112701

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EEE BRANCH REVIEW

DATE: IN 9/6/78 OUT 4/26/79 IN 5/2/79 OUT 8/31/79 IN _____ OUT _____
FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO(S). 10182-EA, EE, EG, EI, EL, EN, EO, ER, EU

PETITION OR EXP. PERMIT NO. _____

DATE DIV. RECEIVED _____

DATE OF SUBMISSION _____

DATE SUBMISSION ACCEPTED _____

TYPE PRODUCT(S): I, D, H, F, N, (R), S _____

DATE ACCESSION NO(S). _____

PRODUCT MGR. NO(S). (16) Miller

PRODUCT NAME(S) TALON

COMPANY NAME ICI Americas

SUBMISSION PURPOSE registration of formulating materials (2) and formulations (7) for commensal rodent control.

CHEMICAL & FORMULATION 3-[3-(4'-bromo[1,1'-biphenyl]4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]4-hydroxy-2H-1-benzopyran-2-one
0.005 % bait
0.25 % liquid concentrate
99.75 % technical

100.0 Pesticidal Use

Talon pelleted bait is formulated as a 0.005 % rodenticide proposed for indoor control of commensal rats and mice. This submission deals with following formulations of Talon:

1. 10182-EA Talon rodenticide pellets
2. 10182-EE Talon rodenticide pellets in trays
3. 10182-EG Talon bait bits in trays
4. 10182-EI Talon 0.25 % liquid concentrate for formulating use only.
5. 10182-EL Talon bait pack (mini pellets) in mouse box
6. 10182-EN Talon rodenticide mini pellets
7. 10182-EO brodifacoum 90 % technical for formulating use only
8. 10182-ER Talon rodenticide bait pack (mini pellets)
9. 10182-EU Talon rodenticide bait packs

100.1 Applications methods/rates/directions

The labeled directions are similar for all of bait products. The label for the rodenticide pellets (10182-EA) reads as follows:

For control of rodents in homes, industrial and agricultural buildings. Place bait in areas which are inaccessible to children, pets, domestic animals and wildlife or in a tamper-proof bait box.

Limit alternate food sources as much as possible. Replace moldy bait promptly. Collect all rodent bodies and unused bait and dispose of in accordance with State and local regulations.

Norway and Roof Rats:

Place at least 4 oz. of bait* (usually at intervals of 15 to 30 feet) along walls or runways, in rat burrows and in sheltered areas where rats are known to live or feed. Maintain an uninterrupted supply of fresh bait for 10 days or until signs of rat activity cease.

House Mice

Place at least 2 oz. of bait* (usually at intervals of 8 to 12 feet) along walls or runways, in mouse burrows and in sheltered areas where mice are known to live or feed. Maintain an uninterrupted supply of fresh bait for 15 days or until signs of mouse activity cease.

* The underlined portion is the only part of the use directions that differs on the various labels. This portion reads as follows for the various formulations:

Reg. No.	formulation	norway and roof rats	house mice
10182-EE	pellets in trays	one tray	one tray
10182-EG	bait bags in trays	one tray	
10182-EL	mini pellets in mouse box	two boxes	one box
10182-EN	mini pellets	4 oz. of bait	2 oz. of bait
10182-ER	mini pellets in bait pack	2 bait packs	one bait pack
10182-EU	bait packs	2 bait packs	one bait pack

Since the technical material (10182-EO) and 0.25 % liquid concentrate (10182-EI) are for formulating use only, no use directions appear on these labels.

100.3 Precautionary labeling

The Environmental Hazards Section of the label is the same for all 7 end use and 2 formulating use products:

"This product is toxic to fish and wildlife. Keep out of lakes, streams, or ponds."

101.0 Chemical and Physical Properties

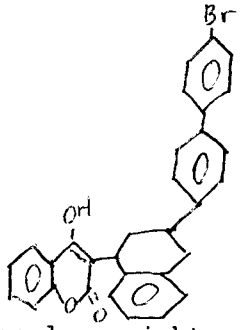
101.1 Chemical name

3-[3-(4'-bromo[1,1'-biphenyl]4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl] 4-hydroxy-2 H-1-benzopyran-2-one.

101.2 Common name

brodifacoum, PP 581, WBA 8119, Talon®, Volak®

101.3 Structural formula



$C_{32}H_{23}O_3Br$

101.4 Molecular weight

523.4

101.5 Physical state

off-white or buff, odorless solid

101.6 Solubility

Solvent	g/100 ml at 20° C
water	<.01
acetone	.06
ethanol	.01
chloroform	3.0

102.0 Behavior in the Environment

In a previous review (L. Turner, 9/5/78), it was reported by EFB that they had no file on brodifacoum. Another call was made on 4/25/79 to Ron Ney who stated again that he had no knowledge of the existence of this pesticide.

103.0 Toxicological Properties

103.1 Acute toxicity

103.1.1 Mammal

(reference: Toxicology Branch memo by R. A. Gessert, 8/2/78.)

male rat acute oral LD_{50} (tech) = 0.27 mg/kg
female rat acute oral LD_{50} (tech) = 0.50 mg/kg
mouse acute oral LD_{50} (tech) = 0.4 mg/kg
rabbit acute oral LD_{50} (tech) = 0.29 mg/kg
cat acute oral LD_{50} (tech) = 25 mg/kg
guinea pig acute oral LD_{50} (tech) = 2.78 mg/kg
dog acute oral LD_{50} (tech) = 0.25 - 1 mg/kg
sheep acute oral LD_{50} (tech) = 25 mg/kg

103.1.2 Bird

(validated this submission)
Mallard acute oral LD_{50} (? %) = 2.0 mg/kg supplemental

103.1.3 Fish

(validated by R. Balcomb, 4/4/78; revalidated this submission)
The bluegill and rainbow trout tests were originally not considered acceptable because the LC_{50} values were calculated from nominal, rather than measured, concentrations, and because the percent active ingredient tested was not identified. Registrant has submitted additional data identifying the percent a.i. and recalculating the LC_{50} values by both Finney probit and Litchfield-Wilcoxon, using measured concentrations (Acc 237703). The values from Finney probit analysis, which are nearly identical with Litchfield-Wilcoxon values, are reported below. Both tests are now considered acceptable to support registration.

Rainbow trout 96-hour LC_{50} (99.3 %) = 0.04 mg/l measured (95 % c.i. 0.03 - 0.05 mg/l) or 0.056 mg/l nominal — Core

Bluegill 96-hr LC_{50} (99.3 %) = 0.123 mg/l measured (95 % c.i. 0.11 - 0.14 mg/l) or 0.180 mg/l nominal — Core

Additional fish tests were submitted and have been validated in this review.

1. Rainbow trout 96-hour LC_{50} (92.5 %) = 0.0528 ppm nominal or 0.039 ppm mean measured. — Core
2. Rainbow trout 96-hour LC_{50} (0.25 %) = 17.36 ppm nominal or 10.6 ppm mean measured. Supplemental (core for formulation)
3. Bluegill 96-hour LC_{50} (0.25 %) = 12.89 ppm nominal or 7.5 ppm mean measured. — Supplemental
4. In adult rainbow trout fed or offered Talon 0.005 % pellets for four days, 3 of 4 treated fish died 15 - 30 days after feeding was stopped. — Supplemental
5. In adult bluegill fed or offered Talon 0.005 %pellets for four days, 3 of 5 treated fish died 10 - 25 days after feeding was stopped. One fish that died had not fed on the Talon pellets at all. — Supplemental

103.1.4 Aquatic invertebrate

(validated this submission)

Daphnia magna 48 hr LC_{50} (92.5 %) - very erratic.	invalid
Daphnia magna 48 hr LC_{50} (0.25 %) = 0.059 mg/l.	invalid
Daphnia magna 48 hr LC_{50} (0.005 %) = 0.34 mg/l.	invalid
Daphnia magna 48 hr LC_{50} (93.3 %) - 0.89 mg/l.	core

103.3 Subacute toxicity

Two 8-day avian dietary studies were validated as core by R. Balcomb (4/4/78). However, in a meeting with ICI representatives on 6/28/78, EEB was informed that these tests were likely inaccurate because the acute oral tests showed mortality occurring 20 days after dosing. ICI requested that these studies not be used and therefore, they have been reclassified from core to supplemental. These tests and additional avian dietary tests that were validated in the present submission are sumarized below. All tests used technical material.

Mallard 8-day dietary LC_{50} = 778 ppm	supplemental
Bobwhite 8-day dietary LC_{50} = 201 ppm	supplemental
Bobwhite 40-day dietary LC_{50} = 0.8 ppm	core
Mallard 33-day dietary LC_{50} < 100 ppm	supplemental
Mallard 40-day dietary LC_{50} = 2.7 ppm	core

103.5.2 Secondary toxicity

(validated this submission)

1. One of six beagle dogs fed rats killed with high, intubated doses of brodifacoum died; three others had slight to moderate hemorrhaging detected in autopsy. Investigators concluded no severe secondary hazard to dogs. This reviewer disagrees and feels the study does indicate hazard. An invalid study because of a major discrepancy between text and tables.

2. Two of five foxes (4 red, 1 gray) died after being fed rats killed with large, intubated doses of brodifacoum. The three survivors exhibited slight to moderate hemorrhage as detected during autopsy. Investigators conclude no severe hazard to wild canids. This reviewer reached the opposite conclusion from the submitted data. A supplemental report because it indicates a secondary hazard, but is notably deficient because amounts of brodifacoum ingested by the foxes are completely unknown.

3. (not validated) In a study conducted by Patuxent Wildlife Research Center, 5 of 6 barn owls fed brodifacoum killed rats for 1 - 10 days died. The survivor ingested 67 g of rat in one day. Barn owls that died had been fed 154, 299, 370, 492, and 368 g of poisoned rat for 3, 3, 6, 10, and 10 days, respectively. Rats had died after free-choice feeding on 0.002 % brodifacoum bait and untreated lab chow. Owls died 8 - 11 days after dosing.

104.0 Hazard Assessment

104.1 Discussion

The various bait formulations of Talon are all proposed for indoor use to control commensal rats and mice in homes, industrial, and agricultural buildings. Because moderate amounts (2 - 4 ounces) of Talon will be placed at a given site and because of the indoor use, determination of resiudes per acre is meaningless.

104.1.1 Likelihood of exposure to non-target organisms

Normally, indoor uses might be considered to present no hazard to non-target organisms other than humans and domestic animals. A hazard assessment for these two groups of non-target organisms is the province of Toxicology Branch. However, it is felt that an Ecological Effects hazard assessment is quite pertinent to this use pattern and toxicant because of the potential for secondary toxicity.

First, it should be noted that this reviewer expects no significant primary hazard to native, non-target organisms, as long as the labeled directions are followed. The specific directions protecting non-targets read "Place bait in areas that are inaccessible to children, pets, domestic animals and wildlife or in a tamper-proof bait box." If these directions are adhered to, the non-target organisms that would be affected would be non-target, native rodents such as Peromyscus, Microtus, Neotoma, and others. In many cases the presence of these rodents would be considered an economic nuisance, and their destruction would be welcomed - even if they are not a labeled target. In any case, all of the non-target rodents that might be affected are quite common. The possibility that a few individuals might be killed will certainly not affect any local population levels. Thus, no significant primary hazard is expected from this essentially indoor use.

It is also felt that no significant secondary hazard, except for domestic or stray dogs, exists for the indoor use in homes or industrial buildings. However, use in agricultural buildings appears to present a very real hazard to non-target organisms, particularly in those buildings that allow for substantial ingress and egress of animals, such as barns. Two modes of secondary exposure appear likely. First, in a discussion headed "Recovery of Carcasses" in Accession No. 237703 submitted by the registrant, it is stated that almost 80% of the recovered rodent carcasses were found inside the test structures. This leaves 20+%, a significant minority, that were apparently recovered outside the test structures. Second, there is a strong likelihood for exposure of barn owls, an avian predator that frequently occurs in barns.

The registrant has submitted two secondary toxicity studies on dogs and foxes (validated as study numbers FF1 and FF2 of this review) in which it is concluded that no severe secondary hazard exists. This reviewer cannot help but reach the opposite conclusion from the data presented in these studies. In these studies, 1 of 6 dogs and 2 of 5 foxes died after consuming rat meat containing an unknown amount of Talon. Three other dogs and all three surviving foxes exhibited slight to moderate hemorrhaging. Although the rats received 55 times the LD_{50} dose, it is quite likely that much or most was lost through excretion or detoxification. It is also considered likely by this reviewer that both the dogs and foxes that survived but had hemorrhages would have had a more demonstrable effect had they been free-ranging and engaging in normal activities or if the observation period following treatment had been longer. Thus, these studies do not adequately address the concern for secondary toxicity.

In exurban situations, such as in and around agricultural buildings, there is a probability that predators or scavengers could ingest some of the approximately 20% of the rodent carcasses that could be outside the buildings. This could include foxes, coyotes, skunks, weasels, bobcats, raccoons, possums, vultures, various accipiters and buteos, and owls. Although some of these would not routinely eat carcasses, they could catch and ingest rodents that are carrying lethal doses of Talon but have not yet died.

Of particular concern are barn owls, predators known to occupy barns and other accessible buildings. Although the barn owl is not federally listed as endangered or threatened, it is listed in the 1978 Audubon blue-list of species showing evidence of population decline. It is also more likely to be exposed than other raptors. That the barn owl may be affected is indicated in a study by Patuxent Wildlife Research Center that has been submitted for publication (Mendenhall, V. M. and L. N. Pank, Secondary poisoning of owls by anticoagulant rodenticides). In this study 5 barn owls that consumed 154-492 grams of Talon-poisoned rats over a 3 to 10 day period all died. A sixth barn owl that ate 67 grams of poisoned rat offered for one day only survived without external symptoms. Rats had received the toxicant as a 0.002% concentration in oat-groat baits on a free choice basis for five days. The authors speculated that effects might be exacerbated under field conditions because of stress, diet changes, or increased activity. They noted that a minor injury even before exposure could increase susceptibility, since one Talon-fed owl suffered a massive hemorrhage at the site where blood had been sampled 17 days earlier.

This study is solid evidence that avian predators may be affected secondarily. In addition the registrant has unofficially provided summary data (in EEB file) showing that 4 of 4 red tailed hawks and 1 of 2 rough-legged hawks died after being fed one Talon-killed rat each day for four days. Unfortunately, these tests have not been officially submitted and no evaluation of them can be made with just the results summary.

The toxicity data presented above are strongly suggestive of a potential effect through secondary poisoning. The agricultural use, specifically in barns and other outbuildings, will expose barn owls, and barn owls are demonstrably sensitive to secondary poisoning by brodifacoum. These owls could ingest poisoned, but not yet dead, rodents that are outside the barn. During times when young are being reared, it is likely that these owls could prey upon rodents within a barn. And when young are fledging, it is also likely that they could capture rodents inside a barn. The chances of ingesting affected rodents seems very high, since predators are well known for their ability to select prey individuals that are even slightly weakened by injuries, disease,

parasites, and, quite likely, poisoning. It is, therefore, the conclusion of this reviewer that barn owls will be slightly to substantially affected, possibly to the point of causing marked reductions in local and/or national populations of these owls.

In summary, EEB feels that no significant, primary, non-target hazard exists for any proposed use as long as label directions are followed. No significant secondary hazard to non-target organisms is expected from use in homes, industrial buildings, or some agricultural buildings (e.g. grain elevators). However, a strong possibility of secondary hazard from use in farm and ranch barns and other outbuildings exists for barn owls, a species that appears to be declining somewhat, which should be considered an ally of agriculturalists with rodent problems, and which has a demonstrated susceptibility for mortality from feeding on brodifacoum-killed rats. Repeated and widespread use of brodifacoum in barns and other outbuildings could lead to substantial reductions in national populations of barn owls.

104.1.2 Endangered Species Considerations

It is not expected that the proposed use will adversely affect endangered species. This opinion is based on the distribution and habits of endangered species and the exposure potential that centers around human structures and habitations. Endangered terrestrial species that could be affected are unlikely to exist so close to civilization as to be exposed enough for adverse effects to occur.

104.1.3/4 Data adequacy/data requests

See Sections 107.4 and 107.5.

107.0 Conclusions

107.1 Environmental Fate and Toxicology

Toxicology data was obtained from Toxicology Branch memo by R. A. Gessert, 8/2/78. There appears to be no Environmental Fate data for brodifacoum. Several studies have been submitted, but apparently review of these has not been completed.

107.2 Classification

Although additional data are required before a decision on classification can be made, it is the opinion of this reviewer that use in agricultural buildings should be considered as restricted, at least. This opinion is based primarily on the extreme acute,

dietary, and secondary hazard of Talon to birds. This reviewer also notes that the directions must be interpreted ("areas which are inaccessible to ... wildlife or in a tamper-proof bait box") by the user and then followed precisely to avoid excessive non-target hazard. It is also noted that this pesticide and use could become a potential RPAR candidate because of significant reductions in barn owl populations (Section 162.11 (a)(3)(ii)(C)), however, there ~~is~~ are insufficient data to state at this time that the proposed use can "reasonably be anticipated" to cause such reductions.

107.3 Labeling

As with classification, additional data and clarification are needed prior to determining appropriate labeling. If no changes are made by the registrant in the proposed use pattern, subsequent reviewers should consider and/or modify the following precautionary labeling:

> This product is toxic to fish and wildlife. Use with caution in areas frequented by wildlife. Barn owls and other predators that eat rodents may be killed by feeding on poisoned rodents. Recover and remove rodent carcasses at frequent intervals. Keep out of lakes, ponds, and streams.

107.4 Data Adequacy

Ecological Effects has the following comments on the submitted fish and wildlife studies:

1. The mallard acute oral study (report 6I) is not acceptable as submitted. It is possible that this study may be considered acceptable upon the receipt of additional information. Ecological Effects notes that not all birds were tested at the same time. Registrant should supply information about the exact dates that the various groups were tested, the percent active ingredient of the test material, and complete information on the statistical analysis, including log-probit graphs. Registrant should also justify why the test should not be considered unacceptable on the basis of a high chi squared value indicating heterogeneous data.

2. Because the registrant requested in a meeting (4/17/78) that we not use the LC_{50} values reported in the 8-day dietary tests for bobwhite and mallard (reports 1I and 2I), these tests have been reclassified as not acceptable.

3. The 33-day dietary study on mallards (report 15I) is not acceptable to support registration because no definitive LC_{50} value was determined.

4. The 40-day dietary studies on mallard and bobwhite (reports 16I and 17I) are acceptable to support registration.

5. The previously submitted 96-hour LC_{50} studies on rainbow trout and bluegill (reports 3I and 4I) have been re-evaluated upon receipt of additional information and are now considered acceptable to support registration.

6. The 96-hour LC_{50} study on rainbow trout (report 8I) is considered acceptable to support registration.

7. The 96-hour LC_{50} studies with formulation JFU 5074 on rainbow trout and bluegill (reports 8I and 9I) are not required for the proposed use and are considered supplementary. The trout study could be considered acceptable if a requirement exists, but the bluegill results appear too imprecise because of quite variable toxicant concentrations and substantial difference in the results of the two series of fish that were tested.

8. The 96-hour feeding studies with rainbow trout and bluegill (reports 11I and 12I) are not required for the proposed use and are considered supplementary.

9. The 48-hour Daphnia LC_{50} study (report 13I) is considered invalid because of erratic results (technical material), significant heterogeneity of data according to chi squared tests (0.25% and 0.005% formulations), and extremely low dissolved oxygen concentrations (0.005% formulation). Tests on the 0.25% liquid concentrate are not required for the proposed use, but may be reconsidered as supplementary if registrant can justify in detail why certain dose levels were excluded from statistical analysis.

10. The part of the 48-hour Daphnia LC_{50} study (report 18I) using the technical material is acceptable to support registration. The parts using the formulated products are identical to report 13I.

11. The secondary toxicity study on dogs (report 37H) is considered invalid because there is a discrepancy between the text and the tables about which dog died. If this discrepancy is clarified, this study may be re-evaluated as supplementary. This study and the secondary toxicity study on foxes (report 38H) cannot be considered as acceptable to support registration because the amount of Talon actually contained in the rat meat was not determined and because the method of poisoning the rats was not realistic of field situations wherein rats eat pellets over a period of time. While it does not affect the validity of the reports, registrant should note that EEB feels that these reports do give evidence of a secondary hazard to canids, in contrast to the conclusions of the investigator.

107.5 Additional data required

1. An avian acute oral LD_{50} for mallard duck or bobwhite quail. This request can be satisfied by supplying information noted in #1 of section 107.4.

2. A secondary toxicity study on canids from rats or mice wherein the amount of brodifacoum residues contained in the poisoned rodents are actually measured. By analyzing the residues in the rodents, the poisoned rodents can be pooled if evenly mixed into the diet. Ecological Effects is aware that the registrant has, in the past, not developed a method for analyzing residues in tissue. If there is still no such methodology, a secondary test would be acceptable if rats are allowed to ingest Talon bait in a manner similar to what is expected in the field. Intubation of rats with excessive single doses of brodifacoum is not acceptable unless actual residues ingested by the predators are known.

3. Ecological Effects requests that the avian secondary toxicity tests on raptors that were mentioned in the 4/17/78 meeting with this branch be submitted in full detail. Ecological Effects also requested that the registrant conduct an LD_{50} test on mink or weasels, with a possible follow-up on secondary toxicity to mustelids, in conjunction with the VOLAK formulation of brodifacoum. If either or both of these tests have been completed, they should be submitted.

Subject: Supplement to Review dated 8/31/79
Reg. File No. 10182-ET-EO

Physical and Chemical characteristics of TALON 0.25% liquid concentrate.

1. Talon is a rodenticide concentrate containing 0.25% bradifacoum and is used at 2% in the formulation to provide 50 ppm in the finished product.

2. Chemical Name: 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzo-pyran-2-one

3. Chemical Structure:

4. Common Name: Brodifacoum

5. Solubility: Soluble in benzene and chloroform. Moderately soluble in acetone, ethanol, ethyl acetate, glycerol and polethylene glycol. Insoluble in water and pertoleum ether.

6. Physical State: solid
7. Color: off-white
8. Odor: not detectable
9. Stability: Active ingredient is stable for at least 12 months at temperatures from ambient to 50°C. Crystallizes at temperatures below 10°C.

10. Vapor Pressure: 1.0 mm hg at 20°C

11. Boiling point: 186°C

12. Specific gravity: 1.043

M. Nawar
Review Section 1
Environmental Fate Branch
Hazard Evaluation Division

Ronald E. Ney, Jr.