2$.
Molecular Weight: 461.16.
Physical state: Solid.
Solubility: 0.027 ppm in water at 18°C.

2. TEST MATERIAL:

Studies 1-3: Active ingredient (uniformly benzoyl ring-labeled [^{14}C] and uniformly aniline ring-labeled [^{14}C]).

3. STUDY/ACTION TYPE:

D192427: Review of three environmental fate studies submitted in support of a New Chemical Screen.

D192760: Application for an EUP for testing of bait stakes (0.1 g ai/100 g [REDACTED]) in "structures" in 21 states.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

4. STUDY IDENTIFICATION:

Jackson, R., and D.A. Yon. 1992. The hydrolysis of hexaflumuron in buffered distilled water at pH 5, 7 and 9. Laboratory Study ID: 4B; Report No. GHE-P-2795. Unpublished study performed by DowElanco Europe, Oxon, United Kingdom, and submitted by DowElanco, Indianapolis, IN. (42648526)

Letter from Jeffery D. Pinkham, Product Registration Manager, DowElanco, dated January 27, 1993, to Joe Tavano (PM-10), Registration Division. (42695900)

Pinkham, J.D. 1993. Bait station assembly. Laboratory Project Study ID: JDP/0011893. Unpublished document study compiled and submitted by DowElanco, Indianapolis, IN. (42648528)

Racke, K.D. 1993a. Aerobic and anaerobic soil metabolism of hexaflumuron. Laboratory Study ID: GH-C 2970. Unpublished study performed by Huntingdon Research Centre Ltd., Huntingdon, United Kingdom, and DowElanco Europe, Oxon, United Kingdom; and submitted by DowElanco, Indianapolis, IN. (42695901)

Racke, K.D. 1993b. Leaching and adsorption/desorption of hexaflumuron. Laboratory Study ID: GH-C 2969. Unpublished summary of GHE-P-1863 and GHE-P-1892 prepared and submitted by DowElanco, Indianapolis, IN. (42648527-C)

Robertson, A.S. 1993. Proposed experimental program: Hexaflumuron termite bait. DowElanco Laboratory Study ID: ASR052893. Unpublished document compiled and submitted by DowElanco, Indianapolis, IN. (No MRID)

Yon, D., and R.K. Grant. 1989. The aged desorption characteristics of Dowco 473. Laboratory Project Study ID: GHE-P-1892. Unpublished study performed by Dow Chemical Company Limited, Wantage, Oxon, United Kingdom. (42648527-B)

Yon, D., and G. Morrison. 1988. The leaching characteristics of hexaflumuron. Laboratory Project Study ID: GHE-P-1863. Unpublished study performed by Dow Chemical Company Limited, Wantage, Oxon, United Kingdom. (42648527-A)

5. REVIEWED BY:

Stephanie Syslo
Environmental Scientist
Review Section #2
OPP/EFED/EFGB

Stephanie Syslo

11/2/93

6. APPROVED BY:

Mah Shamim, Ph.D.
Acting Section Chief
Review Section #2
OPP/EFED/EFGB

Mah Shamim

NOV 02 1993

7. CONCLUSIONS:

New Chemical Screen:

Hydrolysis (161-1)

A hydrolysis study (MRID 42648526; Study # 1) was reviewed in this report and is acceptable.

Uniformly benzoyl ring-labeled [¹⁴C]hexaflumuron [1-(3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl)-3-(2,6-difluorobenzoyl)urea; radiochemical purity >99%], at 0.015 ug/mL, was stable in sterile aqueous pH 5 buffer solutions (containing 10 ppm mercuric chloride) and relatively stable (<5% degraded) in pH 7 buffer solutions (no mercuric chloride); the solutions were incubated in the dark at 25 ± 1°C for 33 days. In pH 9 buffer solutions (no mercuric chloride), uniformly benzoyl and aniline ring-labeled [¹⁴C]hexaflumuron (radiochemical purities >99%) degraded with registrant-calculated half-lives of 21-22.5 days. Degradates identified in the benzoyl-labeled pH 9 solutions were: 2,6-difluorobenzoic acid (maximum of 55% of the applied at 33 days posttreatment); and 2,6-difluorobenzamide (maximum of 8% of the applied at 33 days posttreatment). Degradates identified in the aniline-labeled pH 9 solutions were: 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylurea (maximum of 59% of the applied at 37 days posttreatment); and 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylamine (maximum of 10% of the applied at 33 days posttreatment).

This study fulfills EPA Data Requirements for Registering Pesticides by providing information on the hydrolysis of benzoyl ring-labeled [¹⁴C]hexaflumuron in aqueous buffered solutions at pH 5, 7, and 9.

Aerobic Soil Metabolism (162-1)

The aerobic soil metabolism portion of a study reviewed in this report (MRID 42695901; Study # 2) does not meet present guidelines and should be upgraded. However, the data are adequate to support the proposed use.

The portion of the aerobic soil metabolism study conducted with aniline ring-labeled [¹⁴C]hexaflumuron is scientifically sound, but does not meet Subdivision N guidelines for the following reasons:

one compound (M8) detected in the soil extracts at a maximum of 11% of the applied (0.11 ppm; in one soil at 180 days posttreatment) was not identified.

The portion of the aerobic soil metabolism study conducted with benzoyl ring-labeled [¹⁴C]hexaflumuron is unacceptable for the following reason:

the material balances were incomplete; up to 55% of the applied radioactivity was not accounted for by the termination of the experiments (365 days posttreatment).

Because the material balances in the portion of this study conducted using benzoyl ring-labeled [¹⁴C]hexaflumuron were incomplete, these data are of uncertain value and should not be used to predict the behavior of benzoyl ring-labeled [¹⁴C]hexaflumuron and its degradates in the environment.

The study does provide supplemental information on the metabolism of aniline ring-labeled [¹⁴C]hexaflumuron in aerobic soils.

Aniline ring-labeled [¹⁴C]hexaflumuron [1-(3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl)-3-(2,6-difluorobenzoyl)urea] degraded with half-lives of 180 and 260 days in US silt loam and sandy loam soils, respectively, and 110 and 130 days in UK sandy loam and clay loam soils, respectively, that were incubated in the dark at 25°C and 75% of field moisture capacity for 365 days. One degradate, 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylamine (M4), was identified in the four soils at maximums of 12-20% of the applied at 30-120 days posttreatment.

Anaerobic Soil Metabolism (162-2)

The portion of the anaerobic soil metabolism study conducted with aniline ring-labeled [¹⁴C]hexaflumuron and reviewed in this report (MRID 42695901; Study # 2) is acceptable.

Uniformly aniline ring-labeled [¹⁴C]hexaflumuron [1-(3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl)-3-(2,6-difluoro-benzoyl)urea; radiochemical purities >98%], at 1 mg/kg, degraded with registrant-calculated half-lives of 40-72 days in four US and UK soils that were incubated in the dark at 25.3 ± 1.3 C under anaerobic conditions (flooded plus nitrogen atmosphere) for 60 days following 30 days of aerobic incubation. The floodwater contained ≤1% of the applied (≤0.01 ppm) in all samples at all sampling intervals. 3,5-Dichloro-4-(1,1,2,2-tetrafluoroethoxy)-phenylamine (M4) was identified in the soils treated with aniline ring-labeled [¹⁴C]hexaflumuron at maximums of 15-18% of the applied at 30-60 days posttreatment; an unidentified "polar" compound (designated M8) was also present at 2-5% at 60 days posttreatment.

The portion of this study conducted with aniline ring-labeled [¹⁴C]hexaflumuron partially fulfills EPA Data Requirements for Registering Pesticides by providing information on the anaerobic metabolism of aniline ring-labeled [¹⁴C]hexaflumuron in four US and UK soils.

The portion of the anaerobic soil metabolism study conducted with benzoyl ring-labeled [14C]hexaflumuron and reviewed in this report (MRID 42695901; Study # 2) does not meet present guidelines and should be upgraded. However, the data are adequate to support the proposed use.

This portion of the study is unacceptable for the following reason:

the material balances were incomplete; up to 60% of the applied radioactivity was not accounted for by the termination of the experiments (90 days posttreatment).

Because the material balances in the portion of this study conducted using benzoyl ring-labeled [¹⁴C]hexaflumuron were incomplete, these data are of uncertain value and should not be used to predict the behavior of benzoyl ring-labeled [14C]hexaflumuron and its degradates in the environment.

Mobility - Leaching and Adsorption/Desorption (163-1)

1) The column leaching (unaged hexaflumuron) portion of a mobility - leaching and adsorption/desorption study reviewed in this report (MRID 42648527-A, -B, -C; Study # 3) is acceptable and can be used towards the fulfillment of data requirements.

[¹⁴C]Hexaflumuron was immobile in columns of silt loam, clay loam, and two sandy loam soils that were treated with uniformly aniline or benzoyl ring-labeled [¹⁴C]hexaflumuron [1-(3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)-phenyl)-3-(2,6-difluorobenzoyl)urea; radiochemical purities >99%] at 150 g ai/ha and leached with approximately 50.8 cm of 0.1 N calcium chloride solution.

[¹⁴C]Residues remained concentrated in the upper 6 cm of each column; the topmost soil segment (upper 3 cm) contained 96-101% of the applied radioactivity in the Hanford sandy loam soil columns, 89-95% in the silt loam soil columns, 69-82% in the clay loam soil columns, and 92% in the Castle Rising sandy loam soil columns. Parent hexaflumuron was the only [¹⁴C]compound detected in the soil extracts. No [¹⁴C]residues were detected in the soil below the 6-cm depth or in the leachate from any column. The material balances for all columns ranged from 93.9% to 100.8%.

This portion of the study is acceptable and partially fulfills EPA Data Requirements for Registering Pesticides by providing information on the mobility (column leaching) of unaged aniline and benzoyl ring-labeled [¹⁴C]hexaflumuron in silt loam, clay loam, and two sandy loam soils.

2) The adsorption/desorption (aged hexaflumuron residues) portion of a mobility - leaching and adsorption/desorption study reviewed in this report (MRID 42648527-A, -B, -C; Study # 3) does not meet present guidelines because:

the experimental design and data manipulation by the study authors was atypical and severely limited the interpretation of the results. Batch equilibrium experiments are not appropriate for determining the adsorption and desorption of individual compounds from mixtures of degradates and parent as were present in the hexaflumuron-treated, aerobically aged soil used in this study.

Since adsorption-desorption batch equilibrium experiments are not appropriate for mixtures of degradates and parent as were present in the aerobically aged soil used in this study, this study cannot be upgraded with the submission of additional data.

Although these data are of uncertain value and should not be used to predict the behavior of hexaflumuron and its degradates in the environment, this study does provide supplemental information adequate to support the proposed use on the mobility of hexaflumuron and its degradates.

Based on qualitative estimates of K_{des} for hexaflumuron and its degradates determined in this report (" K_d "s), it can be inferred that hexaflumuron and its phenylamine and phenylurea degradates are not easily desorbed in the soils tested; the benzoic acid degradate would be considered easily desorbed. No inferences can

be made concerning K_{ads} of the degradates, since adsorption of the degradates could not be separated from other processes occurring during metabolism in the soil. However, because of the marginal validity of the reported " K_d "s, these numbers should not be used in risk assessments based on computer models that require these numbers as inputs to those models.

ENVIRONMENTAL FATE ASSESSMENT

Although the environmental fate data base for hexaflumuron is incomplete, the following information is available:

Hexaflumuron is stable to hydrolysis at neutral to acidic pHs; the material will not be subject to photodegradation when used as proposed (bait stakes in buried cylinders). Hexaflumuron's persistence in soil under aerobic conditions and the nature of formation and decline of its degradates have not been adequately determined; however, since the bait stakes containing the active will not be in contact with soil when used as proposed, and the maximum loading of the soil surrounding the stakes is 0.1 g/stake, hexaflumuron does not present a great concern when used under the conditions of this EUP. Hexaflumuron will not be mobile in soils; although the mobility of hexaflumuron degradates has not been adequately determined, it appears that the degradates, which are produced in small quantities, are not highly mobile. Field dissipation data for hexaflumuron are not required when the chemical is used as proposed in this EUP.

Although there are gaps in the acceptable information on the persistence and mobility of degradates, it is EFGWB's opinion that, when used under the conditions of the EUP, hexaflumuron will not present a hazard to groundwater.

Experimental Use Permit:

1. The following data requirements have been imposed for the termiticide hexaflumuron (DOWCO 473; 062719-EUU) when used as described in the EUP. (Hexaflumuron is to be formulated as bait stakes containing 0.1 g of ai/100 g [REDACTED] Proposed use rates are five stakes per "structure;" bait stakes are to be enclosed in plastic bait stations, which will be buried in soil in close proximity to potential termite activity.)

- 161-1 Hydrolysis
- 162-1 Aerobic soil metabolism
- 162-2 Anaerobic soil metabolism
- 163-1 Leaching and adsorption/desorption

One data requirement fully meets present guidelines for the proposed EUP:

Hydrolysis (161-1)

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Three data requirements do not meet present guidelines but are considered adequate to support the proposed EUP:

Aerobic Soil Metabolism (162-1)	(Aniline ring-labeled [¹⁴ C]hexaflumuron only)
Anaerobic Soil Metabolism (162-2)	(Aniline ring-labeled [¹⁴ C]hexaflumuron only)
Leaching and Adsorption/Desorption (163-1)	(unaged parent)

The following data requirements are not satisfied, but the reviewed studies do provide supplemental information:

Aerobic Soil Metabolism (162-1)	(Benzoyl ring-labeled [¹⁴ C]hexaflumuron only)
Anaerobic Soil Metabolism (162-2)	(Benzoyl ring-labeled [¹⁴ C]hexaflumuron only)
Leaching and Adsorption/Desorption (163-1)	(aged)

2. Because of the proposed use, EFGWB requested a reduced data set (see above). Although the data submitted are not fully acceptable according to EPA guidelines, based on our review and evaluation of the submitted data, Hexaflumuron is relatively stable in the environment. That is, any residues moving from the stake to the soil will not rapidly degrade. The data submitted do not allow EFGWB to reach a conclusion about the identity of the major degradates; however, those residues that do move into the soil medium will likely be tightly adsorbed to the soil matrix and not be mobile. Since the maximum loading of soil is 0.1 g ai/stake, this complete information (identity of the major degradates) may not be important prior to granting of the EUP.

8. RECOMMENDATIONS:

Registration:

Based on the acceptable and supplemental information provided in the review of studies submitted in support of the registration of the New Chemical Hexaflumuron (see discussion in Conclusions section above), and on information provided with the request for an EUP, EFGWB concludes that the data are adequate to support the proposed use.

However, the additional information requested below would be needed to support registration for any additional uses of Hexaflumuron.

1. EFGWB recommends that RD notify the registrant that no additional information on the hydrolysis of hexaflumuron or the anaerobic soil metabolism of aniline ring-labeled [¹⁴C]hexaflumuron is needed at this time.
2. EFGWB recommends that RD notify the registrant that the aerobic/anaerobic soil metabolism study reviewed in this report (MRID 42695901; Study # 2) may be upgraded with the submission of additional data. In order for the portions of this study conducted with aniline ring-labeled [¹⁴C]hexaflumuron to contribute towards the fulfillment of the aerobic soil metabolism data requirements, the registrant must identify the degradate M8. In order for the portions of this study conducted with benzoyl ring-labeled [¹⁴C]hexaflumuron to contribute

towards the fulfillment of the aerobic and anaerobic soil metabolism data requirements, the registrant must support the claim that [¹⁴C]residues not recovered at the termination of the experiment were lost as volatiles by providing additional data on the quantification and characterization of these volatiles.

3. EFGWB recommends that RD notify the registrant that no additional information on the mobility of unaged hexaflumuron in soil columns is required at this time. However, if in the future the registrant proposes any changes in use patterns, it may be necessary for the registrant to generate fully acceptable K_d s to support those use patterns.

4. EFGWB recommends that RD notify the registrant that, in order to fulfill the Mobility - Leaching and Adsorption/Desorption (163-1) data requirement, acceptable data on the mobility-adsorption/desorption of hexaflumuron degradates must be submitted. In order to accurately determine the mobility-adsorption/desorption of the parent and each degradate identified at 10% or higher of the applied in the aerobic soil metabolism study, standard batch equilibrium experiments must be conducted using four soils and at least four different concentrations of each compound so that valid Freundlich K values can be calculated.

9. BACKGROUND:

A. Introduction -

In early 1993, DowElanco submitted data to the Agency as part of an application for registration of the new chemical Hexaflumuron [1-(3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl)-3-(2,6-difluorobenzoyl)urea; Chemical # 118202] as a termiticide (Attachment 1). At that time, because of the nature of the proposed use (chemically impregnated bait stakes contained in buried perforated polypropylene cylinders), EFGWB recommended that a reduced set of environmental fate data requirements be imposed, consisting of:

- 161-1 Hydrolysis
- 162-1 Aerobic soil metabolism
- 162-2 Anaerobic soil metabolism
- 163-1 Leaching and adsorption/desorption

(EFGWB memo dated 4/30/93, Attachment 2).

The registrant has also submitted an application for an Experimental Use Permit for testing NAF-46 (EPA Reg. No. 62719-EUG) in 21 states for efficacy in the control of termites for the time period October 1, 1993, through January 1, 1995.

B. Directions for Use -

Hexaflumuron (DOWCO 473; 062719-EUU) is an insecticide for the proposed use of controlling termites. The test material is formulated as bait stakes containing 0.1 g of ai/100 g [REDACTED]

[REDACTED] Proposed use rates are five stakes per "structure;" bait stakes are to be enclosed in plastic bait stations, which will be buried in soil in close proximity to potential termite activity.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

10. DISCUSSION OF INDIVIDUAL STUDIES:

New Chemical Screen:

Please refer to attached DERs.

EUP:

The document submitted (Attachment 3) includes the proposed experimental program, which is summarized below.

- The test material (NAF-46; 062719-EUG) consists of bait stakes, composed of 0.1 g of hexaflumuron/100 g cellulose-based matrix on [REDACTED] (Confidential Statement of Formula; Attachment 4).
- The termite species targeted (subterranean termites; *Reticulitermes* spp, *Coptotermes formosanus*, *Heterotermes aureus*) contribute to severe economic losses from property damage to wooden structures.
- Treatment sites will be located in 21 states (table on page 6 of Attachment 3).
- The delivery system is a monitoring station consisting of a plastic frame with a lockable cap (Attachment 5). A perforated plastic sleeve ("toxicant delivery device") is placed inside the frame and the station is buried at the treatment site. Monitoring stakes (untreated wood) will be placed inside the sleeve until termite activity is observed; a bait stake will then be placed in the sleeve until termite activity is no longer observed. The author references a draft label; however, no draft label was included in the submission.
- Application is to be made to "structures" (no further description) that are to average 1500 ft² in area.
- It is proposed that 10 structures per state per year will be treated at an average treatment of 5 stakes per structure, resulting in a total application per state of 5 g ai for each of the two years of the study. Total nationwide use of the active per year is 105 g.
- The proposed use period is October 1, 1993, through January 1, 1995.

As previously stated, no draft label for NAF-46 was included; a proposed label for the technical product is attached (Attachment 6)

EFGWB has analyzed the environmental fate data base (consisting of the three studies reviewed in this report) and has the following conclusions:

Hexaflumuron is stable to hydrolysis at neutral to acidic pHs; the material will not be subject to photodegradation when used as proposed (bait stakes in buried cylinders). Hexaflumuron's persistence in soil under aerobic conditions and the nature of

INERT INGREDIENT INFORMATION IS NOT INCLUDED

formation and decline of its degradates have not been adequately determined; however, since the bait stakes containing the active will not be in contact with soil when used as proposed, and the maximum loading of the soil surrounding the stakes is 0.1 g/stake, hexaflumuron does not present a great concern when used under the conditions of this EUP. Hexaflumuron will not be mobile in soils; although the mobility of hexaflumuron degradates has not been adequately determined, it appears that the degradates, which are produced in small quantities, are not highly mobile. Field dissipation data for hexaflumuron are not required when the chemical is used as proposed in this EUP.

The above environmental fate assessment is based on studies that do not full meet present guidelines. However, the information is considered adequate to support the assessment given above. For a more complete prediction of the fate of this chemical in the environment, EFGWB would need acceptable data for the Aerobic Soil Metabolism (162-1), Anaerobic Soil Metabolism (162-2), and aged Leaching/Adsorption/Desorption studies (163-1).

11. COMPLETION OF ONE-LINER:

The EFGWB One-Liner for this chemical was updated 11/2/93.

12. CBI INDEX:

This document includes a Confidential Statement of Formula and should be considered CBI.