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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS

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MEMORANDUM

SUBJECT: OCCUPATIONAL AND RESIDENTIAL EXPOSURE ASSESSMENT AND
RECOMMENDATIONS FOR THE REREGISTRATION ELIGIBILITY
DECISION DOCUMENT FOR BRODIFACOUM

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Edward Zager

Please observe the OREB review of Brodifacoum.

DP Barcode: D231156

Pesticide Chemical Codes: 112701

EPA Reg. Nos.: 3782-79, 10182-340, 10182-336, 10182-335, 3282-74,
10182-48, 3286-66, 10182-334, 11715-218, 10182-338,
182-384, 3282-81

EPA MRID Nos.: None

LUIS Report Date: 10/17/96

PHED:

OCCUPATIONAL AND RESIDENTIAL EXPOSURE CHAPTER

In this document, which is for use in EPA's development of the brodifacoum registration Eligibility Decision document (RED), EPA presents the results of its review of the potential human health effects of occupational and residential exposure to brodifacoum. Included is a

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discussion of the adequacy of the occupational and residential exposure data that have been submitted in support of the reregistration of brodifacoum.

(RED SECTION III - TOXICITY, EXPOSURE, AND RISK)

(EXPOSURE)

Occupational and Residential

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete.

Use Summary

Use Patterns

Brodifacoum 3-[3-(4-bromo[1,1-biphenyl]4-yl)-1,2,3,4-tetra-hydro-1-naphthalenyl]4-hydroxy-2H-1-benzophyran-2-one is a rodent control agent. It is a warfarin-like compound that acts as an anticoagulant and is formulated as meal bait, paraffinized pellets, rat and mouse bait ready-to-use place packs, and paraffin blocks, cakes, and slabs.¹ All products are 0.005 percent active ingredient.¹

Brodifacoum is currently registered for the control of rodents in and around farm structures, households, and domestic dwellings, uncultivated agricultural and nonagricultural areas, commercial transportation facilities, industrial areas, in sewage systems, aircraft, ships, boats, railway cars, and food processing, handling, and storage areas and facilities. Application may be made as frequently as is necessary. Both general use and restricted use brodifacoum products are currently registered.^{1,2}

Baits and bait packs are placed at 15 to 30 foot intervals for rats and 8 to 12 foot intervals for mice. When bait blocks are used in sewage systems, wire is used to secure blocks above the high water mark. The rate of application is 16 ounces per 15 foot interval for rats and 2 ounces per 8 to 12 foot interval for mice. According to labels, all baits are to be placed out of the reach of children, pets, domestic animals and nontarget wildlife, or in tamper resistant bait stations. Bait stations must be resistant to destruction by dogs and by children under 6 years of age, and must be used in a manner that prevents children from reaching into bait compartments and obtaining bait. If bait can be shaken from stations when they are lifted, stations must be secured or otherwise immobilized.²

Occupational-use products and homeowner-use products

At this time some products containing brodifacoum are intended primarily for homeowner use and some are intended primarily for occupational use.

Summary of Toxicity Concerns Impacting Occupational and Residential Exposures

Acute Toxicity

The toxicological data base for brodifacoum is adequate and will support reregistration. Guideline studies for acute toxicity indicate that brodifacoum is classified as toxicity category I for acute oral toxicity, category I for acute dermal toxicity, category I for acute inhalation toxicity, category IV for skin irritation potential, and category III for eye irritation potential. It is not classified as a skin sensitizer. The vapor pressure of brodifacoum is 9.8×10^{-7} Torr.

Other Adverse Effects

The *Toxicology Endpoint Selection Document* dated November 7, 1996, indicates that there is a toxicological endpoint of concern for brodifacoum. The endpoints employed in the occupational exposure assessment are a short-term and intermediate-term NOEL of 0.002 mg/kg/day from a 21-day dermal toxicity study and a NOEL of 0.002 mg/kg/day from a developmental toxicity study. No chronic toxicological endpoints have been identified for brodifacoum as appropriate for use to quantify occupational or residential exposure assessments.³

Because the vapor pressure of brodifacoum is low (9.8×10^{-7}), the potential for risk resulting from inhalation of brodifacoum vapors is not a significant concern despite a very low LC_{50} (4.86 mg/L).³ However, if fine particles become airborne during the handling of brodifacoum baits and/or tracking powder, individuals may inhale these particles. Because these particles also could potentially be ingested, such exposure would contribute to the individual's risk resulting from accidental ingestion/oral exposure.

There is no cancer classification for brodifacoum.

No dermal absorption data are available for brodifacoum. However, the assumption of 100 percent dermal absorption is reasonable. It is noted that the LD_{50} values for dermal and oral toxicity are dissimilar (acute dermal LD_{50} is 1/10 of the acute oral LD_{50}), although this may be indicative of greater susceptibility in the rabbit (employed in the dermal study) than the rat (employed in the oral study).³

Epidemiological Data

A review of Poison Control Center data on brodifacoum and other anticoagulant rodenticides shows a relatively high frequency of exposure among young children and pets. In 1989, brodifacoum had an estimated ratio of 1.5 exposures per 1,000 containers for children ages 0-5 years in residential settings compared to a ratio for all pesticides of 0.2 exposures per 1,000

containers for such children in 1989 and 1990. Other anticoagulants had similarly high ratios of exposure to estimated containers in U.S. homes.⁴

Over 10,000 anticoagulant exposures were reported in young children in 1995. However, the overwhelming majority of exposures (95%) did not result in any symptoms. Those with symptoms were almost always reported to be minor with little or no need for any medical attention. Despite the lack of need for medical attention, over one-third of cases are seen in a health care facility, often because parents or child caretakers bring in the children without first checking with a Poison Control Center. As a result, the average brodifacoum incident has estimated medical costs of \$151.00, whereas the average per-incident cost for non-anticoagulant pesticides is \$106.00. These costs are based only on those cases called into Poison Control Centers. The average estimated costs (adjusted to 1989 dollars) include: the cost of the call at \$20.00, the cost of emergency department treatment at \$338, and the cost of hospitalization at \$801.00⁴

Pets exposed to anticoagulants accounted for over 5,000 incidents in 1987 according to the University of Illinois National Animal Poison Control Center. The anticoagulant rodenticides are a cause of serious and costly poisonings in domestic animals, especially dogs. Secondary poisoning through consumption of poisoned rodents is also a concern. Although most of the reports to the NAPCC were for exposure only and clinical signs were not evident, there still may be significant cost to the pet owner in diagnostic tests and monitoring.⁴

Handler Exposures & Assumptions

EPA has determined that there is a potential exposure to applicators or other handlers during typical use-patterns associated with brodifacoum. Specifically, EPA is concerned about potential dermal and inhalation exposures to handlers during the loading and application of brodifacoum.

Based on the use patterns and potential exposures described above, four major handler exposure scenarios were identified for brodifacoum: (1) placing bait packs; (2) loading bait boxes or bait stations with meal bait, grain bait, bait pellets, or other food-based bait from larger containers; (3) breaking paraffinized slabs, cakes, and blocks into pieces and placing the pieces at bait stations; (4) securing large paraffin blocks at bait stations in sewers; (5) applying bait by hand; (6) applying bait (e.g., pellets) in broadcast treatments using ground equipment.

It is unclear from labels and other available information (1) the extent to which it is necessary, due to size or design of packages, for handlers to directly handle or contact the bait during bait station loading (which may result in dermal exposures); or (2) the extent to which it is possible for dusts associated with meal baits, grain baits, or pellets to result in inhalation exposure to handlers during bait station loading.

Calculations of daily exposure to brodifacoum by handlers are used to assess risk to those handlers. There are no handler exposure data available for the use patterns associated with brodifacoum mixing, loading, and application.

Post-Application Exposures and Assumptions

EPA has determined that there is a potential for exposure to homeowners and others following applications of brodifacoum, particularly in residences. EPA has concerns about possible post-application exposures if (1) baits are not placed out of reach of children or are not placed in tamper-resistant bait stations, as specified in labeling; (2) baits are available to homeowners in packages which are not tamper resistant and could be accessible to children prior to application; and (3) baits are brightly colored or packaged in a way in which they could be appealing to children or mistaken by children for food or candy. Also recommend in caution section that users remove poisoned rodents from areas accessible to domestic animals. Under note to physicians, many of the labels recommend that vitamin K₁ be administered intravenously (IV) or intramuscularly (IM). The veterinary literature states that Vitamin K₁ can cause anaphylactic reactions if given IV and extensive hemorrhage after IM administration. Sheldon Wagner, M.D., a consultant to OPP, confirmed that Vitamin K₁ should not be given IV unless there is a hemorrhagic crisis. IM administration is acceptable in humans. The recommendation for IV administration should be deleted from the label.

RISK

Occupational and Residential

Because EPA currently has no data on occupational or residential exposures to brodifacoum, the Agency is unable to calculate daily doses. EPA has risk concerns for persons exposed to brodifacoum in both occupational and residential scenarios. These concerns are based on (1) very high acute toxicity (short- and intermediate-term NOEL of 0.2 mg/kg/day based on systemic toxicity); (2) potentially high (e.g., 100 percent) dermal absorption values; (3) an absence of exposure data for all exposure scenarios considered; and (4) a relatively high number of incidents associated with brodifacoum use as compared to non-anticoagulant pesticides.

Risk From Handler Exposures

There are no exposure data currently available for calculating risks to handlers resulting from exposures to brodifacoum. However, EPA has several concerns about the risks to handlers of brodifacoum products, particularly commercial handlers (1) handling large quantities of product, (2) handling dusty, non-paraffinized products, or (3) applying products by hand.

OREB recommends that all labels for occupational-use products require commercial handlers to wear chemical-resistant gloves while handling all brodifacoum formulations that are not contained in a tamper-resistant bait station or in place packs. This would reduce dermal exposure to brodifacoum and diminish the potential oral exposure that could result from hand-to-mouth transfer. Though no exposure data are available, EPA believes that both tamper-proof bait stations and place packs greatly reduce the potential for dermal contact with brodifacoum.

In addition, OREB recommends that occupational handlers (commercial applicators) wear chemical-resistant eyewear and a dust/mist respirator when handling non-paraffinized brodifacoum formulations, such as meal or grain-based baits, unless those formulations are contained in tamper-resistant bait stations or place packs. The eyewear and respirator would reduce the possibility of inhalation and ingestion of dusts resulting from the pouring and application of these products and reduce the potential ocular absorption that could result from contact with such dusts.

Risk from Post-Application Exposures

There are no data currently available to address post-application exposure for brodifacoum. The group most at risk would be children less than 6 years old. Only the following rough calculations are possible.

The dose a 10 kilogram child would receive from a one gram packet of brodifacoum at 0.005% active ingredient would equal 0.005 mg/kg (1 gram x 0.005% / 10 kg). This exposure will result in a Margin of Exposure less than 1 (MOE = 0.002 mg/kg/day / 0.005 mg/kg/day = 0.4). OREB considers this MOE to be of concern.

OREB believes that requiring "tamper-resistant bait stations" is consistent with 40 CFR Section 157.22 Criteria for Child-Resistant Packaging which states:

"The pesticide or device has such characteristics that, based upon human toxicological data, use history, accident data or such other evidence as is available, the Agency determines there is serious hazard of accidental injury or illness which child-resistant packaging could reduce. The product's labeling either directly recommends residential use or reasonably can be interpreted to permit residential use."

OREB is recommending that the sale of brodifacoum products that are not prepackaged in tamper-resistant bait stations should be limited to professional or commercial handlers. OREB believes that this will mitigate the risk to children under six years of age and to domestic pets. The current label restricts use to an "inaccessible area" which is difficult to define. Further, OREB believes that brodifacoum should be applied only in tamper-resistant bait stations at any residence and in other areas where children frequent, such as schools, recreation areas, and libraries. In addition, OREB is recommending that products that are labeled for use at residential sites (both occupational-use and homeowner-use products) contain a bittering agent at a dose level palatable to rats but not to humans. A bittering agent should help reduce repeated ingestion exposures by young children.

Additional Occupational/Residential Exposure Studies

Handler Studies

Handler exposure studies are not required at this time, but may be required pending the outcome of discussions between EPA and the registrant.

Post-Application Studies

Post-application exposure studies are not required at this time, but may be required pending the outcome of discussions between EPA and the registrant.

(SECTION IV - REGULATORY POSITION AND LABELING RATIONALE)

Occupational/Residential Labeling Rationale/Risk Mitigation

At this time, some products containing brodifacoum are intended primarily for occupational use and some are intended primarily for homeowner use.

Requirements for Handlers

For each end-use product, personal protective equipment and engineering control requirements for pesticide handlers are set during reregistration as follows:

- ☐ *Based on risks posed to handlers by the active ingredient, EPA may establish active-ingredient-specific ("a-i specific") handler requirements for end-use products containing that active ingredient. If the risks to handlers posed by the active ingredient are minimal, EPA may establish no a-i-specific handler requirements.*
- ☐ *Based on the acute toxicity characteristics of the end-use product, EPA usually establishes handler PPE requirements for each end-use product.*
- ☐ *If a-i-specific requirements have been established, they must be compared to the end-use-product-specific PPE and the more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product. Engineering controls are more stringent than PPE requirements.*

Occupational-Use Products

EPA is establishing a-i-specific requirements for occupational handlers for brodifacoum due to concerns about toxicity and poisoning incidents. EPA has determined that certain brodifacoum end-use products should be limited to use by occupational handlers (commercial applicators) and should not be available for sale or use by homeowners. Epidemiological evidence, the extremely low oral and dermal LD50 values, the low inhalation LC50 value, and the low NOEL for short- and intermediate-term effects have convinced the Agency that no formulation should be sold to or used by homeowners unless contained in tamper-resistant bait stations. In addition, due to these concerns, the Agency has determined that brodifacoum used in and around any residence and in and around schools, recreation areas, and other places where children may frequent must be contained in tamper-resistant bait stations even if it is applied by occupational handlers (commercial applicators). Furthermore all products labeled for use in and around residences or other areas where children frequent must be formulated with a bittering agent at a dose level palatable to rats but not to humans.

Limiting formulations that are not sold in tamper-resistant bait stations to occupational handlers (commercial applicators) allows EPA to require personal protective equipment for such

users. In addition, such users are more likely to have received training about the hazards of pesticides and safe use practices, such as washing thoroughly after use. Finally, EPA believes that formulations not contained in child-resistant bait stations should not be stored at or applied in residences due to the risk of accidental poisonings, particularly to children and pets.

EPA is requiring all occupational handlers (commercial applicators) who handle any brodifacoum formulation that is not already contained in tamper-resistant bait stations or place packs to wear chemical-resistant gloves. In addition, the Agency is requiring all occupational handlers who handle any other non-paraffinized formulation of brodifacoum to wear a dust/mist respirator and protective eyewear during open pouring and application.

Homeowner-Use Products

EPA is allowing brodifacoum end-use products formulated as baits to be sold to and used by homeowners, provided such products are contained in tamper-resistant bait stations during sale, storage, and application. The tamper-resistant bait station must meet the standards set forth in PR Notice 94-7, be resistant to destruction by dogs and by children under six years of age, and must be used in a manner that prevents such children from reaching into bait compartments and obtaining bait.

EPA is not establishing minimum (baseline) handler PPE for brodifacoum end-use products that are intended primarily for homeowner use, because the Agency has determined that limiting the formulations available for homeowner use to baits contained in tamper-resistant bait stations will adequately mitigate the concerns about the high acute toxicity and poisoning incidents.

Post-Application/Entry Restrictions

EPA is not establishing entry restrictions at this time for brodifacoum end-use products. The Agency is relying on the use restriction statement, "Apply bait in locations out of reach of children, pets, domestic animals and nontarget wildlife" and on the requirement for the use tamper-resistant bait stations in and around any residence and in other locations where children may frequent to reduce post-application exposures, particularly to children.

Other Labeling Requirements

The Agency is also requiring other use and safety information to be placed on the labeling of all end-use products containing brodifacoum. For the specific labeling statements, refer to Section V of this document.

(RED SECTION V - LABELING REQUIREMENTS)

LABELING REQUIREMENTS FOR END-USE PRODUCTS

PPE/Engineering Control Requirements for Pesticide Handlers

For **sole-active-ingredient** end-use products that contain brodifacoum, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain brodifacoum, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use

Minimum (Baseline) PPE/Engineering Control Requirements

EPA is limiting the use of some end-use products containing brodifacoum to occupational handlers (i.e., commercial applicators). These include all brodifacoum-containing end-use products formulated as a bait, unless contained in a tamper-resistant bait station during sale, storage, and use. All occupational-use products — all formulations that are not sold in tamper-resistant bait stations — must bear the following statement in a prominent location on the front panel of the end-use product labeling:

"For sale to and use by occupational handlers (commercial applicators) only. Sale to or use by the general public is prohibited."

The minimum (baseline) PPE for brodifacoum end-use products formulated in a non-paraffinized form (except those products in place packs or tamper-resistant bait stations) is:

"Applicators and other handlers must wear the following:
--long-sleeved shirt and long pants,
--chemical-resistant gloves*,
--shoes plus socks,
--protective eyewear,
--a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C).

If the product is placed into a tamper-resistant bait station, persons handling the bait stations need not wear the chemical-resistant gloves, protective eyewear, or respirator."

The minimum (baseline) PPE for brodifacoum end-use products formulated as paraffinized baits that are not in tamper-resistant bait stations is:

"Applicators and other handlers must wear:

- long-sleeved shirt and long pants,
- chemical-resistant gloves*, and
- shoes plus socks.

If the product is placed into a tamper-resistant bait station, persons handling the bait stations need not wear the chemical-resistant gloves."

* For the glove statement, use the statement established for brodifacoum through the instructions in Supplement Three of PR Notice 93-7.

If the end-use product is classified as toxicity category I or II for eye irritation potential, protective eyewear is also required.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7, and the format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Products Intended Primarily for Homeowner Use

EPA is not establishing active-ingredient-based minimum (baseline) handler PPE for brodifacoum end-use products that are intended primarily for homeowner use.

Entry Restrictions

There are no entry restrictions.

For **sole-active-ingredient** end-use products that contain brodifacoum the product labeling must be revised to remove any entry restrictions on the current labeling.

For **multiple-active-ingredient** end-use products that contain brodifacoum the entry restrictions on the current labeling must be retained.

Other Labeling Requirements

Products Intended Primarily for Occupational Use

The Agency is requiring the following labeling statements to be located on all end-use products containing brodifacoum that are intended primarily for occupational use.

Use Restrictions

The following language must appear on the label directly below the heading "DIRECTIONS FOR USE". The captions "READ THIS LABEL" and "IMPORTANT" must be printed in conspicuous type, preferably in a color which contrasts with the remainder of the text in this section and with the background.

"It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

READ THIS LABEL: Read this entire label and follow all use directions and use precautions.

IMPORTANT: Do not expose children, pets, or other nontarget animals to rodenticides. To help to prevent accidents:

1. Store product not in use in a location out of reach of children and pets.
2. Apply bait in locations out of reach of children, pets, domestic animals and nontarget wildlife. All applications in and around any residence and in and around schools, recreation areas, and other places where children may frequent must be contained in tamper-resistant bait stations. These stations must be resistant to destruction by dogs and by children under six years of age, and must be used in a manner that prevents such children from reaching into bait compartments and obtaining bait. If bait can be shaken from stations when they are lifted, units must be secured or otherwise immobilized. Even stronger bait stations are needed in areas open to hooved livestock, raccoons, bears, other potentially destructive animals, or in areas prone to vandalism.
3. Dispose of product container, and unused, spoiled, and unconsumed bait as specified on this label."

Application Restrictions

"Do not apply this product in a way that will contact workers, other persons, pets, or domestic animals.

User Safety Requirements

- ☐ "With detergent and hot water, wash all equipment and utensils used for applying bait. Such equipment and utensils must be designated as and clearly marked for pesticide use only. Do not allow such equipment or utensils to contact any food or feed."
- ☐ "Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry."

User Safety Recommendations

- ☐ "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- ☐ "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."
- ☐ "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Products Intended Primarily for Home Use

Use Restrictions

The following language must appear on the label directly below the heading "DIRECTIONS FOR USE". The captions "READ THIS LABEL" and "IMPORTANT" must be printed in conspicuous type, preferably in a color which contrasts with the remainder of the text in this section and with the background.

"It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

READ THIS LABEL: Read this entire label and follow all use directions and use precautions.

IMPORTANT: Do not expose children, pets, or other nontarget animals to rodenticides. To help to prevent accidents:

1. Store product not in use in a location out of reach of children and pets.
2. Place bait stations in locations out of reach of children, pets, domestic animals and nontarget wildlife, when possible. If bait can be shaken from stations when they are lifted, units must be secured or otherwise immobilized. Even stronger bait stations are needed in areas open to hoofed livestock, raccoons, bears, other potentially destructive animals, or in areas prone to vandalism.
3. Dispose of product container, and unused, spoiled, and unconsumed bait as specified on this label."

Application Restrictions

"Do not apply this product in a way that will contact any person or pet. Keep people and pets out of the area during application."

User Safety Recommendations

- ☐ "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- ☐ "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

References

1. U.S. EPA 1995. Label Use Information System Report for brodifacoum, dated 17 October 1996.
2. Brodifacoum Labels: EPA Reg. No. 3782-79, 10182-340, 10182-336, 10182-335 10182-48, 3286-66, 10182-334, 11715-218, 10182-338, 10182-384, 3282-81.
3. Toxicology Endpoint Selection Document for Brodifacoum, dated November 4, 1996.
4. Review of Rodenticide Poisoning Data, Memo from Virginia A. Dobozy to Tom Campbell, 12/18/96.

Attachments

1. Toxicology Endpoint Selection Document for Brodifacoum, 11/4/96.
2. Review of Rodenticide Poisoning Data, Memo from Virginia A. Dobozy to Tom Campbell, 12/18/96.

cc: Thomas Campbell, OREB/HED
John Redden, RCAB/HED
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Chemical File
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