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United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508W) | EPA738-R-98-007 July 1998

Reregistration Eligibility Decision (RED)

Rodenticide Cluster

US EPA ARCHIVE DOCUMENT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

I am pleased to announce that the Environmental Protection Agency has completed its reregistration eligibility review and decisions on the rodenticide cluster pesticide case which includes the active ingredients brodifacoum, bromodialone, bromethalin, chlorophacinone and diphacinone and its sodium salt, and pival and its sodium salt. The enclosed Reregistration Eligibility Decision (RED), which was approved on **September 30, 1997**, contains the Agency's evaluation of the data base of these chemicals, its conclusions of the potential human health and environmental risks of the current product uses, and its decisions and conditions under which these uses and products will be eligible for reregistration. The RED includes the data and labeling requirements for products for reregistration. It also includes requirements for additional data (generic) on the active ingredients to confirm the risk assessments.

To assist you with a proper response, read the enclosed document entitled "Summary of Instructions for Responding to the RED." This summary also refers to other enclosed documents which include further instructions. You must follow all instructions and submit complete and timely responses. **The first set of required responses is due 90 days from the receipt of this letter. The second set of required responses is due 8 months from the date of this letter.** Complete and timely responses will avoid the Agency taking the enforcement action of suspension against your products.

Please note that the Food Quality Protection Act of 1996 (FQPA) became effective on August 3, 1996, amending portions of both pesticide law (FIFRA) and the food and drug law (FFDCA). This RED takes into account, to the extent currently possible, the new safety standard set by FQPA for establishing and reassessing tolerances. However, it should be noted that in continuing to make reregistration determinations during the early stages of FQPA implementation, EPA recognizes that it will be necessary to make decisions relating to FQPA before the implementation process is complete. In making these early case-by-case decisions, EPA does not intend to set broad precedents for the application of FQPA. Rather, these early determinations will be made on a case-by-case basis and will not bind EPA as it proceeds with further policy development and any rulemaking that may be required.

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If EPA determines, as a result of this later implementation process, that any of the determinations described in this RED are no longer appropriate, the Agency will pursue whatever action may be appropriate, including but not limited to reconsideration of any portion of this RED.

If you have questions on the product specific data requirements or wish to meet with the Agency, please contact the Product Reregistration representative Venus Eagle at (703) 308-8045. Address any questions on required generic data to the Special Review and Reregistration Division representative Dennis Deziel at (703)308-8176.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
Reregistration Division

Enclosures

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SUMMARY OF INSTRUCTIONS FOR RESPONDING TO THE REREGISTRATION ELIGIBILITY DECISION (RED)

1. **DATA CALL-IN (DCI) OR "90-DAY RESPONSE"**--If **generic data** are required for reregistration, a DCI letter will be enclosed describing such data. If **product specific data** are required, another DCI letter will be enclosed listing such requirements. If **both generic and product specific data** are required, a combined Generic and Product Specific letter will be enclosed describing such data. Complete the two response forms provided with each DCI letter (or four forms for the combined) by following the instructions provided. **You must submit the response forms for each product and for each DCI within 90 days of the date of this letter (RED issuance date); otherwise, your product may be suspended.**

2. **TIME EXTENSIONS AND DATA WAIVER REQUESTS**--No time extension requests will be granted for the 90-day response. Time extension requests may be submitted only with respect to actual data submissions. Requests for data waivers must be submitted as part of the 90-day response. Requests for time extensions should be submitted in the 90-day response, but certainly no later than the 8-month response date. All data waiver and time extension requests must be accompanied by a full justification. All waivers and time extensions must be granted by EPA in order to go into effect.

3. **APPLICATION FOR REREGISTRATION OR "8-MONTH RESPONSE"--You must submit the following items for each product within eight months of the date of this letter (RED issuance date).**

a. **Application for Reregistration** (EPA Form 8570-1). Use only an original application form. Mark it "Application for Reregistration." Send your Application for Reregistration (along with the other forms listed in b-e below) to the address listed in item 5.

b. **Five copies of draft labeling** which complies with the RED and current regulations and requirements. Only make labeling changes which are required by the RED and current regulations (40 CFR 156.10) and policies. Submit any other amendments (such as formulation changes, or labeling changes not related to reregistration) separately. You may delete uses which the RED says are ineligible for reregistration. For further labeling guidance, refer to the labeling section of the EPA publication "General Information on Applying for Registration in the U.S., Second Edition, August 1992" (available from the National Technical Information Service, publication #PB92-221811; telephone number 703-487-4650).

c. **Generic or Product Specific Data**. Submit all data in a format which complies with PR Notice 86-5, and/or submit citations of data already submitted and give the EPA identifier (MRID) numbers. Before citing these studies, you must **make sure that they meet the Agency's acceptance criteria** (attached to the DCI).

d. **Two copies of the Confidential Statement of Formula (CSF)** for each basic and each alternate formulation. The labeling and CSF which you submit for each product must comply with P.R. Notice 91-2 by declaring the active ingredient as the **nominal concentration**. You have two options for submitting a CSF: (1) accept the standard certified

limits (see 40 CFR §158.175) or (2) provide certified limits that are supported by the analysis of five batches. If you choose the second option, you must submit or cite the data for the five batches along with a certification statement as described in 40 CFR §158.175(e). A copy of the CSF is enclosed; follow the instructions on its back.

e. **Certification With Respect to Data Compensation Requirements**. Complete and sign EPA forms 8570-34 and 8570-35 for each product.

4. **COMMENTS IN RESPONSE TO FEDERAL REGISTER NOTICE**--Comments pertaining to the content of the RED may be submitted to the address shown in the Federal Register Notice which announces the availability of this RED.

5. **WHERE TO SEND PRODUCT SPECIFIC DCI RESPONSES (90-DAY) AND APPLICATIONS FOR REREGISTRATION (8-MONTH RESPONSES)**

By U.S. Mail:

Document Processing Desk **(RED-SRRD-PRB)**
Office of Pesticide Programs (7504C)
EPA, 401 M St. S.W.
Washington, D.C. 20460-0001

By express:

Document Processing Desk **(RED-SRRD-PRB)**
Office of Pesticide Programs (7504C)
Room 266A, Crystal Mall 2
1921 Jefferson Davis Hwy.
Arlington, VA 22202

6. **EPA'S REVIEWS**--EPA will screen all submissions for completeness; those which are not complete will be returned with a request for corrections. EPA will try to respond to data waiver and time extension requests within 60 days. EPA will also try to respond to all 8-month submissions with a final reregistration determination within 14 months after the RED has been issued.

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REREGISTRATION ELIGIBILITY DECISION

RODENTICIDE CLUSTER

LIST B

CASES 2100, 2205, 2755, 2760, 2765, 2810

ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
SPECIAL REVIEW AND REREGISTRATION DIVISION

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RODENTICIDE CLUSTER REREGISTRATION ELIGIBILITY DECISION TEAM

Office of Pesticide Programs:

Biological and Economic Analysis Assessment

Frank Hernandez	Economic Analysis Branch
William Gross	Biological Analysis Branch

Environmental Fate and Effects Risk Assessment

Sharlene Matten	Science Analysis and Coordination Staff
James Goodyear	Ecological Effects Branch
William Erickson	Ecological Effects Branch
Harry Craven	Ecological Effects Branch
Richard Mahler	Environmental Fate and Groundwater Branch
Larry Liu	Environmental Fate and Groundwater Branch
John Jordan	Environmental Fate and Groundwater Branch

Health Effects Risk Assessment

Byron T. Backus	Toxicology Branch II
Thomas Campbell	Occupational and Residential Exposure Branch
John Redden	Risk Characterization and Analysis Branch
Whang Phang	Toxicology Branch II
John Leahy	Occupational and Residential Exposure Branch

Registration Support Risk Assessment

Daniel Peacock	Insecticide-Rodenticide Branch
Bill Jacobs	Insecticide-Rodenticide Branch

Risk Management

Dennis Deziel	Reregistration Branch I
William Wooge	Reregistration Branch I

Registration Support Risk Assessment

Carol Glasgow	Reregistration Support Branch
Debbie McCall	Registration Support Branch

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GLOSSARY OF TERMS AND ABBREVIATIONS

ADI	Acceptable Daily Intake. A now defunct term for reference dose (RfD).
AE	Acid Equivalent
a.i.	Active Ingredient
ARC	Anticipated Residue Contribution
CAS	Chemical Abstracts Service
CI	Cation
CNS	Central Nervous System
CSF	Confidential Statement of Formula
DFR	Dislodgeable Foliar Residue
DRES	Dietary Risk Evaluation System
DWEL	Drinking Water Equivalent Level (DWEL) The DWEL represents a medium specific (i.e. drinking water) lifetime exposure at which adverse, non carcinogenic health effects are not anticipated to occur.
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EC_{50}	Median Effective Concentration. The concentration at which 50% of an exposed test population is effected sublethally.
EP	End-Use Product
EPA	U.S. Environmental Protection Agency
FAO/WHO	Food and Agriculture Organization/World Health Organization
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GLC	Gas Liquid Chromatography
GM	Geometric Mean
GRAS	Generally Recognized as Safe as Designated by FDA
HA	Health Advisory (HA). The HA values are used as informal guidance to municipalities and other organizations when emergency spills or contamination situations occur.
HDT	Highest Dose Tested
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LD_{lo}	Lethal Dose-low. Lowest Dose at which lethality occurs.
LEL	Lowest Effect Level
LOC	Level of Concern
LOD	Limit of Detection
LOEL	Lowest Observed Effect Level
MATC	Maximum Acceptable Toxicant Concentration
MCLG	Maximum Contaminant Level Goal (MCLG) The MCLG is used by the Agency to regulate contaminants in drinking water under the Safe Drinking Water Act.
µg/g	Micrograms Per Gram
mg/l	Milligrams Per Liter
MOE	Margin of Exposure
MP	Manufacturing-Use Product
MPI	Maximum Permissible Intake
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.

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N/A	Not Applicable
NOEC	No effect concentration
NPDES	National Pollutant Discharge Elimination System
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
OP	Organophosphate
OPP	Office of Pesticide Programs
Pa	Pascal, the pressure exerted by a force of one newton acting on an area of one square meter.
PADI	Provisional Acceptable Daily Intake
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PCO	Pesticide Certified Operator
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRN	Pesticide Registration Notice
Q^*_1	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RS	Registration Standard
RUP	Restricted Use Pesticide
SLN	Special Local Need (Registrations Under Section 24 (c) of FIFRA)
TC	Toxic Concentration. The concentration at which a substance produces a toxic effect.
TD	Toxic Dose. The dose at which a substance produces a toxic effect.
TEP	Typical End-Use Product
TGAI	Technical Grade Active Ingredient
TLC	Thin Layer Chromatography
TMRC	Theoretical Maximum Residue Contribution
torr	A unit of pressure needed to support a column of mercury 1 mm high under standard conditions.
μg/L	Micrograms per liter
WP	Wettable Powder
WPS	Worker Protection Standard

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ABSTRACT

The U. S. Environmental Protection Agency (EPA) has completed its reregistration eligibility decision of the pesticides brodifacoum, bromadiolone, chlorophacinone, diphacinone and its sodium salt, bromethalin, and pival and its sodium salt. This decision includes a comprehensive reassessment of the required target data and the use patterns of currently registered products. These chemicals are rodenticides used in urban, suburban, and rural areas for the control of commensal rodents. Chlorophacinone and diphacinone are also used in the field to control a variety of vertebrate pests, mainly rodents but also jackrabbits (lagomorphs), moles (insectivores), and mongoose (carnivores). With the exception of bromethalin, which is a neurotoxin, the chemicals being reregistered in this decision document are anticoagulants. With the exception of pival and its sodium salt, the Agency has concluded that the uses, as prescribed in this document, with additional labeling requirements and a number of risk mitigation measures, will not cause unreasonable risks to humans or the environment.

The Agency has determined that all uses of brodifacoum, bromethalin, and bromadiolone are eligible for reregistration.

The Agency has determined that all uses of chlorophacinone and diphacionone and its salt are eligible for reregistration, with the exception of certain field bait uses. The Agency has determined that field-bait uses containing .005% chlorophacinone and diphacionone and its salt are eligible for reregistration.

The Agency has determined that field-bait uses containing more than .005% chlorophacinone and diphacionone and its salt are ineligible for reregistration. Field tests have adequately demonstrated that products with lower-concentrations of these active ingredients are sufficiently efficacious for target pest species, and that the uses with higher concentrations have the potential to cause unnecessary secondary poisonings to avian and mammalian consumers.

The EPA has determined that all uses of pival and its sodium salts are ineligible for reregistration. Pival and its sodium salt was suspended by the Agency in December 1994 for failure of the registrant, Motomco, Incorporated, to respond to the Agency's Data Call-In Notice (DCI) and submit the required data to support the continued registration. In the future, EPA may seek cancellation of the registration for pival and its sodium salt.

Rodenticides, when used as currently sold and marketed, are responsible for a number of human incidents and accidental exposures each year. As with human exposures, EPA is concerned about the increased risk posed to non-target domestic animals, as well as primary and secondary risks to nontarget mammals and birds, from the use of rodenticides used. However, EPA also

recognizes the important public health benefits of rodenticides. Specifically, the Agency considered the benefits from rodent control relating to prevention of disease transmission, property damage, and attacks on humans.

In order to address the risk concerns posed from the use of these products and still maintain the benefits afforded by their use, the Agency has developed a two-phased approach to mitigating risk. The first phase will put into place in short-term measures that will serve to identify when an exposure has occurred, to lessen the amount of exposures, and monitor exposures. The second phase will reduce exposures in the long term. Ideally, the Agency would have preferred to impose measures to immediately eliminate opportunities for exposures; however, it recognizes that new technologies do not exist and must be developed to accomplish this while still maintaining the efficacy of the product. The Agency has therefore developed this phased approach to allow time for the development and testing of this new technology.

In addition, outside the scope of this RED process, the Agency is requiring similar risk mitigation measures to the registrations of other rodenticide active ingredients such as zinc phosphide, warfarin and salts, difethialone, vitamin D-3, and red squill and, if necessary, registrations of new rodenticide active ingredients.

The Agency recently became aware of incident data which suggests that there may be a potential incident problem specifically involving the active ingredient brodifacoum. At this time the Agency is reviewing the data; no final conclusions have been reached. Additionally, through the "Notice of Availability" for this document, the Agency requests state incident data on all rodenticides to better understand the extent of this potential problem. After review, the Agency may impose additional restrictions on the use of brodifacoum.

Phase One: Short-Term Risk Mitigation Measures

(A) Indicator Dye and Bittering Agent

All registrants of rodenticides, other than those with products used exclusively at agricultural sites, must incorporate an indicator dye into their formulations. The dye is intended to help identify whether a child or household pet has actually consumed a rodenticide by dying their mouth and/or hands a bright color. EPA believes the dye will play an important role in identifying when an exposure has occurred, thereby helping to determine if treatment is required. Typically, it is very difficult for parents and guardians of children and pet owners to discern whether an exposure or ingestion has actually occurred, which may lead to unnecessary treatment at a medical facility as a precautionary measure. In turn, the Agency believes this measure will also enable parents and guardians of children and pet owners to seek medical or veterinarian attention sooner rather than later and avoid a serious medical episode. EPA recognizes that many of the formulations currently contain a dye. All registrants may present data demonstrating that the current dye meets the intent of this requirement.

All registrants of rodenticides, other than those with products used exclusively at agricultural sites, must incorporate a bittering agent into their formulations to make the bait less palatable to humans. EPA believes that the bittering agent may cause some children to expel the

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bait if placed in the mouth. The Agency is fully aware that children younger than one year old do not have fully formed taste buds and may not be fully protected by this measure. However, this measure should prevent some exposures to children older than one year of age. Likewise, the EPA is also aware that this measure may not affect exposures to non-target household animals.

(B) Improved Labeling Requirements

EPA is requiring a number of label revisions to rodenticide registrations. These requirements are set forth in Section V of this RED document and are in addition to those in PR Notice 94-7 that have already been implemented.

Labels which currently allow placement of rat and mouse baits "in and around buildings" must be amended to "indoors and against the outside walls of buildings." Rat and mouse bait placements will be allowed "around" buildings only if registrants demonstrate from secondary toxicity testing that secondary risks to birds and mammals are likely to be minimal.

(C) Annual Submission of American Association of Poison Control Centers (AAPCC) Data

Under the authority of FIFRA section 3(c)(2)(B), the Agency is requiring registrants of rodenticides subject to this RED document, to submit to the Agency annual American Association of Poison Control Centers' (AAPCC) data. The Agency is requiring AAPCC data for the years 1999 through 2009. Registrants are encouraged to share the cost of generating data, whenever appropriate. If needed, the Agency may ask registrants of rodenticides for additional annual submission of AAPCC data. These data will enable the Agency to determine whether the imposed risk mitigation measures are reducing incidents/exposures to humans, in particular children. AAPCC data obtained by the Agency for 1995 and 1996 will serve as baseline data.

(D) Restricted Use Classification for Tracking Powders

EPA has determined that the use of these chemicals as tracking powders in and around residences, schools, recreation areas, and other places that children may frequent, pose a significant risk to children, household pets, and non-target animals. EPA believes that children and pets can easily come in contact with rodenticides used as tracking powders simply based on their use patterns and use locations. To protect children and non-target animals from exposure, all products formulated as tracking powders must must remain classified and labeled as restricted use because of acute toxicity and undue secondary risk to non-target species. Certified applicators receive training on the importance of following label directions and overall application, and, therefore are more likely to apply the product correctly. Moreover, tracking powder products must bear a strong precautionary statement and new restrictions limiting placement of powder to locations not accessible to children, household pets, and non-target animals.

EPA is also concerned about the potential exposure (inhalation and dermal) to the certified applicators of these types of product formulations. Due to the low inhalation LC_{50} value and the possibility of users inhaling or ingesting powders during pouring and application, EPA is limiting use of the powder formulations to use by certified applicators, EPA is requiring protective

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eyewear and dust/mist respirators for such users in addition to other personal protective equipment.

(E) Restricted Use for Field Products

All products labeled for field uses, except for those limited to manual underground baiting, must be reclassified and relabeled as restricted use because of acute toxicity and high potential for primary and secondary risks to nontarget mammals and birds.

Phase Two: Long-Term Risk Reduction

The Agency believes that the required risk mitigation measures outlined in Phase One should be followed by further exposure/risk reduction measures for rodenticides. EPA is also aware that a safer technology, which is efficacious and equally effective to eliminate human and household pet exposures may not currently exist. However, the Agency will require the development of and movement into a new, safer rodenticide use technology. The EPA is convinced that development of this technology can be achieved. Therefore, Phase Two of the Agency's risk mitigation approach, is the requirement to move rodenticides into a safer use technology. To achieve this end, within 120 days of the issuance of the REDs, the Agency will form a Stakeholder group and hold a series of meetings to discuss means of significantly reducing exposures to children and pets. The Stakeholder group will consist of members from industry, states, CDC, CPSC, AAPCC, rodent control experts, members of environmental groups, the medical community, and the veterinary community.

The Agency will conclude the Stakeholder process within 9 months from the issuance of the REDs. The Agency expects, at the conclusion of this process, to have a recommendation on how to further mitigate risk to children and household pets and a implementation plan to achieve significant risk reduction.

Risk Mitigation Measures for Products Intended for Occupational Use

The Agency has determined that all labels for occupational use products require commercial handlers to wear gloves while handling these rodenticide chemicals not already contained in place packs to reduce dermal exposure unless registrants submit data which indicate there is no dermal exposure. The Agency has determined that occupational handlers (commercial applicators) must wear protective eyewear, and a dust mask/mist respirator when handling non-parafinized formulations of these chemicals such as meal or grain-based baits, unless these formulations are contained in place packs or the registrants can determine via data that there is no inhalation exposure. In addition, the Agency is requiring all occupational handlers who handle powder formulations or any other non-parafinized formulation of chlorophacinone to wear a dust/mist respirator and protective eyewear during open pouring and application unless registrants submit data indicating there is no inhalation exposure.

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I. INTRODUCTION

In 1988, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act provides a schedule for the reregistration process to be completed in nine years. There are five phases to the reregistration process. The first four phases of the process focus on identification of data requirements to support the reregistration of an active ingredient and the generation and submission of data to fulfill the requirements. The fifth phase is a review by the U.S. Environmental Protection Agency (referred to as "the Agency") of all data submitted to support reregistration.

FIFRA Section 4(g)(2)(A) states that in Phase 5 "the Administrator shall determine whether pesticides containing such active ingredient are eligible for reregistration" before calling in data on products and either reregistering products or taking "other appropriate regulatory action." Thus, reregistration involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criterion of FIFRA.

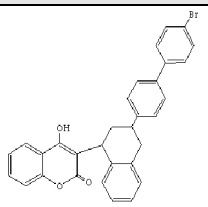
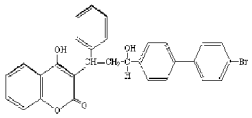
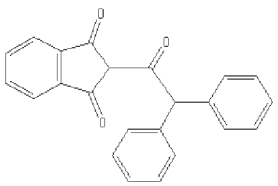
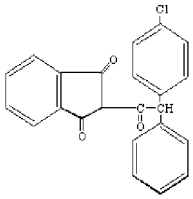
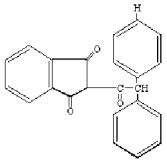
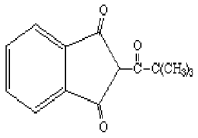
On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) (Public Law 104-170) was signed into law. FQPA amends both the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 301 et seq, and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136 et seq. The FQPA amendments went into effect immediately. Among other things, FQPA amended the FFDCA by establishing a new safety standard for the establishment of tolerances. The FQPA does not, however, amend any of the existing reregistration deadlines set forth in Sec. 4 of FIFRA. Thus, EPA is embarking on an intensive process, including consultation with registrants, States, and other interested stakeholders, to make decisions on the new policies and procedures that will be appropriate as a result of enactment of FQPA. This process will include a more in-depth analysis of the new safety standard and how it should be applied to both food and non-food pesticide applications. However, in light of the statutory deadlines with respect to reregistration, the Agency will continue its ongoing reregistration program while it continues to determine how best to implement FQPA.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of brodifacoum, bromadiolone, bromethalin, chlorophacinone, diphacinone and its sodium salt, and pival and its sodium salt . The document consists of six sections. Section I is the introduction. Section II describes these chemicals' uses, data requirements and regulatory history. Section III discusses the concerns regarding human health and environmental assessment based on the data available to the Agency. Section IV presents the reregistration decision for brodifacoum, bromadiolone, chlorophacinone, diphacinone and its sodium salt, bromethalin, and pival and its sodium salt. Section V discusses the reregistration requirements for brodifacoum, bromadiolone, chlorophacinone, diphacinone and its sodium salt, and bromethalin. Finally, Section VI contains the Appendices supporting this Reregistration Eligibility Decision. Additional details concerning the Agency's review of applicable data are available on request.

II. CASE OVERVIEW

A. Chemical Overview

Table 1 - Chemical Overview

Common/ Case Name	Reregistration Case #	OPP Chemical Code	Chemical Name	CAS Registry #	Empirical Formula	Structural Formula	Basic Manufacturer
Brodifacoum	2755	112701	3-[3-(4'-bromo[1,1'biphenyl]-4yl)-1,2,3,4-tetrahydro-1-napthalenyl]-4-hydroxy-2H-1-benzopyran-2-one	56073-10-0	$C_{32}H_{23}BrO_3$		Zenica; Bell Laboratories
Bromadiolone	2760	112001	3-[3-(4'-Bromo[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2H-1-benzopyran-2-one	28772-56-7	$C_{30}H_{23}BrO_4$		Lipha; Bell Laboratories
Bromethalin	2765	112802	N-Methyl-2,4-dinitro-N(2,4,5-tribromophenyl)-6(trifluoromethyl) benzenamine	63333-35-7	$C1_3H_7Br_3F_3N_3O_4$		PM Resources.
Chlorophacinone	2100	67707	2-[(4-Chlorophenyl)phenyl acetyl]-1H-indene-1,3-(2H)-dione	3691-35-8	$C_{23}H_{15}ClO_3$		Lipha
Diphacinone	2205	67701	2-(diphenylacetyl)-1,3-indanedione	82-66-6	$C_{23}H_{16}O_3$		Bell laboratories; HACCO, Inc.
Pival	2810	67703	2-(trimethyacetyl)-1,3-indanedione	83-26-1	$C_{14}H_{14}O_3$		Motomco

B. Use Profile

The following table (Table 2) lists the sites, pests, formulations (as applied), and application methods for rodenticides covered by this RED document. These chemicals are for the control of mammal pests, particularly commensal rats and mice but also a variety of field rodents [note: commensal rodents are Norway rat, roof rat, and house mouse].

Table 2 - Use Profile

Category	Name of Rodenticide					
Sites	Pival	Diphacinone or its Sodium Salt	Chlorophacinone	Brodifacoum	Bromadiolone	Bromethalin
In/Around Buildings	X	X	X	X	X	X
Inside Transport/Cargo Vehicles				X	X	X
Sewers		X	X	X	X	X
Landfills		X				
Terrestrial Nonfood		X	X			
Forestry Plantings		X	X			
Nurseries		X				
Levees/Ditch banks		X	X			
Orchards (dormant or nonbearing)		X	X			
Small Grains		X				
Small Fruits (dormant or nonbearing)		X	X			
Terrestrial food Crops (bait boxes)		X	X			
Terrestrial Food Crops		X	X			
Artichokes			X			
Aquatic, Non-Food (bait boxes)		X	X			
Pests	Pival	Diphacinone or its Sodium Salt	Chlorophacinone	Brodifacoum	Bromadiolone	Bromethalin
Norway Rat	X	X	X	X	X	X
Roof Rat	X	X	X	X	X	X
House Mice	X	X	X	X	X	X
White-footed Mice		X	X			
Meadow Mice/Voles		X	X			
Ground Squirrels		X	X			
Chipmunks		X	X			
Jackrabbits		X	X			
Cottontail Rabbits		X				
Pocket Gophers		X	X			
Cotton Rats		X	X			
Wood Rats		X	X			
Rice Rats		X				
Florida Water Rat		X				
Muskrat		X	X			
Polynesian Rat		X				
Moles			X			
Mongoose		X				
FORMULATIONS (as applied)	Pival	Diphacinone or its Sodium Salt	Chlorophacinone	Brodifacoum	Bromadiolone	Bromethalin
Solid Baits	X	X	X	X	X	X
Liquid Sprays			X			
Liquid Baits (salt)	X	X				
Tracking Powders		X	X			
APPLICATION METHODS	Pival	Diphacinone or its Sodium Salt	Chlorophacinone	Brodifacoum	Bromadiolone	Bromethalin
Hand Placement	X	X	X	X	X	X
Hand Broadcast (field use)		X	X			
Ground Broadcast (field use)		X	X			
Aerial Broadcast (field use)		X	X			

1. Brodifacoum Summary of Use Patterns and Formulations

Brodifacoum (3-[3-(4-bromo[1,1-biphenyl]4-yl)-1,2,3,4-tetra-hydro-1-napthalenyl]4-hydroxy-2H-1-benzophyran-2-one) is a rodent control agent for use against commensal rats and mice only. It is an anticoagulant and is formulated as meal bait, paraffinized pellets, rat and

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mouse bait ready-to-use place packs, and paraffin blocks. All end-use products contain 0.005 percent active ingredient.

Brodifacoum is currently registered for the control of rats and mice in and around farm structures, households and domestic dwellings, uncultivated agricultural and non-agricultural areas, inside transport vehicles, commercial transportation facilities, industrial areas, 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. Only general-use brodifacoum products are currently registered.

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 maximum rates of application are 16 ounces of product per 15 foot interval for controlling commensal rats and 2 ounces of bait per 8 to 12 foot interval for controlling house 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. Tamper-resistant 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 the bait. If the bait can be shaken from stations when they are lifted, stations must be secured or otherwise immobilized. Baits may be loaded into bait stations by hand (place packs, cakes, blocks, and slabs), or by using a scoop for loose baits (meal baits, grain baits) and pellets.

2. Bromadiolone Summary of Use Patterns and Formulations

Bromadiolone (3-(3-(4'-bromo-(1,1'-biphenyl)-4-yl)-3-hydroxy-1-phenylpropyl)-4-hydroxy-2H-1-benzopyran-2-one) is a rodent control agent for rats and mice in and around buildings, inside transport vehicles and sewers. It acts as an anticoagulant and is formulated as meal bait, paraffinized pellets, rat and mouse bait ready-to-use place packs, and paraffin blocks, (all formulations contain 0.005 percent a.i.).

Baits and bait packs are placed at 15 foot intervals for rats and 8 foot intervals for mice. When bait blocks are used in sewage systems, wire is used to secure blocks above the high water mark. The maximum rates of application are 16 oz per 15 ft interval for controlling commensal rats and 2 oz of bait per 8 ft interval for house 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 the bait can be shaken from stations when they are lifted, stations must be secured or otherwise immobilized.

3. Bromethalin Summary of Use Patterns and Formulations

Bromethalin (N-methyl-2,4-dinitro-N-(2,4,6-tribromophenyl)-6-(trifluoromethyl) benzenamine) is a rodent control agent for use against roof rats, Norway rats, and house mice in and around buildings and in transport vehicles. It is a single-dose poison that blocks nerve transmissions. Bromethalin is formulated as paraffinized blocks, meal bait, "all-weather bait," bait pellets, bait cups, place packs, bait packs, rat pellets, mouse pellets, and "mouse poison bait

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stations." All products are 0.01 percent a.i., with the exception of one, which is 0.005 percent active ingredient.

Bromethalin is currently registered for the control of commensal rats and mice in and around sewers, homes, industrial and agricultural buildings, and similar man-made structures. It may also be used in alleys located in urban areas, inside transport/cargo vehicles such as ships, trains, and aircraft, and in and around related port or terminal buildings. Baits may be placed in rodent burrows. Placement of bromethalin formulated as pellets or meal baits is prohibited in sewers. Baits are not to be applied to water or areas where surface water is present, or where there is the possibility of contaminating food or surfaces that come in direct contact with food. Applications may be made as frequently as necessary. At this time the Agency is aware of only general-use bromethalin products.

The maximum application rate is 8 ounces of bait per 15 foot interval for controlling commensal rats and 3 ounces of bait per 8-foot interval for controlling house mice. Several labels recommend baiting rodent burrows. When baiting rodent burrows, labels specify inserting bait into the burrow far enough so only a person who knows the bait is there would be likely to see it.

Bromethalin product labels specify that baits are to be applied in locations out of the reach of children, pets, domestic animals and non-target wildlife, or in tamper-resistant bait stations. Bait 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 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.

4. Chlorophacinone Summary of Use Patterns and Formulations

Chlorophacinone 2-[(p-chlorophenyl)phenylacetyl)] 1,3-indandione is a vertebrate control agent used to control a variety of vertebrate pests, mainly rodents, but also jackrabbits (lagomorphs), and moles (insectivores). It is an anticoagulant and is formulated as tracking powder, (0.2% a.i.) as loose-grain bait, paraffinized pellets, rat and mouse bait ready-to-use place packs, and paraffin blocks. Baits are mostly formulated as 0.005 % active ingredient, but some 0.01% active ingredient baits are registered. Chlorophacinone is currently registered for the control of rodents in and around buildings, households and domestic dwellings, uncultivated agricultural and non-agricultural areas, commercial transportation facilities; industrial areas, and food processing, handling, and storage areas and facilities. Baits are applied as frequently as needed only for commenal rats and mice; most field uses have a limited number of applications. Both general use and restricted use chlorophacinone products are currently registered.

For chlorophacinone, as well as all the rodenticides discussed in this RED, baits and bait packs are placed at 15 to 30 foot intervals for rats and 8 to 12 foot intervals for mice. The rate of application is 16 ounces of bait per 15 foot interval for controlling commensal rats and 2 ounces of bait per 8 foot interval for controlling housemice. According to labels, all baits are to

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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. Baits may be loaded into bait station by hand (place packs, cakes, blocks, and slabs), or by using a scoop for loose baits (meal baits, grain baits) and pellets.

Twenty states currently have special local needs (SLNs) registrations for field uses of Chlorophacinone. Most SLNs are for control of meadow and/or pine voles in orchards (17 states), mainly dormant fruit orchards, or for control of ground squirrels (8 states). Most products are food baits (pellets or treated whole grains), but a spray concentrate exists for vole control (4 states). Other SLNs include control of moles in Oregon and Washington; jackrabbits in Oregon and California; and pocket gophers, ground squirrels, deer mice, chipmunks, muskrats, woodrats, and commensal rats and mice in California.

5. Diphacinone Summary of Use Patterns and Formulations

Diphacinone and salt 2-(diphenylacetyl)-1,3-Indandione products are formulated predominantly as 0.005% a.i. food baits (loose bait, feeder boxes, place packs, or paraffinized bait blocks) for control of commensal rats (Norway rat, roof rat) and mice (house mouse). Food baits also are registered for controlling ground squirrels and pocket gophers. One product is registered as a tracking powder (0.2% a.i.) for control of rats and mice indoors and at burrows located along the periphery of buildings. Because Diphacinone salt is highly soluble, it is also used to prepare water baits for indoor control of rats and mice. Use sites for rat and mouse food baits are predominantly in and around buildings and similar man-made structures. Some labels include sewers or other wet or damp sites such as dumps, irrigation ditches, along fences, gullies, and other such areas. Ground squirrels can be baited in bait stations placed in or near levee or ditch banks, around farm buildings, along fence lines, in orchards, in or near crops, and in noncrop areas. Pocket gophers can be baited in underground burrow systems located in rangeland, cropland, forest, and noncrop areas.

Twenty-three states currently have one or more special local needs (SLNs) registrations for field uses of Diphacinone. Most SLNs are for control of meadow and/or pine voles in dormant or non-bearing orchards and tree plantations or for control of ground squirrels. Other SLNs target meadow voles around perimeters of small grain crops in Washington and Idaho, commensal rats, cotton rats, rice rats, and Florida water rats in noncrop areas adjacent to crop fields in Florida, mongoose and commensal rats, including the Polynesian rat, in forests, offshore islands, and other noncrop outdoor areas in Hawaii, and deer mice, jackrabbits, chipmunks, muskrats, woodrats, voles, and commensal rats and mice in California.

C. Estimated Usage of Pesticide

The total annual usage of the rodenticides included in this RED is estimated to have been about 250,000 lbs. of active ingredient over the last few years [Note: usage data based on proprietary information].

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Pest control operators (PCOs) use rodenticides primarily to control mice and rats in residential, industrial and institutional buildings. The majority of PCOs use single dose anticoagulants. Brodifacoum and bromadiolone-based products account for virtually all sales of single dose anticoagulants.

According to proprietary sources, approximately 60 percent of total rodenticides used by PCOs are for the commercial (non-residential) segment of the market. Residential applications account for approximately 40%. Local health departments contract PCOs, who primarily use anticoagulant rodenticides like brodifacoum, bromadiolone, chlorophacinone and diphacinone.

Over the past few years, the single dose anticoagulant brodifacoum represented about 30 percent of total pounds of rodenticide active ingredient. Bromadiolone ranked second with about 20 percent of the rodenticide market. Multiple-dose anticoagulants chlorophacinone and diphacinone, and the acute poison bromethalin accounted for another 20 percent market share.

D. Data Requirements

Appendix B includes all data requirements identified by the Agency for currently registered uses needed to support reregistration.

E. Regulatory History

The Agency's predecessor, the U.S. Department of Agriculture (USDA), first regulated vertebrate control agents after Congress passed FIFRA in 1947. During the initial year of regulation, the USDA registered the four mammalian poisons: strychnine, strychnine sulfate, zinc phosphide and red squill. Two of these chemicals are still registered 50 years later, but with several restrictions.

This Reregistration Eligibility Decision (RED) covers the neurotoxin bromethalin and five anticoagulant active ingredients (brodifacoum, bromethalin, bromadiolone, chlorophacinone and diphacinone and its sodium salt) applied as baits or tracking powders to control small mammals, such as rodents. This RED covers 243 of the currently registered 406 products, including Section 3 and 24(c) used to control vertebrate pests by baits and tracking powders. However, decisions made in this RED may impact many of the remaining 182 vertebrate control products, which were the subject of past REDs (e.g., warfarin and its sodium salt, strychnine and strychnine sulfate), or those that will be the subject of future reregistrations (e.g., difethialone, zinc phosphide, cholecalciferol/Vitamin D-3).

The following table (Table 3) includes all active ingredients with use patterns similar to those chemicals covered by this RED document and, those active ingredients (e.g., fumarin and its sodium salt) that are no longer registered.

Table 3 includes the name of each active ingredient grouped under "Anticoagulant Rodenticides" or "Other Rodenticides". Also, the table groups the anticoagulants by structural similarity and indicates which groups are considered to be "multiple-dose" or "single-dose" toxicants. Multiple-dose anticoagulants require repeated feedings over several days to kill, but

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single-dose ones typically require only a single-day's feeding. Brodifacoum and bromadiolone are considered "second-generation" anticoagulants because they are capable of killing rats that are resistant to warfarin, the original "first generation" anticoagulant rodenticide, which was registered in 1950.

Table 3 also lists the year of first registration and the current numbers of interstate (section 3 of FIFRA) and intrastate (section 24(c)) products.

Table 3 - Regulatory History of Mammalian Toxicants Used as Baits and Tracking Powders. The names of active ingredients covered by this RED are bold.

Name of Active Ingredient/Type of Rodenticide		Year First Registered	Number of Products	
			Sec 3	Sec 24(c)
I. ANTICOAGULANT RODENTICIDES				
A. Type I, 4-hydroxycoumarin - Multiple-Dose	1. Warfarin	1950	40	0
	2. Sodium Salt of Warfarin	1954	1	0
	3. Fumarin	1954	0	0
	4. Sodium Salt of Fumarin	1958	0	0
B. Type I, 1,3 indandione - Multiple-Dose	1. Pival	1953	4	0
	2. **Sodium Salt of Pival**	1954	1	0
	3. Calcium Salt of Pival	1967	0	0
	4. PMP	1962	0	0
	5. Calcium Salt of PMP	1963	0	0
C. Type II, 1,3 indandione - Multiple-Dose	1. **Diphacinone**	1960	61	40
	2. **Sodium Salt of Diphacinone**	1962	5	0
	3. **Chlorophacinone**	1971	16	43
D. Type II, 4-hydroxycoumarin - Single-Dose	1. **Brodifacoum**	1979	32	0
	2. **Bromadiolone**	1980	27	0
	3. Difethialone	1995	6	0
II. OTHER RODENTICIDES				
A. Single-Dose	1. Strychnine	1947	39	6
	2. Strychnine Sulfate	1947	0	0
	3. Red Squill (Scilliroside)	1947	0	0
	4. Zinc Phosphide	1947	40	20
	5. **Bromoethalin**	1984	19	0
B. Multiple-Dose	1. Cholecalciferol (Vitamin D-3)	1984	4	1

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III. SCIENCE ASSESSMENT

A. Physical Chemistry Assessment

Table 4 - Physical Chemistry Assessment

Common/Case Name	Brodifacoum	Bromadiolone	Bromethalin	Chlorophacinone	Diphacinone	Pival
Reregistration Case #	2755	2760	2755	2100	2205	2810
OPP Chemical Code	112701	112001	112802	67707	67701	67703
Color	Cream	White	White Crystals	Pale Yellow	White	Data Gap
Physical State	Fine Powdery Solid	Powdered Solid	Powder at 25°C	Microcrystalline Powder	Powder at Rm. Temp.	Data Gap
Odor	Not Reported	Odorless	Not Available	Not Reported	Not Reported	Data Gap
Melting Point	Decomposes at 201 - 205°C	198 - 199.8°C	148.2 - 154.1°C	141 - 145°C	141 - 145°C	Data Gap
Bulk Density	1.42 g/cm^{-3}	1.5164 g/ml	2.169 ± 0.001 g/ml at 23°C	0.56 g/cc	1.87 g/ml	Data Gap
Solubility	Water at pH 5.2 0.00038 7.4 0.24 9.3 1.00 Hexane 0.00088 Toluene 0.72 Dichloromethane 5.00 Acetone 2.30 Acetonitrile 0.32 Methanol 0.27	Mean Solubility (g/100 ml Solvent) Water 1.25 x 10^{-3} Hexane 7.15 x 10^{-4} Methanol 6.93 x 10^{-1}	Data Gap	Water 0.002 Dichloromethane 30.2 Chloroform 28.7 Ethyl Acetate 3.08 Acetone 1.93 Diethyl Ether 1.13 Hexane 0.113 Methanol 0.109 Ethanol 0.074	Data Gap	Data Gap
Dissociation Constant	Not Reported	Not Applicable/Very Low Water Solubility	Waived	Waived	Waived	Data Gap
Octanol/Water Partition Coefficient	8.5	Log P_{OW} = 4.27	P_{OW} = 1.8 x 10^4 Log P_{OW} = 4.26	Log P_{OW} = 4.22	Log P_{OW} = 4.27	Data Gap
Stability	Stable for 14 days at 54°C	Stable for 14 days at 54°C Not Stable in Sunlight (> 99% degradable)	Data Gap	Stable for 14 days at 54°C	Stable for 14 days at 54°C	Data Gap

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B. Human Health Assessment

1. Toxicology Assessment

The toxicological data bases for, brodifacoum, bromadiolone, chlorophacinone, diphacinone and its sodium salt, and bromethalin are adequate and will support reregistration eligibility.

a. Acute Toxicity

(1) Brodifacoum Acute Toxicity

Results of the acute toxicity studies conducted with technical brodifacoum are summarized below in Table 5:

Table 5 - Acute Toxicity Values of Technical Brodifacoum

Route	Species	Results	MRID	Toxicity Category
Oral	Rat	LD_{50} (M) = 0.418 mg/kg LD_{50} (F) = 0.561 mg/kg	42687501	I
Dermal	Rabbit	LD_{50} (M) = 5.21 mg/kg LD_{50} (F) = 3.16 mg/kg	42232101	I
Inhalation	Rat	LC_{50} (M) = 4.86 µg/L LC_{50} (F) = 3.05 µg/L	43110501	I
Eye Irritation[a]	Rabbit	Some minor eye irritation, clearing by day 7.	66938	III
Skin Irritation[a]	Rabbit	Unlikely to cause anything more than mild irritation; the high toxicity (note the dermal LD_{50} values above) precludes necessity for testing the technical for dermal irritation potential.	None	-
Dermal Sensitization[a,b]	Guinea Pig	Non sensitizer	None	N/A

[a] Not required for TGAI, however, presented here for informational purposes.
[b] Conducted on the 0.25% Brodifacoum Formulation Concentrate; see below.

In an oral LD_{50} study in which technical brodifacoum (96.1%) was administered as a suspension in polyethylene glycol to 300 rats, there were no mortalities or signs of toxicity in males or females at 0.25 mg/kg, nor in males at 0.35 mg/kg (females were not tested at this dose level). However, 5/5 males and 1/5 females died following dosage at 0.5 mg/kg, and 5/5 females died following dosage at 0.75 mg/kg (males were not tested at this dose level). Signs of toxicity at 0.5 and 0.75 mg/kg included pallor, bleeding from the nose and/or rectum and/or other sites. Deaths occurred in the period from 3-8 days after dosing. *Post mortem* examination of those animals that died or were sacrificed *in extremis* and/or showed signs of bleeding, revealed the presence of free or clotted blood in the abdominal and/or thoracic cavity. Discoloration or pallor of a number of organs was also observed. These findings are consistent with the known anticoagulant activity of brodifacoum. The LD_{50} is calculated to be 0.418 mg/kg for males (95% confidence interval between 0.35 and 0.5 mg/kg) and 0.561 mg/kg for females (95% confidence interval 0.472-0.667 mg/kg). These results place brodifacoum in Toxicity Category I (MRID 42687501) by the oral exposure route.

In a dermal LD_{50} study with rabbits, brodifacoum technical (95.6%) was applied as a suspension in corn oil (500 mg/kg), olive oil (10 mg/kg), or polyethylene glycol 600 (1 mg/kg), with 24-hour occluded dermal exposure. At 500 mg/kg, all the males were euthanized *in extremis* on days 5-6, and all females between days 5 and 8. At 10 mg/kg, 4/5 males were found dead or were euthanized *in extremis* between days 7 and 11, and 5/5 females between days 6 and 8. The animals that died or were euthanized showed signs of extreme toxicity consistent with anticoagulant activity (pallor, bleeding/bruising, breathing abnormalities) immediately prior to death. There were practically no signs of skin irritation on any of the animals. The dermal LD_{50} of brodifacoum technical was calculated to be 5.21 mg/kg (95% confidence interval 1.95-13.8 mg/kg) for males, and 3.16 mg/kg (95% a.i. 1.00-10.00 mg/kg) for females. These results place technical brodifacoum in toxicity category I (MRID 42232101) in terms of dermal toxicity potential.

In an inhalation LC_{50} study in rats, groups of young adult Wistar-derived rats, 5/sex, were exposed (nose only) for 4 hours to aerosols of brodifacoum (96.1% a.i.) generated from an acetone solution. The mean particulate concentrations were 0.82, 1.88, or 4.96 µg/L; corresponding brodifacoum concentrations were 0.69, 1.72 or 4.40 µg/L. The mass median diameters were 0.80, 0.89 and 0.68 µm, and the geometric standard deviations were 3.09, 1.91 and 2.54, respectively. Animals were observed for 14 days after exposure. Mortalities (accompanied by symptoms consistent with anticoagulant activity) occurred on days 4-6 in 3/5 males and 5/5 females exposed to the highest concentration (4.96 µg/L). The inhalation LC_{50} for males = 4.86 µg/L (based on particulate concentration), and for females = 3.05 µg/L. Brodifacoum technical (96.1%) is in toxicity category I (inhalation LC_{50} at or below 50 µg/L) based on the LC_{50} values in both sexes (MRID 43110501).

In an eye irritation study in rabbits, aliquots of 100 mg technical brodifacoum (92.5%) were instilled in the conjunctival sac of the left eye in each of 9 New Zealand white rabbits. Three of the rabbit eyes were irrigated for one minute with lukewarm tap water starting 30 seconds after instillation of the test material. In some of the rabbits, there was subsequent iritis and/or slight redness of the conjunctivae with slight chemosis and discharge; with all irritation clearing by day 7. Brodifacoum technical (92.5%) is in toxicity category III in terms of eye irritation potential (MRID 00066938). However, it is noted that because of the high toxicity of brodifacoum, absorption of any significant amount of the technical material by the ocular exposure route might result in mortality (and the animals in this study were followed for only 7 days after exposure). Technical brodifacoum is in toxicity category III in terms of its ocular irritation potential.

There are no dermal irritation studies on technical brodifacoum. Because of the relatively high toxicity, dermal exposure to undiluted (or mixtures containing a relatively high percentage of) technical brodifacoum would probably be fatal (the dermal LD_{50} of brodifacoum technical in rabbits is given above as 5.21 mg/kg for males, and 3.16 mg/kg for females).

Because of the high toxicity of technical brodifacoum, end-use products (mostly containing 0.005% brodifacoum) are usually manufactured from a formulation containing 0.25% brodifacoum. Results of the acute toxicity studies conducted with brodifacoum Formulation Concentrate are summarized below in Table 6:

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Table 6 - Acute Toxicity Values of Brodifacoum Formulation Concentrate (0.25%)

Route	Species	Results	Toxicity Category	MRID
Oral	Rat	LD_{50} (M) = 163 mg/kg LD_{50} (F) = 152 mg/kg	II	44021701
Dermal	Rat[a]	LD_{50} (M) > 2000 mg/kg LD_{50} (F) > 2000 mg/kg	III	44021702
Skin Irritation	Rabbit	Test material stained the skin pink at application site, but no indication of an inflammatory response	IV	44021703
Dermal Sensitization	Guinea Pig	Evaluation complicated by pink staining at the application site, but no evidence of a sensitization response.	N/A	44021704

[a]Study conducted with rats; however, rabbits may be a more sensitive species

In an acute oral toxicity study (MRID No. 44021701), groups of fasted, young Alpk:APfSD (Wistar-derived) rats, 5/sex were given a single oral dose of brodifacoum Formulation Concentrate (active ingredient: brodifacoum: label declaration 0.25%; analytical concentration 0.259%) in deionized water at doses of 50, 200, or 500 mg/kg (males), and doses of 100, 150 or 200 mg/kg (females), and were subsequently observed for 14 days.

LD_{50} Males = 163 (95% C.I.: 97-275) mg/kg
Females = 152 (95% C.I.: 132-175) mg/kg
Combined = not reported

Brodifacoum Formulation Concentrate (0.25%) is in toxicity category II based on the oral LD_{50} in both sexes.

Animals that died or subsequently showed symptoms were generally normal through day 4; symptoms (decreased activity, pallor, piloerection, stains around nose) in some animals were observed only on the day of (or the day before) death. Some rats that were found dead had showed no previous signs of toxicity. Mortalities occurred 4-7 days after dosing. Necropsy findings in rats that died included pallor of the kidney, liver, lung, pancreas and spleen, and clotted and/or free blood in the thymus and/or thoracic cavity, consistent with the anticoagulant activity of brodifacoum. There were no consistent effects on body weight.

In an acute dermal toxicity study (MRID No. 44021702), a group of five male and two groups each with five female young adult Alpk:APfSD (Wistar-derived) rats received a single 24-hour occluded dermal exposure to 2000 mg/kg undiluted brodifacoum Formulation Concentrate (active ingredient: brodifacoum: label declaration 0.25%; analytical concentration 0.259%). At 24 hours the application site was cleansed with cotton swabs. In order to prevent ingestion of any residual material, rats were fitted with collars that were kept in place until day 4 for the males and first group of females, and throughout the observation period for the second group of females. The animals were observed for 14 days following removal of the occlusive dressings. 1/5 males and 2/10 females died on days 7-9 with symptoms consistent with anticoagulant activity. One of the dead females was reported to have chewed and partly removed the dressing.

Dermal LD_{50} Males > 2000 mg/kg
Females > 2000 mg/kg
Combined > 2000 mg/kg

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Brodifacoum Formulation Concentrate (0.25%) is in Toxicity Category III in terms of dermal toxicity potential, based on the dermal LD_{50} values in both sexes. It is noted that this study was conducted with rats as opposed to rabbits. Rats may be a less sensitive species than rabbits which are generally used in dermal toxicity studies.

Among the survivors, one female showed bruising at the application site on days 10-15. Necropsy findings (pallor of the brain, liver, lung, pancreas and/or spleen) for animals that were euthanized in extremis were consistent with anticoagulant activity of brodifacoum. Survivors all gained weight.

In a primary dermal irritation study (MRID No. 44021703), a group of six female young adult rabbits (New Zealand white), weights ranging from 3940-4290 g, each received a single 4-hour occluded dermal exposure to 0.5 ml of undiluted brodifacoum formulation concentrate (0.25% a.i.), with scoring for dermal irritation within the first hour after removal of the occlusive wrap, and at 1, 2 and 3 days. There was slight edema in one rabbit, which occurred within one hour following exposure. The test material stained the skin pink at the application sites thereby preventing full assessment of erythema. However, subsequent histopathological examination of application and unexposed skin sites showed no indications of an inflammatory response associated with exposure to the test material.

Brodifacoum formulation concentrate (0.25%) is in Toxicity Category IV in terms of dermal irritation potential, based on the lack of any significant irritation (slight edema observed in only one animal within one hour following exposure, and lack of inflammatory response observed in histopathological examination).

In a dermal sensitization study (MRID 44021704) with brodifacoum Formulation Concentrate (0.25% a.i.), administered at challenge undiluted and as 30% and 10% w/v suspensions in deionized water, young adult Crl:(HA)BR male guinea pigs were tested using the method of Buehler. There were no indications of a sensitization reaction, although evaluation was complicated by pink staining at the application sites. Skin samples were examined histopathologically, with no indications of a significant inflammatory response. In this study, brodifacoum Formulation Concentrate (0.25% a.i.) is not a dermal sensitizer.

(2) Bromadiolone Acute Toxicity

The acute toxicity data for bromadiolone are summarized in Table 7.

Table 7 - Acute Toxicity Values for Bromadiolone

Study	Results	Category	MRID
Oral LD_{50}-rat[a]	between 0.56 and 0.84 mg/kg	I	41900001
Dermal LD_{50}-rabbit	1.71 mg/kg	I	42673701
Acute inhalation LC_{50}-rat	0.43 µg/kg	I	4197690
Eye irritation-rabbit	Irritation cleared by 4 days	III	88113
Dermal irritation-rabbit	Minimally irritating	IV	88112
Dermal sensitization	Not a dermal sensitizer	n/a	41847401

[a]This study was conducted with a concentrate which provides an understanding of the acute oral toxicity of bromadiolone.

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A number of acute toxicity studies have been conducted with bromadiolone in the technical form or as a concentrate. The acute oral LD_{50} in rats was tested using a concentrate (2.5 gm/L) and doses were between 0.56 and 0.84 mg/kg (Toxicity Category I, MRID 41900001). An acceptable acute oral toxicity study with technical grade is currently unavailable, but the available data indicate that bromadiolone is very toxic. Requiring another acute oral toxicity with the technical grade may not add more information than what is currently available. The acute dermal LD_{50} in rabbits was 1.71 mg/kg (Toxicity Category I, MRID No. 42673701. This study satisfies Guideline 81-2 requirement). The LC_{50} for acute inhalation toxicity in rats is 0.43 µg/L (Toxicity Category I, MRID No. 41976901. This study satisfies Guideline 81-3).

A primary eye irritation study in rabbits indicated that bromadiolone technical produced no irritation in washed eyes. Conjunctivitis and iritis were seen in the unwashed eyes for 4 days. No corneal opacity was seen in either the washed or unwashed eyes (Toxicity Category III, MRID No. 00088113. This study satisfies the Guideline 81-4).

A primary dermal irritation study in rabbits showed that, after 24 hours of dermal application, bromadiolone produced minimal irritation on the application site (Toxicity Category IV; MRID No. 00088112. This study satisfies Guideline 81-5)

A dermal sensitization study in guinea pig showed that bromadiolone was not a dermal sensitizer (MRID No. 41847401. This study satisfies Guideline 81-6).

(3) Bromethalin Acute Toxicity

Results of the acute toxicity studies conducted with technical bromethalin are summarized below in Table 8:

Table 8 - Acute Toxicity Values of Technical Bromethalin

Route	Species	Results	Toxicity Category	MRID
Oral	Rat	LD_{50} (Males) = 10.7 mg/kg LD_{50} (Females) = 9.1 mg/kg	I	00026524
Dermal	Rabbit	LD_{50} = 2000 mg/kg	II	00026524
Inhalation	Rat	LC_{50} = 0.024 mg/L	I	00026524
Eye Irritation[a]	Rabbit	Slight irritation	III	00026524
Skin Irritation[a]	Rabbit	Not an irritant	IV	00026524
Dermal Sensitization[a]	Guinea Pig	Non sensitizer	N/A	41653001

[a]Not required for TGAI, however, presented here for informational purpose

An acute delayed neurotoxicity study was conducted in the hen. White rock strain hen (30 animals) were initially dosed with bromethalin in PEG-400 at 9 mg/kg and redosed on day 3 with 15 mg/kg. Observation was for 24 days. Bromethalin did not produce acute delayed neurotoxicity in the hen. (MRID 00101543).

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An acute neurotoxicity study was conducted in rats. Male and female Sprague-Dawley CD rats were orally gavaged with bromethalin in mineral oil at doses of 0, 0.8, 1.5 or 3 mg/kg. The NOEL was greater than 3 mg/kg (HDT) and the LOEL was not determined in this study. Although this study was classified as unacceptable, the study can be upgraded if the registrant can provide the following data: the rationale of vehicle choice and volume used, the stability of test material in mineral oil, the rationale for choice of testing time on dosing day, and body temperature measurements. Body temperature is a measurement that should have been taken, given the mechanism of action of bromethalin (uncoupler of oxidative phosphorylation) (MRID 42793101). However, a new study will not be required since adequate information is available to determine an acute NOEL for bromethalin neurotoxicity.

(4) Chlorophacinone Acute Toxicity

Results of the acute toxicity studies conducted with technical chlorophacinone are summarized in Table 9:

Table 9 - Acute Toxicity Values of Technical Chlorophacinone

Route	Species	Results	Toxicity Category	MRID
Oral	Rat	LD_{50} (M) = 3.15 mg/kg LD_{50} (F) = 10.95 mg/kg combined = 6.26 mg/kg	I	41875301
Dermal	Rabbit	LD_{50} (M) = 0.329 mg/kg LD_{50} (F) = not done	I	41702801
Inhalation	Rat	LC_{50} (M) = 7 µg/L LC_{50} (F) = 12 µg/L	I	41981102
Eye Irritation[a]	Rabbit	No eye irritation at 1, 24, 48, or 72 hours.	IV	41874001
Skin Irritation[a]	Rabbit	PIS = 0, but mortalities occurred (same study as dermal LD_{50} assay)	IV	41702801
Dermal Sensitization[a,b]	Guinea Pig	Non sensitizer	N/A	41578601

[a] Not required for TGAI, however, presented here for informational purposes.
[b] 2/10 animals died

In an oral LD_{50} study in which technical chlorophacinone (99.36% by potentiometry, 102% by UV spectrophotometry) was administered as a suspension in polyethylene glycol 300 to Sprague-Dawley rats, there were mortalities at all dose levels in males (2.0 mg/kg: 4/10; 3.2 mg/kg: 6/10; 5.2 mg/kg: 4/10; 8.2 mg/kg: 8/10; 13.2 mg/kg: 10/10; 21 mg/kg: 9/10). There were no mortalities in females receiving doses of 2.0 or 3.2 mg/kg, but mortalities occurred at higher dose levels (5.2 mg/kg: 2/10; 8.2 mg/kg: 3/10; 13.2 mg/kg: 6/10; 21 mg/kg: 9/10). Deaths, with symptoms consistent with internal hemorrhage or other evidence of anticoagulant activity, occurred on days 4-13 after dosage. The acute oral LD_{50} for males was calculated as 3.15 mg/kg, with 95% confidence limits of 1.48-6.68 mg/kg. For females it was 10.95 mg/kg, with 95% confidence limits of 6.46-18.57 mg/kg. The combined oral LD_{50} for both sexes was calculated as 6.26 mg/kg (95% confidence limits of 3.96 to 9.89 mg/kg). These results place technical chlorophacinone in Toxicity Category I (MRID 41875301) by the oral exposure route.

In a dermal LD_{50} study with male New Zealand white rabbits chlorophacinone technical (100%) was dissolved in acetone and spread onto 2.0 x 2.0 cm pads. Each pad was allowed to dry before it was applied to a shaven dermal area on one of 10 male rabbits/dose level. Doses applied were 0.25, 0.5 or 0.75 mg/kg, with 24-hr occluded dermal exposure. Animals were observed for 21 days (instead of the usual 14 days) after exposure. Deaths occurred between days 5 and 19. Symptoms (which included bloody nasal discharge) and necropsy findings (hemorrhage in the thoracic cavity and large intestine) were consistent with anticoagulant activity. There were mortalities at each dose level (0.25 mg/kg: 4/10; 0.50 mg/kg: 6/10; 0.75 mg/kg: 9/10). There were no indications of skin irritation in any of the animals. The dermal LD_{50} of chlorophacinone technical was calculated to be 0.329 mg/kg (95% confidence interval 0.21-0.52 mg/kg) for males. Females were not tested. This was because males had been previously observed to be more sensitive to the anticoagulant effects of chlorophacinone than females. With a dermal LD_{50} below 200 mg/kg, technical chlorophacinone is in Toxicity Category I (MRID 41702801) by the dermal exposure route.

There were no indications of skin irritation from dermal exposure to technical chlorophacinone at doses which resulted in mortality (this is the dermal LD_{50} study indicated above, in MRID 41702801). The test material is in toxicity category IV in terms of its dermal irritation potential.

In an inhalation LC_{50} study in rats, groups of young adult Sprague-Dawley rats, 7-9/sex/exposure level, were exposed (nose only) for 4 hours to analytically-determined concentrations of 1.33, 10.3, 11.5 or 14.5 µg/L (the respective nominal values were 72.3, 88.63, 440 and 166 µg/L), with a subsequent 21-day observation. "To minimize human exposure, continuous observation of the animals during the 4-hour exposure was not maintained." Observations were made at 0.5, 1 and 2.5 hours during the exposure period. Between observations some animals turned in the restrainers and, as a result, died from suffocation. The deaths from suffocation were considered stress-related. All animals that died within the first 5 hours showed no clinical signs of hemorrhage. At the lowest concentration level (1.33 µg/L) there were no compound-related mortalities in 5 males and 7 females; but mortalities accompanied by signs of anticoagulant activity occurred on post-exposure days 3-8 in rats exposed to the higher concentrations (10.3 µg/L: 4/6 males, 2/8 females; 11.5 µg/L: 8/8 males, 5/6 females; 14.5 µg/L: 2/5 males and 3/6 females). The inhalation LC_{50} for males = 7.00 µg/L, with 95% confidence limits (C.L.) of 0.83 - 59 µg/L. For females, the inhalation LC_{50} = 12.0 µg/L, with 95% C.L. of 7.8 - 18 µg/L; and the combined LC_{50} = 9.3 µg/L, with 95% C.L. of 2.3 - 38 µg/L. Chlorophacinone technical (analyzed concentration: 101%) is in Toxicity Category I (inhalation LC_{50} at or below 50 µg/L) based on the LC_{50} values in both sexes (MRID 41981102).

In an eye irritation study in rabbits, 0.1 g technical chlorophacinone (99.88%) was instilled in the conjunctival sac of the left eye in each of 6 female New Zealand white rabbits, with no subsequent eye wash. Eyes were scored at 1, 24, 48 and 72 hours after exposure, but there were no indications of any irritation (all scores zero). Technical chlorophacinone (99.88%) is in Toxicity Category IV in terms of eye irritation potential (MRID 41874001). It is noted that the rabbits were only observed for 72 hours following ocular exposure, and the possibility exists that if observations had been continued mortalities might have subsequently been noted.

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A dermal sensitization study (MRID 41578601) of male Hartley strain guinea pigs with chlorophacinone technical (99.88%), using the Buehler procedure and a 3-week induction period with 2 inductions/week was conducted. A first attempt was made using a dosage level of 0.2 g/animal/induction, but after one induction there was 40% mortality in the test group. In a second attempt, 0.01 g/animal/induction was used as a dose level. Subsequently, the dosage amount was reduced to 0.005 g/animal/induction using new animals. This part of the study was also terminated "due to high mortality in the test group." The final assay attempt utilized a dosage level of 0.003 g/animal/induction. Dosing chambers were secured with hypoallergenic tape, and following each 6-hour exposure period, the application site was wiped to remove as much of the test material as possible. Even so, two animals died during the induction period (on days 8 and 13). There were no indications of dermal irritation at the application sites during either the induction phase or following challenge. This study adequately demonstrates that technical chlorophacinone is not a dermal sensitizer as a result of exposure to non-lethal doses.

(5) Diphacinone and its sodium salt Acute Toxicity

Results of the acute toxicity studies conducted with technical diphacinone are summarized below in Table 10:

Table 10 - Acute Toxicity Values of Technical Diphacinone

Route	Species	Results	Toxicity Category	MRID
Oral	Rat	LD_{50} (M) = 2.5 (1.32-3.44) mg/kg LD_{50} (F) = 2.1 (1.55-2.86) mg/kg combined = 2.3 (1.86-2.88) mg/kg	I	00060605
Oral	Rat	LD_{50} (M) = 6.8 mg/kg LD_{50} (F) = 8.0 mg/kg combined = 7.0 (5.2-9.5 mg/kg	I	42245202
Dermal	Rabbit	LD_{50} (M) = 3.6 (0.6-20.8) mg/kg LD_{50} (F) = not done	I	42507001
Inhalation	Rat	LC_{50} (M) < 0.6 µg/L LC_{50} (F) < 0.6 µg/L	I	43000401
Eye Irritation	Rabbit	Moderate irritation clearing by day 4	III	42245203
Skin Irritation	Rabbit	Slight erythema clearing within 48 hours, but 4/6 rabbits died between days 8 and 10	IV	
Dermal Sensitization	Guinea Pig	neither a dermal irritant nor a sensitizer at a non-lethal dose level (2.5 mg/day)	N/A	42132501

In an oral LD_{50} study (MRID 00060605) technical diphacinone (purity not specified), was administered as a suspension in corn oil (volumes of 10 mL/kg were administered at all dosage levels) to Spartan rats (5/sex/dose level), at dose levels of 0, 0.79, 1.25, 1.98, 3.15, 5.00, 7.94, 12.60, 20.01, 31.76, 50.40 or 201.7 mg/kg, with a subsequent 14-day observation. The following mortality pattern was observed as outlined in Table 11.

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Table 11 - Dose Levels and Mortality in an Oral LD_{50} Study with Diphacinone

Dose Level (mg/kg)	Males Deaths /Rats Dosed	Females Deaths /Rats Dosed	Combined Deaths /Rats Dosed	Days after dosage deaths occurred
0.79	0/5	0/5	0/10	-
1.25	0/5	1/5	1/10	6
1.98	2/5	1/5	3/10	4
3.15	3/5	5/5	8/10	3-7
5.00	5/5	5/5	10/10	3-6
7.94	5/5	5/5	10/10	3-7
12.60	5/5	5/5	10/10	4-6
20.01	5/5	4/5	9/10	3-8
31.76	5/5	5/5	10/10	4-9
50.40	5/5	5/5	10/10	3-7
201.70	5/5	5/5	10/10	3-6

Data extracted from tables 4, 5 and 6 of MRID 00060605

Symptoms occurred at all doses, and were not necessarily associated with subsequent mortality. These included clear or colored nasal discharge, soft stool and/or diarrhea (possibly associated with the corn oil vehicle used), decreased motor activity and occasional drying of the corneal surface. Symptoms at higher dose levels included lacrimation, ataxia, cyanosis and bloody exudate from nose and eyes. Hemorrhage into the body cavities and of various organs was observed in animals which died. The acute oral LD_{50} for males was calculated as 2.50 mg/kg, with 95% confidence limits of 1.82-3.44 mg/kg. For females. it was 2.10 mg/kg, with 95% confidence limits of 1.55-2.86 mg/kg. The combined oral LD_{50} for both sexes was calculated as 2.31 mg/kg (95% confidence limits of 1.86 to 2.88 mg/kg). These results place technical diphacinone in Toxicity Category I (MRID 00060605) by the oral exposure route. The study defines such a high degree of toxicity for technical diphacinone that the Agency can accept the findings, even in the absence of information as to the purity of the test material.

In a second oral LD_{50} study (MRID 42245202), technical diphacinone (reported as having "at least 98% purity") was administered as a 0.2% w/w suspension in corn oil to groups of 5 rats/sex/dose level. The dose levels were 4, 6, 8 or 10 mg diphacinone/kg body weight, with observation for 14 days after dosage. Signs of toxicity included nasal staining (usually red), paleness, red staining on the tail. Most animals that survived (including 2/3 at the highest dose level) appeared healthy throughout the test period. Necropsy findings of animals which died during the 14-day observation period were consistent with anticoagulant activity (such as red fluid in the thoracic and/or abdominal cavities, apparent testicular hemorrhage). The acute oral LD_{50} for males was calculated as 6.8 mg/kg, and for females 8 mg/kg. The combined oral LD_{50} for both sexes was calculated as 7 mg/kg (95% confidence limits of 5.2 to 9.5 mg/kg). The results of this second oral LD_{50} study (MRID 42245202) are reasonably consistent with those of the first (MRID 60605), as both define a Toxicity Category I hazard potential for technical diphacinone by the oral exposure route, although the second study indicates somewhat less toxicity (or perhaps the strain of rat used in the second study was less susceptible). See Table 12 below.

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Table 12 - Dose Levels and Mortality in a Second Oral LD_{50} Study with Diphacinone

Dose Level (mg/kg)	Males Deaths/Rats Dosed	Females Deaths/Rats Dosed	Combined Deaths/Rats Dosed	Days after dosage deaths occurred
4	1/5	1/5	2/10	5
6	3/5	3/5	6/10	3-9
8	3/5	1/5	4/10	3-7
10	4/5	3/5	7/10	3-7

Data extracted from tables 1, 2, 5, 8 and 11 of MRID 42245202

It is noted that the mouse is considerably less susceptible to the toxic effects of diphacinone than other mammalian species (see discussion in Mutagenicity section under MRID 42406801). The NIOSH Registry of Toxic Effects of Chemical Substances 1985-86 reports a mouse LD_{50} for diphacinone as 300 mg/kg, and the rat LD_{50} as 1.5 mg/kg. This is also supported by a report from the open literature (Correll et. al., 1952) which states that the acute oral LD_{50} for diphacinone was found to be 3 mg/kg for rats, 340 mg/kg for mice, and 35 mg/kg for rabbits.

In a dermal LD_{50} study (MRID 42507001) with male New Zealand white rabbits, diphacinone technical (97.4%) was dissolved in acetone and the appropriate amount of the test substance solution was applied to the foil side of Scotch Pak pads. The acetone was allowed to evaporate, and the Scotch Pak pad, test substance side down, was applied to the application site, with 24-hour occluded exposure. In a range-finding trial, dose levels of 0, 1, 5, 10, 25 or 50 mg/kg were administered to groups consisting of 1 animal/sex/dose level. The findings in this range-finding study were used to set the doses in the subsequent definitive study. Females at the three highest dose levels - 10, 25, or 50 mg/kg - died. Those at the two lower dose levels - 1 and 5 mg/kg - survived. Deaths occurred on days 7-13. Males at all dose levels died. The performing laboratory suggested that only male rabbits should be used for the LD_{50} determination, as they had been the more sensitive sex. The doses for the dermal LD_{50} determination were 0.05, 0.20 and 0.80 mg/kg, with subsequent 21-day observation. The following mortality pattern was observed as outlined in Table 13.

Table 13 - Dose Levels and Mortality in a Dermal LD_{50} Study with Diphacinone

Dose Level (mg/kg)	Males Deaths/Rabbits Dosed	Days after dosage deaths occurred
0.05	0/10	-
0.20	1/10	4
0.80	2/10	4

Data extracted from tables IIA, IIB and IIC of MRID 42507001

The animals that died (both in the preliminary range-finding and subsequent LD_{50} determination studies), showed symptoms (hemorrhage, discoloration of various organs) indicative of anticoagulant activity. No clinical signs were observed at the lowest dose level (0.05 mg/kg). Symptoms at the two higher dose levels included somnolence, loss of fluids, absence of feces and vasoconstriction. Based on the mortality, the estimated dermal LD_{50} in male rabbits is 3.6 mg/kg. These results place technical diphacinone in Toxicity Category I (MRID 42507001) by the dermal exposure route.

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In an inhalation LC_{50} study in rats (MRID 43000401), a group of young adult Sprague-Dawley rats, 5 of each sex, were exposed (whole body) for 4 hours to a time-weighted average aerosol concentration (gravimetrically determined) of 6 µg/L, with subsequent 14-day observation. The mass median aerodynamic diameter was 2.3 µm, with a geometric standard deviation of ±2.1 µm. The percentage of particles ≤ 4.0 µm was equal to 78%. Mortality occurred (days 4-8) in 5/5 males and 4/5 females. Symptoms (including red staining of abdominal and urogenital regions, reddish material around ears and in cage tray) and necropsy findings (hemorrhage in the thoracic cavity and/or cranial cavity and/or various organs) were consistent with anticoagulant activity. The dose in the LC_{50} study was based on findings in a preliminary range-finding study, in which groups of one rat/sex/exposure level were exposed for one-hour to concentrations of 0, 0.01, 0.11, or 1.1 mg/L, with subsequent 7-day observation. All the males died (deaths occurred days 4-7), as did the female exposed to the lowest concentration (0.01 mg/L). However, the two females exposed to the two higher concentrations (0.11 and 1.1 mg/L) showed an array of symptoms (decreased activity, labored breathing, distended abdomen) on day 7 similar to those observed in other rats in the day or so before they died. These females underwent scheduled euthanasia. Diphacinone technical (percentage active ingredient not reported) is in Toxicity Category I (inhalation LC_{50} at or below 50 µg/L) based on the LC_{50} value of less than 6 µg/L in both sexes (MRID 43000401).

In an eye irritation study with New Zealand white rabbits (MRID 42245203), an attempt was made to place as much technical diphacinone (with at least 98% active ingredient) as possible into the conjunctival sac of one eye of each of nine rabbits. The report notes that the test material at 0.1 g exceeded the capacity of the rabbits' eye. The treated eyes of 3 rabbits were irrigated approximately 20-30 seconds after instillation of the test material. The eyes of the remaining 6 rabbits were not washed. No corneal opacity was observed, although some eyes showed iritis, and all eyes (washed and unwashed) showed some conjunctival irritation, with clearing by day 4. Technical diphacinone is in Toxicity Category III in terms of eye irritation potential (MRID 42245203). It is noted that the rabbits were only observed for 96 hours following ocular exposure, and the possibility exists that if observations had been continued mortalities might have subsequently been noted.

In a dermal irritation study with New Zealand white rabbits, 0.5 g of undiluted technical diphacinone (with at least 98% active ingredient) was applied to a single intact site, with 4-hour occluded exposure. Barely perceptible erythema was observed at 2 treated sites one hour after patch removal and at one treated site at 24 hours, with no evidence of erythema at 48 or 72 hours. No occurrence of edema was observed. The Primary Dermal Irritation Score was reported to be 0.09. Technical diphacinone (at least 98% active ingredient) is in Toxicity Category IV in terms of its primary dermal irritation potential. However, the report also notes "There were no signs of gross toxicity, adverse pharmacological effects or abnormal behavior during the test period. However, it should be noted that 4 of 6 rabbits died after the last scoring interval (i.e. between days 8 and 10 post-dosing). These spontaneous deaths may have been due to the anticoagulant properties of the test product."

In a dermal sensitization study (MRID 42132501) with Hartley albino male guinea pigs with diphacinone technical (96.57%), the test material was administered as a topical application

at various dose concentrations. The test article was kept in contact with the skin surface for a six hour period. After the initial exposure, the test article was administered on alternate days three days a week such that each animal received 10 sensitizing treatments. Following the tenth treatment, animals were rested for two weeks, and then given an eleventh (challenge) dose.

The major problem in this dermal sensitization study was on determining a non-lethal dose level. In the initial assay application of 500 mg caused death and/or severe hemorrhage from the external nares in some animals and evident discomfort in others, with the result that all surviving animals were euthanized. Further testing at doses of 5, 10, 20, 40 or 80 mg with two male guinea pigs/dose resulted in all animals either dying or being euthanized on or about the seventh day after the initial dose. Additional dosing at 0.1, 0.5, 1.0 or 2.5 mg with two animals/dose resulted in the death of one animal in the 0.5 mg group. As a result, the final dose selected was 2.5 mg in 10 guinea pigs (one of these animals died 13 days after the initial dose). Signs of dermal irritation were not observed in any of the guinea pigs at any dose level during the study, and there were no indications of any sensitization reaction in the survivors of the final assay (dose level: 2.5 mg/animal). There were 3 guinea pigs in a positive control group (each received 2.5 mg/application). One of these positive control animals died before the challenge application, but positive responses were elicited in the remaining 2 guinea pigs. The findings of this study (MRID 42132501) adequately demonstrate that technical diphacinone at a non-lethal exposure level is neither a dermal irritant nor a sensitizer.

b. Subchronic Toxicity

(1) Brodifacoum Subchronic Toxicity

The Agency has no record that any subchronic toxicity studies on brodifacoum have been received and/or reviewed. However, it is noted that there are a number of multiple-dose studies which the Agency has received (including a special study Brodifacoum: Blood Kinetics Study in the Pregnant Rat, MRID 42641902, see below), which include prothrombin time measurements, which appears to be the most sensitive indicator of toxicity for the anticoagulants.

Although the current toxicological data base is sufficient for the purposes of this RED, because of the potential for non-purposeful dermal exposure, and to more accurately assess the margins of exposure associated with potential incidental exposure, a 21-day dermal toxicity study (Guideline 82-2) is required as confirmatory data. Such a study must include prothrombin and activated partial thromboplastin time measurements, including pre-exposure, as well as on days 7, 14 and 21 of exposure.

(2) Bromadiolone Subchronic Toxicity

In a 90-day study, groups of beagle dogs (4/sex/dose) received bromadiolone in gelatin capsules at variable daily doses for different lengths of time. The dosages were low-dose, 5/10 µg/kg; mid-dose, 10/15/20 µg/kg; and high-dose, 15/25/50/100 µg/kg. The control dogs received starch in gelatin capsules. The high-dose animals died or were sacrificed moribund prior

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to the study's termination. In addition, the high-dose animals also showed signs of loose, bloody stools following the 15 µg/kg dosing. After five days of following 100 µg/kg dosing high-dose animals also showed signs of hypothermia, respiratory difficulties, pale mucosa, drowsiness, atonia, bloody urine, hematomas, and external hemorrhage. Both mid- and high-dose dogs had increased prothrombin time and hematuria. Histological examination showed that in high-dose groups, 4/4 male or female dogs had hemorrhage, congestion and/or edema of the spleen, kidneys, lungs, urinary bladder, small intestine, liver, thyroid, and skin. No compound-related histological lesions were found in mid- and low-dose dogs. Based upon the clinical and hematological findings, the LOEL for subchronic toxicity of bromadiolone was 15 µg/kg; NOEL, 10 µg/kg (MRID 92196013).

In a multiple-dose toxicity study, groups of female rats (10/dose) received bromadiolone (technical grade) by gavage at doses of 6.4, 12.4, or 24.8 µg/kg for 20 days. By study day 13, the mid- and high-dose rats were all dead, and 8/10 rats in the 6.4 µg/kg group were also dead by day 20. The clinical signs included hemorrhage in the orbital sinus, nasal cavity, and nail beds, anorexia, and polydypsia. At necropsy, the dead rats showed general internal bleeding and hemorrhagic spots in liver, intestinal tract, and kidneys. No NOEL for subchronic toxicity could be established for bromadiolone (MRID 00107035).

The above two studies are classified as supplementary and do not meet the data requirements for a subchronic toxicity study in dogs and rats (Guideline No. 82-1). However, when the data from the 90-day dog study and the 20-day rat study are analyzed together with the results from rat and rabbit developmental toxicity studies, the results provided sufficient information for the understanding of the subchronic toxicity of bromadiolone. Additional subchronic toxicity tests would probably not yield much more new information. Therefore, a new subchronic toxicity study in either the rat or dog is not requested at this time.

(3) Bromethalin Subchronic Toxicity

Sprague Dawley rats (10/sex/group) received daily gavage doses of 0 (25% polyethylene glycol in H_2O), 5, 25, or 125 micrograms/kg/day (ug/kg/day) of bromethalin technical for 13 weeks. Parameters evaluated included daily observation, weekly body weight and food consumption, ophthalmoscopy, clinical pathology, necropsy, organ weights, and histopathology. The NOEL is 25 µg/kg/day. The LOEL is 125 µg/kg/day, based on spongy degeneration (leukoencephalomyelopathy) observed in most of the central white fiber tracts of the brain, cerebellum, pons, brain stem, and thoracic spinal cord of both sexes and optic nerves of males. There were no effects on mortality, clinical chemistry, ophthalmoscopy, body weight, food consumption, clinical pathology and histopathology of other tissues (MRID 43582102).

In a second 90-day study, groups of 4 male and 4 female beagle dogs were orally dosed by gavage for 90 days at levels of 0, 5, 25, 125, or 200 ug/kg/day with bromethalin technical. Observations included daily clinical evaluations, ophthalmoscopy, body weight, food consumption, clinical pathology evaluations at weeks 6 and 13, necropsy, organ weights and histopathology. The NOEL is 25 µg/kg/day. The LOEL is 125 µg/kg/day based on spongy

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degeneration observed in nervous tissue components (cervical, thoracic, and lumbar spinal cord, brain stem, right and left optic nerves, frontal and median brain, pons, and cerebellum) in both sexes of dogs. At the high dose, 3 male dogs displayed the following neurotoxic signs before death or being sacrificed moribund: salivation and hypoactivity, followed by trembling, myoclonia, hyperesthesia, groaning, and decubitus. Other measured parameters were considered comparable between control and treated dogs of both sexes (MRID 43582101).

The above two subchronic toxicity studies in rats and beagle dogs are not guideline-type subchronic neurotoxicity studies. However, these studies will satisfy the data requirements for a 90-day neurotoxicity screening battery because a NOEL and a LOEL was established in both studies.

(4) Chlorophacinone Subchronic Toxicity

In a subchronic study (MRID 92018013), groups of 10 Sprague-Dawley rats/sex/dose were gavaged at 0, 10, 20 or 40 µg/kg 7 days/week for 113 days. A group was also dosed at 5 µg/kg/day, but was terminated at 77 days due to lack of evident toxicity. Additional groups were tested at 80 and 160 µg/kg, but all animals died between days 3 and 13. At 40 µg/kg/day deaths occurred in 10/10 males (mortalities occurred days 29-82) and 4/10 females (days 69-111); 4/10 males (but 0/10 females) died at 20 µg/kg/day (deaths occurred on days 105-111). "The dominant clinical signs that were responsible for death of animals were related to the anticoagulant activity of chlorophacinone." Although 1/10 males and 1/10 females died in the 10 µg/kg/day group, these deaths were ascribed to intubation error. At termination (112-113 days), hematology (including "coagulation time") and clinical chemistry parameters were determined from the 0, 10, 20 or 40 µg/kg/day groups (but not the 5 µg/kg/day group, which was terminated at 77 days). In the 10 µg/kg/day animals, males showed a 28% increase ($p < 0.01$) in coagulation time, while females showed a 6% increase ($p < 0.05$); at 20 µg/kg/day males showed a $>100\%$ increase ($p < 0.01$) in coagulation time and females an 11% increase ($p < 0.05$); at 40 µg/kg/day females showed a $>100\%$ increase.

The FIFRA 88 Phase 2 and 4 Data requirements for all anticoagulant rodenticides included a generic data request for a 14-day feeding study in the rat to determine a NOEL and LOEL for signs of toxicity and coagulation parameters. This information was requested to more adequately define and evaluate the effects that would result from accidental ingestion of this type of rodenticide. While MRID 92018013 does not adequately satisfy the Guideline requirements for a 90-day feeding or gavage study (Guideline 82-1), sufficient information is provided to satisfy the generic data request for a 14-day feeding study.

At the 5 µg/kg/day dose level there was no mortality or signs of toxicity during the 77-day exposure period. Coagulation values were not evaluated at this dose level. However clotting times were increased by 28% and 6% for males and females, respectively, at the 10 µg/kg/day levels at termination (113 days). Based on these findings, HED considers 5 µg/kg/day as a NOEL in a subchronic oral study, with a LOEL of 10 µg/kg/day (increased coagulation times for both males and females, with males more sensitive than females).

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In a 21-day dermal toxicity study (MRID 42237402), a formulated product (tracking powder) containing 0.2% chlorophacinone was applied dermally with 6 hr occluded exposure/day, 5 days/week at 0.08, 0.40 or 2.0 mg/kg (these doses are in terms of the active ingredient, chlorophacinone) to 5 rabbits/sex/dose. The 0.2% product was used instead of the technical material because of difficulties (encountered in a preliminary range-finding study) in accurately weighing out and working with small quantities of this highly toxic compound. At 2 mg/kg/day, there was mortality (with "widespread" internal hemorrhage) in 4/5 males (deaths occurred on days 14-18) and 1/5 females (one death occurred on day 21). Prothrombin (PT) times were markedly increased on day 21 in surviving animals (the one male had a PT time of 9.0 seconds, while controls had a mean of 6.0. The females had a mean PT time of 17.7 seconds, as compared to a control mean of 5.9). Moderate to severe centrilobular liver necrosis was observed in 3/5 males and 1/5 females. There was no mortality at 0.4 mg/kg, but prothrombin times were markedly increased on day 21 (males: 7.7 vs. a control value of 6.0 seconds; females: 9.5 vs. a control value of 5.9). There were no indications of any effect at 0.08 mg/kg/day.

The following table from the report (in MRID 42237402) summarizes the measurements for prothrombin time (PT) and activated partial thromboplastin time in seconds (APTT):

Table 14 - Prothrombin and Activated Partial Thromboplastin Times in a 21-Day Subacute Dermal Study in Rabbits - Statistically Significant Findings

		Hematology Data - PT/APTT Mean Values							
Sex		Males				Females			
Parameter		Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg/day)		0	0.08	0.4	2.0	0	0.08	0.4	2.0
		Prothrombin time (PT) in seconds							
Pretreatment	Week -2	6.4	6.4	6.4	6.4	6.3	6.1	6.3	6.4
	Week -1	6.3	6.3	6.3	6.2	6.2	6.1	6.3	6.4
	Week - 0	6.6	6.3	6.3	6.3	6.4	6.3	6.2	6.5
Termination	Week - 0	6.0	6.0	7.7	9.0	5.9[a]	6.4[b]	9.5[c]	17.7[c]
		Activated partial thromboplastin time (APTT) in seconds							
	Week -3	32.5	32.4	52.3	24.5	22.9	28.3	59.7[c]	67.0[c]

[a]Examination of the female animals in the concurrent control, for the Week 3 interval, showed a statistically significant decrease based on their own three pretreatment values. This slight decrease in the control female value gave rise to the statistical significance in the Group 2 female value.

[b]Analysis of variance indicated a significant difference from the control value, $p \leq 0.05$; further statistical analyses, using repeated measures analysis of variance and dependent measures t-test procedures, indicated that this value did not vary significantly from the mean prothrombin time recorded at pretreatment intervals for those animals.

[c]Significantly increased, $p \leq 0.05$

The subchronic dermal LOEL is 0.4 mg/kg/day, based on increased prothrombin times in both sexes on day 21. The subchronic dermal NOEL is 0.08 mg/kg/day.

This subchronic dermal study in the rabbit is classified as acceptable (Guideline), and satisfies the guideline requirement for a subchronic dermal toxicity study (§82-2).

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(5) Diphacinone and its sodium salt Subchronic Toxicity

In a 21-day dermal toxicity study (MRID 00074637), diphacinone (99.8%, moistened with 0.9% physiological saline) was applied (6-hr occluded exposure) five days a week for three weeks, at dosage levels of 0, 0.1, 1.0 or 10.0 mg/kg to groups consisting of four male and four female New Zealand white rabbits/dose level. The skin of two males and two females in each group was abraded. The skin of the remaining rabbits was left intact. Most of the animals exposed to diphacinone showed no dermal irritation. The dermal irritation which did occur in 1 or 2 animals/group was slight. However, all of the animals exhibited yellow staining of the test site after a few exposures.

Mortalities or sacrifice *in extremis* occurred in 1/8 controls, 1/8 in the 0.1 mg/kg/day group, 5/8 at 1.0 mg/kg/day, and 6/8 at 10.0 mg/kg/day. Symptoms included clear nasal discharge, pale skin and/or mucous membranes, and hypothermia. On gross pathology, "hemorrhagic areas in different sites were present in the stomach, mouth, ear, muscle, soft tissues, thoracic and abdominal cavities, cecum, colon, kidney and bladder of some animals. These lesions were more frequent in the 1.0 mg/kg and 10.0 mg/kg Diphacinone groups, only one case was present in the control group and one in the 0.1 mg/kg Diphacinone group." Blood samples were taken at preexposure, and on day 19. Determinations included hematocrit, hemoglobin, erythrocyte count, total leucocyte count, platelets, mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration. However, there were no measurements of clotting time.

Finally, while this 21-day dermal toxicity study (MRID 00074637) is classified as acceptable (satisfying the guideline requirement for a subchronic dermal toxicity study §82-2), with a subchronic dermal NOEL of 0.1 mg/kg/day, and a subchronic dermal LOEL of 1.0 mg/kg/day (based on mortality accompanied by indications of anticoagulant activity), it is noted that there are indications in the report of possible anticoagulant activity ("hemorrhagic areas") in one control and one 0.1 mg/kg rabbit. In addition, there were no clotting time determinations (such as prothrombin and/or activated partial thromboplastin times).

In a 21-day subchronic study (MRID 00077319), groups of 2 Swiss Webster mice/sex/dose level were intubated (using a 10 mg/mL solution of technical diphacinone in propylene glycol) at 0.1, 0.5, 1.0, 2.5, 5.0, 10.0 or 20.0 mg/kg/day for 20 days. All the mice dosed at 5, 10 or 20 mg/kg/day died during the first 7 days of the test period, and symptoms (bleeding, paleness) were generally consistent with anticoagulant activity. Three out of 4 intubated at 2.5 mg/kg died by day 14 (with symptoms of bleeding) with only one female surviving to termination. While there were no mortalities at 1.0 mg/kg, hemorrhages, sub-cutaneous accumulation of blood or external bleeding was noted at this dose level. No effects were observed at 0.5 mg/kg/day.

The observations in this study were subsequently used to set the dose levels (0, 0.1, 0.5, 1.0 or 2.5 mg/kg) in a mouse developmental toxicity study (also in MRID 00077319), which utilized 15 pregnant females/dose level. All animals dosed at 2.5 mg/kg/day died (days 4-10 of dosing). There was a considerable proportion of the fetuses in each female of this group

undergoing resorption (6/10, 4/10, 7/12, 3/11, and 4/12). At 1.0 mg/kg/day one pregnant female died on day 10 (2/10 fetuses were being resorbed).The LOEL in the 20-day feeding study is 1.0 mg/kg/day (occurrence of subcutaneous accumulation of blood, hemorrhages and external bleeding, with no mortalities), although no measurements were made for clotting time. While the single-dose LD_{50} for the mouse is about 300 mg/kg, the toxicity of diphacinone in this species is enhanced when administration takes place over a period of several days.

At the 0.5 mg/kg/day dose level there was no mortality or signs of toxicity during the 20-day exposure period, and no mortalities (or other effects) were observed at this dose level in the subsequently conducted mouse developmental toxicity study. The LOEL is 1.0 mg/kg/day (based on the occurrence of subcutaneous accumulation of blood, hemorrhages and external bleeding, with no mortalities in the initial 20-day study, and the occurrence of mortality in 1/5 pregnant females at this dose level in the subsequently conducted mouse developmental toxicity study). It is noted that no information is given in this study as to clotting times. While the information in MRID 00077319 is useful, it is not adequate to satisfy the FIFRA 88 Phase 2 and 4 data requirements for anticoagulant rodenticides for a 14-day feeding study in the rat to determine a NOEL and LOEL for signs of toxicity.

In a single dose toxicity study (MRID 43260702), male and female Sprague-Dawley rats (5/sex) received technical diphacinone (99.0%) as a single oral gavage dose in corn oil at doses of 0, 0.13, 0.20, 1.0 or 2.5 mg/kg. In a 14-day oral toxicity study (MRID 43260701) groups of 5 rats/sex/dose received technical diphacinone (99.0%) by oral gavage in corn oil once a day for 14 days at doses of 0, 0.025, 0.040, 0.085 or 0.175 mg/kg/day. The purpose of these experiments were to demonstrate a NOEL and LOEL for overt signs of toxicity, lethality, and anticoagulant effects in young adult Sprague-Dawley rats following single and repeated dosage with technical diphacinone. Following single doses at up to 2.5 mg/kg (HDT), there were no overt clinical signs of toxicity. Following repeated dosing, there were no signs of toxicity at the 0.025, 0.040 or 0.085 mg/kg/day dose levels. At the 0.175 mg/kg/day dose level, there were increased incidences of dyspnea, lethargy, hemorrhage from the nose, ptyalism, and few feces. At this dose level 3/5 males died (2/5 were found dead and one was sacrificed *in extremis*). All of the female rats in this dose group had died by day 11. The following Prothrombin (PT) and Activated Partial Thromboplastin Times (APTT) were observed as outlined in Tables 15, 16, 17 and 18.

Table 15 - Prothrombin Time in Seconds in Rats Following a Single Dose of Diphacinone[a]

	Prothrombin Time in Seconds				
Diphacinone (mg/kg)	0	0.13	0.20	1.00	2.50
Males - 24 hrs after dosing	15.5 ± 0.9	15.1 ± 0.5	15.2 ± 0.2	56.6 ± 9.2	70.7 ± 8.1
Males - 96 hrs after dosing	14.0 ± 0.3	14.5 ± 0.3	14.3 ± 0.5	14.3 ± 0.3	22.9 ± 16.6
Females - 24 hrs after dosing	15.1 ± 0.3	14.8 ± 0.4	15.6 ± 0.5	30.9 ± 6.6	51.8 ± 14.9
Females - 96 hrs after dosing	14.4 ± 0.2	14.6 ± 0.4	14.4 ± 0.3	14.0 ± 0.3	15.1 ± 0.9

[a]Data taken from pages 51-58 of the report (MRID 43260702)

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Table 16 - Activated Partial Thromboplastin Time in Seconds in Rats Following a Single Dose of Diphacinone[a]

	Activated Partial Prothrombin Time in Seconds				
Diphacinone (mg/kg)	0	0.13	0.20	1.00	2.50
Males - 24 hrs after dosing	24.5 ± 2.6	22.1 ± 3.5	24.0 ± 1.3	49.8 ± 18.3	42.2 ± 5.3
Males - 96 hrs after dosing	21.7 ± 3.1	21.2 ± 2.7	19.4 ± 2.8	21.1 ± 1.7	30.3 ± 11.0
Females - 24 hrs after dosing	20.3 ± 1.6	19.3 ± 1.1	32.1 ± 6.6	39.6 ± 3.6	33.9 ± 7.8
Females - 96 hrs after dosing	21.4 ± 3.9	19.8 ± 2.0	18.4 ± 0.5	20.6 ± 1.7	29.3 ± 4.5

[a]Data taken from pages 51-58 of the report (MRID 43260702)

Table 17 - Prothrombin Time in Seconds in Rats Following Repeated Doses of Diphacinone[a]

	Prothrombin Time in Seconds				
Diphacinone (mg/kg/day)	0	0.025	0.040	0.085	0.175
Males - 24 hrs after last dose	14.0 ± 0.2	14.2 ± 0.2	14.4 ± 0.2	15.2 ± 0.7	20.0 ± 1.3
Males - 96 hrs after last dose	14.4 ± 0.4	14.4 ± 0.3	14.0 ± 0.7	14.1 ± 0.4	14.3 ± 0.4
Females - 24 hrs after last dose	14.3 ± 0.3	14.6 ± 0.3	14.4 ± 0.2	14.4 ± 0.3	--b
Females - 96 hrs after last dose	14.4 ± 0.8	14.6 ± 0.3	14.3 ± 0.4	14.7 ± 0.1	--b

[a]Data taken from pages 51-58 of the report (MRID 43260702)
[b]All animals were dead by day 11

Table 18 - Activated Partial Thromboplastin Time in Seconds in Rats Following Repeated Doses of Diphacinone[a]

	Activated Partial Thromboplastin Time in Seconds				
Diphacinone (mg/kg/day)	0	0.025	0.040	0.085	0.175
Males - 24 hrs after last dose	20.2 ± 1.1	20.0 ± 1.2	22.0 ± 1.2	25.9 ± 2.1	38.3 ± 11.0
Males - 96 hrs after last dose	20.4 ± 2.0	20.3 ± 1.0	19.9 ± 1.0	19.9 ± 0.9	19.7 ± 0.7
Females - 24 hrs after last dose	20.7 ± 1.9	19.7 ± 0.8	20.6 ± 0.7	24.4 ± 2.1	--b
Females - 96 hrs after last dose	21.4 ± 2.9	20.2 ± 0.9	20.2 ± 0.5	20.0 ± 0.9	--b

[a]Data taken from pages 51-58 of the report (MRID 43260702)
[b]All animals were dead by day 11

The LOEL from single dose administration is 0.20 mg/kg, based on increased activated partial thromboplastin time in female rats. The NOEL from single dose administration is 0.13 mg/kg. The LOEL from repeated dose administration is 0.085 mg/kg/day, based on increased prothrombin and activated partial thromboplastin times in male and female rats. The NOEL from repeated dose administration is 0.040 mg/kg/day. The information in MRIDs 43260701 and 43260702 satisfies the FIFRA 88 Phase 4 Data requirements to determine effects in the rat (and defining the NOELs and LOELs for signs of toxicity and coagulation parameters) following a single dose and following repeated oral dosage over a 14-day period.

c. Chronic toxicity

Given the exclusively non-food uses of these chemicals, no chronic studies were required.

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d. Carcinogenicity

Given the exclusively non-food uses of these chemicals, no carcinogenicity studies were required.

e. Developmental Toxicity

(1) Brodifacoum Developmental Toxicity

In a developmental toxicity study (MRID 00052443, along with additional data in MRID 40307202), brodifacoum (92.5%) was administered to 30 Alderley Park, Wistar-derived mated female rats/dose level by gavage in 10% v/v ethanol:water at dose levels of 0 (vehicle only), 0.001, 0.01 or 0.02 mg/kg/day from days 6 through 15 of gestation. There was blood in the uteri of one 0.01 and three 0.02 mg/kg females. This was considered to be possibly related to the administration of brodifacoum. There were no indications of any dose-related developmental effects associated with exposure to brodifacoum at doses up to and including 0.02 mg/kg/day. The dose level of 0.02 mg/kg/day is considered adequate, based on the occurrence of 100% mortality at a nominal value of 0.05 (analytical value of 0.35) mg/kg/day in a preliminary study, and blood measurements in a special study (Brodifacoum: Blood Kinetics Study in the Pregnant Rat, MRID 42641902, see below).

The rat maternal toxicity NOEL is 0.001 mg brodifacoum/kg/day (based on the equivocal finding of blood in the uteri of one 0.01 and three 0.02 mg/kg females).

The rat developmental NOEL is 0.02 mg brodifacoum/kg/day (HDT).This developmental toxicity study in the rat is classified as acceptable (Guideline) (83-3a), and satisfies the guideline requirement for a developmental toxicity study in the rat.

In a special study (MRID 42641902), mixtures of unlabeled brodifacoum (98.7%) and radiolabeled brodifacoum (radiochemical purity > 95%) were administered to Alderley Park, Wistar-derived mated female rats by gavage at nominal doses of 0.0125 mg/kg (Group A: 24 rats, starting on day 1 of gestation, with sacrifice by exsanguination of 3 rats on days 1, 3, 5, 7, 9, 11, 13, 16) or 0.02 mg/kg (Group B: 15 rats, starting on day 7, with sacrifice of 3 rats on days 7, 9, 11, 13 and 16). The test material was administered as a suspension in polyethylene glycol 600. Terminal blood samples were analyzed for brodifacoum levels.

The following mean nanogram (ng.) equivalents of brodifacoum/gram of maternal blood were observed:

Group A (0.0125 mg/kg/day, days 0-16): day 1: 0.560; day 3: 0.924; day 5: 1.556; day 7: 1.809; day 9: 2.015; day 11: 2.795; day 13: 2.168; day 16: 3.396.

Group B (0.02 mg/kg/day, days 7-16): day 7: 0.691; day 9: 1.362; day 11: 3.087; day 13: 2.427; day 16: 4.488.

The relative proportions of mean blood brodifacoum levels in group B rats as compared to group A rats were the following: Day 7: 0.382; Day 9: 0.666; Day 11: 1.10; Day 13: 1.12; and Day 16: 1.32.

This study showed a steady increase of blood brodifacoum levels with continued dosage of both 0.0125 mg/kg/day and 0.02 mg/kg/day, consistent with findings of a previously reviewed metabolism study (MRID 00080235). In that study. three rats were given a single oral dose of 0.25 mg labeled brodifacoum and retained a mean of 77.73% of the initial dose (mean total label recovery was 91.51%) after 10 days. The combination of high toxicity and body accumulation of brodifacoum would have eventually resulted in mortalities at these dosage levels at some time after 16 days. The study is classified as acceptable (Non-guideline) as it is not a required guideline study. It is acceptable for the purposes for which it was intended as a special study, and the findings adequately justify the dosing schedule and doses used in the rat developmental toxicity study (MRID 00052443 and 40307202; summarization in MRID 92195013).

In a developmental toxicity study in rabbits (MRIDs 00052442 and 40307201), brodifacoum (92.5%) was administered to 15 mated female Dutch rabbits/dose level by gavage in 5% v/v ethanol:water at dose levels of 0 (0.5% v/v aqueous Tween 80), 0 (5% v/v aqueous ethanol, the vehicle used with brodifacoum), 0.001, 0.002 or 0.005 mg brodifacoum/kg/day from days 6 through 18 of gestation. Ten of the 15 rabbits receiving 0.005 mg/kg/day died or were humanely euthanized. All were found to have internal hemorrhage. Nine of these does had loss of blood (in some cases heavy) from the vagina. All of the implants of one doe (#47; euthanized on day 16) in the 0.005 mg/kg/day group are reported to have had a hemorrhagic appearance, but otherwise there were no indications of any dose-related developmental or toxic effects associated with exposure to brodifacoum at doses up to and including 0.005 mg/kg/day. Because only three litters (and only 20 fetuses) were available from the 0.005 mg/kg/day group at 29 days (and taking into consideration the hemorrhagic appearance of the implants of #46), the NOEL for fetal toxicity is 0.002 mg/kg/day, and the LOEL is 0.005 mg/kg/day. The only possible indication of toxicity in the 0.002 mg/kg/day does was the occurrence of a small hemorrhage beneath the lid of one eye on gestation day 14 in one rabbit (#44) which was not pregnant, but a similar finding was not reported for the 0.005 mg/kg/day females. In addition, the prothrombin time was significantly increased at 0.005 mg/kg/day on day 20 relative to controls (to 26.5 [seconds?] from 14.5) in a preliminary range-finding study. The following table shows the prothrombin time measurements (presumably in seconds) on day 20 in a preliminary range-finding study.

Table 19 - Prothrombin Time in the Preliminary Developmental Toxicity Range-Finding Study in the Rabbit (Day 20)*

	Control	0.001 mg/kg/day	0.005 mg/kg/day
Mean	14.5	17.4	26.5**
SD	2.0	-	5.1
No. of samples	4	1	3

** Statistically significant at the 1% level (Student's t-test) compared with the control group
*Data extracted from appendix 1 of MRID 00052442 (p. 31)

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The rabbit maternal NOEL is 0.002 mg brodifacoum/kg/day. The LOEL is 0.005 mg/kg/day (based on 75% mortality associated with hemorrhage in pregnant females at this dose level). The developmental toxicity NOEL is 0.002 mg/kg/day, as only 3 litters (with a total of 20 fetuses) were available for evaluation at 0.005 mg/kg/day). It is reported that all of the implants from a 0.005 mg/kg/day doe which was euthanized on day 16 had a hemorrhagic appearance. This developmental toxicity study in rabbits is classified as acceptable (Guideline 83-3b).

(2) Bromadiolone Developmental Toxicity

Groups of pregnant Sprague-Dawley rats received bromadiolone (technical grade) in aqueous vehicle by gavage from gestation days (gd) 6 through 16 at doses of 0, 17.5, 35, and 70 µg/kg bw/day. There was an increase in the incidence of vaginal bleeding, hypotonicity, pale eyes, and deaths in 70 µg/kg dams. None of the above findings were seen in the controls or the two lower dose groups. No developmental toxicity was found in the test animals. The NOEL for developmental toxicity was 70 µg/kg (HDT). Based on the increased incidence of vaginal bleeding, hypotonicity, pale eyes, and deaths, the LOEL for maternal toxicity was 70 µg/kg. The NOEL was 35 µg/kg. This study satisfies the data requirements for a developmental toxicity study in rats (Guideline No. 83-3(a); MRID No. 92196014).

Groups of artificially inseminated New Zealand White rabbits received bromadiolone (99.8% purity) in aqueous media by gavage from gestation days (gd) 6 through 18 at doses of 0, 2, 4, and 8 µg/kg bw/day. Vaginal bleeding was found in 8/19 does of the 8 µg/kg group, in 1/19 does of the 2 µg/kg group, and none in the 4 µg/kg group and the controls. Since bromadiolone is an anticoagulant, the vaginal bleeding seen in the 2 µg/kg group could be conservatively considered as a compound-related effect in spite of the lack of a dose-related response. The prothrombin times of the highest dose group and the controls were comparable at sacrifice (11 days after dosing). This result was consistent with that seen in an antidote study where bromadiolone (up to 5.6 mg/kg bw) did not affect the prothrombin times of rats which received bromadiolone in the diet 2 weeks prior to the prothrombin time measurement (Tox. Document No. 009423; MRID No. 420933-01). Under the conditions of this study, conservatively, the incidence of vaginal bleeding seen in the lowest dose group (2 µg/kg) was considered as a threshold effect. The Peer Review/RfD Committee had analyzed the results of this study, and considered the 2 µg/kg as the "threshold" NOEL. The LEL was 4 µg/kg. There was no developmental toxicity in any dose group, and the NOEL for developmental effect was 8 µg/kg (HDT). This study satisfies the data requirements for a developmental toxicity study in rabbits (Guideline No. 83-3(b); MRID No. 92196015).

(3) Bromethalin Developmental Toxicity

A developmental toxicity study was conducted with Harlan Wistar rats (25 rats/group). Rats were orally gavaged on gestation days 6 through 15 at a dosing volume of 5 ml/kg with 0 (vehicle, PEG-200), 0.1, 0.3, or 0.5 mg/kg/day bromethalin technical. Surviving dams were sacrificed on gestation day 20, necropsied and reproductive findings were recorded. The NOEL for developmental toxicity is 0.5 mg/kg/day (HDT). There were no compound-related external, visceral or skeletal effects in bromethalin-treated fetuses in comparison to controls on either a litter or fetal basis.

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The NOEL for maternal toxicity is 0.3 mg/kg/day and the LOEL is 0.5 mg/kg/day. Several effects occurred at the 0.5 mg/kg/day including four deaths during gestation (gestation days 12, 16, 17, and 17). Three high-dose females revealed upper respiratory tract infections which was regarded as secondary due to physiological stress from treatment. Additionally, in 10 of the 25 high-dose females, including the four which died, clinical signs consisting of hind leg weakness and decreased muscle tone were seen. Other observations included poor grooming, weakness, ventral soiling, chromodacryorrhea, decreased respiration, labored respiration, hypothermia, hind leg paralysis, prostration and dehydration.

During the dosing period, high-dose dams had a 30.2% decrease in weight gain in comparison to controls. During the post dosing period, weight gain in the high-dose females was decreased by only 11.7% in comparison to controls. Due to the substantial decreased weight gain during the dosing period, the high-dose females experienced a 13.9% decrease in weight gain for the entire gestation period in comparison to controls. These decreased weight gains are considered to be treatment-related. Food consumption was decreased by 8.7% in high-dose animals in the post dosing period in comparison to controls. The observed decrease in weight gain during the post dosing period may be because of decreased food consumption. The food consumption was comparable between controls and treated groups, including the high-dose group at other times (MRID 00086731).

A second developmental toxicity study was conducted with Dutch Belted rabbits (15/group). In this study, rabbits were orally gavaged at a volume of 1 ml/kg with bromethalin at doses of 0 (PEG-200, vehicle), 0.10, 0.25, or 0.50 mg/kg/day during gestation days 6 through 18. Surviving does were sacrificed on gestation day 28 and reproductive parameters were determined. The NOEL for developmental toxicity is 0.5 mg/kg/day (HDT). There were no compound-related external, visceral or skeletal effects in bromethalin-treated fetuses in comparison to controls on either a litter or fetal basis.

The NOEL for maternal toxicity is 0.10 mg/kg/day. Clinical signs of toxicity were observed in two females at 0.25 mg/kg/day and 5 females in the 0.50 mg/kg/day group. These signs included nasal discharge, loss of muscle tone, weakness, decreased respiration, coolness, and prostration. Two high-dose does died; one on gestation day 16 and one on day 21. The two high-dose does that died had clinical signs before death. One female that died had pneumonia and an empty gastrointestinal tract, and the other had an acute upper respiratory tract infection. Additionally, two high-dose does, one mid-dose doe and one low-dose doe aborted. The two high-dose and the one low-dose does that aborted had gastric trichobezoars in an otherwise empty gastrointestinal tract. The mid-dose doe which aborted had an empty gastrointestinal tract. The clinical signs, abortions and deaths at the top dose and the clinical signs at the mid-dose are considered compound-related. Mid and high-dose animals had decreased weight gains during the dosing period, which are considered compound-related. Food consumption was comparable between control and treated does during gestation. Although values for the mid-dose animals were lower than controls, this finding was not dose-related and is not considered compound-related (MRID 00101545).

(4) Chlorophacinone Developmental Toxicity

In a preliminary range-finding study in rats (MRID 43349501) chlorophacinone (analytically determined concentration 101%) was administered at days 6-15 of gestation at doses

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of 0, 1, 5, 25, 50, 100 or 200 µg/kg/day to groups of 8 mated Sprague-Dawley female rats. Mortalities occurred at 100 and 200 µg/kg/day. Five rats/dose level in the 0, 1, 5, 25 and 50 µg/kg/day groups were sacrificed on gestation day 16, and prothrombin and activated partial thromboplastin times were determined (Refer to Table 20).

It is noteworthy that while there was clotting in at least one sample from the controls and 3 lowest dose groups, this apparently did not occur in the 5 samples from rats of the 50 µg/kg/day group.

Table 20 - Prothrombin (PT) and Activated Partial Thromboplastin Times (APTT) in a Preliminary Rat Developmental Toxicity Study

	Dose Level (µg/kg/day)				
	0	1	5	25	50
Prothrombin Time (sec)[a]	12.2 ± 0.6 N = 4[b]	12.9 ± 1.3 N = 2[b]	12.8 ± 0.3 N = 4[b]	12.6 ± 0.4 N = 3[b]	13.0 ± 0.2 N = 5
Activated Partial Thromboplastin Time (sec)[a]	15.5 ± 2.1	23.9 ± 12.4	16.1 ± 1.4	16.2 ± 1.3	17.0 ± 0.9

[a]Reported as the mean ± S.E.M.
[b]decrease in N is due to the clotting of some of the samples on which the analysis could not be done.

In the subsequent developmental toxicity study (also in MRID 43349501) chlorophacinone (analytically determined concentration: 101% a.i.) was administered to groups of 25 Sprague-Dawley female rats/dose level by gavage at doses of 0 (vehicle only), 12.5, 25, 50 or 100 µg/kg/day on gestation days 6-15 inclusive. The test compound was administered as a suspension in corn oil. Eighteen high-dose (100 µg/kg/day) rats died or were sacrificed moribund (gestation days 12-16) with necropsy findings (blood in vagina and amniotic sacs, blood in stomach and/or small and/or large intestines) indicative of anticoagulant effects. There were no indications of maternal toxicity at 50 µg/kg/day. Treatment-related effects for developmental anomalies, were noted at the lowest dose and above as increased fetal and litter incidences of distended ureter (Refer to Table 21).

Table 21 - Fetal and Litter Incidences of Treatment Related Effects in a Rat Developmental Toxicity Study (doses in µg/kg/day)

	Control 0	Low 12.5	Low Mid 25	High Mid 50	High 100
# pups/# litters examined	205/25	186/24	206/25	196/24	55/7
Hydroureter:					
Bilateral	4/4	8/4	23/10	21/9	12/3
Left	2/2	3/3	3/3	5/4	0/0
Right	0/0	0/0	0/0	1/1	1/1
TOTAL INCIDENCE	6/6	11/5	26/11	27/11	13/4
% Incidence	2.9/24.0	5.9/20.8	12.6/44.0	13.8/40.7	23.6/57.1
Distended ureter:					
Bilateral	1/1	2/2	3/2	4/4	1/1
Left	1/1	4/3	3/3	6/6	1/1
TOTAL INCIDENCE	2/2	6/4	6/5	10/7	2/2
% Incidence	1.0/8.0	3.2/16.7	2.9/20.0	5.1/25.9	3.6/28.6
Total ureter anomaly:					
incidence:	8/6	17/10	32/13	37/14	15/5
% Incidence	3.9/24.0	9.1/41.7	15.5/52.0	18.9/51.9	27.3/71.4

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At the highest dose (100 µg/kg/day) there was an increased total incidence (16/55 fetuses in 5/7 litters; controls: 14/205 fetuses in 10/25 litters) of enlarged lateral ventricle. At 50 µg/kg/day there was an increased incidence of extra rib on lumbar vertebrae I (not noted at 100 µg/kg/day; however, fewer litters were available for examination). For malformations, there were increased fetal and litter incidences of bilateral hydroureter at 25 µg/kg/day.

The rat maternal toxicity NOEL = 50 µg/kg/day.
The rat maternal toxicity LOEL = 100 µg/kg/day (based on mortality)
The rat developmental NOEL is < 12.5 µg/kg/day.
The rat developmental LOEL is < = 12.5 µg/kg/day (increased incidences of hydroureter, distended ureter and total ureter anomaly).

This developmental toxicity study in the rat is classified as acceptable and satisfies the guideline 83-3(a) requirement for a developmental toxicity study in the rat.

In a preliminary range-finding developmental toxicity study in rabbits (MRID 43570801). chlorophacinone (analytically determined concentration 101%) was administered at 0, 1, 2, 5, 10, 50 or 100 µg/kg/day to groups of 5 mated female rabbits. In addition, there were five satellite groups, each containing 3 rabbits dosed at 0, 1, 2, 5 or 10 µg/kg/day. The dosing period was from gestation days 7 through 19; satellite females were sacrificed on gestation day 20 and their blood was analyzed for Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) measurements. Both the mean PT and APTT were elevated in the 10 µg/kg/day females (refer to Table 22).

Table 22 - Prothrombin (PT) and Activated Partial Thromboplastin Times (APTT) in a Preliminary Rabbit Developmental Toxicity Study Chlorophacinone (µg/kg/day)

	0	1	2	5	10
No. of female rabbits bled	3	3	3	3	3
Prothrombin Time (sec)[a]	8.1 ± 0.5	7.8 ± 0.2	7.9 ± 0.1	8.7 ± 0.6	11.6 ± 2.1
Activated Partial thromboplastin Time (sec)[a]	26.5 ± 5.7*	26.6 ± 3.7	23.2 ± 1.5	26.4 ± 4.9	53.0 ± 14.3

[a]Reported as the mean ± S.E.M.
*p < 0.05; Jonckheere's Test (significant by trend test)
Table from page 167 of MRID 43570801.

In the subsequent developmental toxicity study in rabbits (MRID 43570801), chlorophacinone (analytically determined concentration reported as 101%) was administered to 16 New Zealand white rabbits/dose level by oral gavage at dose levels of 0, 5, 10, 25 or 75 µg/kg/day from gestation days 7 through 19, inclusive.

There was maternal mortality in 13/16 high mid (25 µg/kg/day) and 16/16 high dose (75 µg/kg/day) rabbits, with hemorrhage (neck, thoracic cavity, vagina, uterus, amniotic sacs, and GI tract). Increased incidences of external bleeding around the mouth, ears, and urogenital system, along with pale eyes, ears, lips/gums, lethargy and blood in the pan beneath the cage, were noted in the two highest dose groups. No evidence of treatment-related fetotoxicity was

noted in the cesarean section observations. However, due to the low number of surviving litters (3) at 25 µg/kg/day, and the lack of surviving litters at the highest dose (75 µg/kg/day), developmental toxicity cannot be assessed at these doses, and 10 µg/kg/day will be considered as the NOEL for developmental toxicity. This developmental toxicity study in the rabbit is classified as Acceptable (Guideline 83-3(b), and satisfies the guideline requirement for a developmental toxicity study in the rabbit.

The rabbit maternal toxicity NOEL is 5 µg chlorophacinone/kg/day. The LOEL is 10 µg/kg/day (based on increased prothrombin and activated partial thromboplastin times in the preliminary range-finding study. These measurements were not made in the subsequent developmental toxicity study). The rabbit developmental toxicity NOEL is 10 µg/kg/day, based on the lack of sufficient fetuses/litters at the next highest dose level (25 µg/kg/day) available for evaluation. This developmental toxicity study (Guideline 83-3(b) in the rabbit is classified as acceptable.

(5) Diphacinone and its sodium salt Developmental Toxicity

In a developmental toxicity study in rats (MRID 42834801), technical diphacinone (purity > 97%) in corn oil was administered via gavage to groups of 25 mated female Sprague-Dawley rats/dose level at 0, 10, 25 or 75 µg/kg/day on gestational days 6-15, inclusive. There were no effects on maternal body weight or weight gain. Reddish vaginal discharge, reddish urogenital staining and/or reddish fluid in the cage/tray were observed in one dam from the control group, two dams at 10 µg/kg/day, three dams at 25 µg/kg/day, and six dams at 75 µg/kg/day. One dam (with these symptoms) in the 75 µg/kg/day group was euthanized *in extremis* on day 15. A NOEL was not established for maternal toxicity then, as there was a dose-related increase in incidence of clinical signs of the anticoagulant effects of diphacinone through all dose levels. No compound-related altered growth and/or developmental anomalies were observed. There was an increased number of early resorptions and resorptions/dam at 75 µg/kg/day (52 and 2.2 ± 1.8, respectively, compared to control values of 33 and 1.4 ± 1.5). These increases were not statistically significant, and were within the upper limit of historical control data. However, 33% mortality was observed at 100 µg/kg/day in a range-finding study, and the increased number of resorptions is consistent with what was observed in a mouse developmental toxicity study (MRID 00077319) at a dose level (2.5 mg/kg/day) at which 5/5 pregnant females died.

The rat maternal toxicity NOEL < 10 µg/kg/day.
The rat maternal toxicity LOEL = 10 µg/kg/day (based on signs consistent with anticoagulant activity)
The rat developmental NOEL = 25 µg/kg/day.
The rat developmental LOEL = 75 µg/kg/day (based on an increased incidence of resorptions)

This developmental toxicity study in the rat is classified as acceptable, and satisfies the guideline (Guideline 83-3(a) requirement for a developmental toxicity study in the rat).

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It is noted that no clotting time measurements were obtained in this rat developmental toxicity study, and that there is no rabbit developmental toxicity study. The Agency has received, for brodifacoum and chlorophacinone, both rat and rabbit developmental toxicity studies. For both of these anticoagulants, the rabbit is the more sensitive species, particularly with respect to mortality.

f. Mutagenicity

Results of mutagenicity studies for brodifacoum, bromadiolone, bromethalin, chlorophacinone and diphacinone and its sodium salt indicate the following:

Salmonella typhimurium. There were no indications of an increased number of revertants at the histidine locus in any of the strains used.

In Vivo Testing. While different species were used such as Chinese hamsters and mice, results were consistent and there was no evidence of induced mutagenicity response to any strains at any non-activated or activated dose levels.

In Vitro Testing. Testing was performed for chlorophacinone and bromadiolone. Based on this testing it can be concluded that at doses up to and including those associated with cytotoxicity (50 µg/ml), did not induce a clastogenic response in human lymphocytes under the conditions of this assay either in the presence or absence S9.

Appendix C of this document provides the MRID numbers and names of studies used to support these mutagenicity findings.

g. Metabolism

(1) Brodifacoum Metabolism

In the first part of a metabolism study (MRID 44021705) brodifacoum, 3-[3-(4'-bromo-[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one, radiochemical purity > 98%, radiolabeled (^{14}C) in the benzene ring of the benzopyran, was administered to 3 previously bile-duct cannulated Crl:CD(SD)BR strain male rats as a single oral administration at a nominal dose level of 10 mg/kg body weight, well above the LD_{50} value of 0.3 mg/kg. The rats had been pre-dosed with vitamin K_1 in their drinking water, but showed symptoms of anticoagulant toxicity before sacrifice at 48 hours. Bile, urine and feces were collected at pre-dose, 6, 12, 24, and 48 hr post-dose, and radioactivity was determined in these samples, as well as in the livers and residual carcasses. The metabolite profiles of ^{14}C-brodifacoum in bile and bile extracts were examined by chromatographic and spectroscopic techniques.

Total mean recovery of radioactivity was 102.9 ± 8.1%. Recovery from feces (presumably unabsorbed brodifacoum) was 36.11 ± 8.83%; from liver was 14.79 ± 0.41; from the residual carcass: 42.85 ± 5.06%. The mean from bile (all 3 animals) was 6.40 ± 5.45%, but one rat had poor bile flow, possibly from blockage in the cannula. The two remaining animals had a mean 9.53% of the label in bile.

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The major (and only identified) metabolite of brodifacoum in bile was the glucuronide (attachment to the 4-hydroxy moiety of brodifacoum), which accounted for 39.43 to 77.28% of the total radioactivity in individual bile samples, while brodifacoum represented 0.00 to 24.95% of the total activity. Further characterization appeared to split the glucuronide peak into 2 components, and while the cis:trans ratio of parent material was 70:30, the ratio in the glucuronide was reversed (30:70). One unidentified metabolite (region 10) ranged from 1.59 to 21.7% total radiolabel.

Although only one metabolite (the glucuronide) is identified, it is the parent compound which is of toxicological concern, and the registrant has adequately demonstrated in previously submitted studies (refer to MRIDs 00080235 and 42007502) that a high proportion of unmetabolized compound is retained, particularly in the liver.

In a second study (*in vitro* perfusion, also in MRID 44021705) the lower vena cava of a single male rat was ligated. The hepatic portal vein was then cannulated and the liver was cleared of blood and the bile duct cannulated. The liver was perfused and, after equilibration, ^{14}C-brodifacoum, at a dose of 10 mg/kg, was added to the main perfusate reservoir. Bile and perfusate were collected at pre-dose, 1 minute (perfusate only), 1, 2, 3, 4 and 6 hr post-dose. The radioactivity present in bile, perfusate, terminal perfusate supernatant, supernatant filtrate and liver was determined. There was 74.32% recovery after 6 hours, with 59% of the total in perfusate, and 15.19% in liver. Metabolite profiling was attempted, but no metabolites were identified. All radioactivity in the perfusate supernatant was bound to perfusate proteins, with no activity being measured in the aqueous filtrate.

In a metabolism study (MRID 42007502), groups of male rats received single oral doses of ^{14}C-labeled brodifacoum at different dose levels (Group 2: 0.02 mg/kg; Group 3: 0.15 mg/kg; Group 4: 0.35 mg/kg), and blood was taken from 1-3 rats/group at various intervals following this dosage. The following Kaolin Cephalin Time (KCT) and Prothrombin Time (PT) measurements were made as outlined in Table 23 below:

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Table 23 - Kaolin Cephalin and Prothrombin Time in a Metabolism Study in Male Rats

	Clotting times (seconds)					
	Group 2: 0.02 mg/kg		Group 3: 0.15 mg/kg		Group 4: 0.35 mg/kg	
Time after Dosing	KCT	PT	KCT	PT	KCT	PT
6 hr	-	-	-	-	ND	14.3 ± 1.7
12 hr	-	-	-	-	ND	20.7 ± 3.7
18 hr	-	-	-	-	43.7 ± 2.1	37.2 ± 5.4
24 hr	14.9[a] ± 4.2	13.0[a] ± 1.8	15.8 ± 4.8	13.0 ± 1.1	58.9 ± 7.6	95.5 ± 2.7
48 hr	-	-	-	-	113.7 ± 10.6	147.6 ± 6.9
72 hr	-	-	-	-	92.8 ± 49.4	39.7 ± 19.4
96 hr	-	-	-	-	32.3 ± 7.2	18.8 ± 2.0
Day 8	-	-	-	-	21.3[a] ± 2.4	15.8[a] ± 1.2
Day 14	-	-	14.0 ± 1.1	14.3 ± 0.2	15.4 ± 4.5	17.4 ± 0.5
Day 28	14.9[a] ± 1.1	12.7[a] ± 0.3	21.3 ± 2.9	13.6 ± 0.6	20.2 ± 2.9	13.4 ± 0.4
Day 56	-	-	16.2[a] ± 2.4	12.7[a] ± 0.6	19.6[a] ± 2.2	13.3[a] ± 0.2
Day 84	-	-	-	-	17.2 ± 2.9	12.5 ± 0.4
Week 13	14.1[a] ± 1.1	15.4[a] ± 0.6	16.5 ± 1.4	13.8 ± 0.2	-	-
Week 26	-	-	12.3[b]	16.1[b]	-	-
Week 39	16.6 ± 4.3	13.5 ± 1.2	15.0 ± 1.7	13.8 ± 0.5	-	-
Week 52	-	-	15.6 ± 6.2	12.7 ± 1.2	-	-
Week 65	16.7 ± 3.3	13.5 ± 0.8	18.0 ± 3.2	13.2 ± 0.5	-	-
Week 78	-	-	18.6 ± 1.3	12.8 ± 1.2	-	-
Week 91	16.8 ± 2.0	14.6 ± 0.4	19.8 ± 2.2	15.1 ± 1.5	-	-
Week 104	14.7 ± 3.0	11.1 ± 1.0	13.2 ± 0.5	10.9 ± 0.6	-	-

The standard deviation (SD) is derived from data obtained with 3 animals per group.
[a] 2 values only
[b] single value only
ND = not determined
Table taken from p. 26 of MRID 42007502.

The results given above clearly show an increase in clotting time in rats which had received a single oral dose of 0.35 mg/kg. Assuming the effect was manifested as a doubling of the normal clotting time (to approximately 30 seconds for kaolin cephalin and/or prothrombin times), effects were evident as soon as 18 hours after dosage, and were still present at 96 hours post-dosage. In addition, the metabolism study in MRID 42007502 demonstrates that considerable amounts of the radiolabel are retained in the liver following dosage (refer to the Table 24).

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Table 24 - Percentage of radioactivity retained in the liver following single-dose administration of ^{14}C Brodifacoum

Time after dosing	Group 2: 0.02 mg/kg Mean SD	Group 3: 0.15 mg/kg Mean SD	Group 4: 0.35 mg/kg Mean SD
Day 1	47.33 ± 10.87	29.71 ± 4.40	28.92 ± 1.79
Week 4	39.16 ± 3.50	37.07 ± 1.94	23.47 ± 1.21
Week 8	-	30.86 ± 4.23	23.00 ± 0.09
Week 12	-	-	21.24 ± 3.19
Week 13	34.01 ± 2.49	31.74 ± 5.13	-
Week 39	20.33 ± 0.42	22.02 ± 2.83	-
Week 65	15.97 ± 2.33	15.36 ± 3.03	-
Week 91	10.57 ± 1.08	12.39 ± 3.08	-
Week 104	11.78 ± 0.97	11.74 ± 1.64	-

Table from data on pages 30-32 of MRID 42007502.

It is concluded that overall there is sufficient metabolism data (including excretion, distribution, retention half-life and amounts retained within different organs). This metabolism study in the rat, taken with previously submitted metabolism studies (in MRIDs 00080235 and 42007502) is classified as acceptable. The combination of these studies is adequate to satisfy the 85-1 data (metabolism study) guideline requirement.

Groups of male Sprague-Dawley rats received a single dose (0.2 mg/kg bw) of brodifacoum, bromadiolone, or flocoumafen by gavage. A control group consisting of 9 male rats which received nothing was also included in the study. The results showed that the levels of brodifacoum in the liver declined very slowly during the duration of the study as indicated by the difference between day 1 (1.107 µg/g) and day 200 (0.539 µg/g). During the first 28 days after dosing, the decline of the liver concentrations of bromadiolone and flocoumafen was faster than that of brodifacoum as indicated by the $t_{1/2}$'s of these 3 chemicals at the first 28 days (brodifacoum: $t_{1/2}$, 63 days; bromadiolone: $t_{1/2}$, 17 days; flocoumafen: $t_{1/2}$, 6 days). The decline of the liver concentrations of these 3 test chemicals occurred in a "bi-exponential manner". The second $t_{1/2}$'s were estimated to be 282, 318, and 159 days for brodifacoum, bromadiolone, and flocoumafen, respectively. In general, oral administration of any of these 3 chemicals would result in substantial retention of the chemical in the liver for a very long time. The initial report of this study contained deficiencies which were rectified in subsequent supplemental data submission. This study satisfies the data requirement for a modified metabolism study on bromadiolone (Guideline No. 85-1; MRID No. 42596801).

(2) Bromadiolone Metabolism

Groups of male Sprague-Dawley rats received a single dose (0.2 mg/kg bw) of brodifacoum, bromadiolone, or flocoumafen by gavage. A control group consisting of 9 male rats which received nothing was also included in the study. The results showed that the levels of brodifacoum in the liver declined very slowly during the duration of the study as indicated by the difference between day 1 (1.107 µg/g) and day 200 (0.539 µg/g). During the first 28 days

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after dosing, the decline of the liver concentrations of bromadiolone and flocoumafen was faster than that of brodifacoum as indicated by the $t_{1/2}$'s of these 3 chemicals at the first 28 days (brodifacoum: $t_{1/2}$, 63 days; bromadiolone: $t_{1/2}$, 17 days; flocoumafen: $t_{1/2}$, 6 days). The decline of the liver concentrations of these 3 test chemicals occurred in a "bi-exponential manner". The second $t_{1/2}$'s were estimated to be 282, 318, and 159 days for brodifacoum, bromadiolone, and flocoumafen, respectively. In general, oral administration of any of these 3 chemicals would result in substantial retention of the chemical in the liver for a very long time. The initial report of this study contained deficiencies which were rectified in subsequent supplemental data submission. This study satisfies the data requirement for a modified metabolism study on bromadiolone (Guideline No. 85-1; MRID No. 42596801).

(3) Bromethalin Metabolism

A metabolism study was conducted in Fischer 344 rats following oral administration of ^{14}C-bromethalin at 1 mg/kg. Blood samples were taken from the orbital sinus at 0.25, 0.5, 1, 2, 4, and 24 hours, and at 2, 3, 4, 6, 8, 11, 14, 17, and 21 days after dosing. Based on radiolabeled material, the plasma half-life was 134 hours (5.6 days). The half-life of the distributive phase suggested distribution in total body water. The T ½ of bromethalin is 5.6 days. The major metabolite formed in the rat is desmethyl bromethalin. The study (MRID 0004724) was classified as acceptable.

(4) Diphacinone and its sodium salt Metabolism

In a metabolism study (MRID 92049009), the disposition of 14-C diphacinone was studied in Sprague-Dawley rats, Swiss albino mice, and Diphacinone-tolerant Norway rats. Sprague-Dawley rats received single oral doses of 0.18, 0.4 mg/kg (group A, 2 rats/group), 0.5, or 1.0 mg/kg (group B, 1 rat/group) labeled diphacinone and urine and feces collected up to 3 days post-dose (group A) or 8 days post-dose (group B). Swiss mice (1 mouse/group) received 0.6 mg/kg labeled diphacinone by oral intubation or sandwich method and urine and feces collected up to 4 days post-dose. Norway rats (1 rat) received 4 consecutive doses of 3.5 mg/kg labeled diphacinone and 1 dose of 6.1 mg/kg labeled diphacinone. Blood samples were obtained at 4, 6, 7, and 8 hours after the last dose and at 26 hours (time of sacrifice). A group of 10 diphacinone-tolerant Norwegian rats received 1.5 mg/kg labeled diphacinone in DMSO daily for 2-3 days to obtain enough excreta for metabolite identification. Because 4 different batches of labeled diphacinone were prepared for this study (label in different positions for each batch), eight Sprague-Dawley rats (2 females/group) received approximately 42 μg of labeled diphacinone from each labeled batch as a single oral dose, and TLC autoradiograms from these 4 labels were compared.

Absorption appeared fairly rapid but was only estimated in one rat, as judged by the blood levels measured over time. Distribution data showed that the liver, muscle, blood, fat, and lung were the tissues demonstrating the greatest retention of the test chemical in the order liver (14-25% of the dose), muscle (0.18-4.4% of the dose), fat (0.55-1.16% of the dose), and lung (0.04-0.5% of the dose). Rats appeared to show greater retention than mice of test chemical, but data were inconclusive based on limited numbers of animals and poor experimental design.

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Half-life, as estimated in the single Norway rat, was stated as 17 hours, but is likely an underestimation. Elimination of diphacinone derived radioactivity was primarily in feces, with between 47-77% of the dose in feces of rats, and 69-73% of the dose in mice. At least five metabolites of diphacinone were identified in urine, feces, and/or liver. These metabolites represent hydroxylated products of diphacinone occurring on the phenyl and indandionyl rings.

This study is classified as unacceptable and does not satisfy the guideline requirement 85-1 for a metabolism study in rats. The unacceptable classification is based on the following deficiencies observed in this study:

1) Inadequate number of animals per dose group.

2) Four different radiolabeled parent compounds were administered in this study. Distribution data show that blood, liver, muscle and fat contained the highest amount of radioactivity, but the percentages found might depend on the label position. The excretion of only two different radiolabeled compounds was followed to any degree.

3) Inadequate experimental design for analysis of half-life.

4) Inadequate data on recovery of radioactivity from dosed animals.

5) No stated rationale for doses used.

The Agency requires metabolism data more adequately defining the half-life of diphacinone in the rat, as well as retention data for the liver.

(5) Chlorophacinone Metabolism

Agency records indicate only one metabolism study (MRID 00155540) on chlorophacinone has been received. Several experiments were conducted, including blood kinetics (2 experiments with a determination of radioactivity in organs 4 and 48 hours following dosage; urinary, fecal and biliary excretion).

In the first blood kinetics assay, four rats each received orally 1 mg of ^{14}C-labeled chlorophacinone. The following mean blood concentrations were measured as outlined in Table 25 below:

Table 25 - Mean blood concentration of chlorophacinone (in µg equivalents) following oral administration of 1 mg chlorophacinone

	30 min.	1 hr.	2 hr.	4 hr.	6 hr.	8 hr.	24 hr.	48 hr.
Mean Blood Conc.	1.4	2.4	4.1	6.4	6.4	5.9	1.8	0.3

Chromatography and autoradiography demonstrated that the chlorophacinone remained unchanged in plasma, with a blood half-life of about 10 hours.

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Organs of the rats used in the first blood kinetics study were assayed for radioactivity. The following results were obtained as outlined in Table 26 below:

Table 26 - Mean concentration of chlorophacinone (µg/g of organ)

Organ	4 hours	48 hours
Liver	31.1	2.9
Kidney	6.6	1.2
Lung	4.5	0.4
Heart	3.1	0.2
Muscle (thigh)	2.0	0.1
Fat	1.2	0.7
Carcass	5.2	0.3

In a second blood kinetics study, two rats each received 1.43 mg of ^{14}C-labeled chlorophacinone/day for 3 days. Blood samples were taken at various times following the third dose, with the following blood concentration measurements as outlined in Table 27 below.

Table 27 - Mean blood concentration of chlorophacinone (in µg equivalents) following three daily oral administrations of 1.43 mg chlorophacinone

	30 min.	1 hr.	2 hr.	4 hr.	6 hr.	8 hr.
Mean Blood Conc.	7.1	8.9	10.2	11.5	12.2	14.2

In an elimination assay, two rats were used. One received 1.43 mg of ^{14}C-labeled chlorophacinone and the second received 1.28 mg ^{14}C-labeled chlorophacinone. Daily assays were made of urine, feces and CO_2 for four days. The rats were sacrificed and radioactivity was measured in blood, organs and carcass. Urine and feces were extracted and measured by TLC and autoradiography.

Urine and CO_2 radioactivity were less than 1% of the total dose. Most of the radioactivity was excreted in the feces (94.7% in one rat and 108.6% in the other over the 4-day period). Excretion reached 90% in the first two days.

In a biliary excretion assay, two rats were used. Each received 1.4 mg of chlorophacinone intraduodenally. Bile was collected for 8 hours and total radioactivity was measured. TLC and autoradiography were performed on the bile directly before and after hydrolysis with glucuronidase.

Two hours after administration of chlorophacinone in the duodenum, biliary elimination was constant. At the end of 8 hours, an average of 26% of the administered radioactivity was eliminated in the bile.

The information provided in MRID 00155540 adequately addresses the guideline requirements 85-1 for a metabolism study for a highly toxic anticoagulant with no chronic

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exposure. Although it is reported that there is over 90% excretion in the two days following dosage, the findings in the subchronic study (MRID 92018013) indicate there is a potential for bioaccumulation (or cumulative toxicity). In the subchronic study, there were mortalities at 40 µg/kg/day in 10/10 males (deaths occurred days 29-82) and 4/10 females (deaths on days 69-111), and there were also mortalities at 20 µg/kg/day in 4/10 males (deaths on days 105-111).

h. Other Toxicological Considerations

(1) Brodifacoum - Other Toxicological Considerations

In an antidotal study (MRID 42007501), four male beagle dogs each received a single oral dose of 5 mg/kg brodifacoum (96.8%). Prothrombin times for each of the dogs were then monitored over a period of five weeks. "Doses of 2 mg/kg vitamin K_1 were administered to dogs by the intramuscular route whenever their prothrombin times were elevated to levels consistent with a life-threatening effect on coagulation." Individual dogs required 12-15 vitamin K_1 treatments in the period from days 2 to 29 post-dosing. All four dogs survived to the end of this study (5 weeks after the test material was administered). However, based on elevations in prothrombin time, vitamin K_1 had to be administered to one dog on day 29. This dog had also been treated with vitamin K_1 on days 23 and 24 as well as on previous occasions, and the last prothrombin time measurement for this dog was on day 34. The possibility exists that this dog would have required additional vitamin K_1 treatments after day 34.

(2) Bromadiolone - Other Toxicological Considerations

In an antidotal treatment study, groups of male Crl:CD^R rats (10/dose) were exposed to bromadiolone baited pellets (0.005% a.i.) for 24, 48, or 78 hours. The estimated mean total bromadiolone doses were 5.69, 9.76, and 15.63 mg/kg for 24-, 48-, and 72-hour groups, respectively. At the end of the exposure period, the first 5 surviving rats of each group were given vitamin K_1 at 5 mg/kg. Initially, a loading dose was given subcutaneously, and subsequently, vitamin K_1 was administered daily by gavage for 13 days. The survivors were sacrificed at 8 to 10 days after discontinuing the vitamin K_1 treatment.

The animals which did not receive vitamin K_1 died in each exposure group. The deaths frequently occurred within 3 to 4 days of the study. The clinical and gross pathology findings were hemorrhage-related toxicity in all test-article treated animals. The death rates in vitamin K_1 treated animals were 1/5, 2/5, and 5/5 in the 24-, 48-, and 72-hour exposure groups, respectively. With vitamin K_1 treatment, the clinical findings (hemorrhagic-related toxicity) were resolved by the 5^{th} day of the antidote treatment, and the decrease in body weight observed during the bromadiolone treatment was also restored in the surviving animals. At the 2^{nd} week of the study, the prothrombin times of the vitamin K_1 treated animals were essentially comparable to those of the controls. However, for the 48-hour exposure group, the prothrombin time was slightly decreased relative to that of the control.

The results demonstrate that vitamin K_1 treatment, as employed in this study, can restore the clotting process of an animal which is exposed to bromadiolone below an estimated total dose of 15.63 mg/kg body weight during a 72 hour period. However, the antidotal treatment may not completely prevent death (i.e. all the rats died in 72-hour exposure groups with vitamin K^1

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treatment) when rats are exposed to bromadiolone even at the lowest exposure dose (5.69 mg/kg) in this study. This study satisfies the data requirements for an antidotal study (Guideline 86-1; MRID No. 42093301).

(3) Bromethalin - Other Toxicological Considerations

The following information is in the Agency's files and are supportive of the endpoint of toxicological concern identified in the above studies.

Ph.D. Dissertation entitled "Bromethalin-Based Rodenticides: Mode of Action, Toxicity, Clinical Effects, and Treatment Efficacy in Rats, Dogs, and Cats", by D. Dorman, University of Illinois, Dept. of Veterinary Biosciences (MRID 42759602).

This dissertation is a summary of information found in the literature. According to the summary page of the dissertation, "The purpose of these studies was to define the toxicity of bromethalin-based rodenticides, develop treatments, and determine new modes of action of bromethalin….. Sublethal doses of bromethalin to dogs and cats resulted in delayed CNS depression, hind-limb ataxia, paresis, and paralysis. Higher doses given to dogs resulted in rapid severe muscle tremors and generalized seizures. Bromethalin toxicosis was also associated with increased cerebrospinal fluid pressure and cerebral edema. Bromethalin toxicosis produced acute and chronic EEG changes. Predominant abnormal EEG changes included spike and spike-and-wave EEG patterns; high voltage slow wave activity; photoconvulsive or photoparoxysmal irritative responses, and marked voltage depression. Histologic lesions included diffuse white matter spongiosis, mild microgliosis, and optic nerve vacuolization. Ultramicroscopic examination of brainstem revealed occasional swollen axons, intramyelenic vacuolization, and myelin splitting at the intraperiod line."

The Toxicity and Mechanism of Action of Bromethalin (MRID 42795603).

This publication is a journal article with only summary data. The study authors state " Doses in excess of the LD_{50} (2 mg/kg in rats) will cause death within 8-12 hours and it is preceded by one to three episodes of clonic convulsions with death usually due to respiratory arrest. Multiple low doses or sublethal intoxication yield hind leg weakness and loss of tactile sensation in rodents. Histopathology of the brain and spinal cord of these animals revealed a spongy degeneration of the white matter which was shown upon ultramicroscopic examination to be intramyelenic edema. …Mechanistic studies showed that bromethalin is rapidly converted to the desmethyl analog which is an extremely potent uncoupler of oxidative phosphorylation. It was theorized that if this occurs in the central nervous system, a fluid imbalance may ensue due to insufficient adenosine triphosphate (ATP). Fluid buildup in the cranium was determined by measuring cerebrospinal fluid pressure (CSFP), brain and spinal cord moisture, and cation concentrations."

Toxicity and Efficacy of Bromethalin (MRID 42795604).

This report is a published journal article with no raw data. The study authors state "Acute oral LD_{50} values range between 1 and 13 mg/kg for several mammalian and avian species.

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Results of experiments designed to determine the physiological and biochemical mechanism of action suggest that treatment with bromethalin results in the uncoupling of oxidative phosphorylation in central nervous system mitochondria."

(4) Chlorophacinone - Other Toxicological Considerations

In an antidotal study (MRID 41981101) groups of 10 male rats were offered pelleted end-use product (containing 0.005% chlorophacinone) as their sole dietary source of food for 24, 48 or 72 hours. Reported mean dose levels were 5.28, 4.73 and 5.03 mg chlorophacinone/day. About 1-2 hours after the end of their respective exposure periods, five males in each group received a subcutaneous injection of 5 mg/kg vitamin K_1, followed by vitamin K_1 by daily oral gavage (5 mg/kg/day) for the next 13 days. Animals were sacrificed 8-10 days after the last oral dose of vitamin K_1. Five animals in each dose group did not receive vitamin K_1 treatment.

All rats that ate the chlorophacinone-containing pellets and did not receive vitamin K_1 died. All rats treated with vitamin K_1 after 24-hour exposure to the chlorophacinone diet survived, as did 3/5 rats fed the chlorophacinone-containing diet for 48 hours. All of the vitamin K_1-treated rats which had been fed the chlorophacinone-containing diet for 72 hours died.

While vitamin K_1 has been shown to be a somewhat effective treatment following chlorophacinone ingestion, there were some mortalities among the rats which were given vitamin K_1 at 48 hours. This suggests a potential hazard if incidents occur involving pets or small children in which it is not known or realized that ingestion has occurred. It is noted that this antidotal study does not include prothrombin times. Such information, while not necessary for purposes of reregistration, could be useful to the Agency in defining hazards associated with exposure to chlorophacinone.

(5) Diphacinone and its sodium salt - Other Toxicological Considerations

A collection of published articles (in MRIDs 42791201, 42791202, 42791203) from the literature has been submitted to support the use of Vitamin K_1 as an antidote in treating diphacinone poisoning.

In one report (Mount, M. E. and B. F. Feldman, 1983. The Mechanism of Diphacinone Rodenticide Toxicosis in the Dog Clarified and Its Therapeutic Implications. Am. J. of Vet. Res. 44(11): 2009-2017; in MRID 42791201) the clinical effectiveness of Vitamin K_1 therapy in reversing anticoagulant effects of two rodenticides in male dogs was investigated. Warfarin and diphacinone were administered in the diet twice daily for 3 days. Warfarin was fed to one dog at a total dose of 5 mg (a.i.)/kg and diphacinone was fed to three dogs at 2.5 mg (a.i.)/kg. These doses would generally be lethal for repeated exposure. Evidence of coagulopathy was observed by day 3, and Vitamin K_1 therapy was initiated for all dogs on day 6 at divided doses 3 times/day over a 5-day interval. One warfarin and one diphacinone-dosed dog received 2.5 mg K_1/kg/day, while the other two diphacinone-dosed dogs received 5 mg K_1/kg/day. All animals survived to the termination of the study.

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A single regime of vitamin K_1 (2.5 mg/kg/day for 5 days) was effective in reversing hypoprothrombinemia of the warfarin-treated dog. However, this regimen was ineffective for diphacinone-treated dogs, which required either 5 mg vitamin K_1/kg/day administered in repeated doses 3 times/day on days 6-10 and 16-20, or 2.5 mg vitamin K_1 in repeated doses on days 6-10, 16-20 and 26-30. In addition, one diphacinone-dosed dog received fresh plasma with the first vitamin K_1 injection.

The three diphacinone-exposed dogs had prolonged bleeding at venepuncture sites the last day of treatment. All dogs became clinically ill within the subsequent 3 days. Bleeding was observed in the diphacinone-exposed dogs as long as 2 weeks following exposure. An important finding was that the vitamin K-enzyme complex was inhibited in diphacinone-exposed dogs for approximately 30 days as indicated by routine coagulation screen tests and coagulation factor inhibition. No hepatic dysfunction was observed. There was a statistically significant reduction ($p < 0.001$) in pancreatic exocrine function although the resulting values were within the laboratory's reference range.

According to the published paper in MRID 42791201:

> "The liver synthesizes the vitamin-K dependent coagulation proteins, factors II, VII, IX, and X, to inactive precursor forms dependent upon vitamin K for activation by a postribosomal protein modification. The inactive precursor proteins contain several glutamic acid residues which serve as the site for vitamin K function. These amino acids are carboxylated to form gamma-carboxyglutamic acid (G1a) residues which are responsible for activation of the coagulation protein. Calcium binding is dependent upon this cluster of carboxylic groups; without calcium binding the factor is nonfunctional. Hence, vitamin K serves as an essential cofactor for the enzyme that carboxylates protein-bound glutamic acid residues to G1a.
>
> The molecular role of vitamin K in the carboxylation event is unclear. The carboxylase enzyme has been studied and its activity measured. A reductase, epoxidase (carboxylase-epoxidase enzyme), and epoxide reductase enzymes are also closely associated with the metabolic role of vitamin K… This…collectively represents the vitamin K-enzyme complex. This term is used since the complete biochemical mechanisms of vitamin K metabolism are not completely understood. The site of the biochemical lesion caused by anticoagulant rodenticides is the epoxide reductase enzyme… The carboxylase-epoxidase enzyme interaction…is not understood but results in G1a formation and conversion of vitamin K to the inactive epoxide. The epoxide can then be reconverted to the vitamin K quinone through the epoxide reductase enzyme… Without this enzyme vitamin K cannot be recycled. This results in rapid depletion of body stores of vitamin K…"

The material in MRID 427912201 satisfies the guideline data requirement (§86-1) for an antidotal study.

Diphacinone (as "Dipaxin") has been investigated and used as a therapeutic anticoagulant in humans (Correll, J.; Coleman, L.; Long, S.; Willy, R., 1952). According to this report, a single oral dose of 16 mg given to a healthy man weighing over 200 lbs resulted in no significant change in prothrombin determinations over a period of 48 hours. A second man of similar weight was given 32 mg, and changes in the prothrombin time were evident within a period of 4 hours. The maximum effect was seen at about 16 hours, with decrease in prothrombin time at 30 hours, and recovery to normal at 70 hours. A third patient, a 95-lb 22-year-old man received 32 mg as

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a single dose; definite increase of prothrombin time was measurable within 23 hours, and a "therapeutic" effect (prothrombin time > 15 seconds) was evident within 48 hours. Following this single dose, 12 days were required for the prothrombin time to return to normal range. The dosage was then repeated, and prothrombin time was prolonged to 31 seconds (normal is about 12 seconds) within 36 hours. The following day, the patient received 50 mg of vitamin K intravenously. One hour later the prothrombin time was 26 seconds; 2 hours later it was 19 seconds, and approximately normal prothrombin values had been restored at 7 hours.

Dipaxin was given to a 30-year-old woman with post-operative venous thrombosis. Definite prolongation of the prothrombin time (to approximately 22 seconds) developed 24 hours after a single 32-mg dose. Repetition of this dose on the third day brought prolongation of the prothrombin time into the optimal therapeutic range (24-36 seconds), where it was maintained by 5 mg of Dipaxin daily. On the day of the last dose (day 13) the prothrombin time was 26 seconds, returning to normal range 3-4 days later.

Additional information on clinical investigations of Dipaxin in humans are given in Katz et al. 1954 (in which it is stated that "The prothrombopenic action of Dipaxin is readily counteracted with vitamin K_1 administered either orally or intravenously) and Field et al. 1952 (in which it is stated that, in man: "This agent induces an effective hypoprothrombinemia in single doses of as little as 4 mg… After single doses of 20 mg a marked hypoprothrombinemia was usually evident in 48 hours which persisted from 6 to 10 days… The recommended starting dose is about 20 mg… The maintenance of adequate clinical hypoprothrombinemia was obtained with daily doses of 2 to 4 mg. Hypoprothrombinemia was readily overcome with vit. K_2, the natural vitamin being more effective than the synthetic…".

2. Exposure Assessment

a. Dietary Exposure

These chemicals are non-food use pesticides. Therefore, it is unlikely that there will be any exposure to food sources or to residues in ground or surface water contamination.

b. Occupational and Residential Exposure

The following assumptions were made:

- All formulations are 0.005% a.i. (note: some end-use products formulations have a higher percent a.i., but using these would make a comparison of MOEs more difficult). In order to calculate MOEs for a higher percent a.i. the calculations would be adjusted accordingly;
- A child weighs 10 kilograms; and
- Poison specialists estimate that a child would consume approximately 5 grams in one bite.

These assumptions were extracted from the various rodenticides in this RED.

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Using bromethalin as an example, the exposure (dose), and resulting MOE, a 10 kilogram child would receive from 5 grams of bromethalin at 0.005% active ingredient (a.i.) is:

5 grams X 1000 mg/gram = 5000 mg
5000 mg X .00005 (percent a.i.) = 0.25 mg technical a.i. in 5 grams
0.25 mg / 10 kg = 0.025 mg/kg (note: for any 0.005% formulation this number will remain consistent for the listed rodenticides.
MOE = NOEL / Exposure; NOEL = 0.025 mg/kg
MOE = 0.025 mg/kg / 0.025 mg/kg = 1

Table 28 summarizes the relative MOEs for the chemicals in the Rodenticide Cluster and for zinc phosphide. Normally any MOE less than one is expressed as: < 1. However, for comparison purposes the actual MOE has been put in the table. The Agency acknowledges that there is little confidence in the significant figures of results less than one.

Table 28 - Relative MOEs for the Chemicals in the Rodenticide Cluster and Zinc Phosphide

Chemical	a.i. of Typical EP	Tox. Endpoint	Amount consumed in one bite	Amount of technical consumed in one bite (mg/kg)	MOE
Bromethalin	0.05%	0.025 mg/kg/day	5 grams	0.025	1
Brodifacoum	0.05%	0.002 mg/kg/day	5 grams	0.025	0.08
Bromadiolone	0.05%	0.002 mg/kg/day	5 grams	0.025	0.08
Chlorophacinone	0.05%	0.005 mg/kg/day	5 grams	0.025	0.2
Diphacinone	0.05%	0.13 mg/kg/day	5 grams	0.025	5.2
Zinc Phosphide	2.0%	5 mg/kg	5 grams	0.10	0.5

The Agency notes that all the above rodenticides result in MOEs of concern assuming 0.05 percent active ingredient and a 5 gram dose for a 10 kg child, except for zinc phosphide. The Agency also notes the only zinc phosphide baits not restricted are 1 and 2 percent. To facilitate a risk management decision the rodenticides can be ranked, based on the above table. Zinc phosphide formulations contain 1 and 2 percent a.i. at a minimum, which results in MOEs of 1 and 0.5 respectively.

(1) Brodifacoum Occupational and Residential Exposure Assessment

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

(a) Handler Exposures & Assumptions

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

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Based on the use patterns and potential exposures described above, six 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; and (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. Although the vapor pressure of brodifacoum is relatively low (9.8×10^{-7} Torr), the Agency is concerned about potential inhalation of particulates, fine particles and dusts associated with baits which could be inhaled resulting in ingestion/oral exposure.

Calculations of daily exposure to pesticidal active ingredients 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.

(b) Post-Application Exposures & Assumptions

EPA has determined that there is a potential for exposure to users 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 re resistant or child 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.

(c) Occupational and Residential Characterization

Risk from Dermal and Inhalation 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. These concerns are based on (1) very high acute toxicity; (2) potential dermal absorption of toxicologically significant amounts; and, (3) absence of exposure data for all scenarios considered.

(2) Bromadiolone Occupational and Residential Exposure Assessment

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

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(a) Handler Exposures & Assumptions

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

Based on the use patterns and potential exposures described above, four major handler exposure scenarios were identified for Bromadiolone: (1) placing bait packs at bait stations; (2) loading bait boxes or bait stations with meal bait or bait pellets from larger containers; (3) breaking paraffinized slabs, cakes, and blocks into pieces and placing the pieces at bait stations; and (4) securing large paraffin blocks at bait stations in sewers.

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 or pellets to result in inhalation exposure to handlers during bait station loading.

Calculations of daily exposure to Bromadiolone by handlers are used to assess risk to those handlers.

(b) Post-Application Exposures and Assumptions

EPA has determined that there is a potential for exposure to consumers and others following applications of bromadiolone, 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; or (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.

(3) Bromethalin Occupational and Residential Exposure

At this time, some products containing bromethalin are intended primarily for occupational use, and some products are intended primarily for residential use.

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) during use or to persons entering treated sites after application is complete.

(a) Handler Exposures and Assumptions

The Agency has determined that there is potential for exposure to applicators or other handlers during typical use-patterns associated with bromethalin. Specifically, the Agency is

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concerned about potential accidental oral and inhalation exposures to handlers resulting from the loading and application of bromethalin at bait stations.

Occupational Handler Exposures

Based on the use patterns described above, four major handler exposure scenarios were identified for occupational handlers of bromethalin: (1) placing bait packs and bait cups at bait stations; (2) loading or recharging bait stations and bait trays with loose baits (meal baits, bait pellets, etc.); (3) putting loose baits into plastic or paper bags for placement in rodent burrows; and (4) removing baits that have not been touched by target rodents for relocation or disposal.

Frequency of handling activities and amount of product handled are expected to vary among handlers; some occupational handlers may use bromethalin products several times in a 90-day period resulting in possible intermediate-term exposures, while others may use bromethalin infrequently resulting in possible short-term exposures.

No data are currently available for any of the occupational handler exposure scenarios identified. It is unclear from labels and other available information the extent to which exposure is possible or likely during the activities associated with each exposure scenario.

Homeowner Handler Exposures

Because bromethalin products are available to homeowners, the Agency has determined that there is potential for exposure to applicators or other residential handlers during typical use-patterns associated with bromethalin. Specifically, the Agency is concerned about accidental oral and inhalation exposures to homeowner handlers during the loading and application of bromethalin at bait stations.

Residential handlers are expected to have fewer than seven days of exposure during a 90-day period.

Based on the use patterns and potential exposures described above, four major handler exposure scenarios were identified for residential handlers of bromethalin: (1) placing bait packs and bait cups at bait stations; (2) loading or recharging bait stations and bait trays with loose meal baits or bait pellets; (3) putting loose baits into plastic or paper bags for placement in rodent burrows; and (4) removing baits that have not been touched by target rodents for relocation or disposal.

No data are currently available for any of the homeowner handler exposure scenarios identified. It is unclear from labels and other available information the extent to which exposure is possible or likely during the activities associated with each exposure scenario.

(b) Post-Application Exposures and Assumptions

The Agency has determined that there is a potential for exposure to residential and others following applications of bromethalin, particularly in residential areas. the Agency has special

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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 product labeling; (2) baits are available to homeowners in packages which are not child resistant and could be accessible to children; or (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.

Occupational Post-Application Exposures

The Agency has determined that there is potential for occupational post-application exposure to bromethalin. Accidental exposures may occur in a variety of industrial and other occupational settings if bromethalin baits have not been applied in tamper-resistant bait stations or ready-to-use packages and workers come into contact with or handle the bait material. Because exposures of this nature are expected to be infrequent and relatively short in duration, at this time the Agency does not expect such exposures to significantly affect worker risk. Furthermore, based on available incident data, the Agency believes it is unlikely that adult workers mistake bromethalin baits for food.

Residential Post-Application Exposures

The Agency has determined that the potential for post-application residential exposure exists following residential applications made either by users or professional pest control operators (PCOs).

For adults, the Agency has determined that there is potential for user post-application exposure to bromethalin for situations similar to those described above for workers. Accidental exposures may occur following applications in residential settings if baits have not been applied in tamper-resistant or child resistant bait stations and consumer handle or otherwise come in contact with bait material, or if adults in residential settings mistake bromethalin baits for food. For the reasons described above for workers, the Agency does not expect such post-application exposure scenarios to pose a significant risk to an adult user, but recommends confirmation from the registrant(s).

The Agency has special concerns, however, about possible post-application exposures to children if (1) baits are not placed out of reach of children or are not applied in tamper-resistant or child resistant bait stations as specified in product labeling; and (2) baits are brightly colored or packaged in a way in which they could be appealing to children or be mistaken by children for food or candy. These concerns are supported by the high number of accidental child ingestion incidents relative to the number of adult ingestion incidents for rodenticide baits in general, and for bromethalin specifically.

(c) Occupational and Residential Risk Characterization

Calculations of daily dose of bromethalin are used to assess occupational and residential risks resulting from bromethalin use. Because the Agency currently has no data on occupational or residential exposures to bromethalin, the Agency is unable to calculate daily doses.

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The Agency has risk concerns for persons exposed to bromethalin in both occupational and residential scenarios. These concerns are based on (1) very high acute toxicity (category I for acute oral toxicity); (2) very low short-term and intermediate-term NOELs (0.1 mg/kg/day and 0.025 mg/kg/day respectively); (3) the potential for acute, short-term, and intermediate-term exposures for occupational handlers, and for acute and short-term homeowner exposures; (4) a relatively high number of incidents associated with rodenticide baits in general; and (5) an absence of exposure data for all exposure scenarios considered.

(4) Chlorophacinone Occupational and Residential Exposure

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

(a) Handler Exposures & Assumptions

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

Because the vapor pressure of chlorophacinone is low (3.6×10^{-6} Torr), the potential for exposure resulting from inhalation of chlorophacinone vapors is not a significant concern despite a very low LC_{50} (0.007 mg/L). However, if fine particles become airborne during the handling of chlorophacinone baits, individuals may inhale these particles. Because these particles could potentially be ingested, such exposure would contribute to the individual's risk resulting from accidental ingestion/oral exposure.

Based on the use patterns and potential exposures described above, eight major handler exposure scenarios were identified for chlorophacinone: (1) mixing concentrate into baits (if end-use products which are concentrates that are intended to be mixed with food based do not exist, then this scenario can be eliminated), (2) placing bait packs; (3) loading bait boxes or bait stations with meal bait, grain bait, bait pellets, or other food-based bait from larger containers; (4) breaking paraffinized slabs, cakes, and blocks into pieces and placing the pieces in bait stations; (5) securing large paraffin blocks in bait stations in sewers; (6) applying bait by hand; (7) applying bait (e.g., pellets) in broadcast treatments using ground equipment; and (8) pouring and applying tracking powders (For some workers involved in major applications, exposure could last 8 hours a day, 5 days a week), and (9) spray application in orchards at 0.2 lb a.i./acre.

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, tracking powders, or pellets to result in inhalation exposure to handlers during bait station loading.

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(b) Post-Application Exposures & Assumptions

Occupational and Residential

EPA has determined that there is a potential for exposure to consumers and others following applications of chlorophacinone, 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 consumers 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. These factors, among others, can be expected to lead to numerous exposures among small children Under Note to Physicians, many of the labels recommend that Vitamin K_1 be administered intravenously (IV) or intramuscularly (IM). The veterinary literature states that vitamin K_1 can cause anaphylactic reactions if given IV and extensive hemorrhage after IM administration. Sheldon Wagner, M.D., a consultant to OPP, confirmed that Vitamin K_1 should not be given IV unless there is a hemorrhagic crisis. IM administration is normally acceptable in humans. The recommendation for IV administration should be deleted from the label.

(5) Diphacinone and its sodium salt Occupational and Residential Exposure

Because EPA currently has no data on occupational or residential exposures to diphacinone, the Agency is unable to calculate daily doses. EPA has risk concerns for persons exposed to diphacinone in both occupational and residential scenarios. These concerns are based on (1) very high acute toxicity (short- and intermediate - term NOEL of 0.1 mg/kg/day based on developmental 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 diphacinone use as compared to non-anticoagulant pesticides.

(a) Handler Exposures & Assumptions

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

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

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In addition, the Agency recommends that occupational handlers (commercial applicators) wear protective eyewear and a dust/mist respirator when handling diphacinone powder or other non-paraffinized diphacinone formulation, 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 exposure that could result from contact with such dusts.

(b) Post-Application Exposures & Assumptions

There are no data currently available to address post application exposure for diphacinone. Only the following rough calculations are possible.

The dose a 10 kg child could receive from a 43 gram packet (average packet size) of diphacinone at (0.005%) equals 0.215 mg/kg. Assuming a NOEL of 0.13 mg/kg, this exposure will result in a Margin of Exposure (MOE = NOEL/Exposure) of 0.6, more than 167 fold less than the acceptable MOE of 100.

3. Risk Assessment

a. Occupational and Residential

The Agency has determined that there is a potential exposure to applicators and other handlers during typical use patterns associated with these chemicals. Specific concerns are those of dermal and inhalation exposure to handlers during the loading and application of the chemicals. The Agency is therefore recommending that gloves be worn when handling formulations not already contained in tamper-resistant bait stations or place packs. In addition the Agency is requiring all those who handle powder formulations or any other non-parafinized formulations to wear a dust mask or respirator and protective eyewear during open pouring and application.

The Agency has special concerns, however, about possible post-application exposures to children if (1) baits are not placed out of reach of children or are not applied in tamper-resistant or child resistant bait stations as specified in product labeling; and (2) baits are brightly colored or packaged in a way in which they could be appealing to children or be mistaken by children for food or candy. These concerns are supported by the high number of accidental child ingestion incidents relative to the number of adult ingestion incidents for rodenticide baits in general, and for bromethalin specifically.

EPA is concerned about the continued risk of human exposure, especially to children, to rodenticides used in residential settings. In fact, EPA has gone on record, over the years, to express its concern regarding human exposures and incidents to rodenticides used in and around the home. PR Notice 94-7, Label Improvement Program for the Revision of Use Directions for Commensal Rodenticides and Statement of the Agency's Policies on the Use of Rodenticide Bait Stations, issued by the Agency on September 16, 1994, required registrants of certain rodenticide

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products claimed to control commensal rodents to revise the labeling of such products to bear certain statements concerning "tamper-resistant bait stations." It also informed rodenticide registrants, applicants, and other interested persons of EPA's continued concern for the safe use of rodenticides. Moreover, PR Notice 94-7 outlined EPA's policies regarding the isolation of commensal rodenticides from children, dogs, other pets, domestic animals, and non-target wildlife. PR Notice 94-7, in part, stated the following:

> "Historically, more than 1000 incidents of human exposure to rodent poisons have been reported annually in the U.S. Numbers of human incidents reported have increased greatly in recent years with the advent of a new reporting network. In 1988, more than 10,000 rodenticide incidents were reported in the American Association of Poison Control Center's National Data Collection System. Nearly 90% of these cases involved children under six years of age. Nearly all of such exposures are classed as accidents. The human exposure incidents that are reported may represent less than half of those which occur. Well over 80% of reported human rodenticide exposures involve anticoagulant compounds.
>
> Young children thought to have been exposed to rodenticides are often given some medical attention, although symptoms of poisoning usually are not observed, especially in cases involving anticoagulants which act very slowly. Although young children have been killed by rodenticides, most rodenticide-related deaths of humans result from intentional ingestions by persons much older than five years of age.
>
> While reports summarizing incidents typically do not indicate exactly how exposures have occurred, it is likely that most accidents are related to improper use rather than to improper storage. Accidents of both types are preventable. EPA believes that the large numbers of exposure incidents provide evidence that current policies for promoting bait protection have not been sufficient and, therefore, that tougher, more explicit policies are needed. EPA has not been persuaded by contentions that the relatively low incidences of serious human illnesses caused by accidental exposures to compounds such as warfarin justify selective relaxations of requirements for bait protection…"

Based on available data, young children experience excessive exposures to anticoagulant rodenticides. An analysis of pesticide ingestions in 1989 in children less than 6 years of age compared the number of ingestions to the number of containers reported in U.S. homes in 1990. When 83 active ingredients were ranked, the top 5 products responsible for childhood ingestion per 1000 containers were all anticoagulant rodenticides. The ratio of cases for these rodenticide baits was up to a 100 times higher than the median for all pesticides.

A relatively large percentage of children accidentally exposed to anticoagulant rodenticides are treated in health care facilities. For 99 percent of all cases, however, only minor or no adverse health effects are reported. In some published reports, it has been claimed that children exposed to anticoagulants often are given unnecessary treatments as a precautionary measure. Over several years, some 36 percent of the victims of all anticoagulant rodenticide cases reported to poison control centers are brought to health care facilities for treatment.

Furthermore, rodenticides are acutely toxic to humans. Margins of Exposures (MOEs), when bait is ingested, are less than one. Generally, the Agency considers a MOE of 100 or above to be protective of the public's health. The Agency, for example, has calculated the dose a 10 kg child receives from a 43 gram packet (standard commercial package). The Agency's calculation resulted in a MOE of 0.6 (using the diphacinone NOEL of 0.13 mg/kg).

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Rodenticides, when used as currently sold and marketed, are responsible for a high number of accidental exposures each year. In the recent past, poison control centers have enhanced their ability to capture incident data. Even with improved data collection, the high number of human unintentional or accidental exposures to rodenticides remain constant each year, or may be increasing. From the number of exposures to children, it is clear that children under six years-old are disproportionately more at risk to the continued use of these products in and around the home. Based on these facts, EPA is concerned regarding the risk of exposure to these chemicals to the public, particularly children.

Ingestion of an entire 43 gram packet by a one year old is unlikely. Poisoning specialists estimate the risks to children by assuming a one year old child weighing 10 kg would get one swallow (approximately 5 grams). This provides an estimated dose of 500 mg/kg. For diphacinone and other anticoagulants formulated at 0.005% active ingredients, the dose would be 0.025 mg/kg. Therefore, the margin of exposure from the lowest dose causing clinical effects in adults (0.1 mg/kg) to the dose if a child consumed one swallow (0.1/.025) would be 4.0. In other words, if a child consumed four swallows, the child would be expected to experience clinical effects. Note this assumes that children are no more sensitive to anticoagulants than adults, which may not be the case.

1995 data collected by the American Association of Poison Control Centers (AAPCC) show 17,187 human exposures to all rodenticides. Of these numbers, 14,710 (~ 86%) exposures were attributed to the anticoagulant rodenticides. Of concern to EPA is the number of exposures to children less than six years-old; in 1995, there were a total of 14,900 or approximately 87% of the total exposures. Six thousand four hundred and fifty (6,450) of the total number of human exposures to rodenticides, were significant enough to result in treatment at a health care facility.

1996 data collected by the AAPCC indicate that 17,601 rodenticide exposures occurred to humans. The anticoagulant rodenticides (brodifacoum, bromadiolone, chlorophacinone, diphacinone and its sodium salt, and pival and its sodium salt), accounted for 14,836 or over 84% of the total exposures. Of these exposures, 13,362 (90%) occurred in children less than six years-old. Approximately 5,300 exposures resulted in people seeking treatment at a health care facility.

C. Environmental Assessment

1. Ecological Toxicity Data

Primary toxicity to mammals is very high for all five of these rodenticides. Primary toxicity to birds is high to very high for the single-feeding compounds (brodifacoum, bromadiolone, bromethalin) but mostly moderate for the multiple-feeding compounds (diphacinone, chlorophacinone). Toxicity to aquatic organisms ranges from moderate to very high.

Some secondary toxicity data exist for avian and mammalian predators and/or scavengers for some but not all of these rodenticides. These studies are required to support rodenticides used

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in the field and around buildings in non-urban (i.e., rural, suburban areas). The available laboratory and/or field data indicate that rodents poisoned with brodifacoum or bromadiolone baits can kill avian and mammalian secondary consumers. Sufficient data also exist to indicate that 0.01% a.i. diphacinone bait is secondarily hazardous to birds and mammals and that 0.01% a.i. chlorophacinone bait is hazardous to mammalian predators. Avian data are not available for 0.01% a.i. chlorophacinone bait. Adequate secondary data are not available for birds and mammals for 0.005% a.i. chlorophacinone and diphacinone bait or bromethalin and is being required in this RED. These data are required to support all uses except those bait placements limited to indoors and immediately against the outside walls of buildings.

a. Toxicity to Terrestrial Animals

(1) Birds, Acute and Subacute

(a) Brodifacoum - Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of brodifacoum to birds. The preferred test species is either mallard duck (a waterfowl) or bobwhite quail (an upland gamebird). Results of this test are summarized in Table 29 below.

Table 29 - Brodifacoum Avian Acute Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)	Toxicity Category	MRID No. Author, Year	Study Classification[1]
Mallard duck *(Anas platyrhynchos)*	97.6	0.26	Very highly toxic	41563303 Ross, 1980	Core

[1]Core (study satisfies guideline). Supplemental (study is scientifically sound, but does not satisfy guideline)

Since the LD_{50} falls two orders of magnitude below the 10 mg/kg standard, brodifacoum is very highly toxic to avian species on an acute oral basis. The guideline (71-1) is fulfilled (MRID 41563303).

Two subacute dietary studies using the TGAI are required to establish the toxicity of brodifacoum to birds. The preferred test species are the mallard duck and bobwhite quail. Results of these tests are summarized in Table 30 below.

Table 30 - Brodifacoum Avian Subacute Dietary Toxicity

Species	% a.i.	40-Day LC_{50} (ppm)[1]	Toxicity Category	MRID No. Author, Year	Study Classification
Northern bobwhite quail *(Colinus virginianus)*	97.6	0.8	Very Highly Toxic	124477 Fink, 1978	Core
Mallard duck *(Anas platyrhynchos)*	97.6	2	Very Highly Toxic	124476 Fink, 1978	Core

[1]Test organisms observed an additional three days while on untreated feed.

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Since the LC_{50} is an order of magnitude less than 10 ppm, brodifacoum is very highly toxic to avian species on a subacute dietary basis. The guideline (71-2) is fulfilled (MRIDs 124477 and 124476).

(b) Bromadiolone - Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of bromadiolone to birds. The preferred test species is either mallard duck (a waterfowl) or bobwhite quail (an upland gamebird). Results of this test are summarized in Table 31 below.

Table 31 - Bromadiolone Avian Acute Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)	Toxicity Category	MRID Author, Year	Study Classification
Northern Bobwhite (*Colinus virginianus*)	99.75	170	Moderately toxic	257770 Roth, 1985	Core
Northern Bobwhite	99.75	138	Moderately toxic	41707301 Shapiro	Core

Because the LD_{50} is in the range of 51 to 500 mg/kg, bromadiolone is considered moderately toxic to birds on an acute oral basis. The guideline (71-1) is fulfilled (MRID 257770, 417073-01)).

Two subacute dietary studies using the TGAI are required to establish the toxicity of bromadiolone to birds. The preferred test species are mallard duck and bobwhite quail. Results of these tests are summarized in Table 32 below.

Table 32 - Bromadiolone Avian Subacute Dietary Toxicity

Species	% a.i.	LC_{50} (ppm)	Toxicity Category	MRID Author, Year	Study Classification
Northern Bobwhite (*Colinus virginianus*)	99.75	37.6	Highly toxic	257770 Roth, 1985	Core
Mallard (*Anas platyrhynchos*)	99.75	158	Highly toxic	257770 Fletcher, 1985	Core
Mallard	94.4	440	Highly toxic	249995 Beavers, 1979	Core

Because the LC_{50} values are in the range of < 50 to 500 ppm, bromadiolone is highly to very highly toxic to birds on a subacute dietary basis. The guideline requirements are fulfilled (MRID 257770, 249995).

(c) Bromethalin - Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient is required to establish the toxicity of bromethalin to birds. The preferred test species is either the mallard duck or the bobwhite quail. Results from these tests are summarized in Table 33 below.

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Table 33 -Bromethalin Avian Acute Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)	Toxicity Category	MRID Author, Year	Study Classification
Bobwhite quail (*Colinus virginianus*)	96.3	4.6	Very highly toxic	246173 van Lier, 1981	Core
Bobwhite quail	96.3	11.0	Highly toxic	86741 van Lier, 1981	Core

These results indicate that bromethalin is highly to very highly toxic to birds on an acute oral basis. The guideline requirement (71-1) is fulfilled (MRIDs 246173, 86741, and 86745).

Two subacute dietary studies using the technical grade of the active ingredient are required to establish the toxicity of bromethalin to birds. The preferred test species are mallard duck (a waterfowl) and bobwhite quail (an upland gamebird). Results of these tests are summarized in Table 34 below.

Table 34 - Bromethalin Avian Subacute Dietary Toxicity

Species	% a.i.	LC_{50} (ppm)	Toxicity Category	MRID Author, Year	Study Classification
Bobwhite quail (*Colinus virginianus*)	96.3	210	Highly toxic	86745 van Lier, 1981	Core
Mallard duck (*Anas platyrhynchos*)	96.3	620	Moderately toxic	26526 van Lier, 1981	Core

These results indicate that bromethalin is moderately to highly toxic to avian species on a subacute dietary basis. The guideline requirement (71-2) is fulfilled (MRID 86745 and 26526).

(d) Chlorophacinone - Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of chlorophacinone to birds. The preferred test species is either mallard duck (a waterfowl) or bobwhite quail (an upland gamebird). Results of this test are listed in Table 35 below.

Table 35 - Chlorophacinone Avian Acute Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)[1]	Toxicity Category	MRID No. (Author/Year)	Study Classification
Northern bobwhite quail *(Colinus virginianus)*	100	258[2]	moderately toxic	41513101 (Fletcher and Pedersen 1989)	core

[1] birds were observed for 30 days after dosing
[2] all mortality (28 of 50 birds dosed) occurred within 5 days

Because the LD_{50} is in the range of 51 to 500 mg/kg, chlorophacinone is considered moderately toxic to birds on an acute oral basis. The guideline (71-1) is fulfilled (MRID 41513101).

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Two subacute dietary studies using the TGAI are required to establish the toxicity of chlorophacinone to birds. The preferred test species are mallard duck and bobwhite quail. Results of these tests are summarized in Table 36 below.

Table 36 - Chlorophacinone Avian Subacute Dietary Toxicity

Species	% a.i.	5-Day LC_{50} (ppm)[1]	Toxicity Category	MRID No. (Author/Year)	Study Classification
Northern bobwhite quail *(Colinus virginianus)*	100	56[2]	highly toxic	41513102 (Fletcher and Pedersen 1989)	core
Mallard duck *(Anas platyrhynchos)*	100	172[3]	highly toxic	41513103 (Fletcher and Pedersen 1989)	core

[1] birds were observed an additional 25 days while on untreated feed
[2] all mortality (37 of 60 birds dosed) occurred within 9 days
[3] all mortality (28 of 60 birds dosed) occurred within 22 days

Because the LC_{50} values are in the range of 50 to 500 ppm, chlorophacinone is considered highly toxic to birds on a subacute dietary basis. The guideline (71-2) is fulfilled (MRIDs 41513102, 41513103).

(e) Diphacinone and its sodium salt - Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of diphacinone to birds. The preferred test species is either mallard duck (waterfowl) or bobwhite quail (upland gamebird). Results of this test are summarized below.

Table 37 - Diphacinone and its sodium salt Avian Acute Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)[1]	Toxicity Category	MRID No. (Author/Year)	Study Classification
Northern bobwhite quail *(Colinus virginianus)*	96.9	$400 < LD_{50} < 2000$	moderately toxic	42245201 (Campbell et al. 1991)	supplemental

[1] quail were observed for 21 days after a single oral dose

A reliable LD_{50} was not determined in this study. The 95% confidence interval ranged from 0 to ∞, in part because test concentrations were separated by a factor of 5X rather than the 1.6X separation recommended in the study guideline. Visual inspection of the data indicate that the LD_{50} is less than 2000 mg/kg but greater than 400 mg/kg. Therefore, until an adequate study is submitted, 400 mg/kg will be used as a conservative estimate of the LD_{50}. The guideline (71-1) is not fulfilled.

Two subacute dietary studies using the TGAI are required to establish the toxicity of diphacinone to birds. The preferred test species are mallard duck and bobwhite quail. Results of these tests are summarized in Table 38 below.

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Table 38 - Diphacinone and its sodium salt Avian Subacute Dietary Toxicity

Species	% a.i.	5-Day LC_{50} (ppm)[1]	Toxicity Category	MRID No. (Author/Year)	Study Classification
Northern bobwhite quail *(Colinus virginianus)*	96.9	> 5000[2]	practically nontoxic	42408801 (Long et al. 1992)	core
Mallard duck *(Anas platyrhynchos)*	96.9	906[3]	moderately toxic	42408802 (Long et al. 1992)	core

[1]test organisms (10/level; 6 test concentrations, 3 control groups) were observed an additional 20 days while on untreated feed.
[2]all mortality (10% at 5000 ppm, 30% at 1667 ppm, and 10% at 185 ppm) occurred within 18 days.
[3] all mortality (20 of 60 birds dosed) occurred within 16 days.

Because the lowest LC_{50} value is between 501 to 1000 ppm, diphacinone is considered moderately toxic to birds on a subacute dietary basis. The guideline (71-2) is fulfilled (MRID 42408801, 42408802).

(2) Birds, Chronic Toxicity

Avian reproduction studies are not required for these rodenticides, except for one product. Chronic exposure of birds is not expected for rodenticides used inside and along the outside walls of buildings. Only chlorophacinone and diphacinone have field uses, but applications are either made outside the avian breeding season or bait is applied in enclosed bait stations or other sites (e.g., rodent burrows) inaccessible to nontarget wildlife. The one exception is chlorophacinone product CA890023. Its use according to label directions could subject birds to repeated or continuous exposure during or preceding the breeding season, because it allows an uninterrupted supply of unprotected bait to be maintained for up to four weeks.

(3) Mammals

Wild mammal testing is required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies, intended use pattern, and pertinent environmental fate characteristics. In most cases, rat or mouse toxicity values obtained from the Agency's Health Effects Division (HED) substitute for wild mammal testing. These toxicity values are reported in Tables 39 through 43 below.

(a) Brodifacoum - Mammals, Acute and Chronic

Table 39 - Brodifacoum Mammalian Acute Oral Toxicity

Species Study Duration	% a.i.	Toxicity Value	MRID No.
Laboratory rat *(Rattus norvegicus)*	97.6	♂ 0.418 mg/kg ♀ 0.561 mg/kg	426875

Since the acute and dietary toxicities are much less than 10 mg/kg, brodifacoum is very highly toxic to mammals on an acute and a dietary basis.

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(b) Bromadiolone Mammals, Acute and Chronic

Table 40 - Bromadiolone Mammalian Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)	Toxicity Category	MRID	Study Classification
White lab rat (*Rattus norwegicus*)	0.005	1.1 (female)	Very highly toxic	226423	Supplemental
Substitute for wild rodents	1.0	60 (TEP?)	Moderately toxic	241703	Minimum
White lab mice (House mouse, *Mus musculus*)	Doc.# 007425	1.75	Very highly toxic	007425	Minimum
Substitute for wild rodents	2.5 g/l	.56 -.84	Very highly toxic	009423	Minimum
Beagle dogs Substitute for wild canids 90 day gavage	Unknown	(in μg/kg/day) NOEL = 8 4 of 6 died @ 20 6 of 6 died @ 50	n/a	254001 Chempar, 1981	Supplemental
Beagle dogs Maximum tolerated dose	Unknown	10 mg/kg	n/a	254000 Chabert, 1975	Not rated
Cat - Substitute for wild felids Maximum tolerated dose (Continued)	Unknown	25 mg/kg	n/a	254000 Chabert, 1975	Not rated
Pig	Unknown	5 mg/pig/day killed 3 pigs in 8, 9 & 10 days	n/a	257769 Lyon Vet. School, 1984	Not rated
Ground squirrel	0.005%	Died	n/a	264384	Not rated

The available mammalian data indicate that bromadiolone is moderately to very highly toxic to mammals on an acute oral basis (MRID 226423 and 241703).

(c) Bromethalin - Mammals, Acute and Chronic Toxicity

Table 41 - Bromethalin Mammalian Oral Toxicity

Species	% a.i.	Test type	LD_{50} (mg/kg)	Classification	Toxicity Category	MRID
Laboratory rat (*Rattus norvegicus*)	TGAI in Acacia 0.005%	Acute oral	♀ = 9.1 ♂ = 10.7	Minimum	Very highly toxic	241521
Laboratory rat	TGAI in Acacia 0.005%	Acute oral	♀ = > 500 (> 2.5 a.i.)	Minimum	Very highly toxic	246172
Laboratory Mouse (*Mus musculus*)	TGAI in PEG-200	Acute oral	♀ = 8.1 ♂ = 5.3	Minimum	Very highly toxic	241521
Laboratory Mouse	TGAI in Acacia	Acute oral	♀ = 28.9 ♂ = 35.9	Minimum	Very highly toxic	241521
House cat (*Felis domesticus*)	TGAI in PEG-200	Acute oral	18	Minimum	Highly toxic	241521
Domestic dog (*Canis familiaris*)	TGAI in PEG-200	Acute oral	4.8	Minimum	Very highly toxic	241521

The results indicate that bromethalin is highly to very highly toxic to small mammals on an acute oral basis.

(d) Chlorophacinone - Mammals, Acute and Chronic Toxicity

Table 42 - Chlorophacinone Mammalian Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)	Toxicity Category	MRID No.
Laboratory rat *(Rattus norvegicus)*	100	6.2[1,2]	Very highly toxic	418753-01

[1] ♂ = 3.15 mg/kg, ♀ = 10.95 mg/kg
[2] mortalities occurred 4 to 9 days after treatment

The results indicate that chlorophacinone is very highly toxic to small mammals on an acute oral basis.

(e) Diphacinone and its sodium salt - Mammals, Acute and Chronic Toxicity

Table 43 - Diphacinone and its sodium salt Mammalian Oral Toxicity

Species	% a.i.	LD_{50} (mg/kg)	Toxicity Category	MRID No.
Laboratory rat *(Rattus norvegicus)*	96.9	7.0	very highly toxic	422452-02
Coyote *(Canas latrans)*	not reported	0.6	very highly toxic	(Savarie et al. 1979)[1]
Mongoose *(Herpestes auropunctatus)*	not reported	0.2	very highly toxic	(DWRC)[2]

[1]reported by the Denver Wildlife Research Center (Savarie et al. 1979, ASTM STP 693, pp. 69-79)
[2]reported by the Denver Wildlife Research Center in EUP application for mongoose control in Hawaii

These results indicate that diphacinone is very highly toxic to mammals.

b. Toxicity to Aquatic Animals

(1) Toxicity to Freshwater Fish

Two freshwater fish toxicity studies using the TGAI are required to establish the toxicity of brodifacoum to fish. The preferred test species are rainbow trout (a coldwater fish) and bluegill sunfish (a warmwater fish). Results of these tests are summarized in Tables 44 through 48 below.

(a) Brodifacoum - Freshwater Fish Acute Toxicity

Table 44 - Brodifacoum Freshwater Fish Acute Toxicity (Flow through)

Species	% a.i.	96-hour LC_{50} (ppm)	Toxicity Category	MRID No. Author, Year	Study Classification
Rainbow trout *(Oncorhynchus mykiss)*	97.6	0.015 measured stock	Very Highly Toxic	088011 Hill, 1976	Supplemental, but satisfies the requirement
Bluegill sunfish (*Lepomis macrochirus*)	97.6	0.025 measured stock	Very Highly Toxic	124472 Hill, 1978	Supplemental, but satisfies the requirement

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Since the LC_{50} is in the range 0.1 to 1 ppm for the bluegill and is an order of magnitude less than 0.1 ppm for the trout, brodifacoum is highly toxic to very highly toxic to freshwater fish on an acute basis. Although all the studies were "supplemental," they were accepted as fulfilling the Guidelines' requirement (72-1), because of the use pattern and the extremely low solubility of brodifacoum (MRID 088011, 124474, and 124473).

(b) Bromadiolone - Freshwater Fish Acute Toxicity

Table 45 - Bromadiolone Freshwater Fish Acute Toxicity

Species	% a.i.	LC_{50} ppm a.i.	MRID	Toxicity Category	Study Classification
Rainbow trout	94.4	0.24	232567 Stiefer, 1978	Moderate	Fulfills Guideline Requirement
Bluegill sunfish	94.4	3.0	232567 Stiefer, 1978	Moderate	Fulfills Guideline Requirement

The results of the 96-hour bluegill sunfish and rainbow trout acute toxicity studies indicate that bromadiolone is moderately toxic to fish. The guideline requirements are fulfilled (MRID 232567).

(c) Bromethalin Freshwater Fish Acute Toxicity

Table 46 - Bromethalin Freshwater Fish Acute Toxicity

Species	% a.i.	LC_{50} (ppb)	Toxicity Category	MRID Author, Year	Study Classification
Bluegill sunfish (*Lepomis macrochirus*)	99	598	Very highly toxic	42733501 Conner, 1993	Supplemental
Rainbow trout (*Oncorhynchus mykiss*)	99	38	Very highly toxic	42733502 Conner, 1993	Supplemental

These results indicate that bromethalin is very highly toxic to freshwater fish on an acute basis. The guideline requirement (72-1) is fulfilled (MRID 42733501 and 42733502).

(d) Chlorophacinone - Freshwater Fish Acute Toxicity

Table 47 - Chlorophacinone Freshwater Fish Acute Toxicity*

Species	% a.i.	96-hour LC_{50} (ppb)	Toxicity Category	MRID No. (Author/Year)	Study Classification
Rainbow trout *(Oncorhynchus mykiss)*	100	450	highly toxic	42356103 (Machado 1992)	core
Bluegill sunfish *(Lepomis macrochirus)*	100	710	highly toxic	42356102 (Machado 1992)	core

*Using flow-through (measured) testing

Because the LC_{50} falls in the range of 100 to 1000 ppb, chlorophacinone is considered highly toxic to freshwater fish on an acute basis. The guideline (72-1) is fulfilled (MRID 42356102, 42356103).

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(e) Diphacinone and its sodium salt - Freshwater Fish Acute Toxicity

Table 48 - Diphacinone and its sodium salt Freshwater Fish Acute Toxicity*

Species	% a.i.	96-hour LC_{50} (ppm)	Toxicity Category	MRID No. (Author/Year)	Study Classification
Rainbow trout *(Oncorhynchus mykiss)*	95.8	2.6	moderately toxic	43249502 (Machado 1994)	core
Bluegill sunfish *(Lepomis macrochirus)*	95.8	7.5	moderately toxic	43249501 (Machado 1994)	core

*Using flow-through (measured) testing

Because the LC_{50} falls in the range of 1 to 10 ppm, diphacinone is considered moderately toxic to freshwater fish on an acute basis. The guideline (72-1) is fulfilled (MRID 42356102, 42356103).

(2) Toxicity to Freshwater Invertebrates

(a) Brodifacoum - Acute Toxicity to Freshwater Invertebrates

A freshwater aquatic invertebrate toxicity test using the TGAI is required to establish the toxicity of brodifacoum to aquatic invertebrates. The preferred test species is *Daphnia magna*. Results of this test are summarized in Table 49 below.

Table 49 - Brodifacoum Freshwater Invertebrate Acute Toxicity

Species	% a.i.	48-hour LC_{50}/EC_{50} (ppm)	Toxicity Category	MRID No. Author, Year	Study Classification
Waterflea *(Daphnia magna)* Static	97.6	0.98 nominal	Highly Toxic	128442 Gerry, 1978	Supplemental, but satisfies requirements

Since the LC_{50} falls in the range 0.1 to 10 ppm, brodifacoum is Highly Toxic to aquatic invertebrates on an acute basis. Although the study was "Supplemental," it was accepted as fulfilling the Guidelines' requirement (72-1), because of the use pattern and the extremely low solubility of brodifacoum (MRID 128442).

(b) Bromadiolone-Acute Toxicity to Freshwater Invertebrates

The minimum testing required to assess the hazard of a pesticide to freshwater invertebrates is a freshwater aquatic invertebrate toxicity test, preferably using first instar *Daphnia magna* or early instar amphipods, stoneflies, mayflies, or midges. The available information is summarized in Table 50 below.

Table 50 - Bromadiolone Freshwater Invertebrate Acute Toxicity

Species	% a.i.	EC_{50} (ppm)	Toxicity Category	MRID Author, Year	Study Classification
Waterflea *(Daphnia magna)*	Unknown	0.24	Highly toxic	232567 LeBlanc, 1977	Core
Waterflea	98.7	2	Moderately toxic	420933-02 Boeri, 1991	Core

Because the EC_{50} falls in the range of 0.1 to 10 ppm, bromadiolone is considered moderately to highly toxic to freshwater invertebrates on an acute basis. The guideline requirement is fulfilled (MRID 232567, 420933-02).

(c) Bromethalin - Acute Toxicity to Freshwater Invertebrates

A freshwater aquatic invertebrate toxicity test using the technical grade of the active ingredient is required to establish the toxicity of bromethalin to invertebrates. The preferred test species is *Daphnia magna*. Results of this test are summarized in Table 51 below.

Table 51 - Bromethalin Freshwater Invertebrate Acute Toxicity

Species	% a.i.	EC_{50} (ppb)	Toxicity Category	MRID Author, Year	Study Classification
Waterflea (*Daphnia magna*)	96.3	2.0	Very highly toxic	86751 van Lier, 1981	Supplemental
Waterflea	99	5.1	Very highly toxic	42733503 Conner, 1993	Supplemental

The results indicate that bromethalin is very highly toxic to aquatic invertebrates on an acute basis. The guideline requirement (72-2) is fulfilled (MRIDs 86751 and 42733503).

(d) Chlorophacinone - Acute Toxicity to Freshwater Invertebrates

A freshwater aquatic invertebrate toxicity test using the TGAI is required to establish the toxicity of chlorophacinone to aquatic invertebrates. The preferred test species is *Daphnia magna*. Results of this test are summarized in Table 52 below.

Table 52 - Chlorophacinone Freshwater Invertebrate Acute Toxicity*

Species	% a.i.	48-hour EC_{50} (ppb)	Toxicity Category	MRID No. (Author/Year)	Study Classification
Waterflea *(Daphnia magna)*	100	640	highly toxic	42356101 (Putt 1992)	core

*Using Flow-through (measured) testing

Because the EC_{50} is between 100 to 1000 ppb, chlorophacinone is considered highly toxic to aquatic invertebrates. The guideline (72-2) is fulfilled (MRID 42356101).

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(e) Diphacinone and its sodium salt - Acute Toxicity to Freshwater Invertebrates

A freshwater aquatic invertebrate toxicity test using the TGAI is required to establish the toxicity of diphacinone to aquatic invertebrates. The preferred test species is *Daphnia magna*. Results of this test are summarized in Table 53 below.

Table 53 - Diphacinone and its sodium salt Freshwater Invertebrate Acute Toxicity*

Species	% a.i.	48-hour EC_{50} (ppm)	Toxicity Category	MRID No. (Author/Year)	Study Classification
Waterflea *(Daphnia magna)*	98.7	1.8	moderately toxic	42282201 (Putt 1992)	core

*Using Flow-through (measured) testing

Because the EC_{50} in the range of 1 to 10 ppm, diphacinone is considered moderately toxic to aquatic invertebrates on an acute basis. The guideline (72-2) is fulfilled (MRID 42282201).

c. Birds and Mammals, Secondary Toxicity Tests

The Agency requires data to determine if vertebrate pesticides labeled for outdoor use pose a hazard to secondary consumers. A whole body residue analysis with a target species is initially required to determine the toxicant load in the carcass of a primary consumer. If a significant toxicant load occurs, secondary poisoning studies with a mammalian predator and a predacious bird are required. If the toxicant load is not significant, the secondary studies are not required. For chlorophacinone, studies are required on the 0.005% a.i. bait only if a hazard exists for the 0.01% a.i. bait. The study in Table 54 was previously submitted.

Table 54 - Mammalian Secondary Toxicity

Species	Food/Test Material	Food Amount	Results	MRID No. (Author/Year)	Study Classification
Coyote *(Canis latrans)*	Ground squirrels poisoned with 0.01% Chlorophacinone bait over a 6-day period	1 dead ground squirrel/day for 5 consecutive days[1]	3 of 7 coyotes died (1 adult, 2 subadult) during the 30-day posttreatment period	427609-02 (Marsh and Howard 1986)	core

[1]the coyotes were held an additional 30 days for observation

Three coyotes died from multiple feedings on ground squirrels poisoned with 0.01% a.i. bait. One of four adults died of internal hemorrhaging, whereas the other three remained healthy with no observable symptoms. Of the three subadults tested, two died of internal hemorrhaging; the survivor remained healthy. The amount of toxicant ingested secondarily was not determined. The study is adequate to indicate that rodents poisoned with 0.01% Chlorophacinone baits pose a secondary hazard to coyotes and presumably other mammalian carnivores and scavengers. No whole body residue analysis or avian data have been submitted.

Because the 0.01% a.i. bait resulted in secondary mortality to coyotes, a study is required using the 0.005% a.i. bait. The data requirement (70-A-SS) for a secondary poisoning study with

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a mammal is fulfilled for the 0.01% a.i. bait (MRID 427609-02) but is outstanding for the 0.005% a.i. bait. The data requirements for a secondary poisoning study (70-B-SS) and whole body residues in a target species (70-C-SS) are not fulfilled for the 0.01% a.i. and 0.005% a.i. bait.

d. Terrestrial Field and Simulated Field Testing

The studies summarized in Table 55 below were submitted to support Chlorophacinone registrations for California ground squirrel control or for vole control in orchards.

Table 55 - Chlorophacinone Terrestrial and Simulated Field Tests

Target Species	Treatment	Nontarget Kill	MRID No. (Author/Year)	Study Classification
California Ground Squirrel *(Spermophilus beecheyi)*	0.01% a.i. and 0.005% a.i. grain baits	poisoning confirmed in 14/15 mice and 2/2 woodrats examined on 5 0.01% a.i. bait plots and 9/13 mice and 3/3 woodrats on 5 0.005% a.i. bait plots[1]	439222-01 (Baroch 1996)	supplemental[2]
California Ground Squirrel	bait station with 0.005% a.i. grain bait	poisoning confirmed in 3/3 mice examined on 2 bait plots[1]	439222-02 (Baroch 1996)	supplemental[2]
California Ground Squirrel	0.005% a.i. pelleted bait	poisoning confirmed in 2 dead rabbits (residue levels of 0.011 and 1.16 ppm in GI tract)	416493-01 (Poché 1991)	supplemental[2]
Pine vole *(Microtus pinetorum)*	1 ground spray at 0.3 lb ai/acre	No mortality or adverse affects were observed in six captive opossums exposed for 14 days to sprayed ground vegetation in an orchard	234579 (Libke et al. 1972)	supplemental[3]

[1]poisoning was indicated by blue-dyed bait in the GI tract, blue stain in fatty tissues, subdermal hematomas, and/or internal hemorrhaging
[2]the study was an efficacy test that provided some information on nontarget hazards
[3]sample size (6 opossums) was small

The food bait studies were designed primarily to assess efficacy of 0.01% a.i. and 0.005% a.i. chlorophacinone baits to the California ground squirrel in the field. The orchard spray study was designed to determine if opossums exposed to sprayed ground vegetation in an orchard setting were adversely effected. All four studies were too limited in scope for a broad evaluation of the potential impacts of chlorophacinone on nontarget species. However, the information obtained indicates that chlorophacinone baits pose a primary risk to some nontarget species, especially granivorous rodents. In two of the food baiting studies (MRID Nos 43922201, 43922202), an effort was made to collect carcasses found during spot-baiting trials with 0.01% a.i. and 0.005% a.i. grain baits and a bait station trial in which 0.005% a.i. grain bait was available in bait stations. Based on the presence of blue dye incorporated into the bait and/or signs of internal or external hemorrhaging, 91% (130/143) of the ground squirrels recovered and 86% (31/36) of nontarget mice (*Peromyscus spp., Perognathus inornatus*) and woodrats (*Neotoma fuscipes*) examined were poisoned. There was no evidence that the 4 rabbits (*Sylvilagus auduboni*), 2 pocket gophers (*Thomomys bottae*), or 1 mourning dove (*Zenaida macroura*) found were poisoned. Although no evidence was found to indicate that birds consumed baits or that avian and

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mammalian predators and scavengers were adversely effected in any of these studies, none were designed to assess such risks. In another study (MRID No. 416493-01) designed to assess efficacy of 0.005% a.i. chlorophacinone bait against the California ground squirrel, two dead rabbits were recovered. Both had bait in the GI tract. How the rabbits were exposed is not known; presumably, they entered bait stations or gleaned spilled bait.

e. Birds and Mammals, Secondary Toxicity Tests

The Agency requires data to determine if vertebrate pesticides labeled for outdoor use pose a hazard to secondary consumers. A whole body residue analysis with a target species is required to determine the toxicant load in the carcass of a primary consumer. Secondary poisoning studies with a mammalian predator and a predacious bird are required only if a biologically significant toxicant load exists. The studies summarized in Table 56 below were previously submitted or published.

Table 56 - Diphacinone Avian and Mammalian Secondary Toxicity

Species	No. Tested	Food/ Test Material	Days Dosed	Results	MRID No. (Author/Year)	Study Classification
Barn owl *(Tyto alba)*	2	wild rats poisoned with 0.005% a.i. grain bait[1] or deer mice poisoned with 0.01% a.i. grain bait[2]	10	both barn owls survived with no apparent signs of intoxication; 2 great horned owls died after 14 days; the saw-whet owl died after 7 days[3]	40077202 (Mendenhall and Pank 1980)	supplemental[4]
Great-horned owl *(Bubo virginianus)*	3		10			
Saw-whet owl*(Aegolius acadicus)*	1		5			
Golden eagle *(Aquila chrysaetos)*	7	sheep muscle containing 2.7 ppm Diphacinone	5-10	all survived, but prothrombin times and hematocrit values were temporarily affected	(Savarie et al. 1979)[6]	n/a
Rat *(Rattus norvegicus)*	72	muscle tissue from captive coyotes killed with a single oral dose	6	coyote muscle containing 0.5 ppm Diphacinone killed 4 of 8 rats; muscle with < 0.5 ppm Diphacinone caused no mortality	(Savarie et al. 1979)[6]	n/a
Mink *(Mustella vison)*,	3	nutria[5] poisoned with 0.01% a.i. carrot bait	5-18	mink died on days 5, 8, and 18; dogs died days 6, 6, and 10	(Evans and Ward 1967)[7]	supplemental[4]
Dogs	3		6-10			
Ermine *(Mustela erminea)*	2	deer mice (2/day) poisoned with 0.01% a.i. grain bait[2]	5	1 ermine died after eating 10 mice in 7 days, the other ate only 2 mice and survived; all skunks survived	002467 (Pank and Hirata 1976)	supplemental[4]
Striped skunk *(Mephitis mephitis)*	5		5			

[1]dead rats *(Rattus spp.)* fed to barns owls were given a free choice of poisoned bait or untreated lab. chow for five days
[2]dead mice *(Peromyscus maniculatus)* fed to great-horned owls, saw-whet owls, ermine, and striped skunks had received 10 daily doses of 1 g oat groats containing 0.01% Diphacinone
[3]the 3 great-horned owls, including the survivor, and the saw-whet owl were necropsied at the end of the test and all displayed severe symptoms of anticoagulant poisoning; coagulation times were elevated from 0.5 to 1.5 min. prior to exposure to 22 to 34+ min. on day 8; coagulation had only partially recovered (6 min.) by day 15 in the owl that survived
[4] small sample size and uncertain dosage levels
[5]*Myocastor coypus*
[6]in E.E. Kenaga (ed.), Avian and Mammalian Wildlife Toxicology, ASTM STP 693, pp. 69-79
[7]J. Amer. Veterinary Med. Assoc. 151:856-861

Collectively, these studies indicate that some birds and mammals are susceptible to secondary poisoning from consuming diphacinone residue in animal tissue. The toxicant loads

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of the rats, mice, and nutria fed to raptors, mustelids, and dogs are not known but were sufficiently high to cause mortality in most species. The relationship between target loads in poisoned target species and the levels presented in coyote and sheep muscle was not established. Moreover, the amount of toxicant present in the coyote muscle was found to be considerably lower than that contained in the small intestine, liver, kidney, and heart tissues. The data are adequate to demonstrate that avian and mammalian predators may be killed from consuming target species poisoned with 0.01% a.i. bait. Therefore, the data requirements for secondary toxicity tests with a mammal (70-A-SS) and bird (70-B-SS) are fulfilled for the 0.01% a.i. bait but not for the 0.005% a.i. bait. Because toxicant loads in a target species have not been determined, that data requirement (70-C-SS) also is not fulfilled for the 0.005% a.i. bait.

2. Environmental Fate

a. Environmental Fate and Transport

(1) Brodifacoum Environmental Fate and Transport

Based on the use pattern of brodifacoum, only hydrolysis (161-1), aerobic soil metabolism (162-1), and mobility (163-1) data are required. The Agency has valid data for hydrolysis, aerobic soil metabolism, and 30-day unaged mobility. The degradates and their accumulation and decline pattern were not identified in the aerobic soil metabolism study. However, because brodifacoum is typically applied in bait stations and/or only in and around structures, bait is only 50 ppm (0.005%) a.i., and brodifacoum is immobile in soil, potential contamination of surface and ground water is low. Therefore, degradate identification, accumulation and decline, aged column leaching, field dissipation, and adsorption/desorption data are not required.

Brodifacoum is stable to hydrolysis at pH 5, 7, and 9, persistent in soil (t-1/2 = 157 days), and immobile in soil columns. Unaged column leaching studies indicated that parent brodifacoum is immobile in columns of British sand, sandy clay loam, silty clay and clay; 78-94% of the applied radioactivity remained in the layer of unaged soil and < 0.32 % was recovered in the leachate. Valid Kds were not obtained, but they are expected to be relatively high because of the immobility indicated in the column leaching studies. Brodifacoum is persistent, but little, if any, contamination of surface and ground waters is expected because of its use pattern and immobility in soil.

(a) Brodifacoum Degradation

Hydrolysis: Brodifacoum is stable to hydrolysis at pH 5, 7, and 9. The guideline requirement (161-1) is fulfilled. (MRID 42237701).

(b) Brodifacoum Metabolism

Aerobic Soil Metabolism: Brodifacoum degraded with a half-life of 157 days in sandy clay loam soil incubated in the dark at 21 C and 75% of 0.33 bar moisture capacity. No volatile

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degradates other than $^{14}CO_2$ were identified; $^{14}CO_2$ comprised 36% of the applied radioactivity at 52 weeks posttreatment. Up to eleven [^{14}C]compounds other than [^{14}C]brodifacoum were isolated from the soil extracts at 2.07 to 17.34% of the applied (0.008 to 0.067 ppm), but none were identified. Identification and accumulation and decline of a major metabolite (17.34% of applied) is not required for currently registered uses because of the limited potential for metabolite contact with the soil. The guideline requirement (162-1) is fulfilled. (MRID 42579401)

(c) Brodifacoum Mobility

Unaged Column Leaching: Based on column leaching experiments, aged 30 days, brodifacoum residues (89-97% as brodifacoum) were relatively immobile in columns of sand, sandy clay loam, silty clay, or clay soils from Great Britain that were leached with 20 inches of 0.01 M calcium chloride solution. Following leaching, 78.8 - 94.8% of the applied radioactivity remained in the layer of aged soil and $\underline{<}$ 0.32% was recovered in the leachate. No degradates were identified in the soil or leachate. The test material was aged for 30 days, but after 30 days the major brodifacoum degradates had not been formed, and parent brodifacoum remained essentially intact. Therefore, this study satisfied requirements for unaged column leaching rather than aged column leaching for which the study was originally designed. Due to the very limited potential for contact with the soil, aged column leaching data are not required. The guideline requirement (163-1) is fulfilled. (MRID 42568301)

Adsorption/Desorption: These data are considered to be of uncertain value and should not be used to predict the environmental behavior of brodifacoum residues. This study is unacceptable because acetone was used as a co-solvent, resulting in brodifacoum concentrations far in excess of possible concentrations in the field. Brodifacoum is soluble in acetone at up to 20,000 parts per million. Brodifacoum was applied to a 2 g soil/20 ml water slurry at 0.9 - 4.5 ppm, although the study author stated that brodifacoum solubility in water is < 0.1 ppm in 0.01 N $CaCl_2$ solution. It is not possible to extrapolate these results into realistic solubility ranges, or to discount the likelihood that brodifacoum was partitioned out of the aqueous solution and into the acetone co-solvent. Also, Freundlich K values were not calculated. (MRID 42024501)

(2) Bromadiolone Environmental Fate and Transport

Based on the use pattern of bromadiolone, only hydrolysis (Guideline 161-1), aerobic soil metabolism (Guideline 162-1), and mobility adsorption/desorption (163-1) data are required. Fish bioaccumulation data also are available. The data requirement for adsorption/desorption is not fulfilled, but the available data are sufficient to characterize the environmental fate of bromadiolone for the labeled rodenticide use. The data requirement for field dissipation studies was waived, because terrestrial non-food use is limited and because baits are typically placed indoors or in bait stations. Additional data may be required if other uses are registered.

Sufficient information exists for a qualitative environmental fate assessment. Parent bromadiolone is not persistent to aerobic soil metabolism ($t_{1/2}$ = 14 days) and can generally be considered immobile except in soils of low organic matter and clay, such as sand. Parent bromadiolone was classified as immobile, based on aged (30 days) and unaged soil column

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leaching studies. Ninety-nine % of the leached radioactivity was bromadiolone isomers. Parent K_ds are 5.4 (silt loam) and 13.2 (loamy sand). Bromadiolone was stable to hydrolysis in pH 5, 7 and 9 buffer solutions.

Although the parent compound is not persistent and is essentially immobile except in soils low in organic matter and clay, two of the major degradates identified in the aerobic soil metabolism study are persistent. These degradates, #1 and #3, reached 19 and 25% of the applied in 120 and 270 days, respectively. Another degradate, bromadiolone ketone, reached 19% of the applied in 14 days. No mobility information is available for the degradates. Additional information to determine the K_ds would be necessary for a more comprehensive fate assessment. However, the available data are sufficient to categorize the environmental fate of bromadiolone for the labeled rodenticide use.

Bromadiolone can leach in soils low in organic matter and clay; leaching was observed in a soil column (silt loam) with 0.5% organic matter and 3.2% clay. Movement is correlated with clay and organic matter content; sand soil, with little or no organic matter and clay, leached 62% of the total radioactivity with the solute. However, because bromadiolone is applied as a food bait (pellets, place packs, or paraffinized blocks), leaching is expected to be minimal.

(a) Bromadiolone Degradation

Hydrolysis: Bromadiolone parent is stable to hydrolysis at 5, 7, and 9. The data requirement for hydrolysis is satisfied. (MRID 42237501)

(b) Bromadiolone Metabolism

Aerobic Soil Metabolism: The half-life of the parent is 14 days. Two major degradates, #1 [1,3-diphenyl-5(4'-bromo-biphenyl) pentane-1-ol] and #3 [1,3-diphenyl-5(4'-bromo-biphenyl) pentane-1,5-diol] are persistent. The mobility and toxicity of these two degradates are unknown. The data requirement for aerobic soil metabolism is satisfied. (MRID 43594301)

(c) Bromadiolone Mobility

Leaching/Adsorption/Desorption: The parent is generally immobile except in soils low in organic matter and clay. Aged and unaged column leaching studies showed no movement of radioactive bromadiolone; 97% of radioactivity remained in the top one inch. Two major degradates identified in the "new" aerobic soil metabolism study (MRID 43594301) have not been tested for mobility.

Bromadiolone can leach in soils low in organic matter and clay. Leaching was observed in a soil column (silt loam) with 0.5% organic matter and 3.2% clay. Movement of bromadiolone is correlated with clay and organic matter content. Sandy soil (little or no organic matter and clay) leached 62% of the total radioactivity with the solute.

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Two major degradates, #1 [1,3-diphenyl-5(4'-bromo-biphenyl) pentane-1-ol] and #3 [1,3-diphenyl-5(4'-bromo-biphenyl) pentane-1,5-diol], detected in the aerobic soil metabolism study (MRID 43594301) are persistent. The mobility and toxicity of these two degradates are unknown. Therefore, the adsorption/desorption data requirement is not satisfied; however, the available data are sufficient to characterize the environmental fate of parent Bromadiolone. Leaching data is needed on the two major degradates noted above. (MRID 43000702, 42237501, 161972, 161973, 161988)

(d) Bromadiolone Accumulation

Accumulation in Fish: Bioaccumulation concentration factors (BCFs) of 160X and 1658X were obtained for edible and non-edible tissues in bluegill sunfish, respectively. The BCF for the non-edible portion was 11.3 higher than the edible portion and 3.2 higher that the value obtained for the whole fish. Twenty-four percent, 35.8% and 16% of Bromadiolone residues were retained in whole, edible tissues, and non-edible tissues, respectively, after 14 days of depuration. Total bluegill mortality during the 44 day test 43.9% (36/82 fish) and only 1.2% for the control. The study for fish bioaccumulation is scientifically valid and is considered supplemental. The data requirement is not satisfied because radioactive residues in the fish tissues were not identified. The identification of extractable residues at concentrations $\geq$ 10% is a critical element of the fish accumulation study. One of the primary reasons this study is conducted is to identify the residues that accumulate in fish after exposure to a constant level of a pesticide. (MRID 00161965)

(3) Bromethalin Environmental Fate and Transport

Based on the use pattern and because bromethalin is formulated as a pelleted rodenticide, it is probable that any contact with soil and water will be minimal. Therefore, only hydrolysis (Guideline 161-1), aerobic soil metabolism (Guideline 162-1) and leaching (Guideline 163-1) data are required at this time. No data were submitted to assess the mobility of bromethalin. However, leaching data are required.

The available data are sufficient for a cursory environmental fate assessment for the current use pattern. The data submitted indicate that bromethalin is stable to hydrolysis and is persistent (half-life = 178 days) to aerobic soil metabolism. Data are not available to assess the mobility of parent bromethalin or its major degradate. However, because bromethalin is formulated as a pelleted food bait, total usage of the active ingredient is low, and field uses do not exist, ground water leaching and surface runoff are expected to be minimal.

(a) Bromethalin Degradation

Hydrolysis: [^{14}C]bromethalin, at approximately 1 ppm, was stable in aqueous buffered pH 5, 7, and 9 solutions that were incubated at 25 °C in the dark for 30 days. At 35 days post-treatment, bromethalin comprised 91.2-99.9% of the radioactivity in the three buffer solutions and was the only [^{14}C]compound detected. At the conclusion of the study, the material balance for the three solutions was 93.0-100.0% of the applied radioactivity. The data requirement (Guideline 161-1) is fulfilled. (MRID 42438701).

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(b) Bromethalin Metabolism

Aerobic Soil Metabolism: Parent compound accounted for 102.4% of the applied radioactivity at the start and decreased to 22.3% by the end of the study. The calculated half-life for parent compound was 178 days (y = -0.0039x + 4.38, r = -0.954). The parent compound would be expected to be relatively stable to microbial/chemical degradation in the soil.

Up to 15.4% of the applied radioactivity was non-extractable residues; while up to 5.1% of the applied radioactivity was ^{14}C-volatiles, including 2.2% CO_2. Because the concentration of volatiles was so low, no attempt was made to characterize them. Unknown degradates ranged up to 3.6% of applied. One degradate at a concentration of 43.8% of the applied was identified as desnitrobromethalin. The data requirement (162-1) is fulfilled. (MRID 43007901)

(c) Bromethalin Mobility

Leaching/adsorption/desorption: The leaching/adsorption/desorption data requirement (Guideline 163-1) is not fulfilled. Mobility data for bromethalin parent are needed. Furthermore, a major degradate detected in the aerobic soil metabolism study, desnitrobromethalin, comprising 43% of the applied, also appears to be persistent and its mobility is unknown. Leaching data also are needed for this degradate. Because bromethalin is formulated as a pelleted rodenticide primarily for use in and around buildings; it is probable that contact with soil and water will be minimal.

(4) Chlorophacinone Environmental Fate and Transport

Data have been submitted for hydrolysis (Guideline 161-1), photolysis in water (Guideline 161-2), photolysis on soil (Guideline 161-3), aerobic soil metabolism (Guideline 162-1), and leaching-adsorption/desorption (Guideline 163-1). These studies are acceptable and can be used to fulfill their respective environmental fate data requirements. No additional data are required to support the reregistration of chlorophacinone.

Based on the available data, chlorophacinone appears to be very immobile and readily degradable in the environment. It has the following characteristics: (1) low water solubility (34 ppm at 25°); (2) stable to hydrolysis at pH 5, 7, and 9; (3) very susceptible to direct photolysis in water (half-life of 37 minutes at pH 7); (4) moderately susceptible to photodegradation on soil (half-life of 4 days); (5) moderately degradable in a sandy clay loam soil under aerobic conditions (half-lives of 21-45 days); (6) expected to be very immobile in soil (K_{ads} = 341; K_{oc} = 43,411); (7) volatilizes slowly from water and soil (vapor pressure = $3.6x10^{-6}$ mm Hg; Henry's Law constant = $5.2x10^{-8}$ at m-m^3/mol); and (8) does not accumulate in fish at a significant level (K_{ow} = 94).

Results from the aqueous photolysis, the soil photolysis, and the aerobic soil metabolism studies suggest that chlorophacinone degrades very rapidly to o-phthalic acid and p-chlorophenylphenyl acetic acid through the cleavage of the indandione ring. The carboxylic acid on the o-phthalic acid was further cleaved and transformed into carbon dioxide.

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In the field, chlorophacinone is expected to be bound very tightly with soil. Most of the chemical is expected to remain in the top soil layers, and its potential to reach ground water is very low. Surface water contamination may occur in less-permeable areas and in areas near water bodies. The mechanism for chlorophacinone to reach surface waters would likely be via adsorption to eroding soil, as opposed to dissolution in runoff water. Because of its high adsorption coefficient, most chlorophacinone would be partitioned in the suspended and bottom sediments instead of in the water column. Chlorophacinone might drift into surface waters from its use as a spray in orchards. However, because the spray is applied at a low height, near ground level, the resulting drift may be decreased by the surrounding orchard trees.

(a) Chlorophacinone Degradation

Hydrolysis: Indan-labeled [^{14}C]chlorophacinone at 1.07 ppm was relatively stable in sterile aqueous buffered solutions (pH 5, 7, and 9) incubated in the dark at 25 $\pm$ 1 C for 30 days. Two degradates (p-chlorophenyl acetic acid and o-phthalic acid) were detected from all three solutions. In the pH 5 solution, chlorophacinone was 113% of the applied immediately posttreatment, 88.5% of the applied at 14 days, and 96% of the applied at 30 days. p-Chlorophenylphenyl acetic acid was a maximum 0.4% of the recovered at 14 days, and o-Phthalic acid was a maximum 0.7% of the recovered at 30 days. In the pH 7 solution, chlorophacinone was 98.5-112.5% of the applied at 0 through 14 days and 84.1-85.9% of the applied at 30 days. p-Chlorophenylphenyl acetic acid and o-phthalic acid were each a maximum 0.2% of the recovered during the study. In the pH 9 solution, chlorophacinone was 68.4-81.2% of the applied at all sampling intervals. p-Chlorophenylphenyl acetic acid and o-Phthalic acid were each a maximum 0.4% of the recovered during the study. The material balances determined prior to partitioning ranged from 94 to 105% of the applied. The hydrolysis data requirement (Guideline 161-1) is fulfilled. (MRID 42205501)

Photodegradation in Water: Indan-labeled [^{14}C]Chlorophacinone at approximately 1 ppm degraded with a half-life of 37 minutes in pH 7 buffered solutions continuously irradiated with a xenon arc lamp for 24 hours at 23.9-25.9 C. In contrast, Chlorophacinone was $\geq$ 97.4% of the applied at all sampling intervals in dark controls incubated at 25 $\pm$ 1 C for 24 hours. During the study, material balances were 94.6-103.3% of the applied for the irradiated samples and $\geq$ 100% for the dark controls.

Photodegradation on Soil: Ring-labeled [^{14}C]Chlorophacinone at 10.8 ppm photodegraded with a half-life of 4 days on sandy clay loam soil irradiated with an artificial light source (xenon lamp) for up to 30 days at 19.9-26.9 C. By comparison, [^{14}C]Chlorophacinone degraded with a half-life of 95 days in the dark controls. Two major degradates (o-phthalic acid and p-chlorophenylphenyl acetic acid) were identified. In the irradiated samples, chlorophacinone was 95.7-99.1% of the applied immediately posttreatment, 77.7-90.5% at 1 day, 60.4-66.2% at 2-3 days, 40.0-41.9% at 5-9 days, and 24.7% at 14 days. o-phthalic acid was 0.4% of the applied immediately posttreatment, 20.9-23.9% at 1 day, 37.1% at 5 days, and 45.5% at 14 days. p-chlorophenylphenyl acetic acid was a maximum of 4.1-4.2% in irradiated samples at 3 days. The material balances were 85.9-122.7% in the irradiated samples and 94.3-121.0% in the dark controls. The photodegradation on soil data requirement (161-3) is fulfilled. (MRID 42452301)

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(b) Chlorophacinone Metabolism

Aerobic Soil Metabolism: Indan-labeled [1,3-^{14}C]Chlorophacinone at 9.7-10.5 ppm degraded with observed half-lives of 45 days in sandy clay loam soil (flushed once daily with humidified air) and 26 days in sandy loam soil (flushed once weekly). During incubation, both soils were maintained in the dark at 24-26 C and 75% of field capacity at 0.33 bar. CO_2 was the major volatile degradate, and two nonvolatile degradates (o-phthalic acid and p-chlorophenylphenyl acetic acid) were isolated from the soils.

In the sandy clay loam soil, [^{14}C]Chlorophacinone comprised 99.0-101% of the applied immediately post-treatment, 55.7-57.9% at 30 days, 19.9-27.3% at 91 days, and 13.7-21.8% at 182 days. o-Phthalic acid was a maximum 3.6-5.4% of the applied at 91 and 182 days post-treatment, and p-chlorophenylphenyl acetic acid was a maximum 1.6-1.9% at 91 days. CO_2, the only volatile compound, totaled 21% of the applied at 30 days post-treatment, 36% at 91 days, and 50% at 182 days. Unextracted soil [^{14}C]-residues were a maximum of 11% of the applied at 182 days post-treatment. Material balances were 99-101% of the applied at 0 and 1 day post-treatment, 92-98% at 3 through 21 days, 86-89% at 30 days, 72-78% at 91 days, and 82-88% at 182 days.

In the sandy loam soil, [^{14}C]Chlorophacinone comprised 90.6-94.1% of the applied immediately post-treatment, 40.3-41.8% at 14 days, 26.3-26.4% at 30 days, and 12.6-12.8% at 70 days. o-Phthalic acid was a 6.6-9.8% of the applied at 14 through 70 days posttreatment, and p-chlorophenylphenyl acetic acid was a maximum 5.3-5.4% at 14 days. $^{14}CO_2$ totaled 34% of the applied at 14 days posttreatment, 50% at 30 days, and 64% at 70 days. Unextracted soil [^{14}C]-residues were 8-10% of the applied at 14 through 70 days post-treatment. Material balances were $\underline{>}$ 95% of the applied at all sampling intervals.

The aerobic soil metabolism (162-1) data requirement is fulfilled. (MRID 43159801)

(c) Chlorophacinone Mobility

Leaching/Adsorption/Desorption: The submitted study on the adsorption/desorption of chlorophacinone is acceptable. The Leaching-Adsorption/Desorption (Guideline 163-1) data requirement is fulfilled. Results from this study are summarized below:

The study's author stated that based on batch equilibrium studies, [^{14}C]chlorophacinone was determined to be relatively immobile in four soils. Freundlich K_{ads} values were 56 for the sand soil, 126 for the loam soil, 183 for the sandy clay loam soil, and 1000 for the clay soil (the averaged $K_{ads} = 341$); K_{oc} values were 95745, 26900, 15600, and 35400, respectively, for the four soils (the averaged $K_{oc} = 43{,}411$). Adsorption increased with increases in clay and soil organic matter content. (MRID 42666001)

(5) Diphacinone and its sodium salt Environmental Fate and Transport

Data have been submitted for hydrolysis (Guideline 161-1), aerobic soil metabolism (Guideline 162-1), and leaching-adsorption/desorption (Guideline 163-1). The hydrolysis and

leaching-adsorption/desorption studies are supplemental and do not fulfill the guideline requirements. The data are sufficient to make a cursory assessment of the environmental fate of diphacinone. However, in order to make a quantitative environmental fate assessment, acceptable hydrolysis and leaching/adsorption/desorption data are needed.

Based on the available data, diphacinone appears to be relatively immobile and moderately degradable. It has the following characteristics: (1) low water solubility (30 ppm at 25°C); (2) stable to hydrolysis at pH 7 and 9 but susceptible to hydrolysis at pH 5 (half-life of 44 days); (3) moderately degradable in a sandy loam soil under aerobic conditions (half-lives of 28 to 32 days); (4) is expected to be immobile in soil; (5) volatilizes slowly from water and soil (vapor pressure = 1.2×10^{-8} mm Hg; Henry's Law constant = 1.8×10^{-10} atm-m^3/mol); and (6) does not accumulate in fish at a significant level (K_{ow} = 43).

Results from the aerobic soil metabolism study suggest that diphacinone degraded to diphenylglycolic acid relatively rapidly. The degradate was further cleaved and transformed into carbon dioxide.

Based on laboratory studies, diphacinone is expected to be bound very tightly with soil in the field. Most of the chemical would remain in the top soil layers and its potential to reach ground water is very low. Surface water contamination may occur in less-permeable areas and in areas near water bodies. The mechanism for diphacinone to reach surface waters would likely be via adsorption to eroding soil rather than dissolution in runoff water. Although no adsorption coefficient is available, most diphacinone is expected to be partitioned in the suspended and bottom sediments instead of in the water column.

(a) Diphacinone and its sodium salt Degradation

Hydrolysis: At a concentration of 10 ppm, Diphacinone was hydrolytically stable at pH 7 and pH 9, but degraded at pH 5 with a half-life of 44 days. However, degradates resulting from hydrolysis at pH 5 were not quantified, nor were they identified other than by reference to a 1977 study (Velsicol Project No. 408398). The 1977 study was unacceptable when submitted and after a current reevaluation. Therefore, it cannot be used to identify the degradates detected in the current study. The current study is supplemental but does not fulfill the guideline requirement for a hydrolysis study (Guideline 161-1). Identification of residues present at levels $\geq$ 10% of the applied is a critical element of the hydrolysis study. Failure to identify one or more significant degradates may result in gaps in the understanding of the environmental fate of the chemical and its degradation products. (MRID 43582401)

(b) Diphacinone and its sodium salt Metabolism

Aerobic Soil Metabolism: Radio-labeled (benzyl ring or both phenyl rings) [^{14}C]Diphacinone, at a concentration of 2 µg/g, was metabolized with a half-life of 28.3 to 31.7 days, respectively, in sandy loam soils incubated aerobically in the dark at 25 ± 1°C for 3.5 months. The major degradate (defined as $\geq$ 10% of the applied) detected in the phenyl ring-labeled study was identified as diphenylglycolic acid and was present at a maximum of 24.5% of the applied at one month after application. Diphenylglycolic acid was also detected in the benzyl ring-labeled study at a very low concentration ($<$ 10% of the applied).

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Benzyl ring-labeled [^{14}C]Diphacinone in soil extracts decreased from 86.4% of the applied radioactivity at day 0 to 39.2% of the applied by day 14 post-treatment, and to 9.6% of the applied by 3.5 months post-treatment. By 3.5 months post-treatment, 42.5% of the applied radioactivity was accounted for as $^{14}CO_2$. Material balances during the study ranged from 93.1 to 104.1%.

Phenyl ring-labeled [^{14}C]Diphacinone in soil extracts decreased from 87.1% of the applied radioactivity at day 0 to 41.6% of the applied by day 7 post-treatment, and to 6.5% of the applied by 3.5 months post-treatment. By 3.5 months post-treatment, 37.3% of the applied radioactivity was accounted for as $^{14}CO_2$. Material balances during the study ranged from 88.6 to 103.1.

The guideline requirement for an aerobic soil metabolism study (162-1) is fulfilled. (MRID 42035001)

(c) Diphacinone and its sodium salt Mobility

Leaching/Adsorption/Desorption: Diphacinone was relatively immobile in columns (60 cm in length) packed with sandy loam, silt loam, sand, and loamy sand soils to a depth of 30 cm. Prior to leaching, the columns had been topped with loamy sand soil that had been treated with technical diphacinone and incubated in a closed container in the dark for 30 days at 18-30∘C. The columns were leached with 20 inches of distilled water.

Diphacinone was detected only in the 0-6 cm layer in the columns with sandy loam and silt loam soils. In the sand soil, diphacinone was detected in the 0-6 cm layer (at 117.1% of the applied) and in the 6-12 cm layer (at < 3% of the applied). Diphacinone was present in the 0-6 cm layer of the loamy sand soil at 76.1% of the applied, and was also present in the 6-12 cm, 12-18 cm, and 18-24 cm layers at 3.4%, 4.8%, and 4.4% of the applied, respectively. Diphacinone was not detected in any of the leachates collected from the four soil columns.

No adsorption values were reported. However, results from the aged column leaching study suggest that diphacinone is relatively immobile in the environment.

Results from this study (MRID 435824-02) are supplemental. The guideline requirement for a leaching-adsorption/desorption study (Guideline 163-1) is not fulfilled primarily because degradates, including CO_2, were not identified or quantified. Identification of residues present at levels $\geq$ 10% of the applied is a critical element of the leaching/adsorption/ desorption study. One reason this study is conducted is to determine the mobility of parent and its degradates in soil. Failure to identify one or more significant degradates may result in gaps in the understanding of the mobility of the chemical and its degradation products and their leaching potential in ground water. A new study is required.

3. Ecological Exposure and Risk Characterization

Risk characterization integrates the results of the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. The means of integrating the results of exposure and

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ecotoxicity data is called the quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic.

RQ = EXPOSURE/TOXICITY

RQs are then compared to OPP's levels of concern (LOCs). LOCs are criteria used by OPP to indicate potential risk to nontarget organisms and the need to consider regulatory action. The criteria indicate that a pesticide used as directed has the potential to cause adverse effects on nontarget organisms. LOCs currently address the following risk presumption categories: (1) **acute high** - potential for acute risk is high; regulatory action may be warranted in addition to restricted use classification; (2) **acute restricted use** - the potential for acute risk is high but may be mitigated through restricted use classification; (3) **acute endangered species** - the potential for acute risk to endangered species is high; regulatory action may be warranted; and (4) **chronic risk** - the potential for chronic risk is high; regulatory action may be warranted.

The ecotoxicity test values (i.e., measurement endpoints) used in the acute and chronic RQs are derived from the results of required studies. Examples of ecotoxicity values derived from the results of short-term laboratory studies that assess acute effects are: (1) LC_{50} (fish and birds); (2) LD_{50} (birds and mammals); and (3) EC_{50} (aquatic invertebrates). For birds, the NOEC value is used as the ecotoxicity test value in assessing chronic effects.

Risk presumptions, RQ methods, and LOCs are summarized in Table 57 below.

Table 57 - Risk Presumptions for Terrestrial and Aquatic Organisms

Risk Presumption	Birds and Mammals		Aquatic Organisms	
	RQ Method	LOC	RQ Method	LOC
Acute High Risk	EEC[1]/LC_{50} or LD_{50}/day[2]	0.5	EEC[3]/LC_{50} or EC_{50}	0.5
Acute Restricted Use	EEC/LC_{50} or LD_{50}/day	0.2	EEC/LC_{50} or EC_{50}	0.1
Acute Endangered Species	EEC/LC_{50} or LD_{50}/day	0.1	EEC/LC_{50} or EC_{50}	0.05
Chronic Risk	EEC/NOEC	1	EEC/MATC or NOEC	1

[1]EEC = Estimated Environmental Concentration (ppm) on avian and mammalian food items (short grass; tall grass; broadleaved plants and small insects; seeds, pods, large insects)

[2]mg toxicant consumed/day ÷ [LD_{50} X bird wt (kg)], where tox. consumed/day = amount food eaten X % a.i. in the food

[3]EEC = aquatic Estimated Environmental Concentration (ppm or ppb)

a. Brodifacoum Ecological Exposure and Risk Characterization

Brodifacoum is a single dose rodent poison for use inside and along the outside walls of buildings. It is very highly toxic to mammals and birds on an acute basis and a dietary basis.

It also is very highly toxic to aquatic organisms, but, due to its extremely low solubility, it is not believed that enough brodifacoum would dissolve in water to create a hazard to nontarget animals. Its use pattern is not likely to bring it into contact with water. There are uses for

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sewers; however, these products are "weather resistant" paraffinized blocks and are not expected to dissolve in the water.

The possibility of plants or bees being unduly exposed to brodifacoum is so small that no plant or bee toxicity studies were required. Since it is being used only inside and along the outside walls of buildings, endangered species will not likely be put at risk.

This risk characterization is based upon the definition of the use pattern "inside and along the outside walls or buildings." The pattern should be put on the label.

If the use pattern is extended, nontarget hazard and secondary poisoning studies will be needed to characterize the risks. The question of endangered species risks would have to be reassessed because it is highly likely that additional species would be exposed. If the Agency can not determine measures to protect those additional species, consultation with the Fish and Wildlife Service may be necessary.

The available toxicity data on the TGAI are interpreted to mean that brodifacoum is very highly toxic to birds (LD_{50} = 260 μg/kg; LC_{50} = 800 ppb), very highly toxic to mammals (LD_{50} = 0.41 mg/kg, male rat), and highly to very highly toxic to freshwater organisms (LC_{50} = 25 ppb). If the use pattern is extended, nontarget hazard and secondary poisoning studies will be needed to characterize the risks.

(1) Brodifacoum Exposure and Risk to Nontarget Terrestrial Animals

There are several terrestrial field studies that were submitted during the initial registration process. They were interpreted as showing that brodifacoum has a primary and secondary nontarget poisoning potential. The reregistration of brodifacoum is for indoor, transportation, and sewer uses only. Therefore, field and secondary poisoning studies are not required and the old studies and the literature were not reviewed. If field uses are requested, additional studies will be required.

(a) Brodifacoum Exposure and Risk to Birds

Brodifacoum's avian toxicity is two orders of magnitude more toxic than is required for the category very highly toxic. It poses a very high hazard to any birds that consume it. If it would be used outdoors it would be a presumptive hazard to birds. However, it is only used indoors, in vehicles, and in sewers, therefore, birds are not expected to be unduly exposed to it.

(b) Brodifacoum Exposure and Risk to Mammals

Brodifacoum is two orders of magnitude more toxic than is required for the category very highly toxic. It poses a very high hazard to any mammals that consume it. If it would be used outdoors it would be a presumptive hazard to mammals. However, it is only used indoors, in vehicles, and in sewers, therefore, wild mammals are not expected to be unduly exposed to it.

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(2) Brodifacoum Exposure and Risk to Nontarget Aquatic Animals

Brodifacoum is an order of magnitude more toxic than is required for the category very highly toxic for the rainbow trout and is highly toxic to the bluegill sunfish. It is only used indoors, in vehicles, and sewers. The sewer use is for a paraffinized bait and is not expected to contaminate water. It is not expected that it will come into contact with aquatic animals. The solubility of brodifacoum is 10 mg/l. If it was put in water it would dissolve sufficiently to produce a concentration of 0.01 ppm, enough to kill some aquatic animals, although it would be below the LC_{50}. Since brodifacoum has no aquatic uses, it is not expected to enter a body of water in a large enough quantity to cause significant contamination. It is not believed that brodifacoum will pose an undue hazard to aquatic organisms.

(3) Brodifacoum Exposure and Risk to Nontarget Plants and Insects

The possibility of plants or bees being unduly exposed to brodifacoum is so small that no plant or bee toxicity studies were required. Since it is being used only outside and along the outside walls of buildings, endangered species will not likely be put at risk.

(4) Brodifacoum Endangered Species Concerns

Brodifacoum was addressed by the U.S. Fish and Wildlife Service in its Biological Opinion of March 1993. Uses considered were control of Norway rats, roof rats, and house mice in and around urban, industrial, commercial, agricultural, and public buildings and in and around transport vehicles (ships, trains, and aircraft and related port buildings. The service made a "jeopardy" or "no jeopardy" determination for the 20 "may affect" species listed below in Table 58. Other species were considered either not at risk of exposure or not likely to be affected.

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Table 58 - USFWS 1993 Biological Opinion for Brodifacoum

Species	Jeopardy	No Jeopardy
Mammals:		
Alabama beach mouse *(Peromyscus polionotus ammobates)*	X	
Anastasia Island beach mouse *(Peromyscus polionotus phasma)*	X	
Choctawhatchee beach mouse *(Peromyscus polionotus allophrys)*	X	
Southeastern beach mouse *(Peromyscus polionotus niveiventris)*	X	
Perdido Key beach mouse *(Peromyscus polionotus trissyllepsis)*	X	
Florida salt marsh vole *(Microtus pennsylvanicus dukecampbelli)*	X	
Salt marsh harvest mouse *(Reithrodontomys raviventris)*	X	
Fresno kangaroo rat *(Dipodomys nitratoides exillis)*	X	
Giant kangaroo rat *(Dipodomys igens)*		X
Morro Bay kangaroo rat *(Dipodomys heermanni morroensis)*	X	
Stephen's kangaroo rat *(Dipodomys stephensi)*		X
Tipton kangaroo rat *(Dipodomys nitratoides nitratoides)*		X
Point Arena mountain beaver *(Aplodontia rufa nigra)*		X
Carolina northern flying squirrel *(Glaucomys sabrinus coloratus)*	X	
San Joaquin kit fox *(Vulpes macrotis mutica)*		X
Louisiana black bear *(Ursus americanus luteolus)*		X
Birds:		
Audubon's crested caracara *(Caracara cheriway audubonii)*	X	
San Clemente loggerhead shrike *(Lanius ludovicianus mearnsi)*	X	
Hawaiian hawk *(Buteo solitarius)*		X
Reptiles:		
Eastern indigo snake *(Drymarchon corais couperi)*		X

b. Bromadiolone Ecological Exposure and Risk Characterization

(1) Bromadiolone Exposure and Risk to Nontarget Terrestrial Animals

(a) Bromadiolone Exposure and Risk to Birds and Nontarget Mammals

Because bromadiolone is a rodenticide, risk is presumed for any small mammals that feed on bait. Mortality of captive subadult coyotes fed poisoned ground squirrels also indicates a potential for secondary poisoning of predators if secondary exposure occurs. However, bromadiolone is used outdoors only in urban areas. Such placements can be made only around buildings or in sewers, and all placements around buildings must be in protective bait stations or in areas inaccessible to nontarget wildlife. Due to paucity of nontarget wildlife (i.e., non-domestic animals) in urban areas, minimal risk is expected. In non-urban areas, bromadiolone baits can be used only indoors therefore, minimal exposure of nontarget species is expected.

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(2) Bromadiolone Exposure and Risk to Nontarget Aquatic Animals

Based on where and how bait is applied, little if any bromadiolone is expected in water bodies. Additionally, because it is extremely insoluble, Bromadiolone is not expected to pose a major risk to aquatic organisms.

(3) Bromadiolone Endangered Species Concerns

The U. S. Fish and Wildlife Service addressed bromadiolone in its Biological Opinion issued in March of 1993. The uses addressed were control of Norway rats, roof rats, and house mice in urban areas in and around the periphery of homes, industrial, commercial and public buildings, alleys, and cargo areas of ships, trains, and aircraft. Table 56 below summarizes the results of the USFWS opinion. The U.S. Fish and Wildlife Service made a "jeopardy" or "no jeopardy" determination for the 12 "may affect" species listed in the jeopardy tables. Other species were considered either not a risk of concern or not likely to be affected.

Table 59 - USFWS 1993 Biological Opinion for Bromadiolone

Species	Jeopardy	No Jeopardy
Mammals:		
Alabama beach mouse *(Peromyscus polionotus ammobates)*	X	
Anastasia Island beach mouse *(Peromscus polionotus phasma)*	X	
Choctawhatchee beach mouse *(Peromyscus polionotus allophrys)*	X	
Southeastern beach mouse *(Peromyscus polionotus niveiventris)*	X	
Perdido Key beach mouse *(Peromyscus polionotus trissyllepsis)*	X	
Salt marsh harvest mouse *(Reithrodontomys raviventris)*	X	
Fresno kangaroo rat *(Dipodomys nitratoides exillis)*		X
Morro Bay kangaroo rat *(Dipodomys heermanni morroensis)*	X	
Stephen's kangaroo rat *(Dipodomys stephensi)*		X
Tipton kangaroo rat *(Dipodomys nitratoides nitratoides)*		X
Point Arena mountain beaver *(Aplodontia rufa nigra)*		X
San Joaquin kit fox *(Vulpes macrotis mutica)*		X

c. Bromethalin Ecological Exposure and Risk Characterization

(1) Bromethalin Exposure and Risk to Nontarget Terrestrial Animals

Because bromethalin is used exclusively in and around buildings or in sewers, primary exposure of birds is expected to be minimal. Bait applications must be contained in protected bait stations or made in areas inaccessible to nontarget wildlife. Because bromethalin is a rodenticide,

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risk is presumed for any small mammals that feed on the bait. Bait applications around buildings in non-urban areas is likely to expose some small mammals.

The Agency's incident data base has no records of wild animals being killed from feeding on rodents poisoned with bromethalin. However, secondary toxicity data are needed before secondary risks can be adequately assessed from bait applications of bromethalin around buildings.

(2) Bromethalin Exposure to Plants and Insects

No data were required.

(3) Bromethalin Exposure and Risk to Nontarget Aquatic Animals

Risks to aquatic organisms are presumed to be minimal. Bromethalin is very highly toxic to aquatic organisms, but its use in and around buildings, cargo vessels, alleys, and sewers is likely to result in minimal contamination of aquatic environments. Some potential for contact with water exists for the sewer use, especially in overflow sewers or if bait blocks are not properly wired above the water line. However, because bromethalin has an extremely low solubility in water and sewer baits are formulated as "weather-resistant" paraffinized blocks, very little, if any, exposure of aquatic organisms is anticipated from sewer use.

(4) Bromethalin Endangered Species Concerns

The U. S. Fish and Wildlife Service addressed Bromethalin in its Biological Opinion issued in March of 1993. The use patterns included control of Norway rats, roof rats and house mice in and around homes, commercial, industrial and agricultural buildings and airports, landing strips and urban alleys. The Service made a "jeopardy" or "no jeopardy" determination for the 14 "may affect" species listed in Table 55. Other species were considered either not at risk of exposure or not likely to be affected.

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Table 60 - USFWS 1993 Biological Opinion for Bromethalin

Species	Jeopardy	No Jeopardy
Mammals:		
Alabama beach mouse *(Peromyscus polionotus ammobates)*	X	
Anastasia Island beach mouse *(Peromyscus polionotus phasma)*	X	
Choctawhatchee beach mouse *(Peromyscus polionotus allophrys)*	X	
Southeastern beach mouse *(Peromyscus polionotus niveiventris)*	X	
Perdido Key beach mouse *(Peromyscus polionotus trissyllepsis)*	X	
Florida salt marsh vole *(Microtus pennsylvanicus dukecampbelli)*	X	
Salt marsh harvest mouse *(Reithrodontomys raviventris)*	X	
Fresno kangaroo rat *(Dipodomys nitratoides exillis)*	X	
Giant kangaroo rat *(Dipodomys igens)*		X
Morro Bay kangaroo rat *(Dipodomys heermanni morroensis)*	X	
Stephen's kangaroo rat *(Dipodomys stephensi)*		X
Tipton kangaroo rat *(Dipodomys nitratoides nitratoides)*		X
Point Arena mountain beaver *(Aplodontia rufa nigra)*		X
Carolina northern flying squirrel *(Glaucomys sabrinus coloratus)*	X	

d. Chlorophacinone Ecological Exposure and Risk Characterization

(1) Chlorophacinone Exposure and Risk to Nontarget Terrestrial Animals

Field and Rural vs Urban/Suburban Risks: The risk assessment for nontarget wildlife pertains to field uses and to bait applications in rural and urban/suburban areas where bait can be applied around buildings (e.g., barns, houses, sheds) for commensal rat and mouse control. Chlorophacinone can be used to control rats and mice around buildings in urban areas. However, due to the paucity of wildlife (i.e., non-domestic animals) in urban areas, primary and secondary risks are expected to be minimal.

EECs: The estimated environmental concentration (EEC) of a pesticide on potential food items of birds and mammals immediately after a foliar application is compared to the most sensitive avian or mammalian LC_{50} value to assess potential risk. Based on the findings of Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994), predicted 0-day maximum and mean residues of a pesticide expected on selected avian or mammalian food items immediately following a direct single application at 1 lb a.i./acre are listed in Table 61. For chlorophacinone, the only spray application is for vole control in orchards. One spray application at 0.2 lb a.i./acre is permitted per year (a repeat application is allowed if rainfall occurs within 12 hours of application). Therefore, EECs resulting from a chlorophacinone spray are presumed to be 20% of the values summarized in Table 61 for a 1 lb a.i./A application.

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Table 61 - EECs[1] on Potential Avian and Mammalian Food Items After a Single Pesticide Spray Application of 1 lb a.i./A and a Chloriphacinone Orchard Spray of 0.2 lb a.i./A

Food Items	1 lb a.i./A pesticide appl.		0.2 lb a.i./A Chlorophacinone appl.	
	Maximum EEC (ppm)	Mean EEC (ppm)	Maximum EEC (ppm)	Mean EEC (ppm)
Short grass	240	85	48	17
Small insects	135	45	27	9
Seeds, Fruits, Large insects	15	7	3	1

[1]Predicted maximum and mean EECs based on on Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994)

(a) Chlorophacinone Birds

Acute primary risk (spray application): Acute RQs for a single spray application of chlorophacinone are summarized in Table 62 below.

Table 62 - Avian Acute RQs for a Single Ground Spray Application of Chlorophacinone[1]

Site/Appl. Rate (lb a.i./A)	Food Item	Maximum EEC (ppm)	Mean EEC (ppm)	Max. Acute RQ (EEC/LC_{50})	Mean Acute RQ (EEC/LC_{50})
Orchard[2] (0.2)	Short grass	48	17.00	0.86***	0.30**
	Small insects	27	9.00	0.48***	0.16*
	Seeds, Fruits, Large insects	3	1.00	0.05	0.02

[1] Single ground spray application of chlorophacinone are based on maximum and mean EECs and a bobwhite quail LC_{50} of 56 ppm.
[2] OR, UT, WA, WV (vole control)
***exceeds LOCs for acute high risk (0.5), restricted use (0.2), and endangered species (0.1)
**exceeds LOCs for acute restricted use (0.2) and endangered species (0.1)
*exceeds the LOC for endangered species (0.1)

Based on maximum EECs for a single application, the avian acute high risk, restricted use, and endangered species, LOCs are exceeded for birds feeding on short grass. restricted use and endangered species LOCs are exceeded for insectivores. Based on mean EECs, restricted use and endangered species, LOCs are exceeded for short grass. Moreover, the endangered species LOC is exceeded for birds feeding on small insects.

Acute primary risk (food baits): The potential for primary exposure of seed-eating birds to food baits exists primarily for field applications of unprotected loose bait (i.e., aerial or ground broadcast or hand applied pellets or treated whole grains). Minimal exposure is expected for applications where bait is placed in protected bait stations or areas inaccessible to nontarget wildlife, if place packs or paraffinized bait blocks are used, and for underground applications for control of pocket gophers. Birds that are mainly herbivorous or insectivorous are not expected to be at risk from grain-based food baits.

RQs for loose food baits are based on the number of LD_{50} doses potentially consumed by a bird in one day. RQs are calculated for three separate weight classes of birds: 500-1000 g (e.g., waterfowl), 100-200 g (e.g., upland gamebird), and 20-50 g (e.g., passerine). Acute RQs for applications of chlorophacinone food baits are summarized in Table 63 below.

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Table 63 - Avian (Granivore) Acute RQs (LD_{50}s/day) for Chlorophacinone Food Baits, Based on a Bobwhite Quail LD_{50} of 258 mg/kg

Site	Bait (% a.i.)	Body Wt Class (g)	Amt Food Eaten (g)[1]	mg a.i. consumed/day	Acute RQ[2,3] (LD_{50}s/day)
Crop and noncrop areas (bare ground)[4]; Forestry[5]	0.01	20-50	3.50	0.35	0.07
		100-200	9.00	0.90	0.04
		500-1000	18.00	1.80	0.01
Orchard[6]; Tree plantation[7]; Noncrop areas, ditch banks, rights of way8; Noncrop areas or unspecified[9]	0.005	20-50	3.50	0.18	0.04
		100-200	9.00	0.45	0.01
		500-1000	18.00	0.90	0.01

[1]estimates of food consumption as a function of body size are based on information provided by Kenaga (1972) and Dunning (1984) for the mallard, bobwhite quail, and red-winged blackbird
[2]LD_{50}s/day = mg toxicant consumed/day ÷ [LD_{50} (mg/kg) * bird wt (kg)]
[3]only the highest RQ value is tabulated
[4] ground squirrel control (CA, MT)
[5] deer mouse control (CA)
[6] vole control (CT, MD, MI, MO, NC, NY, OH, OR, PA, SC, VA, VT, WA, WV)
[7] vole control (ID, NC)
[8] vole control (OR)
[9] ground squirrel, vole, chipmunk, woodrat, and/or jackrabbit control (CA, OR)

Avian acute LOCs are not exceeded for applications of loose bait when risk is based on the number of LD_{50}s potentially consumed by granivorous birds in one day. However, chlorophacinone is a multiple-feeding anticoagulant, and risk to birds that feed on bait for several days is likely greater than predicted by RQ values based on a single feeding. Avian dietary tests indicate that chlorophacinone is more toxic when ingested over a 5-day period than when administered in a single dose. For this scenario, EECs on grains or pellets are 50 ppm (0.005% a.i.baits) and 100 ppm (0.01% a..i baits). Acute RQs based on avian dietary toxicity are summarized in Table 64 below for granivorous birds.

Table 64 - Avian (Granivore) Acute RQs For Chlorophacinone Food Baits, Based on a Bobwhite Quail LC_{50} of 56 ppm

Site	Bait (% a.i.)	EEC(ppm)	Acute RQ (EEC/LC_{50})
Crop and noncrop areas (bare ground)[1]; Forestry[2]	0.01	100	1.78***
Orchard[3]; Tree plantation[4]; Noncrop areas, ditch banks, rights of way[5]	0.005	50	0.89***

[1] ground squirrel control (CA, MT)
[2] deer mouse control (CA)
[3] vole control (CT, MD, MI, MO, NC, NY, OH, OR, PA, SC, VA, VT, WA, WV)
[4] vole control (ID, NC)
[5] vole control (OR)
*** exceeds LOCs for acute high risk (0.5), restricted use (0.2), and endangered species (0.1)

Acute high risk, restricted use, and endangered LOCs are exceeded for granivorous birds for above-ground applications of both 0.01% a.i.and 0.005% a.i. loose food baits when risk is

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based on dietary toxicity. The Agency is not aware of any bird poisoning incidents due to chlorophacinone, nor was any avian mortality observed during efficacy field studies in which small mammal mortality was reported. However, any possible means of reducing primary exposure of birds are important, such as use of protective bait stations, which the Agency addressed in PR Notice 94-7, issued September 16, 1994. The quality of bait stations and the care taken by applicators to secure stations and ensure that bait is not exposed outside bait compartments are important in minimizing exposure of bait to granivorous birds. Stations should be adequate to prevent destruction by wildlife (e.g., raccoons, bears) and/or livestock and protect bait in adverse weather conditions. Stations should be designed with internal bait compartments that minimize spillage and be well secured or anchored. Applicators should be encouraged to use stations with baffles, mazes, and/or small entrance holes that deter birds from entering the bait compartment, and they must ensure that bait spilled outside stations is disposed of properly. Where bait stations may not be feasible, use of products formulated in place packs or paraffinized blocks would help reduce primary exposure of birds.

Chronic risk: Chronic risk is presumed to be minimal for uses where baits are inaccessible (e.g., in bait stations, place packs, or burrows), not likely to be eaten (e.g., paraffinized blocks), if only one application is made, or if applications are made outside or not immediately preceding the breeding season of birds. Based on these criteria, applications of one chlorophacinone product (SLN CA890023) may result in chronic exposure to granivorous birds, because baiting directions specify that "An uninterrupted supply of bait should be maintained as long as any bait is taken, which may be 1 to 4 weeks." Chronic risk from this use cannot be assessed, however, until avian reproduction studies are submitted. This study is required unless label changes are made to eliminate potential chronic exposure.

Secondary risk: Data are lacking to assess potential secondary risks to avian predators and scavengers that may feed on rodents poisoned with chlorophacinone. Two field studies conducted primarily to determine the efficacy of 0.005% a.i.and 0.01% a.i. chlorophacinone food baits to the California ground squirrel also attempted to evaluate potential nontarget hazards. No mortality of avian predators or scavengers was observed in either study. However, the evaluation was based almost exclusively on locating carcasses on treatment plots. Because predatory and scavenging birds are highly mobile and wide-ranging and chlorophacinone takes several days to kill, birds might die away from study sites and not be found. Pre- and post-treatment population censusing of granivorous birds, use of radio telemetry for following and determining fates of raptors and scavengers, and extensive carcass searches on and away from study plots are needed to adequately assess secondary risks to birds. Therefore, these efficacy studies are considered inadequate for evaluating secondary risks to birds from field uses and from commensal rat and mouse control in rural areas. Potential risks will be evaluated when the required laboratory secondary toxicity tests are submitted.

(b) Chlorophacinone Mammals

Acute primary risk (food bait): Because rodents, moles (insectivores), and jackrabbits (lagomorphs) are target species and chlorophacinone is very highly toxic to small mammals, the

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Agency presumes acute high risk to any small mammals that feed on chlorophacinone baits or sprayed food items (e.g., grass, seeds, insects) over a period of several days. Field studies conducted against ground squirrels on the San Joaquin range in California confirm this presumption of high acute risk. Small nontarget mammals, principally mice and woodrats, were found poisoned on plots baited with 0.01% a.i. and 0.005% a.i. Chlorophacinone grain baits. The findings indicated, however, that nontarget mortality might be reduced if 0.005% a.i.bait is used rather than 0.01% a.i. bait. Of the 47 nontarget individuals located on spot-baited plots, 27 (57%) were found on plots treated with 0.01% a.i. bait and 20 (43%) on the plots treated with 0.005% a.i. bait. Evidence of poisoning was found in 80% (16/20) of the individuals necropsied on the 0.01% a.i. plots but only 60% (12/19) of those necropsied on the 0.005% a.i. plots.

Primary risk to larger mammals are reduced for applications requiring protected bait stations, providing that the stations are adequately constructed and secured. Bait stations are designed with openings only large enough to accommodate adults of the target species. Larger species cannot gain entrance to the bait compartment, although smaller species are able to enter and thus have access to the bait. Care should be taken to ensure that bait spillage is minimized and that any bait spilled is immediately removed and not left exposed on the ground. The two dead rabbits found in one field study may have been small enough to enter the bait stations, or more likely they gleaned bait spilled outside the stations.

Acute primary risk (spray application): Sprayed ground vegetation in and around the perimeter of orchards is potentially hazardous to herbivores, and insectivores may be adversely effected by feeding on contaminated insects. Vegetation sprayed at 0.2 lb a.i./acre chlorophacinone apparently is lethal to voles, which are the target species. Mortality occurs when voles consume sprayed vegetation or when they groom fur contaminated from contact with sprayed vegetation. Although opossums exposed for 14 days to sprayed vegetation did not die or exhibit any adverse effects, sample size ($n = 6$) was small. Moreover, opossums are omnivorous and their susceptibility to chlorophacinone may not reflect that of smaller mammalian herbivores that might feed exclusively on green vegetation.

Secondary risk: A secondary hazards study in which poisoned ground squirrels were fed to captive coyotes demonstrates that rodents poisoned with 0.01% a.i. chlorophacinone bait pose a risk to coyotes and presumably other species. In that study, three of seven coyotes died from consuming one poisoned squirrel per day for five consecutive days. In the efficacy studies conducted on the San Joaquin Range in California, carcasses of California ground squirrels poisoned with 0.01% a.i. and 0.005% a.i. grain baits were available at burrow entrances and in open areas on the ground surface away from burrows. It is conceivable that coyotes and other predators (e.g., fox, bobcats, mustelids) could easily find and consume one ground squirrel per day over a 5-day period. Although no dead predators were found in those studies, the techniques used and the search effort for effected nontarget species was not adequate for wide-ranging species.

An adequate assessment of secondary risks to mammalian predators and scavengers cannot be completed until required secondary toxicity tests are conducted for the 0.005% a.i. bait. However, findings from the California ground squirrel field trials indicate that carcasses of ground squirrels poisoned with 0.005% a.i. bait may contain considerably less chlorophacinone

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residue than those poisoned with 0.01% a.i.. bait. Analysis of whole carcass tissue residues found mean residue loads of 0.62 (0.048-1.88) mg chlorophacinone in the 10 squirrel specimens exposed to 0.01% a.i. bait. Mean residue loads were 0.19 (0.032-0.744) and 0.16 (0.043-0.415) mg chlorophacinone in squirrel specimens exposed to 0.005% a.i.bait on spot-baited plots and plots with bait stations, respectively. The hazard of these residue loads is undetermined in the field, although some captive coyotes in the secondary hazards study were killed from exposure to ground squirrels poisoned with 0.01% a.i. chlorophacinone bait. Because the residue levels in poisoned squirrels exposed to 0.005% a.i. bait were only about one-third of those in squirrels exposed to 0.01% a.i. bait, secondary risks from 0.005% a.i. bait likely are less than for 0.01% a.i. bait.

(2) Chlorophacinone Exposure and Risk to Nontarget Aquatic Animals

EFED calculates aquatic EECs using the Generic Expected Environmental Concentration Program (GENEEC). The EECs are used for assessing risk to aquatic organisms. GENEEC uses basic environmental fate data and pesticide label application information to estimate EECs from treatment of 10 hectares. The model calculates the concentration (i.e., EEC) of pesticide in a 1-hectare, 2-m deep pond, taking into account adsorption to soil or sediment, degradation in soil before washoff into the water body, and degradation within the water body. The model also accounts for direct deposition of spray drift into the water body (assumed to be 1% of the application rate for a ground spray). The interval between applications is included in the calculations for multiple applications. The environmental fate values used in the model for chlorophacinone are: soil K_{OC} = 43,411, solubility = 34 ppm, aerobic soil metabolism half-life = 45 days, hydrolysis = > 30 days (stable), and the water photolytic half-life = 0.03 days. Aquatic EECs and RQs for the most sensitive aquatic organism (rainbow trout) are summarized in Table 65 below for those use sites for which the product label specified an application rate in pounds per acre.

Table 65 - Aquatic EECs and Acute RQs For Freshwater Organisms[1]

Site	Type of Application	Appl. Rate (lb a.i./A)	No. Appl./Appl. Interval (days)	Initial EEC (ppb)	Acute RQ (EEC/LC_{50})
Orchard[2]	ground spray	0.2	1 2 (1)	0.271 0.616	< 0.001 0.001
Orchard[3]; Crop and noncrop areas (bare ground)[4]	food bait	0.001	1 2 (30)	0.001 0.002	< 0.001 < 0.001

[1] Aquatic EECs and acute RQs for freshwater organisms are based on a rainbow trout LC_{50} of 450 ppb of chlorophacinone
[2] OR, UT, WA, WV
[3] MI, NC
[4] CA, MT

The results indicate that no aquatic acute LOCs are exceeded for freshwater organisms at maximum registered application rates for orchard ground spray (vole control) or applications of 0.01% a.i. food bait. RQs for the 0.005% a.i. bait and other freshwater organisms would be even lower. Therefore, minimal risk to freshwater organisms is expected.

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(3) Chlorophacinone Endangered Species Concerns

The U.S. Fish and Wildlife Service addressed chlorophacinone in its Biological Opinion of March, 1993. That Opinion is based on its use for control of Norway rats, roof rats, and house mice in and around homes, industrial, and agricultural buildings; pocket gophers in underground runways; mice and voles in Idaho and Delaware; orchard mice in Delaware, Connecticut, and Arizona; control of deer mice in noncrop areas of Florida; ground squirrel control in Arizona; control of deer mice, house mice, and pocket gophers in California; and indoor control of bats. The Service made a "jeopardy" or "no jeopardy" determination for the 28 "may affect" species listed below. Other species were considered either not at risk of exposure or not likely to be affected. See Table 66 below.

Table 66 - USFWS 1993 Biological Opinion for Chlorophacinone

Species	Jeopardy	No Jeopardy
Mammals:		
Alabama beach mouse *(Peromyscus polionotus ammobates)*	X	
Anastasia Island beach mouse *(Peromyscus polionotus phasma)*	X	
Choctawhatchee beach mouse *(Peromyscus polionotus allophrys)*	X	
Southeastern beach mouse *(Peromyscus polionotus niveiventris)*	X	
Perdido Key beach mouse *(Peromyscus polionotus trissyllepsis)*	X	
Amargosa vole *(Microtus californicus scirpensis)*	X	
Florida salt marsh vole *(Microtus pennsylvanicus dukecampbelli)*	X	
Hualapai Mexican vole *(Microtus mexicanus hualpaiensis)*	X	
Salt marsh harvest mouse *(Reithrodontomys raviventris)*	X	
Fresno kangaroo rat *(Dipodomys nitratoides exillis)*	X	
Giant kangaroo rat *(Dipodomys igens)*	X	
Morro Bay kangaroo rat *(Dipodomys heermanni morroensis)*	X	
Stephen's kangaroo rat *(Dipodomys stephensi)*	X	
Tipton kangaroo rat *(Dipodomys nitratoides nitratoides)*	X	
Point Arena mountain beaver *(Aplodontia rufa nigra)*	X	
Utah prairie dog *(Cynomys parvidens)*		X
Carolina northern flying squirrel *(Glaucomys sabrinus coloratus)*	X	
San Joaquin kit fox *(Vulpes macrotis mutica)*	X	
Gray wolf *(Canis lupus)*		X
Florida panther *(Felis concolor coryi)*	X	
Jaguarundi *(Felis yagouaroundi cacomitli)*	X	
Ocelot *(Felis pardalis)*	X	
Grizzly bear *(Ursus arctos horribillis)*		X
Louisiana black bear *(Ursus americanus luteolus)*		X
BIRDS		
Audubon's crested caracara *(Caracara cheriway audubonii)*	X	
REPTILES		
Eastern indigo snake *(Drymarchon corais couperi)*		X
Puerto Rican boa *(Epicrates inornatus)*		X
Virgin Islands tree boa *(Epicrates monensis (=inornatus) granti)*		X

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e. Diphacinone and its sodium salt Ecological Exposure and Risk Characterization

LOCs for diphacinone address the following risk presumption categories: (1) **acute high** - potential for acute risk is high; regulatory action may be warranted; (2) **acute restricted use** - the potential for acute risk is high but may be mitigated through restricted use classification; and (3) **acute endangered species** - the potential for acute risk to endangered species is high; regulatory action may be warranted. The ecotoxicity test values (i.e., measurement endpoints) used in calculating RQs are derived from laboratory studies. Risk presumptions, RQ methods, and LOCs are tabulated below for birds. RQs are not determined for mammals; because diphacinone is a rodenticide, high risk is presumed.

(1) Diphacinone and its sodium salt Exposure and Risk to Nontarget Terrestrial Animals

The risk assessments for birds and small mammals pertains to field uses and to bait applications in rural and suburban areas where baits can be applied around buildings (e.g., barns, houses, sheds) for control of commensal rats and mice. Diphacinone can be used to control rats and mice around buildings, alleys, sewers, and transport vehicles (trains, ships, aircraft) in urban areas. However, due to the paucity of wildlife (i.e., non-domestic animals) in urban areas, primary and secondary risks are expected to be minimal.

(a) Diphacinone and its sodium salt - Birds

Table 67 - Acute Risk Presumptions for Birds

Risk Presumption	RQ	LOC
High Risk	EEC[1]/LC_{50} or LD_{50}/day[2]	0.5
Restricted Use	EEC/LC_{50} or LD_{50}/day	0.2
Endangered Species	EEC/LC_{50} or LD_{50}/day	0.1

[1]EEC = Estimated Environmental Concentration (ppm) on avian and mammalian food items (short grass; tall grass; broadleaved plants and small insects; seeds, pods, large insects)

[2]mg toxicant consumed/day ÷ [LD_{50} X bird wt (kg)], where tox. consumed/day = amount food eaten X % a.i. in the food

Primary risk: The potential for primary exposure of seed-eating birds exists primarily for field applications of unprotected loose bait (i.e., aerial or ground broadcast or hand applied pellets or treated whole grains). Minimal exposure is expected for applications where bait is placed in protected bait stations or areas inaccessible to nontarget wildlife, if place packs or paraffinized bait blocks are used, and for underground applications for control of pocket gophers. Birds that are mainly herbivorous or insectivorous are not expected to be at risk from grain-based food baits.

RQs for loose food baits are based on the number of LD_{50} doses potentially consumed by a bird in one day. RQs are calculated for three separate weight classes of birds: 500-1000 g (e.g., waterfowl), 100-200 g (e.g., upland gamebird), and 20-50 g (e.g., passerine). Acute RQs for applications of diphacinone food baits are summarized in Table 68 below.

Table 68 - Avian (Granivore) Acute RQs (LD_{50}s/day)*

Site[+]	Bait (% a.i.)	Body Wt Class (g)	Amt Food Eaten (g)[1]	mg a.i. consumed/day	Acute RQ[2,3] (LD_{50}s/day)
Unspecified sites[4]; Forestry[5]	0.01	20-50	3.50	0.35	0.05
		100-200	9.00	0.90	0.02
		500-1000	18.00	1.80	0.01
Orchard[6]; Unspecified sites[7]	0.005	20-50	3.50	0.18	0.02
		100-200	9.00	0.45	0.01
		500-1000	18.00	0.90	0.01

[+]the number of LD_{50}s potentially ingested per day are determined only for those use sites where loose, unprotected baits are available (i.e., broadcast or hand-applied, uncovered baits)
[1]estimates of food consumption as a function of body size are based on Kenaga (1972) and Dunning (1984) for the mallard, bobwhite quail, and red-winged blackbird
[2]LD_{50}s/day = mg toxicant consumed/day ÷ [LD_{50} (mg/kg) * bird wt (kg)]
[3]only the highest RQ value is tabulated
[4]ground squirrel control (CA)
[5]deer mouse control (CA)
[6]vole control (CT, GA, ID, MA, MI, NC, NH, OH, OR, PA, SC, UT, VA, VT, WA, WV)
[7]rats, mice, voles, woodrats, jackrabbits (CA)
[*]Acute RQs (LD_{50}s/day) are based on a Diphacinone Bobwhite Quail LD_{50} of 400 mg/kg.

Acute LOCs are not exceeded when RQs are based on the number of LD_{50} doses potentially ingested in a day. However, diphacinone is a multiple-feeding anticoagulant, and risk to birds that feed on bait for several days is likely greater than predicted by RQ values based on a single feeding. Therefore, it may be more appropriate to assess risk based on the 5-day dietary toxicity value. For this scenario, EECs on grains or pellets are 50 ppm (0.005% a.i. baits) and 100 ppm (0.01% a.i. baits). Acute RQs based on subacute dietary toxicity are summarized in Table 69 below.

Table 69 - Avian (Granivore) Acute RQs For Diphacinone Food Baits[1]

Site[+]	Bait (% a.i.)	EEC (ppm)	Acute RQ (EEC/LC_{50})
Unspecified sites[2]; Forestry[3]	0.01	100	0.11***
Orchard[3]; Unspecified sites[5]	0.005	50	0.06***

[+]RQs are calculated only for those use sites where loose, unprotected baits are available (i.e., broadcast or exposed baits)
[1] Acute RQs For Diphacinone Food Baits are based on a Mallard LC_{50} of 906 ppm.
[2]ground squirrel control (CA)
[3]deer mouse control (CA)
[4]vole control (CT, GA, ID, MA, MI, NC, NH, OH, OR, PA, SC, UT, VA, VT, WA, WV)
[5]rats, mice, voles, woodrats, jackrabbits (CA)
[***]exceeds the endangered species LOC

Acute high risk and restricted use LOCs are not exceeded for food bait applications when the RQ is based on the subacute dietary toxicity. However, the endangered species LOC is exceeded for granivores for field and "around" building applications of 0.01% a.i. bait in California.

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Secondary risk: Potential secondary risks exist for some avian predators and scavengers that feed on poisoned rodents. As indicated by a supplemental study, rats and mice poisoned with 0.01% a.i. diphacinone baits can be hazardous to owls and presumably other raptor species that feed on poisoned animals. Such exposure is likely to occur for the uses of 0.01% a.i. diphacinone bait for field uses and around buildings in California. Most field baits and those used to control commensal rats and mice around buildings are 0.005% active ingredient. Risk from 0.005% a.i. bait cannot be assessed until secondary toxicity data become available. However, based on the secondary hazard reported for the 0.01% active ingredient bait, risk is presumed for the 0.005% a.i.bait until data are available to refute that presumption.

(b) Diphacinone and its sodium salt - Mammals

Primary risk: Because diphacinone is a rodenticide with label claims for control of rodents (rats, mice, voles, ground squirrels, pocket gophers, muskrat, chipmunk), lagomorphs (jackrabbit), and carnivores (mongoose), the Agency presumes acute high risk to any small mammals that feed on diphacinone baits. Primary risk is likely to be highest for field uses, because more wildlife is apt to be exposed in orchards and other areas than around buildings where rats and mice are baited. The Agency also presumes that risk from 0.01% a.i. baits is greater than that for 0.005% a.i.baits. High risk to small carnivores also may exist from products containing flavorings such as "meat and blood" and "fish", because the odors and taste of such flavorings may attract and enhance bait consumption by species that might not otherwise be attracted to grain-based bait.

Primary risk can be reduced for mammals larger than the target species if protected bait stations are used for applying bait. Well designed bait stations have entrance holes just large enough for adults of the target species but too small for larger nontarget species. However, because smaller species can enter bait compartments and feed, high risk is presumed for any granivorous mammals in the treatment area that are smaller than the target species.

Secondary risk: Studies conducted by the Denver Wildlife Research Center indicate that animals poisoned with 0.01% a.i. diphacinone bait pose a risk to secondary consumers. In one study (Evans and Ward 1967), 0.01% a.i. carrot baits were fed to nutria for 10 days. Dead nutria (skinned carcass, liver, heart, and lungs) were frozen and subsequently thawed and fed to three mink and three mongrel dogs. The three mink died after 5 to 18 days exposure, and the three dogs died after 6 to 10 days. The authors concluded that nutria poisoned with 0.01% a.i.. diphacinone bait could pose a secondary risk to some nontarget species. In another study, one of two ermine died after eating 10 poisoned mice in 7 days.

Savarie et al. (1979) administered a single oral dose of diphacinone (7 dosage levels) to 10 captive coyotes. The LD_{50} was 0.6 mg/kg, with animals dying 6 to 17 days after dosing. Skeletal muscle from dead coyotes was ground, mixed with 25% oatmeal, reground, and refrigerated until 30 g samples were fed to groups of laboratory rats (8 rats per group) to indicate the potential for secondary hazard. Four of eight rats died 6 to 8 days after feeding on meat mixture containing 0.5 ppm diphacinone. Rats feeding on meat mixtures of less than 0.5 ppm

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survived with no clinical signs of toxicity. However, as the authors emphasized, the amount of residue in liver, kidneys, heart, and small intestine exceeded 0.5 ppm in many or most of the dead coyotes, and selective feeding on these tissues by secondary consumers could result in increased risk of poisoning.

The Agency currently lacks secondary hazards data to assess risk to mammalian predators and scavengers that might feed on rodents poisoned with 0.005% a.i. diphacinone baits. These data are needed to assess risks from the various field uses and for use against commensal rats and mice around buildings in rural areas. However, based on the demonstrated secondary toxicity of 0.01% a.i. bait, the Agency presumes secondary risks to mammals from applications of 0.005% a.i. baits. Secondary risks will be reconsidered when toxicity data are submitted.

(c) Diphacinone and its sodium salt - Exposure and Risk to Nontarget Plants and Insects

No data were required.

(2) Diphacinone and its sodium salt Exposure and Risk to Nontarget Aquatic Animals

Minimal risk to aquatic organisms is expected from the current uses of diphacinone. Outdoor products are food baits, most of which are pelletized and/or paraffinized, and the amount of active ingredient applied per acre is very low. Applications made in bait stations further limit contact of bait with soil. The available environmental fate data indicate that most diphacinone will be tightly bound to soil, and little contamination of surface waters is expected. Moreover, diphacinone has a low solubility in water (30 ppm) and is only moderately toxic to aquatic organisms (EC_{50}/LC_{50}s = 1.8-7.5 ppm). Diphacinone salt, which is highly soluble in water, can be dissolved in water and applied as a liquid bait; however, it is limited to indoor use for rat and mouse control.

(3) Diphacinone and its sodium salt Endangered Species Concerns

The U.S. Fish and Wildlife Service addressed Diphacinone in its Biological Opinion of March, 1993. The use patterns included commensal and field rodent control in and around buildings, in orchards, cropland, pasture, rangeland, ornamentals, forest, rights-of-way, along ditches and banks of waterways, garbage dumps, and sewers. The Service made a "jeopardy" or "no jeopardy" determination for the 34 "may affect" species listed below. Other species were considered either not at risk of exposure or not likely to be affected. See Table 70 below.

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Table 70 - USFWS 1993 Biological Opinion for Diphacinone

Species	Jeopardy	No Jeopardy
Mammals:		
Alabama beach mouse *(Peromyscus polionotus ammobates)*	X	
Anastasia Island beach mouse *(Peromscus polionotus phasma)*	X	
Choctawhatchee beach mouse *(Peromyscus polionotus allophrys)*	X	
Southeastern beach mouse *(Peromyscus polionotus niveiventris)*	X	
Perdido Key beach mouse *(Peromyscus polionotus trissyllepsis)*	X	
Amargosa vole *(Microtus californicus scirpensis)*	X	
Florida salt marsh vole *(Microtus pennsylvanicus dukecampbelli)*	X	
Hualapai Mexican vole *(Microtus mexicanus hualpaiensis)*	X	
Key Largo cotton mouse *(Peromyscus gossypinus allapaticola)*	X	
Salt marsh harvest mouse *(Reithrodontomys raviventris)*	X	
Fresno kangaroo rat *(Dipodomys nitratoides exillis)*	X	
Giant kangaroo rat *(Dipodomys igens)*	X	
Morro Bay kangaroo rat *(Dipodomys heermanni morroensis)*	X	
Stephen's kangaroo rat *(Dipodomys stephensi)*	X	
Tipton kangaroo rat *(Dipodomys nitratoides nitratoides)*	X	
Point Arena mountain beaver *(Aplodontia rufa nigra)*	X	
Silver rice rat *(Oryzomys palustris natator (= Oryzomys argentatus)*	X	
Utah prairie dog *(Cynomys parvidens)*	X	
Carolina northern flying squirrel *(Glaucomys sabrinus coloratus)*	X	
Delmarva fox squirrel *(Sciurus niger cinereus)*		X
Key Largo woodrat *(Neotoma floridana smalli)*	X	
Lower Keys rabbit *(Sylvilagus palustris hefneri)*	X	
Black-footed ferret *(Mustela nigripes)*	X	
San Joaquin kit fox *(Vulpes macrotis mutica)*	X	
Gray wolf *(Canis lupus)*	X	
Florida panther *(Felis concolor coryi)*	X	
Jaguarundi *(Felis yagouaroundi cacomitli)*	X	
Ocelot *(Felis pardalis)*	X	
Grizzly bear *(Ursus arctos horribillis)*	X	
Lousiana black bear *(Ursus americanus luteolus)*	X	
Birds:		
Audubon's crested caracara *(Caracara cheriway audubonii)*	X	
Reptiles:		
Eastern indigo snake *(Drymarchon corais couperi)*		X
Puerto Rican boa *(Epicrates inornatus)*		X
Virgin Islands tree boa *(Epicrates monensis (= inornatus) granti)*		X

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IV. RISK MANAGEMENT AND REREGISTRATION DECISION

A. Determination of Eligibility

Section 4(g)(2)(A) of FIFRA requires the Agency to determine, after submission of relevant data concerning an active ingredient, whether products containing the active ingredient are eligible for reregistration. The Agency has previously identified and required the submission of the generic (i.e., active ingredient specific) data required to support reregistration of products containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, diphacinone and its sodium salt, and pival and its sodium salt, as active ingredients. The Agency has completed its review of these generic data, and has determined that the data are sufficient to support reregistration of all products containing these chemicals, except pival and its sodium salt. Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt. Appendix B also lists the submitted studies that the Agency found acceptable.

The data identified in Appendix B are sufficient to allow the Agency to assess the registered uses of brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt, and to determine that these chemicals can be used without resulting in unreasonable adverse effects to humans and the environment when labeled and used as specified in this RED document. The Agency, therefore, finds that all products containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt as the active ingredient are eligible for reregistration. The reregistration of particular products is addressed in Section V of this document.

With the exception of pival and its sodium salts, the Agency made its reregistration eligibility determination based upon the target data base required for reregistration, the current guidelines for conducting acceptable studies to generate such data, published scientific literature, data from the American Association of Poison Control Centers, etc. and the data identified in Appendix B. Although the Agency has found that all uses of these chemicals are eligible for reregistration, it should be understood that the Agency may take appropriate regulatory action, and/or require the submission of additional data to support the continued registration of products containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt, if new information comes to the Agency's attention or if the data requirements for registration (or the guidelines for generating such data) change.

The chemical pival and its sodium salts was suspended by the Agency in December 1994 for failure of the registrant, Motomco, Incorporated, to respond to the Agency’s Data Call-In Notice (DCI) and submit the required data to support the continued registration. The Agency, during the reregistration process for this rodenticide cluster RED, again solicited the registrant to submit the required data to support the reregistration. The registrant chose not to support the reregistration of pival and its sodium salts. Therefore, the Agency has determined that pival and its sodium salts are *ineligible* for reregistration, and will remain suspended. In the future, the Agency may seek cancellation of the registration for pival and its sodium salt.

1. Eligibility Decision

Based on the reviews of the generic data for the active ingredients brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt, the Agency has sufficient information on the health effects of these chemicals and on their potential for causing adverse effects in fish, wildlife, and the environment. The Agency has determined that these chemicals, labeled and used as specified in this Reregistration Eligibility Decision document, will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, the Agency concludes that products containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt, are eligible for reregistration.

2. Eligible and Ineligible Uses

The Agency has determined that all uses of brodifacoum, bromethalin, and bromadiolone are eligible for reregistration.

The Agency has determined that all uses of chlorophacinone and diphacinone and its sodium salt are eligible for reregistration, with the exception of certain field bait uses. The Agency has determined that field-bait uses containing .005% chlorophacinone and diphacinone and its sodium salt are eligible for reregistration.

The Agency has determined that field-bait uses containing more than .005% chlorophacinone and diphacinone and its sodium salt are ineligible for reregistration. Field tests have adequately demonstrated that products with lower-concentrations of these active ingredients are sufficiently efficacious for target pest species, and that the uses with higher concentrations have the potential to cause unnecessary secondary poisonings to avian and mammalian consumers.

The Agency has also determined that all uses of pival and its sodium salt are ineligible for reregistration and are to remain suspended.

B. Regulatory Position

The following is a summary of the regulatory positions and rationales for brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt. Where labeling revisions are imposed, specific language is set forth in Section V of this document.

1. Summary of Risk Assessment Conclusions

a. Human Health Risk

(1) Dietary

These chemicals are non-food use pesticides. Therefore, tolerance reassessment is unnecessary. Also, it is unlikely that there will be any dietary exposure to humans via food sources or via drinking water through contamination of ground or surface water.

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(2) Residential and Occupational Risk

(a) Residential

EPA is concerned about the continued risk of human exposure, especially children, resulting from the continued use of rodenticides in residential settings. In fact, EPA has gone on record, over the years, to express its concern regarding human exposures and incidents to rodenticides. PR Notice 94-7, Label Improvement Program for the Revision of Use Directions for Commensal Rodenticides and Statement of the Agency's Policies on the Use of Rodenticide Bait Stations, issued by the Agency on September 16, 1994, required registrants of certain rodenticide products claimed to control commensal rodents to revise the labeling of such products to bear certain statements concerning "tamper-resistant bait stations." It also informed rodenticide registrants, applicants, and other interested persons of EPA's continued concern for the safe use of rodenticides. Moreover, PR Notice 94-7 outlined EPA's policies regarding the isolation of commensal rodenticides from children, dogs, other pets, domestic animals, and non-target wildlife. PR Notice 94-7, in part, stated the following:

> "Historically, more than 1000 incidents of human exposure to rodent poisons have been reported annually in the U.S. Numbers of human incidents reported have increased greatly in recent years with the advent of a new reporting network. In 1988, more than 10,000 rodenticide incidents were reported in the American Association of Poison Control Center's National Data Collection System. Nearly 90% of these cases involved children under six years of age. Nearly all of such exposures are classed as accidents. The human exposure incidents that are reported may represent less than half of those which occur. Well over 80% of reported human rodenticide exposures involve anticoagulant compounds.
>
> Young children thought to have been exposed to rodenticides are often given some medical attention, although symptoms of poisoning usually are not observed, especially in cases involving anticoagulants which act very slowly. Although young children have been killed by rodenticides, most rodenticide-related deaths of humans result from intentional ingestions by persons much older than five years of age.
>
> While reports summarizing incidents typically do not indicate exactly how exposures have occurred, it is likely that most accidents are related to improper use rather than to improper storage. Accidents of both types are preventable. EPA believes that the large numbers of exposure incidents provide evidence that current policies for promoting bait protection have not been sufficient and, therefore, that tougher, more explicit policies are needed. EPA has not been persuaded by contentions that the relatively low incidences of serious human illnesses caused by accidental exposures to compounds such as warfarin justify selective relaxations of requirements for bait protection…"

Data collected by the American Association of Poison Control Centers (AAPCC) for 1995 report 17,187 human exposures to all rodenticides. Of these numbers, 14,710 (~ 86%) exposures were attributed to the anticoagulant rodenticides. Of concern to EPA is the number of exposures to children less than six years-old; in 1995, there were a total of 14,900 or approximately 87% of the total exposures. When the total number of human exposures to rodenticides was analyzed, 6,450 were significant enough to result in treatment at a health care facility.

Data collected by the AAPCC for 1996 report that 17,601 rodenticide exposures occurred to humans. The anticoagulant rodenticides (brodifacoum, bromadiolone, chlorophacinone,

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diphacinone and its sodium salt, and pival and its sodium salt), accounted for 14,836 or over 84% of the total exposures. Of these exposures, 13,362 (90%) occurred in children less than six years-old. Approximately 5,300 exposures resulted in people seeking treatment at a health care facility.

Furthermore, rodenticides are acutely toxic to humans. Margins of Exposures (MOEs), when bait is ingested, are less than one. Generally, the Agency considers a MOE of 100 or above to be protective of the public's health. The Agency, for example, has calculated the dose a 10 kg child receives from a 43 gram packet of rodenticide (standard commercial package). The Agency's calculation resulted in a MOE of 0.6 The toxicological endpoint for diphacinone, was 0.13 mg/kg/day.

Rodenticides, when used as currently sold and marketed, are responsible for a high number of human incidents and accidental exposures each year. In the recent past, poison control centers have enhanced their ability to capture incident data. Because of improved data collection, it appears that the high number of human unintentional or accidental exposures to rodenticides remain constant each year, or may be increasing. From the number of rodenticide exposures to children, it is clear that children under six years-old are disproportionately more at risk from the continued use of these products in residential settings. Based on these facts, EPA is concerned regarding the risk of exposure to these chemicals to residential users, particularly children.

(b) Occupational (Mixer/Loader/Applicator)

The Agency has determined that there is potential exposure to applicators and/or other handlers during typical use patterns associated with these chemicals. Specifically, the Agency is concerned about potential dermal and inhalation exposures to handlers during the loading and application of these chemicals.

Based on the use patterns and potential exposures described above, major handler exposure scenarios were identified such as: (l) 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 parafinized blocks into pieces and placing the pieces in bait stations; (4) securing large paraffin blocks in bait stations used in sewers; (5) applying bait by hand; and (6) applying bait, e.g. pellets in broadcast treatments using ground equipment; and (6) spraying.

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 come in contact with the bait during loading into the bait stations (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 loading into bait stations. Hence, the Agency is concerned about potential dermal exposure and inhalation of fine particles, and dusts associated with baits which could be inhaled resulting in an inhalation and/or oral exposure. As a result, the Agency is requiring more stringent PPE for all occupational uses of these chemicals as discussed below and in Section V of this RED document.

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b. Risk to Household Pets

As with human exposures, EPA is concerned about the increased risk posed to household pets to rodenticides used in residential settings. When used as currently sold and marketed, rodenticides account for a high number of incidents and accidental exposures to household pets every year. PR Notice 94-7 stated in part that:

> "Dog incidents account for more than 80% of the reported exposures of nontarget animals to commensal rodenticides. Most dog exposures are believed to be accidental. The annual number of incidents of animals being exposed to rodenticides is not known, but over 4,000 rodenticide-related inquiries were made to the Illinois Animal Poison information Center in each of the years from 1986 to 1988, with a high of 6,272 inquiries having been made in 1987.
>
> Symptoms of rodenticide poisoning are detected more frequently in reported animal cases than in child cases. A larger percentage of asymptomatic exposures of animals may go undetected as pets and livestock generally are not watched as closely as children. Dogs may die as a result of rodenticide exposures, especially if acute poisons are involved. Extended Vitamin K1 therapy may be needed for dogs that have been exposed to certain anticoagulants, such as brodifacoum or diphacinone, which are retained in the body for a relatively long time. For animal exposures reported in 1987 (and probably in other years as well), the animal's owner typically was the source of the rodenticide. Most of these exposures were accidental and occurred in or around human residences."

The American Association of Poison Control Centers (AAPCC) reported 41,854 animal exposure cases (mostly dogs and cats) in 1990. Of these, 3,157 involved rodenticides (8.4%). Most rodenticide poisonings are due to careless placement or overuse of baits, and, much less often, failure to discard poisoned rodents and malicious poisonings. There were a total of 454 deaths reported in animals in 1990, of which 39 (9.2%) were due to anticoagulant rodenticides, the second leading cause of death after ethylene glycol and related compounds.

c. Environmental Risk

(1) Environmental Fate

In general, these rodenticides are very similar in their holistic environmental fate characteristics. However, they differ in specific environmental fate characteristics as discussed earlier in this RED document.

Based on environmental chemistry data, and the use pattern, use of these rodenticides is not expected to result in contamination of surface and ground water. Although persistent, these chemicals tend to be relatively immobile in soil and fairly insoluble in water. Most are applied as a pelleted bait used in and around buildings. They are primarily used in protective bait stations when used outdoors, therefore, their environmental fate risk is negligible.

(2) Ecological Effects

Primary toxicity to mammals is very high for these rodenticides. Primary toxicity to birds is mostly high to very high for the single feeding rodenticides (brodifacoum, bromadiolone, and bromethalin). It is mostly moderate for the multiple feeding compounds (diphacinone and

chlorophacinone). Toxicity to aquatic organisms ranges from moderate to very high. Chronic data are not available for any of the rodenticides.

For only a few of these chemicals do some secondary toxicity data exist for avian and mammalian predators and their scavengers. These studies are required to support the use of rodenticides in fields, and "around" buildings in non-urban (i.e., rural, suburban) areas. Available laboratory and/or field data indicate that rodents, poisoned with brodifacoum or bromadiolone baits, can kill avian and mammalian secondary consumers. Sufficient data exist to indicate that diphacinone bait (0.01%) is secondarily hazardous to birds and mammals and chlorophacinone bait (0.01%) is hazardous to mammalian predators. Avian data are not available for chlorophacinone bait at 0.01%. Adequate data are not available for birds and mammals for chlorophacinone and diphacinone bait or for bromethalin (all at 0.005%).

2. Summary of Rodenticide Benefits

Although the Agency is concerned about the risk posed to humans, especially children, and non-target animals by the use of these products as they are currently sold and marketed, EPA also recognizes the important public health benefits of rodenticides. Specifically, the Agency considered the benefits from rodent control as it relates to prevention of disease transmission, property damage, and attacks on humans.

Rodenticides are one of the most efficient available means for controlling existing infestations of large numbers of rodent pests. These agents also may be the method of choice in controlling certain smaller rodent infestations and often are needed to control individuals which cannot be removed by use of traps.

People control rodent pests primarily because these animals: (1) are associated with the spread of many types of serious diseases; (2) bite humans; (3) damage private and commercial property; (4) destroy and contaminate millions of tons of agricultural crops annually, both in the field and in storage; and, (5) are generally unwelcome in homes, schools, places of business, and other areas occupied or frequented by humans.

The diseases vectored by rodents include: plague, Rickettsial diseases (e.g., murine typhus, Rickettsialpox), leptospirosis, rat bite fever, Salmonellosis, hantavirus, Lyme disease, granulocytic Ehrlichosis, relapsing fever, and others. Rodents transmit diseases either directly or indirectly, via ectoparasites such as fleas, ticks or mites, or bodily waste products and secretions.

Many rodent-transmitted diseases recently have been held in check through the private and public use of rodenticides, along with other pest and disease control and management practices. Improved pest management, including coordination of rodenticide use and other rodent abatement practices, is a principal reason why numbers of cases and deaths associated with many rodent-transmitted diseases have been much lower in the latter part of the 20th Century than was the case in prior decades. For example, there were 3,700 reported cases of murine typhus in the U.S. in

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1942 but only 12 reported cases in 1987. In recent decades, however, "new" rodent-transmitted diseases such as Lyme disease and hantavirus have emerged, primarily in rural and semi-rural areas in the U.S. Of these diseases, the HPS hantavirus strains appear to be the most serious, with a composite fatality rate of approximately 45% for the 170+ human cases reported since 1993.

The number of cases of rats biting humans has been estimated to be 14,000 per year. More recent information is not available on a nationwide basis.

Rodents damage structures by gnawing on integral parts and by contaminating them with bodily waste products and other secretions. Rodents can gnaw through wood, concrete, asphalt, sheet rock, plumbing, and soft metals. Rodent damage to electrical wiring has been cited as the probable cause for certain fires and explosions, as well as an instance of shutting down the Internet. When buildings, including residences, are heavily infested, poisoning generally is an integral component of successful abatement programs.

Field rodents such as ground squirrels, voles, and native mice and rats cause significant damage to crops and rangelands. Certain crops, such as sugarcane, are heavily damaged in the field by commensal rats and mice. Commensal rodent species are responsible for much of the pest damage to stored food and feed in the United States. Chlorophacinone, diphacinone, and zinc phosphide play an important role in the management of rodents associated with agricultural crops.

In general, commensal rats and mice are not "liked" by humans. This may be a factor in rodenticide use; however, disease concerns and desires to protect self and property are present in most cases in which rodenticide baits are used.

Rodenticide baits also are used in certain special circumstances, such as managing or eradicating non-native rodent species at sites where such rodents jeopardize the continued existence of certain threatened or endangered species. Control programs of this nature are run by government agencies and typically are limited to offshore islands or other refuge areas.

EPA has consulted with the Center for Disease Control (CDC), Rodent Control offices in several states (New York; Philadelphia, Pennsylvania; Boston, Massachusetts; Arlington, Virginia; and Chicago, Illinois), and a nationally recognized rodent expert regarding public health benefits and the Agency's risk mitigation measures. Based upon these discussions, the Agency has decided that its reregistration eligibility determination and the risk mitigation measures specified in this document are in the public interest as per FIFRA Section 3(c)(5).

3. Risk Mitigation Overview

As discussed earlier in this RED document, the Agency is concerned about the risks posed to humans, particularly children, household pets, and non-target animals, from the continued use of these products as they are currently sold, marketed, and used.

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While an effective antidote is available, treatment must occur in time. Furthermore, treatment can be traumatic for children, and there are costs both for time and treatment. In addition, the Agency's concerns are heightened by the number of incidents and exposures, reported annually, to these chemicals involving humans (particularly children less than six years-old), and household pets. The Agency, however, is also aware of the public health benefits these chemicals provide. As a result of the Agency's concerns, the following risk mitigation measures are necessary for all registrations of brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt.

a. Reducing Risk for Children and Household Pets

The Agency has concluded that the rodenticides, containing the active ingredients subject to this RED document, which are used in residential settings, schools, recreation areas, and other places that children may frequent, pose the greatest risk of accidental exposure and incidents to humans, particularly children, and household pets. As set forth below, the Agency is requiring the following risk mitigation measures for rodenticide active ingredients subject to this RED document used in residential settings, schools, recreation areas, and other places children may frequent. In addition, outside the scope of this RED process, the Agency is requiring the identical risk mitigation measures to the registrations of other rodenticide active ingredients such as zinc phosphide, warfarin and its salt, difethialone, vitamin D-3, and red squill and, if necessary, registrations of new rodenticide active ingredients to be used in residential settings, schools, recreation areas, and other places that children may frequent.

When reviewing these chemicals for their reregistration eligibility, the Agency carefully considered the acute risk posed by the residential use of these chemicals along with the benefits for allowing them to remain on the commercial market for consumers to use. EPA concludes that although these products pose an acute risk to humans and household pets, the Agency has determined that the continued use of these rodenticides in residential and other settings provide a critical public health benefit.

The Agency recently became aware of incident data which suggests that there may be a potential incident problem involving the active ingredient brodifacoum. At this time the Agency is reviewing the data; no final conclusions have been reached. Additionally, through the “Notice of Availability” for this document, the Agency requests state incident data for all rodenticides to better understand the extent of this potential problem. After review, the Agency may impose additional restrictions on the use of brodifacoum and/or other active ingredients.

b. Incremental Risk Reduction

In order to address the risk concerns posed by the use of these products and still maintain the benefits afforded by their use, the Agency developed a two-phased approach to mitigating risk. The first phase involves measures which can be put in place in the short term that will serve to identify when an exposure has occurred, lessen the number of exposures, and monitor exposures.

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The second phase will move toward eliminating the opportunity for exposures in the long term. Ideally, the Agency would have preferred to impose measures which would have immediately eliminated opportunities for exposures; however, it recognizes that new technologies may not exist and may need to be developed to accomplish this while still maintaining the efficacy of the product. The Agency has, therefore, developed this phased approach to allow time for the development and testing of a new technology. The innovation of the new technology will be coordinated by a Stakeholder group. The two phases to risk mitigation, the time frames, and reporting requirements are described in detail below.

(1) Phase One: Short-Term Risk Mitigation Measures

(a) Indicator Dye and Bittering Agent

All registrants of rodenticides, other than those with products used exclusively at agricultural sites, must incorporate an indicator dye into their formulations. The dye is intended to help identify whether a child or household pet has consumed a rodenticide by dying their mouth and/or hands a bright color. EPA believes the dye will play an important role in identifying when an exposure has occurred, thereby helping to determine if treatment is required.

Typically, it is very difficult for parents and guardians of children and pet owners to discern whether an exposure or ingestion has actually occurred. This uncertainty may lead to unnecessary treatment at a medical facility as a precautionary measure. In turn, the Agency believes this measure will also enable parents and guardians of children and pet owners to seek medical or veterinarian attention sooner rather than later and avoid a serious medical problem.

All registrants of rodenticides, other than those with products used exclusively at agricultural sites, must incorporate a bittering agent into their formulations to make the bait less palatable to humans. EPA believes that the bittering agent may cause some children to expel the bait if placed in the mouth. The Agency is fully aware that children younger than one year old do not have fully formed taste buds and may not be fully protected by this measure. However, this measure should prevent some exposures to children older than one year of age. Likewise, the EPA is also aware that this measure may not affect exposures to non-target household animals. EPA recognizes that many of the formulations currently contain a dye. All registrants may present data demonstrating that the current dye meets the intent of this requirement.

(b) Improved Labeling Requirements

EPA is requiring a number of label revisions to rodenticide registrations. These requirements are set forth in Section V of this RED document and are in addition to those in PR Notice 94-7 that have already been implemented.

Labels which currently allow placement of rat and mouse baits “in and around buildings” must be amended to “indoors and against the outside walls of buildings.” Rat and mouse bait placements will be allowed “around” buildings only if registrants demonstrate in secondary toxicity studies that secondary risks to birds and mammals are minimal.

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Under "Note to Physicians," a few of the labels recommend that Vitamin K_1 be administered intravenously (IV) or intramuscularly (IM). The veterinary literature states that vitamin K_1 can cause anaphylactic reactions if given IV and extensive hemorrhage after IM administration. Sheldon Wagner, M.D., a consultant to OPP, confirmed that Vitamin K_1 should not be given IV unless there is a hemorrhagic crisis. IM administration is acceptable in humans. The recommendation for IV administration must be deleted from the label.

(c) Annual Submission of American Association of Poison Control Centers (AAPCC) Data

Under the authority of FIFRA section 3(c)(2)(B), the Agency is requiring registrants of rodenticides subject to this RED document, to submit to the Agency annual American Association of Poison Control Centers' (AAPCC) data. The Agency is requiring AAPCC data for the years 1999 through 2009. Registrants are encouraged to share the cost of generating data, whenever appropriate. If needed, the Agency may ask registrants of rodenticides for additional annual submission of AAPCC data. These data will enable the Agency to determine whether the imposed risk mitigation measures are reducing incidents/exposures to humans, in particular children. AAPCC data obtained by the Agency for 1995 and 1996 will serve as baseline data. The American Association of Poison Control Centers is located at 3201 New Mexico Avenue NW, Suite 310, Washington, D.C. 20016. They can be reached by telephone on (202) 362-7217 and by fax on (202) 362-8377.

(d) Restricted Use Classification for Tracking Powders

When rodents migrate through tracking powder during their daily activities they contact and accumulate the rodenticide on their bodies and/or fur. Afterward, the rodents ingest the poison while grooming. If enough rodenticide is consumed, death occurs.

EPA has determined that the use of these chemicals as tracking powders in and around residences, schools, recreation areas, and other places that children may frequent, pose a significant risk to children, household pets, and non-target animals. EPA believes that children and pets can easily come in contact with rodenticides used as tracking powders simply based on their use patterns and use locations. To protect children and non-target animals from exposure, all products formulated as tracking powders must remain classified and labeled as restricted use because of acute toxicity and undue secondary risk to non-target species. Certified applicators receive training on the importance of following label directions and overall application, and, therefore are more likely to apply the product correctly. Moreover, tracking powder products must bear a strong precautionary statement and new restrictions limiting placement of powder to locations not accessible to children, household pets, and non-target animals.

EPA is also concerned about the potential exposure (inhalation and dermal) to the certified applicators of these types of product formulations. Due to the low inhalation LC_{50} value and the possibility of users inhaling or ingesting powders during pouring and application, EPA is limiting

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use of the powder formulations to use by certified applicators, EPA is requiring protective eyewear and dust/mist respirators for such users in addition to other personal protective equipment.

Within eight months after receipt of this RED document, the EPA is requiring that all products with tracking powder uses, including field and residential uses, containing brodifacoum, bromadiolone, bromethalin, chlorophacinone, and diphacinone and its sodium salt be classified as restricted use pesticides.

(e) Restricted Use for Field Products

All products labeled for field uses, except for those limited to manual underground baiting, must be reclassified and relabeled as restricted use because of acute toxicity and undue secondary risk to non-target species.

(f) Field Uses of Chlorophacinone and Diphacinone and its sodium salts

Within eight months after the receipt of this RED document, all products containing chlorophacinone and diphacinone and its sodium salt -- at active ingredient percentages higher than 0.005% -- must remove all field-use claims from the label. This is required because of acute toxicity and undue secondary risk to non-target species. This requirement does not apply to products limited to manual, underground applications in field situations (pocket gophers and moles), if this limitation is stated clearly and unambiguously on the products' labels.

(g) Time Frames & Reporting Requirements

PHASE ONE: The Agency is aware that all mitigation measures required during Phase One may not be feasible within the eight-month time frame usually accorded by the RED process to submit labeling changes. While registrants will still be required to submit revised labeling as detailed in Section V within the 8 month time frame, the Agency recognizes that the formulation changes required by the addition of the indicator dye and bittering agent may take longer. The timing for the incorporation of the dye and bittering agent in rodenticide products will be an outcome of a meeting convened by the Agency before the first Stakeholder meeting (as discussed below in Phase Two).

Data from the American Association of Poison Control Centers (AAPCC) must be submitted within one year after the end of the reporting year. For example, 1999 AAPCC data must be submitted to the Agency on or before December 31, 2000. The Agency will schedule a meeting with registrants before the initial Stakeholder meeting to provide registrants with clear guidance on the format, content, and parameters of the data obtained from the AAPCC.

(2) Phase Two: Long-Term Risk Reduction

As discussed previously in this RED document, the Agency believes that the required risk mitigation measures outlined in Phase One should be followed by further exposure/risk reduction

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measures for rodenticides. EPA is also aware that a safer technology is efficacious and equally effective to eliminate human and household pet exposures may not currently exist. However, the Agency will require the development of and movement into a new, safer household rodenticide use technology. The EPA is convinced that this technology can be developed. Therefore, Phase Two of the Agency's risk mitigation approach, is the requirement to move rodenticides into a safer use technology. To achieve this end, within 90 days of the issuance of the REDs, the Agency will form a Stakeholder group and hold a series of meetings to discuss means of significantly reducing exposures to children and pets. The Stakeholder group will consist of members from industry, states, CDC, CPSC, AAPCC, rodent control experts, members of environmental groups, and the medical community.

The Agency will conclude the Stakeholder process within nine months from the issuance of the REDs. The Agency expects, at the conclusion of this process, to have a recommendation on how to further mitigate risk to children and household pets and an implementation plan to achieve significant risk reduction. Agency ideas include: (a) placing rodenticides in bait containing, disposable (non-refillable), child-resistant bait stations, or some other technology, (b) development and implementation of an exhaustive, educational outreach program for consumers and enhanced training for PCOs, (c) tamper-resistant bait stations, and (d) additional labeling improvements, e.g., foreign language labeling, icons on labeling such as "Mr. Yuk," and skull and crossbones.

c. Risk Mitigation Measures for Products Intended for Occupational Use

(1) Gloves

To reduce dermal exposure, the Agency has determined that all labels for occupational-use products will require commercial handlers to wear gloves while handling these rodenticide chemicals that are not already contained in place packs. This requirement will be overturned if registrants submit data which indicate there is no dermal exposure.

EPA is requiring all occupational handlers (commercial applicators) who handle formulations that are not already contained in place packs to wear gloves.

(2) Protective Eyewear and Inhalation Protection

The Agency has determined that occupational handlers (commercial applicators) must wear protective eyewear, and a dust mask/mist respirator when handling non-parafinized formulations of these chemicals such as, meal or grain-based baits, unless these formulations are contained in place packs or the registrants can determine via data that there is no inhalation exposure. The respirator would reduce the possibility of inhalation and ingestion of dusts resulting from the pouring and application of these products. Moreover, the protective eyewear would reduce the potential ocular absorption that could result from contact with such dusts.

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In addition, the Agency is requiring all occupational handlers who handle powder formulations or any other non-paraffinized formulation of chlorophacinone to wear a dust/mist respirator and protective eyewear during open pouring and application unless registrants submit data which indicate there is no inhalation exposure.

There are no handler exposure data available for the use patterns associated with chlorophacinone mixing, loading, and application.

4. Endangered Species Statement

The Agency has developed a program (the "Endangered Species Protection Program") to identify pesticides whose use may cause adverse impacts on endangered and threatened species, and to implement mitigation measures that will eliminate the adverse impacts. At present, the program is being implemented on an interim basis as described in a Federal Register notice (54 FR 27984-28008, July 3, 1989), and is providing information to pesticide users to help them protect these species voluntarily. As currently planned, the final program will call for label modifications referring to required limitations on pesticide uses, typically as depicted in county-specific bulletins or by other site-specific mechanisms as specified by state partners. A final program, which may be altered from the interim program, will be described in a future Federal Register notice. The Agency is not imposing label modifications at this time through the RED. Rather, any requirements for product use modifications will occur in the future under the Endangered Species Protection Program.

The pesticides included in this RED have been subject to a formal consultation with the Fish and Wildlife Service, as noted following each active ingredient. Additional consultation with the Fish and Wildlife Service and/or the National Marine Fisheries Service may be necessary to determine if steps need to be taken to protect newly listed species or from proposed new uses of these pesticides.

Most of the species determined by the Fish and Wildlife Service to be jeopardized or otherwise potentially affected by these pesticides occur in California, Florida, Hawaii, or Texas. Under the Endangered Species Protection Program, these states are working with the Agency and the Fish and Wildlife Service to provide locally based protection to listed species. Interim protective measures are being implemented or are under development. For the few species in other states, the Agency is developing protective measures to be provided to pesticide users in interim county bulletins.

V. ACTIONS REQUIRED OF REGISTRANTS

This section specifies the data requirements and responses necessary for the reregistration of both manufacturing-use and end-use products.

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A. Manufacturing-Use Products

1. Additional Generic Data Requirements

The generic data base supporting the reregistration of brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and salt for the above eligible uses has been reviewed and determined to be substantially complete. The following studies are required to be conducted on the generic ingredients.

a. Brodifacoum

- 21-Day Dermal - rabbit/rat [82-2]
- Estimation of Dermal Exposure at Outdoor Sites [231]
- Estimation of Inhalation Exposure at Outdoor Sites [232]
- Estimation of Dermal Exposure at Indoor Sites [233]
- Estimation of Inhalation Exposure at Indoor Sites [234]

b. Bromadiolone

- Leaching/Adsorption/Desorption [163-1]
- Estimation of Dermal Exposure at Outdoor Sites [231]
- Estimation of Inhalation Exposure at Outdoor Sites [232]
- Estimation of Dermal Exposure at Indoor Sites [233]
- Estimation of Inhalation Exposure at Indoor Sites [234]

c. Bromethalin

- General Metabolism [85-1]
- Leaching/Adsorption/Desorption [163-1]
- Estimation of Dermal Exposure at Outdoor Sites [231]
- Estimation of Inhalation Exposure at Outdoor Sites [232]
- Estimation of Dermal Exposure at Indoor Sites [233]
- Estimation of Inhalation Exposure at Indoor Sites [234]
- Secondary Poisoning, Mammal [70-A-SS]*
- Protocol
- Secondary Poisoning, Bird [70-B-SS]*
- Protocol
- Whole Body Residue, Target Species [70-C-S]*
- Protocol

*Studies are not required for “indoors and along the outside walls of buildings”, but are required for any other uses.

d. Chlorophacinone

- Avian Reproduction, Quail [71-4(a)]*
- Avian Reproduction, Duck [71-4(b)]*
- Estimation of Dermal Exposure at Outdoor Sites [231]
- Estimation of Inhalation Exposure at Outdoor Sites [232]

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- Estimation of Dermal Exposure at Indoor Sites [233]
- Estimation of Inhalation Exposure at Indoor Sites [234]
- Secondary Poisoning, Mammal [70-A-SS]**
- Protocol
- Secondary Poisoning, Bird [70-B-SS]**
- Protocol
- Whole Body Residue, Target Species [70-C-S]**
- Protocol

*Required to support Product CAS 90023.
**Studies are not required for "indoors and along the outside walls of buildings," but are required for any other uses.

e. Diphacinone and its sodium salt

- General Metabolism [85-1]
- Hydrolysis [161-1]
- Leaching/Adsorption/Desorption [163-1]
- Estimation of Dermal Exposure at Outdoor Sites [231]
- Estimation of Inhalation Exposure at Outdoor Sites [232]
- Estimation of Dermal Exposure at Indoor Sites [233]
- Estimation of Inhalation Exposure at Indoor Sites [234]
- Secondary Poisoning, Mammal [70-A-SS]*
- Protocol
- Secondary Poisoning, Bird [70-B-SS]*
- Protocol
- Whole Body Residue, Target Species [70-C-S]*
- Protocol

*Studies are not required for "indoors and along the outside walls of buildings," but are required for any other uses.

2. Submission of Poison Control Centers Data

Under the authority of FIFRA section 3(c)(2)(B), the Agency is requiring registrants of rodenticides subject to this RED document, to submit to the Agency annual American Association of Poison Control Centers' (AAPCC) data. The Agency is requiring AAPCC data for the years 1999 through 2009. Registrants are encouraged to share the cost of generating data, whenever appropriate. If needed, the Agency may ask registrants of rodenticides for additional biannual submission of AAPCC data. Data from the American Association of Poison Control Centers (AAPCC) must be submitted within one year after the end of the reporting year. These AAPCC data requirements are identified in the data requirements listed in Appendix B of this RED document. The American Association of Poison Control Centers is located at 3201 New Mexico Avenue, Suite 310, Washington, D.C. 20016. They can be reached by telephone on (202) 362-7217 and by fax on (202) 362-8377.

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B. End-Use Products

1. Formulation Changes - Indicator Dye and Bittering Agent

All registrants of rodenticides must incorporate an Agency approved indicator dye and bittering agent into their formulations. All registrants must submit to the Agency for approval, a revised CSF and draft labeling reflecting this incorporation into their product's formulation. The Agency recognizes that the formulation changes required by the addition of the indicator dye and bittering agent may take longer than the eight months usually provided by RED Document. The Agency will work with registrants to establish a timeframe for the incorporation of the dye and bittering agent into rodenticide products at a meeting, or through other means, prior to the initial stakeholder meeting. At this time, deadlines and submittal procedures for additional efficacy testing, if required, will also be addressed.

2. Stakeholder Meetings

The Agency is planning to hold the initial stakeholders meeting within 120 days from the issuance of this RED in Washington, D.C. As mentioned earlier, these meetings will provide an open forum to develop workable mitigation measures to adequately protect children from accidental rodenticide exposures. For these meetings to be most efficient and successful, all interested parties and viewpoints will be welcomed and considered. The outcomes of these meetings will effect all rodenticide products with residential uses, including those that were previously reregistered and those that have been registered more recently and, hence, not subject to reregistration.

3. Tracking Powders Classified as Restricted Use

Within eight months after the receipt of this RED document, the Agency is requiring that all products, containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt, with tracking powder uses, must be reclassified and relabeled as RESTRICTED USE PESTICIDES.

4. Field Use Classified as Restricted Use

Within eight months after the receipt of this RED document, the Agency is requiring that all products, containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt, with field uses, except for those limited to manual underground baiting, must be classified and labeled as RESTRICTED USE PESTICIDES.

5. Field Uses of Chlorophacinone and Diphacinone and its sodium salts

Within eight months after the receipt of this RED document, all products, containing chlorophacinone, and diphacinone and its sodium salt, at active ingredient percentages higher than 0.005%, must remove all field use claims from the label. Products which are limited only to manual underground baiting in a field use situation are excluded from the above requirement and must clearly state this limitation on the product label.

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6. Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. Registrants must review previous data submissions to ensure that they meet current EPA acceptance criteria, and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then study MRID numbers should be cited according to the instructions in the Requirement Status and Registrants Response Form provided for each product.

7. PPE/Engineering Control Requirements for Pesticide Handlers

For sole active ingredient end-use products that containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt:

- Revise the product labeling to adopt the handler personal protective equipment/engineering control requirements set forth in this section.

- Remove any conflicting PPE requirements on the current labeling.

a. Products Intended for Occupational Use

The Agency is requiring modifications to the PPE/Engineering Controls requirements on all end-use products containing brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt that are intended primarily for occupational use.

(1) Formulation Specific PPE Requirements

The Agency is establishing formulation-specific PPE for all occupational uses of brodifacoum, bromethalin, bromadiolone, chlorophacinone, and diphacinone and its sodium salt end-use products. Remove any conflicting PPE requirements on the current labeling by eliminating the less stringent requirement. For guidance on choosing glove material, contact the Chemical Review Manager for the specific chemical in question. Please refer to Table 71 for the specific label language required.

(2) Determining PPE Labeling Requirements for End-Use Products

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active ingredient specific personal protective equipment specified above. The more protective PPE must be placed on the product labeling.

For guidance on which PPE is more protective, see PR Notice 93-7.

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(3) 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 language of the PPE requirements must be the same as is specified in PR Notice 93-7.

b. Products Intended for Residential Use

The Agency is not establishing any formulation-specific engineering control or handler PPE requirements for end-use products intended primarily for homeowner use.

8. Other End-Use Product Labeling Requirements

a. All End-Use Products

Labels which currently allow placement of rat and mouse baits "in and around buildings" must be amended to "indoors and against the outside walls of buildings." Rat and mouse bait placements will be allowed "around buildings" only if registrants demonstrate from secondary toxicity studies that risks to birds and mammals are minimal.

All end-use products should have clear, concise and complete labeling instructions. Proper labels can improve reader understanding, thereby reducing misuse and the potential for incidents. Toward this end, the Agency is requiring the labeling modifications listed below.

(1) Directions for Use

Directions for Use must be stated in terms that can be easily read and understood by the average person likely to use or to supervise the use of the pesticide. It must be presented in a format that is easy to understand and follow. The Directions for Use section of a pesticide label must provide the necessary information to answer four major categories regarding the use of the pesticide. These four questions are:

1) Why is the pesticide being used? For what pest(s) or problem?
2) Where is the pesticide to be applied? (Where should it not be applied?)
3) How is the pesticide to be applied (what special precautions must the user take? how much should they use?)
4) When should the pesticide be applied?

"**DIRECTIONS FOR USE"** for products covered by this RED should be organized in the format generally used for rodenticide products registered in the U.S. This format is outlined below and appears in format labels such as the one appended to PR Notice 94-7.

DIRECTIONS FOR USE

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

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

IMPORTANT: [Insert text from PR Notice 94-7 which applies only to products used to control commensal rodents, and to end-use concentrates used to make baits, which may be used to control commensal rodents in and around buildings.]

MIXING DIRECTIONS: [This section applies only to end-use concentrates.]

USE RESTRICTIONS: [Indicate the species for which control is claimed, the sites where the product may be used, general restrictions and precautions on use, and any special seasonal, geographical, or other prohibitions. Requirements for protective clothing and equipment may be stipulated here or under "**MIXING DIRECTIONS:**" or "**APPLICATION DIRECTIONS:**", if more appropriate.]

SELECTION OF TREATMENT AREAS: [This section applies only to products used to control commensal rodents in and around buildings. Text on current labels should be retained.]

APPLICATION DIRECTIONS: [Indicate the correct placement amounts or rates for product application and the specific procedures required for such applications. Add information on follow-up treatments and surveillance of treated areas as appropriate.]

When preparing labels, be sure that this basic format is preserved to ensure that it is clear to readers that all of the subsections indicated above are part of the "**DIRECTIONS FOR USE**".

For products claimed to control a variety of different vertebrate pests, the "**DIRECTIONS FOR USE**" may be subdivided by species groupings. If the same basic set of "**USE RESTRICTIONS:**" applies to all species groupings for which control is claimed, this subdividing should occur at the "**APPLICATION DIRECTIONS:**" level.

If one set of "**USE RESTRICTIONS:**" is not appropriate for all site/pest combinations claimed, such as might occur if certain sites or application methods were permitted or appropriate for only some of the pests claimed, subdivision of the "**DIRECTIONS FOR USE**" should occur at the "**USE RESTRICTIONS:**" level, with each site-pest grouping having separate "**USE RESTRICTIONS:**", "**MIXING DIRECTIONS**" (if appropriate), and "**APPLICATION DIRECTIONS**".

For labels which claim control of commensal rodents "in and around buildings" and other site/pest combinations, the subdivision pertaining to commensal rodent control must include the specific bait protection text indicated in PR Notice 94-7, except that the "It is a violation …" and "**READ THIS LABEL:** …" text may directly precede the subheading which sets directions for controlling commensal rodents in and around buildings apart from the remainder of the "**DIRECTIONS FOR USE**".

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(2) First Aid (Statement of Practical Treatment)

The Agency is requiring that all labels with Statement of Practical Treatment sections be amended so that these sections are entitled, "First Aid." First aid statements must be brief, clear, simple and in straightforward language so that the average person can easily and quickly understand the instructions. These statements should be appropriate for all ages or, when necessary, should include distinctions between the treatments for different ages. Once the Agency has reviewed the data submitted for the RED, it may require additional changes to the "FIRST AID" or "NOTE TO PHYSICIAN" statement."

Under Note to Physicians, many of the labels recommend that Vitamin K_1 be administered intravenously (IV) or intramuscularly (IM). The veterinary literature states that vitamin K_1 can cause anaphylactic reactions if given IV and extensive hemorrhage after IM administration. Sheldon Wagner, M.D., a consultant to OPP, confirmed that Vitamin K_1 should not be given IV unless there is a hemorrhagic crisis. IM administration is acceptable in humans. The recommendation for IV administration must be deleted from the label.

(3) Note to Veterinarian

The Agency is requiring that all labels include a section entitled, "Note to Veterinarian" which reads: "Contains [active ingredient], an anticoagulant with a half-life in the dog of [give number, if known] days. For dogs that have ingested or that are suspected of having ingested [active ingredient], and/or have obvious poisoning symptoms, such as [list major ones, such as bleeding] or have lowered prothrombin times, give [name of antidotal material] as follows: [treatment advice]. For anticoagulants with long half-lives, if known, it might be necessary to check prothrombin times every 3 days until values return to normal.] See 'Note to Physician' for additional information."

(4) PR Notice 94-7

All registrants of rodenticides within eight months after receipt of this RED document, must be in compliance with the labeling requirements outlined in PR Notice 94-7, Notice to Manufacturers, Formulators, Registrants and Users of Pesticides, dated September 16, 1994, if they have not already done so. Any rodenticide products not in compliance will be referred to EPA's Office of Enforcement and Compliance Assurance for action.

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C. Required Labeling Changes

Table 71 - Required Labeling Changes

Description	Required Labeling	Placement
Manufacturing use		
	"Only for formulation into a rodenticide for the following use(s) [fill blank only with those uses that are being supported by MP registrant]."	Directions for Use
One of these statements may be added to a label to allow reformulation of the product for a specific use or all additional uses supported by a formulator or user group	"This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)." "This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)."	
Products Intended Primarily for Homeowner/Residential Use (generally, not marketed for use by professional applicators)		
Indoor sites	"For use in non- food/non-feed areas. Do not contaminate human or pet food preparation items or areas. Do not place near or inside ventilation duct openings."	Use Restriction section in Directions for Use
Products Intended Primarily for Occupational Use (generally, not marketed for use by homeowners)		
	"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. Keep all other persons out of the treated area during application."	Use Restriction section in Directions for Use
	"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." "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." "Any person who retrieves carcasses or unused bait following application of this product must wear gloves."	Hazards to Humans (and domestic animals)
Concentrate formulations that must be diluted prior to use (includes wettable powders and dusts, but does not apply to tracking powders)	"All handlers (including mixers, loaders and applicators) must wear: -- long-sleeve shirt and long pants, -- shoes plus socks, -- glovesl, and mixers and loaders must wear a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C) and protective eyewear."	Hazards to Humans (and domestic animals)

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Description	Required Labeling	Placement
Tracking powder formulations	"All handlers, including mixers/loaders and applicators, must wear: -- long sleeve shirt and long pants, -- shoes plus socks, -- gloves, -- a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C), and -- protective eyewear."	Hazards to Humans (and domestic animals)
Tracking powder formulations	"Tracking powder must be placed in locations not accessible to children, pets, domestic animals or non-target wildlife. If using this product in agricultural buildings where livestock feeds are stored, or in commercial food service, food manufacturing or food processing establishments, limit treatments to concealed, inaccessible places such as spaces between floors and walls. Do not apply tracking powder along walls, in corners or in open floor areas of rooms in which food or feed is handled or stored. Do not place tracking powder in areas where there is a possibility of contaminating water, food, feedstuffs, food or feed handling equipment, or milk or meat handling equipment or surfaces that come in direct contact with food. Do not place near or inside ventilation duct openings."	Use Restriction section in Directions for Use
Pellets or bait formulations	"All handlers, including loaders and applicators, must wear: -- long sleeve shirt and long pants, -- shoes plus socks, and -- gloves. In addition, persons loading the pellets or baits into aircraft or mechanical ground equipment and persons loading/applying with a hand-pushed or hand-held equipment, such as a push-type spreader or cyclone spreader, must wear a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C) and protective eyewear."	Hazards to Humans (and domestic animals)
End-use pellet or premade bait formulation with an acute inhalation toxicity in Category I or II	"All handlers (including mixers, loaders and applicators) must wear: -- long-sleeve shirt and long pants, -- shoes plus socks, -- gloves, -- a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)"	Hazards to Humans (and domestic animals)
Products mixed or applied via equipment	"Do not contaminate water when disposing of equipment wash water or rinsate."	Environmental Hazard Statement
For use in indoor commercial establishments (does not apply to tracking powders)	"Do not use in edible product areas of food or feed processing plants, restaurants or other areas where food or feed is commercially prepared or processed. Do not contaminate food/feed or food/feed handling equipment or place near or inside ventilation duct openings."	Use Restriction section in Directions for Use
Products with Crop Uses (required to maintain non-food classification)		
Orchards/ groves	"Apply after harvest or anytime during the dormant season, but before tree growth begins in the Spring. Do not broadcast over non-orchard/non-grove crops. Do not graze animals on treated areas."	Use Restriction section in Directions for Use
All Products		

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Description	Required Labeling	Placement
Products labeled allowing placement "in and around buildings"	Products must be relabeled to read: "indoors and against the outside walls of buildings"	Directions for Use
	"For information on this pesticide product (including health concerns, medical emergencies, or pesticide incidents), call the National Pesticide Telecommunications Network at 1-800-858-7378." "Do not apply this product by any method not specified on this label."	Directions For Use
	"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."	User Safety Recommendations (directly below Hazards to Humans)
	"Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high-water mark." "Dogs and other predatory and scavenging mammals might be poisoned if they feed upon animals that have eaten this bait."	Environmental Hazard Statements
	"Contains [active ingredient], an anticoagulant with a half-life in the dog of [give number, if known] days. For dogs that have ingested or that are suspected of having ingested [active ingredient], and/or have obvious poisoning symptoms, such as [list major ones, such as bleeding] or have lowered prothrombin times, give [name of antidotal material] as follows: [treatment advice]. For anticoagulants with long half-lives, if known, it might be necessary to check prothrombin times every 3 days until values return to normal.] See 'Note to Physician' for additional information."	Note To Veterinarian

D. Existing Stocks

Registrants may generally distribute and sell products bearing old labels/labeling for 26 months from the date of the issuance of this Reregistration Eligibility Decision (RED). Persons other than the registrant may generally distribute or sell such products for 50 months from the date of the issuance of this RED. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors. Refer to "Existing Stocks of Pesticide Products; Statement of Policy"; Federal Register, Volume 56, No. 123, June 26, 1991.

The Agency has determined that registrants may distribute and sell brodifacoum, bromethalin, bromadiolone, chlorophacinone, diphacinone and its sodium salt products bearing old labels/labeling for 26 months from the date of issuance of this RED. Persons other than the registrant may distribute or sell such products for 50 months from the date of the issuance of this RED. Registrants and persons other than registrants remain obligated to meet pre-existing Agency imposed label changes and existing stocks requirements applicable to products they sell or distribute.

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VI. APPENDICES

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APPENDIX A REPORT

Case 2755 Chemical 112701 [Brodifacoum]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Max. Tex. @ Max. Dose cycle	# Apps Max. Rate unless noted Max. /crop /year	Max. Dose [(AI otherwise)/A] /crop	/year	Min. Interv (days)	Re-Entry Intv.	Allowed	Disallowed	Geographic Limitations Codes	Use Limitations
USES ELIGIBLE FOR REREGISTRATION													
FOOD/FEED USES													
AGRICULTURAL/FARM PREMISES									Use Group: INDOOR FOOD				
Bait station. Use code BAB, When needed, Bait box	B/S	NA ft interval	3.350E-06 lb	*	NS	NS	NS	NS	NS	NS			
	G	NA 1K sq.ft	1.013E-05 lb	*	NS	NS	NS	NS	NS	NS			
FOOD PROCESSING PLANT PREMISES (NONFOOD CONTACT)									Use Group: INDOOR FOOD				
Bait station. Use code BAB, When needed, Bait box	B/S	NA ft interval	2.948E-06 lb	*	NS	NS	NS	NS	NS	NS			
NON-FOOD/NON-FEED													
AGRICULTURAL UNCULTIVATED AREAS									Use Group: TERRESTRIAL NON-FOOD CROP				
Bait station. Use code BAB, When needed, Bait box	B/S	NA ft interval	3.350E-06 lb	*	NS	NS	NS	NS	NS	NS			
	G	NA 1K sq.ft	1.013E-05 lb	*	NS	NS	NS	NS	NS	NS			
AGRICULTURAL/FARM PREMISES									Use Group: INDOOR NON-FOOD				
Bait application, When needed, Bait box	B/S	NA ft interval	3.350E-06 lb	*	NS	NS	NS	NS	AN	NS		C93	
	B/S	NA ft interval	2.513E-06 lb	*	NS	NS	NS	NS	NS	NS		C93, CAC	
	B/S	NA location	3.750E-05 lb	*	NS	NS	NS	NS	NS	NS		C93, CAT	
	B/S	NA .00005 lb * station	UC	*	NS	NS	NS	NS	NS	NS		CAC	

APPENDIX A REPORT

Case 2755 [Brodifacoum] Chemical 112701 [Brodifacoum]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose	Max. # Apps Max. Rate unless noted Max. /crop /year cycle	Max Dose [(AI otherwise)/A] /crop	/year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION												
NON-FOOD/NON-FEED (con't)												
AGRICULTURAL/FARM PREMISES (con't)					Use Group: INDOOR NON-FOOD (con't)							
	B/S	NA	2.344E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		CAT
	P/T	NA	UC	*	NS	NS	NS	NS	NS	NS		CAC
			3.350E-06 lb ft interval	*								
COMMERCIAL TRANSPORTATION FACILITIES-NONFEED/NONFOOD					Use Group: INDOOR NON-FOOD							
Bait application, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	AN	NS		C93
	B/S	NA	2.513E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		C93, CAC
	B/S	NA	3.750E-05 lb location	*	NS	NS	NS	NS	NS	NS		C93, CAT
	B/S	NA	UC	*	NS	NS	NS	NS	NS	NS		CAC
	P/T	NA	UC	*	NS	NS	NS	NS	NS	NS		CAC
			3.350E-06 lb ft interval	*								
COMMERCIAL/INSTITUTIONAL/INDUSTRIAL PREMISES/EQUIP. (INDOOR)					Use Group: INDOOR NON-FOOD							
Bait application, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	AN	NS		C93
	B/S	NA	2.513E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		C93, CAC
	B/S	NA	3.750E-05 lb location	*	NS	NS	NS	NS	NS	NS		C93, CAT

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APPENDIX A REPORT

Case 2755 [Brodifacoum] Chemical 112701 [Brodifacoum]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise) Dose	Soil Tex. @ Max. Rate	Max. # Apps Max. Rate unless noted Max. cycle	Max Dose [(AI otherwise)/A] /crop	/year	Min. Interv (days)	Re-Entry Intv.	Allowed Codes	Disallowed Codes	Use Limitations
USES ELIGIBLE FOR REREGISTRATION												
NON-FOOD/NON-FEED (con't)												
COMMERCIAL/INSTITUTIONAL/INDUSTRIAL PREMISES/EQUIP. (INDOOR) (con't) Use Group: INDOOR NON-FOOD (con't)												
	B/S	NA	UC .00005 lb station	*	NS	NS	NS	NS	NS	NS	CAC	
	B/S	NA	2.344E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAT	
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC	
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval 6.250E-06 lb station	*	NS	NS	NS	NS	NS	NS		
	G	NA	1.013E-05 lb 1K sq.ft	*	NS	NS	NS	NS	NS	NS		
COMMERCIAL/INSTITUTIONAL/INDUSTRIAL PREMISES/EQUIPMENT (OUTDOOR) Use Group: TERRESTRIAL NON-FOOD CROP												
Bait application, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	AN	NS	C93	
	B/S	NA	2.513E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	C93, CAC	
	B/S	NA	3.750E-05 lb location	*	NS	NS	NS	NS	NS	NS	C93, CAT	
	B/S	NA	UC .00005 lb station	*	NS	NS	NS	NS	NS	NS	CAC	
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC	

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APPENDIX A REPORT

Case 2755 [Brodifacoum] Chemical 112701 [Brodifacoum]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose cycle	Max. # Apps Max. Rate unless noted Max. /crop /year	Max. Dose [(AI otherwise)/A] /crop	Min. Interv (days)	Re-Entry Intv.	Allowed	Geographic Limitations Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
COMMERCIAL/INSTITUTIONAL/INDUSTRIAL PREMISES/EQUIPMENT (OUTDOOR) (con'					Use Group: TERRESTRIAL NON-FOOD CROP (con't)						
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
	G	NA	1.013E-05 lb 1K sq.ft	*	NS	NS	NS	NS	NS	NS	
HOUSEHOLD/DOMESTIC DWELLINGS					Use Group: INDOOR RESIDENTIAL						
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
HOUSEHOLD/DOMESTIC DWELLINGS INDOOR PREMISES					Use Group: INDOOR RESIDENTIAL						
Bait application, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	AN	NS	C93
	B/S	NA	2.513E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	C93, CAC
	B/S	NA	3.750E-05 lb location	*	NS	NS	NS	NS	NS	NS	C93, CAT
	B/S	NA	UC	*	NS	NS	NS	NS	NS	NS	CAC
	B/S	NA	1.172E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAT
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval 6.250E-06 lb station	*	NS	NS	NS	NS	NS	NS	

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APPENDIX A REPORT

Case 2755 [Brodifacoum] Chemical 112701 [Brodifacoum]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Max. Tex. @ Max. Dose	# Apps Max. Rate unless noted Max. /crop /year cycle	Max Dose [(AI otherwise)/A] /crop	/year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION												
NON-FOOD/NON-FEED (con't)												
HOUSEHOLD/DOMESTIC DWELLINGS INDOOR PREMISES (con't) Use Group: INDOOR RESIDENTIAL (con't)												
	G	NA	1.013E-05 lb 1K sq.ft	*	NS	NS	NS	NS	NS	NS		
HOUSEHOLD/DOMESTIC DWELLINGS OUTDOOR PREMISES Use Group: OUTDOOR RESIDENTIAL												
Bait application, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	AN	NS		C93
	B/S	NA	2.513E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		C93, CAC
	B/S	NA	3.750E-05 lb location	*	NS	NS	NS	NS	NS	NS		C93, CAT
	B/S	NA	UC	*	NS	NS	NS	NS	NS	NS		CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		
	G	NA	1.013E-05 lb 1K sq.ft	*	NS	NS	NS	NS	NS	NS		
PUBLIC BUILDINGS/STRUCTURES (VERT. PEST CONTROL) Use Group: INDOOR NON-FOOD												
Bait application, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	AN	NS		C93
	B/S	NA	2.513E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		C93, CAC
	B/S	NA	3.750E-05 lb location	*	NS	NS	NS	NS	NS	NS		C93, CAT

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Case 2755 [Brodifacoum] Chemical 112701 [Brodifacoum]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose	Max. # Apps Max. Rate unless noted Max. /crop /year cycle	Max. Dose [(AI otherwise)/A] /crop	Min. Interv (days)	Re-Entry Intv.	Allowed	Geographic Limitations Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
PUBLIC BUILDINGS/STRUCTURES (VERT. PEST CONTROL) (con't)										Use Group: INDOOR NON-FOOD (con't)	
	B/S	NA	UC	*	NS	NS	NS	NS	NS	NS	CAC
	P/T	NA	UC	*	NS	NS	NS	NS	NS	NS	CAC
		3.350E-06 lb ft interval	*								
SEWAGE SYSTEMS										Use Group: AQUATIC NON-FOOD INDUSTRIAL	
Bait application, When needed, Tether	B/S	NA	UC	*	NS	NS	NS	NS	NS	NS	CAC
USE 70001 OR 70009										Use Group: INDOOR NON-FOOD	
Bait station. Use code BAB, When needed, Bait box	B/S	NA ft interval	3.350E-06 lb	*	NS	NS	NS	NS	NS	NS	

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LEGEND
444444

Sort: Uses Eligible or Ineligible for Re-registration, Food/Feed or Non-Food/Non-Feed Uses, Alpha Site Name, Use Group Name, Alpha Application Type/Timing/Equipment Description, Formulation, Maximum Application Rate Unit/Area Quantity, Minimum Application Rate

HEADER ABBREVIATIONS
Min. Appl. Rate (AI unless noted otherwise) : Minimum dose for a single application to a single site. System calculated. Microbial claims only.
Max. Appl. Rate (AI unless noted otherwise) : Maximum dose for a single application to a single site. System calculated.
Soil Tex. Max. Dose : Maximum dose for a single application to a single site as related to soil texture (Herbicide claims only).
Max. # Apps @ Max. Rate : Maximum number of Applications at Maximum Dosage Rate. Example: "4 applications per year" is expressed as "4/1 yr"; "4 applications per 3 years" is expressed as "4/3 yr"
Max. Dose [(AI unless noted otherwise)/A] : Maximum dose applied to a site over a single crop cycle or year. System calculated.
Min. Interv (days) : Minimum Interval between Applications (days)
Re-Entry Intv. : Reentry Intervals
PRD Report Date : LUIS contains all products that were active or suspended (and that were available from OPP Document Center) as of this date. Some products registered after this date may have data included in this report, but LUIS does not guarantee that all products registered after this date have data that has been captured.

SOIL TEXTURE FOR MAX APP. RATE
* : Non-specific
C : Coarse
M : Medium
F : Fine
O : Others

FORMULATION CODES
B/S : BAIT/SOLID
G : GRANULAR
P/T : PELLETED/TABLETED

ABBREVIATIONS
AN : As Needed
NA : Not Applicable
NS : Not Specified (on label)
UC : Unconverted due to lack of data (on label), or with one of following units: bag, bait, bait block, bait pack, bait station, bait station(s), block, briquet, briquets, bursts, cake, can, canister, capsule, cartridges, coil, collar, container, dispenser, drop, eartag, grains, lure, pack, packet, packets, pad, part, parts, pellets, piece, pieces, pill, pumps, sec, sec burst, sheet, spike, stake, stick, strip, tab, tablet, tablets, tag, tape, towelette, tray, unit, --

APPLICATION RATE
DCNC : Dosage Can Not be Calculated
No Calc : No Calculation can be made
W : PPM calculated by weight
V : PPM Calculated by volume
U : Unknown whether PPM is given by weight or by volume
cwt : Hundred Weight

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nnE-xx : nn times (10 power -xx); for instance, "1.234E-04" is equivalent to ".0001234"

USE LIMITATIONS CODES
C93 : Do not apply directly to water.
CAC : Keep out of lakes, streams, and ponds.
CAT : Do not place in locations accessible to children, pets or domestic animals.
* NUMBER IN PARENTHESES REPRESENTS THE NUMBER OF TIME UNITS (HOURS,DAYS, ETC.) DESCRIBED IN THE LIMITATION.

UNIT DESCRIPTIONS
ft interval : Not in LUIS Unit Conversion Vocabulary File
lb : pound
location :
sq.ft : square foot
station :

APPENDIX A REPORT

Case 2760 Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose cycle	Max. # Apps Max. Rate unless noted Max. /crop /year cycle	Max Dose [(AI otherwise)/A] /crop	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
FOOD/FEED USES											
AGRICULTURAL/FARM PREMISES Use Group: INDOOR FOOD											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb / ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb / linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	2.931E-06 lb / ft interval	*	NS	NS	NS	NS	1	NS	CAC
	P/T	NA	3.350E-06 lb / ft interval	*	NS	NS	NS	NS	10	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb / ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.350E-06 lb / ft interval	*	NS	NS	NS	NS	NS	NS	
COMMERCIAL TRANSPORTATION FACILITIES-FEED/FOOD-EMPTY Use Group: INDOOR FOOD											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb / ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb / linear ft	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
			3.350E-06 lb / ft interval	*							
COMMERCIAL TRANSPORTATION FACILITIES-FEED/FOOD-FULL Use Group: INDOOR FOOD											

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APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Max. Tex. @ Max. Dose	# Apps Max. Rate unless noted Max. /crop /year cycle	Max Dose [(AI otherwise)/A] Dose cycle /crop /year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
FOOD/FEED USES (con't)											
COMMERCIAL TRANSPORTATION FACILITIES-FEED/FOOD-FULL (con't) Use Group: INDOOR FOOD (con't)											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
HOUSEHOLD/DOMESTIC DWELLINGS INDOOR FOOD HANDLING AREAS Use Group: INDOOR FOOD											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
NON-FOOD/NON-FEED											
AGRICULTURAL UNCULTIVATED AREAS Use Group: TERRESTRIAL NON-FOOD CROP											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC

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APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose cycle	Max. # Apps Max. Rate unless noted Max. /crop /year	Max. Dose [(AI otherwise)/A] /crop	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
AGRICULTURAL UNCULTIVATED AREAS (con't)					Use Group: TERRESTRIAL NON-FOOD CROP (con't)						
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.141E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
COMMERCIAL STORAGES/WAREHOUSES PREMISES (INDOOR)					Use Group: INDOOR NON-FOOD						
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
COMMERCIAL TRANSPORTATION FACILITIES-FEED/FOOD-EMPTY					Use Group: INDOOR NON-FOOD						
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC

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APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Max. Tex. @ Max. Dose cycle	# Apps Max. Rate unless noted Max. /crop	Max. Dose [(AI unless noted otherwise)/A] /year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
COMMERCIAL TRANSPORTATION FACILITIES-NONFEED/NONFOOD									Use Group: INDOOR NON-FOOD		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
COMMERCIAL/INSTITUTIONAL/INDUSTRIAL PREMISES/EQUIP. (INDOOR)									Use Group: INDOOR NON-FOOD		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC

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APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Rate unless noted Dose cycle	Max. # Apps Max. Rate unless noted Max. /crop /year	Max. Dose [(AI otherwise)/A] /crop /year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
COMMERCIAL/INSTITUTIONAL/INDUSTRIAL PREMISES/EQUIPMENT (OUTDOOR) Use Group: TERRESTRIAL NON-FOOD CROP											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC
HOUSEHOLD/DOMESTIC DWELLINGS INDOOR NONFOOD HANDLING AREAS Use Group: INDOOR RESIDENTIAL											
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC

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APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Rate unless noted Max. Dose cycle	Max. # Apps /crop /year	Max. [(AI otherwise)/A] /crop /year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
HOUSEHOLD/DOMESTIC DWELLINGS INDOOR PREMISES									Use Group: INDOOR RESIDENTIAL		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	UC *	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	* NS	NS	NS	NS	NS	10	NS	CAC
	FM?	NA		UC *	NS	NS	NS	NS	1	NS	CAC
	FM?	NA		UC *	NS	NS	NS	NS	10	NS	CAC
	P/T	NA		UC *	NS	NS	NS	NS	10	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	* NS	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.350E-06 lb ft interval	* NS	NS	NS	NS	NS	NS	NS	
	B/S	NA	3.350E-06 lb ft interval	* NS	NS	NS	NS	NS	NS	NS	CAC
HOUSEHOLD/DOMESTIC DWELLINGS OUTDOOR PREMISES									Use Group: INDOOR NON-FOOD		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	* NS	NS	NS	NS	NS	1	NS	CAC
									Use Group: OUTDOOR RESIDENTIAL		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	* NS	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	* NS	NS	NS	NS	NS	10	NS	CAC
	FM?	NA		UC *	NS	NS	NS	NS	1	NS	CAC

US EPA ARCHIVE DOCUMENT

APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Max. Tex. @ Max. Dose	# Apps Max. Rate unless noted Max. /crop /year cycle	Max. Dose [(AI otherwise)/A] /crop	/year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION												
NON-FOOD/NON-FEED (con't)												
HOUSEHOLD/DOMESTIC DWELLINGS OUTDOOR PREMISES (con't)										Use Group: OUTDOOR RESIDENTIAL (con't)		
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS		CAC
	P/T	NA	UC	*	NS	NS	NS	NS	10	NS		CAC
		3.350E-06 lb ft interval	*									
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS		CAC
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS		CAC
PUBLIC BUILDINGS/STRUCTURES (VERT. PEST CONTROL)										Use Group: INDOOR NON-FOOD		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS		CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS		CAC
	P/T	NA	UC	*	NS	NS	NS	NS	10	NS		CAC
URBAN AREAS										Use Group: TERRESTRIAL NON-FOOD CROP		
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS		CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS		CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS		CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS		CAC

US EPA ARCHIVE DOCUMENT

APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose cycle	Max. # Apps Max. Rate unless noted Max. /crop /year	Max. Dose [(AI otherwise)/A] /crop /year	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
NON-FOOD/NON-FEED (con't)											
URBAN AREAS (con't)				Use Group: TERRESTRIAL NON-FOOD CROP (con't)							
	P/T	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC
USE 66000, 67000 AND/OR 68000				Use Group: TERRESTRIAL NON-FOOD CROP							
Bait application, When needed, By hand	B/S	NA	1.250E-05 lb burrow	*	NS	NS	NS	NS	NS	NS	
USE 70001 OR 70009				Use Group: INDOOR NON-FOOD							
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
Bait station. Use code BAB, When needed, Bait box	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	
	B/S	NA	3.141E-06 lb ft interval	*	NS	NS	NS	NS	NS	NS	CAC
WIDE AREA/GENERAL INDOOR TREATMENT				Use Group: INDOOR NON-FOOD							
Bait application, When needed, By hand	B/S	NA	3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC

US EPA ARCHIVE DOCUMENT

APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. @ Max. Dose	Max. # Apps Max. Rate unless noted Max. /crop /year otherwise)/A] Dose cycle /crop /year	Min. Interv (days)	Re-Entry Intv.	Allowed	Geographic Limitations Disallowed	Use Limitations Codes

USES ELIGIBLE FOR REREGISTRATION

NON-FOOD/NON-FEED (con't)

WIDE AREA/GENERAL INDOOR TREATMENT (con't) Use Group: INDOOR NON-FOOD (con't)

	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC

WIDE AREA/GENERAL OUTDOOR TREATMENT (PUBLIC HEALTH USE) Use Group: TERRESTRIAL NON-FOOD CROP

Bait application, When needed, By hand	B/S	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	1	NS	CAC
	B/S	NA	3.333E-06 lb linear ft	*	NS	NS	NS	NS	10	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	1	NS	CAC
	FM?	NA	UC	*	NS	NS	NS	NS	10	NS	CAC
	P/T	NA	UC 3.350E-06 lb ft interval	*	NS	NS	NS	NS	10	NS	CAC

US EPA ARCHIVE DOCUMENT

APPENDIX A REPORT

Case 2760 [Bromadiolone] Chemical 112001 [Bromadiolone]
4444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444444
LEGEND
444444

Sort: Uses Eligible or Ineligible for Re-registration, Food/Feed or Non-Food/Non-Feed Uses, Alpha Site Name, Use Group Name, Alpha Application Type/Timing/Equipment Description, Formulation, Maximum Application Rate Unit/Area Quantity, Minimum Application Rate

HEADER ABBREVIATIONS
Min. Appl. Rate (AI unless noted otherwise) : Minimum dose for a single application to a single site. System calculated. Microbial claims only.
Max. Appl. Rate (AI unless noted otherwise) : Maximum dose for a single application to a single site. System calculated.
Soil Tex. Max. Dose : Maximum dose for a single application to a single site as related to soil texture (Herbicide claims only).
Max. # Apps @ Max. Rate : Maximum number of Applications at Maximum Dosage Rate. Example: "4 applications per year" is expressed as "4/1 yr"; "4 applications per 3 years" is expressed as "4/3 yr"
Max. Dose [(AI unless noted otherwise)/A] : Maximum dose applied to a site over a single crop cycle or year. System calculated.
Min. Interv (days) : Minimum Interval between Applications (days)
Re-Entry Intv. : Reentry Intervals
PRD Report Date : LUIS contains all products that were active or suspended (and that were available from OPP Document Center) as of this date. Some products registered after this date may have data included in this report, but LUIS does not guarantee that all products registered after this date have data that has been captured.

SOIL TEXTURE FOR MAX APP. RATE
* : Non-specific
C : Coarse
M : Medium
F : Fine
O : Others

FORMULATION CODES
B/S : BAIT/SOLID
FM? : FORM NOT IDENTIFIED
P/T : PELLETED/TABLETED

ABBREVIATIONS
AN : As Needed
NA : Not Applicable
NS : Not Specified (on label)
UC : Unconverted due to lack of data (on label), or with one of following units: bag, bait, bait block, bait pack, bait station, bait station(s), block, briquet, briquets, bursts, cake, can, canister, capsule, cartridges, coil, collar, container, dispenser, drop, eartag, grains, lure, pack, packet, packets, pad, part, parts, pellets, piece, pieces, pill, pumps, sec, sec burst, sheet, spike, stake, stick, strip, tab, tablet, tablets, tag, tape, towelette, tray, unit, --

APPLICATION RATE
DCNC : Dosage Can Not be Calculated
No Calc : No Calculation can be made
W : PPM calculated by weight
V : PPM Calculated by volume
U : Unknown whether PPM is given by weight or by volume
cwt : Hundred Weight
nnE-xx : nn times (10 power -xx); for instance, "1.234E-04" is equivalent to ".0001234"

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USE LIMITATIONS CODES
CAC : Keep out of lakes, streams, and ponds.
* NUMBER IN PARENTHESES REPRESENTS THE NUMBER OF TIME UNITS (HOURS,DAYS, ETC.) DESCRIBED IN THE LIMITATION.

UNIT DESCRIPTIONS
burrow :
ft interval : Not in LUIS Unit Conversion Vocabulary File
lb : pound
linear ft : linear foot

GUIDE TO APPENDIX B

Appendix B contains listings of data requirements which support the reregistration for active ingredients within the case 2665 covered by this Reregistration Eligibility Decision Document. It contains generic data requirements that apply to Rodenticide Cluster active ingredients in all products, including data requirements for which a "typical formulation" is the test substance.

The data table is organized in the following format:

1. Data Requirement (Column 1). The data requirements are listed in the order in which they appear in 40 CFR Part 158. the reference numbers accompanying each test refer to the test protocols set in the Pesticide Assessment Guidelines, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161 (703) 487-4650.

2. Use Pattern (Column 2). This column indicates the use patterns for which the data requirements apply. The following letter designations are used for the given use patterns:

A	Terrestrial food
B	Terrestrial feed
C	Terrestrial non-food
D	Aquatic food
E	Aquatic non-food outdoor
F	Aquatic non-food industrial
G	Aquatic non-food residential
H	Greenhouse food
I	Greenhouse non-food
J	Forestry
K	Residential
L	Indoor food
M	Indoor non-food
N	Indoor medical
O	Indoor residential

3. Bibliographic citation (Column 3). If the Agency has acceptable data in its files, this column lists the identifying number of each study. This normally is the Master Record Identification (MRID) number, but may be a "GS" number if no MRID number has been assigned. Refer to the Bibliography appendix for a complete citation of the study.

US EPA ARCHIVE DOCUMENT

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APPENDIX B

Data Supporting Guideline Requirements for the Reregistration of Brodifacoum

REQUIREMENT		USE PATTERNS	CITATION(S)
PRODUCT CHEMISTRY			
61-1	Chemical Identity	All	129706
61-2A	Start. Mat. & Mnfg. Process	All	129706
61-2B	Formation of Impurities	All	129706
62-1	Preliminary Analysis	All	129706
62-2	Certification of limits	All	129706
62-3	Analytical Method	All	129706
63-2	Color	All	41892201
63-3	Physical State	All	41892201
63-5	Melting Point	All	41892201, 41892202
63-7	Density	All	41892201
63-8	Solubility	All	41892201, 41892202
63-9	Vapor Pressure	All	41892202
63-11	Octanol/Water Partition	All	41892202
63-12	pH	All	41892201
63-13	Stability	All	41892201
ECOLOGICAL EFFECTS			
71-1A	Acute Avian Oral - Quail/Duck	C, F, K	41563303
71-2A	Avian Dietary - Quail	C, F, K	124477
71-2B	Avian Dietary - Duck	C, F, K	124476
72-1A	Fish Toxicity Bluegill	C, F, K	124472
72-1C	Fish Toxicity Rainbow Trout	C, F, K	88011
72-2A	Invertebrate Toxicity	C, F, K	128442

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Data Supporting Guideline Requirements for the Reregistration of Brodifacoum

REQUIREMENT		USE PATTERNS	CITATION(S)
TOXICOLOGY			
81-1	Acute Oral Toxicity - Rat	All	42687501, 4021701
81-2	Acute Dermal Toxicity - Rabbit/Rat	All	42223201,44021702
81-3	Acute Inhalation Toxicity - Rat	All	43110501
81-4	Primary Eye Irritation - Rabbit	All	66938
81-5	Primary Dermal Irritation - Rabbit	All	44021703
83-3A	Developmental Toxicity - Rat	L	52443, 40307202, 42641902
83-3B	Developmental Toxicity - Rabbit	L	52442, 40307201
85-1	General Metabolism	L	80235, 42007502, 42596801, 44021705
86-1	Domestic Animal Safety		42007501
ENVIRONMENTAL FATE			
161-1	Hydrolysis	C, F, K	42237701
162-1	Aerobic Soil Metabolism	C, K	42579401
163-1	Leaching/Adsorption/Desorption	C, F, K	42024501, 42568301

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Bromadiolone

REQUIREMENT		USE PATTERN	CITATION(S)
PRODUCT CHEMISTRY			
61-1	Chemical Identity	All	41717001, 41884701
61-2A	Start. Mat. & Mnfg. Process	All	41717001, 41884701
61-2B	Formation of Impurities	All	41690802, 41717001
62-1	Preliminary Analysis	All	41514101, 41717002
62-2	Certification of limits	All	41514101, 41717002
62-3	Analytical Method	All	41514101, 41717002, 41849601
63-2	Color	All	41849601, 42395901, 42667801
63-3	Physical State	All	41849601, 42395901, 42667801
63-4	Odor	All	41849601, 42395901, 42667801
63-5	Melting Point	All	42395901, 42667801
63-7	Density	All	41849601, 42395901, 42667801
63-8	Solubility	All	42395901, 42667801
63-9	Vapor Pressure	All	42395901, 42667801
63-11	Octanol/Water Partition	All	42395901, 42667801
63-13	Stability	All	42395901, 42667801
ECOLOGICAL EFFECTS			
71-1A	Acute Avian Oral - Quail/Duck	C, K	257770, 41707301
71-2A	Avian Dietary - Quail	C, K	257770
71-2B	Avian Dietary - Duck	C, K	249995, 257770
72-1A	Fish Toxicity Bluegill	C, K	232567
72-1C	Fish Toxicity Rainbow Trout	C, K	232567
72-2A	Invertebrate Toxicity	C, K	232567

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Bromadiolone

REQUIREMENT		USE PATTERN	CITATION(S)
TOXICOLOGY			
81-1	Acute Oral Toxicity - Rat	All	41900001
81-2	Acute Dermal Toxicity - Rabbit/Rat	All	42673701
81-3	Acute Inhalation Toxicity - Rat	All	41976901
81-4	Primary Eye Irritation - Rabbit	All	88113
81-5	Primary Dermal Irritation - Rabbit	All	88112
81-6	Dermal Sensitization - Guinea Pig	All	41847401
82-1A	90-Day Feeding - Rodent	L	107035
82-1B	90-Day Feeding - Non-rodent	L	92196013
83-3A	Developmental Toxicity - Rat	L	92196014
83-3B	Developmental Toxicity - Rabbit	L	92196015
85-1	General Metabolism	L	42596801
86-1	Domestic Animal Safety		42093301
ENVIRONMENTAL FATE			
161-1	Hydrolysis	C, K	42237501
162-1	Aerobic Soil Metabolism	C, K	43594301
163-1	Leaching/Adsorption/Desorption	C, K	161972, 161973, 161988, 42237501, 43000702, 43594301

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Bromethalin

REQUIREMENT		USE PATTERN	CITATION(S)
PRODUCT CHEMISTRY			
61-1	Chemical Identity	All	42333401, 42403001
61-2A	Start. Mat. & Mnfg. Process	All	40617001, 42333401
61-2B	Formation of Impurities	All	42333401, 42403001
62-1	Preliminary Analysis	All	26519, 86718, 86719, 40797401, 42403002
62-2	Certification of limits	All	42433401
62-3	Analytical Method	All	42403002
63-2	Color	All	41599601
63-3	Physical State	All	41599601
63-4	Odor	All	41599601
63-5	Melting Point	All	41599601
63-7	Density	All	41599601
63-9	Vapor Pressure	All	41979600
63-11	Octanol/Water Partition	All	41599603
ECOLOGICAL EFFECTS			
71-1A	Acute Avian Oral - Quail/Duck	All	86741, 246173
71-2A	Avian Dietary - Quail	All	86745
71-2B	Avian Dietary - Duck	All	26526
72-1A	Fish Toxicity Bluegill	All	42733501
72-1C	Fish Toxicity Rainbow Trout	All	42733502
72-2A	Invertebrate Toxicity	All	86751, 42733503

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Data Supporting Guideline Requirements for the Reregistration of Bromethalin

REQUIREMENT		USE PATTERN	CITATION(S)
TOXICOLOGY			
81-1	Acute Oral Toxicity - Rat	All	26524, 241521, 246172
81-2	Acute Dermal Toxicity - Rabbit/Rat	All	26524
81-3	Acute Inhalation Toxicity - Rat	All	26524
81-4	Primary Eye Irritation - Rabbit	All	26524
81-5	Primary Dermal Irritation - Rabbit	All	26524
81-6	Dermal Sensitization - Guinea Pig	All	41653001
81-7	Acute Delayed Neurotoxicity - Hen	All	101543
82-1A	90-Day Feeding - Rodent	All	43582102
82-1B	90-Day Feeding - Non-rodent	All	43582101
82-5B	90-Day Neurotoxicity - Mammal	All	42793101
83-3B	Developmental Toxicity - Rabbit	All	86731, 101545
85-1	General Metabolism	All	4724
86-1	Domestic Animal Safety	All	42759602, 42759603, 42759604
ENVIRONMENTAL FATE			
161-1	Hydrolysis	All	42438701
162-1	Aerobic Soil Metabolism	All	43007901

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Chlorophacinone

REQUIREMENT		USE PATTERN	CITATION(S)
PRODUCT CHEMISTRY			
61-1	Chemical Identity	All	Other Submissions
61-2A	Start. Mat. & Mnfg. Process	All	Other Submissions
61-2B	Formation of Impurities	All	Other Submissions
62-1	Preliminary Analysis	All	41922901
62-2	Certification of limits	All	41922901
62-3	Analytical Method	All	41922901
63-2	Color	All	42237401
63-3	Physical State	All	42237401
63-4	Odor	All	42237401
63-5	Melting Point	All	42237401
63-7	Density	All	42237401
63-8	Solubility	All	42237401
63-9	Vapor Pressure	All	42237401
63-10	Dissociation Constant	All	42237401
63-11	Octanol/Water Partition	All	42237401
63-13	Stability	All	42237401
ECOLOGICAL EFFECTS			
71-1A	Acute Avian Oral - Quail/Duck	All	41513101
71-2A	Avian Dietary - Quail	All	41513102
71-2B	Avian Dietary - Duck	All	41513103
72-1A	Fish Toxicity Bluegill	All	42356102
72-1C	Fish Toxicity Rainbow Trout	All	42356103
72-2A	Invertebrate Toxicity	All	42356101

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Chlorophacinone

REQUIREMENT		USE PATTERN	CITATION(S)
TOXICOLOGY			
81-1	Acute Oral Toxicity - Rat	All	41875301
81-2	Acute Dermal Toxicity - Rabbit/Rat	All	41702801
81-3	Acute Inhalation Toxicity - Rat	All	41981102
81-4	Primary Eye Irritation - Rabbit	All	41874001
81-5	Primary Dermal Irritation - Rabbit	All	41702801
81-6	Dermal Sensitization - Guinea Pig	All	41578601
82-1A	90-Day Feeding - Rodent	All	92018013
82-2	21-Day Dermal - Rabbit/Rat	All	42237402
83-3A	Developmental Toxicity - Rat	All	43349501
83-3B	Developmental Toxicity - Rabbit	All	43570801
85-1	General Metabolism	All	155540
86-1	Domestic Animal Safety	All	41981101
ENVIRONMENTAL FATE			
161-1	Hydrolysis	All	42205501
161-3	Photodegradation - Soil	All	42452301
162-1	Aerobic Soil Metabolism	All	43159801
163-1	Leaching/Adsorption/Desorption	All	42666001
SPECIAL STUDIES			
70-A-SS	Secondary Toxicity Study	All	42760902

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Diphacinone and Salt

REQUIREMENT		USE PATTERN	CITATION(S)
PRODUCT CHEMISTRY			
61-1	Chemical Identity	All	41613401, 41727801, 41612801, 42136001, 42360601
61-2A	Start. Mat. & Mnfg. Process	All	41613401, 41612801, 42136001
61-2B	Formation of Impurities	All	41613401, 41612801, 42136001, 42136002, 42360601
62-1	Preliminary Analysis	All	41613402, 41727802, 41612802, 42136002
62-2	Certification of limits	All	41613402. 41612802, 42136002
62-3	Analytical Method	All	41613402, 41612802, 42136002
63-2	Color	All	41727803, 42360601
63-3	Physical State	All	42360601
63-4	Odor	All	134837
63-5	Melting Point	All	134837
63-7	Density	All	134837
63-8	Solubility	All	134837, 134839
63-9	Vapor Pressure	All	41612802, 134837
63-10	Dissociation Constant	All	41612802
63-11	Octanol/Water Partition	All	41612802, 134840
63-12	pH	All	41612802
63-13	Stability	All	41612802, 42136003
ECOLOGICAL EFFECTS			
71-1B	Acute Avian Oral - Quail/Duck TEP	All	42245201
71-2A	Avian Dietary - Quail	All	42408801
71-2B	Avian Dietary - Duck	All	42408802
72-1A	Fish Toxicity Bluegill	All	43249501
72-1C	Fish Toxicity Rainbow Trout	All	43249502
72-2A	Invertebrate Toxicity	All	42282201
TOXICOLOGY			

US EPA ARCHIVE DOCUMENT

Data Supporting Guideline Requirements for the Reregistration of Diphacinone and Salt

REQUIREMENT		USE PATTERN	CITATION(S)
81-1	Acute Oral Toxicity - Rat	All	43260701, 43260702, 42245202, 60605
81-2	Acute Dermal Toxicity - Rabbit/Rat	All	42507001
81-3	Acute Inhalation Toxicity - Rat	All	43000401
81-4	Primary Eye Irritation - Rabbit	All	42245203
81-6	Dermal Sensitization - Guinea Pig	All	42132501
82-2	21-Day Dermal - Rabbit/Rat	All	074637, 77369
83-3A	Developmental Toxicity - Rat	All	077319, 42834801
84-2B	Structural Chromosomal Aberration	All	42406801
85-1	General Metabolism	All	92049009
86-1	Domestic Animal Safety	All	42791202
ENVIRONMENTAL FATE			
161-1	Hydrolysis	All	43582401
162-1	Aerobic Soil Metabolism	All	42035001
SPECIAL STUDIES			
70-13-SS	Secondary Toxicity Study	All	40077202

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GUIDE TO APPENDIX C

1. CONTENTS OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Reregistration Eligibility Document. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, are included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a "study". In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review and can be described with a conventional bibliographic citation. The Agency has also attempted to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by Master Record Identifier, or "MRID number". This number is unique to the citation, and should be used whenever a specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies (see paragraph 4(d)(4) below for further explanation). In a few cases, entries added to the bibliography late in the review may be preceded by a nine character temporary identifier. These entries are listed after all MRID entries. This temporary identifying number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standard of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

   a Author. Whenever the author could confidently be identified, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as the author. When no author or laboratory could be identified, the Agency has shown the first submitter as the author.

   b. Document date. The date of the study is taken directly from the document. When the date is followed by a question mark, the bibliographer has deduced the date from the evidence contained in the document. When the date appears

as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for the Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission date. The date of the earliest known submission appears immediately following the word "received."

(2) Administrative number. The next element immediately following the word "under" is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter. When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," which stands for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

GENERIC DATA CALL-IN NOTICE

CERTIFIED MAIL

Dear Sir or Madam:

This Notice requires you and other registrants of pesticide products containing the active ingredient(s) identified in Attachment 1 of this Notice, the Data Call-In Chemical Status Sheet, to submit certain data as noted herein to the U.S. Environmental Protection Agency (EPA, the Agency). These data are necessary to maintain the continued registration of your product(s) containing this active ingredient(s). Within 90 days after you receive this Notice you must respond as set forth in Section III below. Your response must state:

1. how you will comply with the requirements set forth in this Notice and its Attachments 1 through 4; or,

2. why you believe you are exempt from the requirements listed in this Notice and in Attachment 3, Requirements Status and Registrant's Response Form, (see section III-B); or,

3. why you believe EPA should not require your submission of data in the manner specified by this Notice (see section III-D).

If you do not respond to this Notice, or if you do not satisfy EPA that you will comply with its requirements or should be exempt or excused from doing so, then the registration of your product(s) subject to this Notice will be subject to suspension. We have provided a list of all of your products subject to this Notice in Attachment 2, Data Call-In Response Form, as well as a list of all registrants who were sent this Notice (Attachment 4).

The authority for this Notice is section 3(c)(2)(B) of the Federal Insecticide, Fungicide and Rodenticide Act as amended (FIFRA), 7 U.S.C. section 136a(c)(2)(B). Collection of this information is authorized under the Paperwork Reduction Act by OMB Approval No. 2070-0107 and 2070-0057 (expiration date 3-31-99).

This Notice is divided into six sections and five Attachments. The Notice itself contains information and instructions applicable to all Data Call-In Notices. The Attachments contain specific chemical information and instructions. The six sections of the Notice are:

Section I	-	Why You Are Receiving This Notice
Section II	-	Data Required By This Notice
Section III	-	Compliance With Requirements Of This Notice
Section IV	-	Consequences Of Failure To Comply With This Notice
Section V	-	Registrants' Obligation To Report Possible Unreasonable Adverse Effects
Section VI	-	Inquiries And Responses To This Notice

The Attachments to this Notice are:

Attachment 1	-	Data Call-In Chemical Status Sheet
Attachment 2	-	Data Call-In Response Form
Attachment 3	-	Requirements Status And Registrant's Response Form
Attachment 4	-	List Of All Registrants Sent This Data Call-In Notice

SECTION I. WHY YOU ARE RECEIVING THIS NOTICE

The Agency has reviewed existing data for this active ingredient(s) and reevaluated the data needed to support continued registration of the subject active ingredient(s). This reevaluation identified additional data necessary to assess the health and safety of the continued use of products containing this active ingredient(s). You have been sent this Notice because you have product(s) containing the subject active ingredient(s).

SECTION II. DATA REQUIRED BY THIS NOTICE

A. DATA REQUIRED

The data required by this Notice are specified in Attachment 3, Requirements Status and Registrant's Response Form. Depending on the results of the studies required in this Notice, additional testing may be required.

B. SCHEDULE FOR SUBMISSION OF DATA

You are required to submit the data or otherwise satisfy the data requirements specified in Attachment 3, Requirements Status and Registrant's Response Form, within the time frames provided.

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C. TESTING PROTOCOL

All studies required under this Notice must be conducted in accordance with test standards outlined in the Pesticide Assessment Guidelines for those studies for which guidelines have been established.

These EPA Guidelines are available from the National Technical Information Service (NTIS), Attn: Order Desk, 5285 Port Royal Road, Springfield, Va 22161 (tel: 703-487-4650).

Protocols approved by the Organization for Economic Cooperation and Development (OECD) are also acceptable if the OECD-recommended test standards conform to those specified in the Pesticide Data Requirements regulation (40 CFR § 158.70). When using the OECD protocols, they should be modified as appropriate so that the data generated by the study will satisfy the requirements of 40 CFR § 158. Normally, the Agency will not extend deadlines for complying with data requirements when the studies were not conducted in accordance with acceptable standards. The OECD protocols are available from 2001 L Street, N.W., Washington, D.C. 20036 (Telephone number 202-785-6323; Fax telephone number 202-785-0350).

All new studies and proposed protocols submitted in response to this Data Call-In Notice must be in accordance with Good Laboratory Practices [40 CFR Part 160.3(a)(6)].

D. REGISTRANTS RECEIVING PREVIOUS SECTION 3(c)(2)(B) NOTICES ISSUED BY THE AGENCY

Unless otherwise noted herein, this Data Call-In does not in any way supersede or change the requirements of any previous Data Call-In(s), or any other agreements entered into with the Agency pertaining to such prior Notice. Registrants must comply with the requirements of all Notices to avoid issuance of a Notice of Intent to Suspend their affected products.

SECTION III. COMPLIANCE WITH REQUIREMENTS OF THIS NOTICE

A. SCHEDULE FOR RESPONDING TO THE AGENCY

The appropriate responses initially required by this Notice must be submitted to the Agency within 90 days after your receipt of this Notice. Failure to adequately respond to this Notice within 90 days of your receipt will be a basis for issuing a Notice of Intent to Suspend (NOIS) affecting your products. This and other bases for issuance of NOIS due to failure to comply with this Notice are presented in Section IV-A and IV-B.

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B. OPTIONS FOR RESPONDING TO THE AGENCY

The options for responding to this Notice are: 1) voluntary cancellation, 2) delete use(s), (3) claim generic data exemption, (4) agree to satisfy the data requirements imposed by this Notice or (5) request a data waiver(s).

A discussion of how to respond if you chose the Voluntary Cancellation option, the Delete Use(s) option or the Generic Data Exemption option is presented below. A discussion of the various options available for satisfying the data requirements of this Notice is contained in Section III-C. A discussion of options relating to requests for data waivers is contained in Section III-D.

There are two forms that accompany this Notice of which, depending upon your response, one or both must be used in your response to the Agency. These forms are the Data-Call-In Response Form (Attachment 2) and the Requirements Status and Registrant's Response Form (Attachment 3). The Data Call-In Response Form must be submitted as part of every response to this Notice. Please note that the company's authorized representative is required to sign the first page of the Data Call-In Response Form and Requirements Status and Registrant's Response Form (if this form is required) and initial any subsequent pages. The forms contain separate detailed instructions on the response options. Do not alter the printed material. If you have questions or need assistance in preparing your response, call or write the contact person identified in Attachment 1.

1. Voluntary Cancellation - You may avoid the requirements of this Notice by requesting voluntary cancellation of your product(s) containing the active ingredient(s) that is the subject of this Notice. If you wish to voluntarily cancel your product, you must submit a completed Data Call-In Response Form, indicating your election of this option. Voluntary cancellation is item number 5 on the Data Call-In Response Form. If you choose this option, this is the only form that you are required to complete.

   If you choose to voluntarily cancel your product, further sale and distribution of your product after the effective date of cancellation must be in accordance with the Existing Stocks provisions of this Notice which are contained in Section IV-C.

2. Use Deletion - You may avoid the requirements of this Notice by eliminating the uses of your product to which the requirements apply. If you wish to amend your registration to delete uses, you must submit the Requirements Status and Registrant's Response Form, a completed application for amendment, a copy of your proposed amended labeling, and all other information required for processing the application. Use deletion is option

number 7 on the Requirements Status and Registrant's Response Form. You must also complete a Data Call-In Response Form by signing the certification, item number 8. Application forms for amending registrations may be obtained from the Registration Support and Emergency Response Branch, Registration Division, (703) 308-8358.

If you choose to delete the use(s) subject to this Notice or uses subject to specific data requirements, further sale, distribution, or use of your product after one year from the due date of your 90 day response, must bear an amended label.

3. Generic Data Exemption - Under section 3(c)(2)(D) of FIFRA, an applicant for registration of a product is exempt from the requirement to submit or cite generic data concerning an active ingredient(s) if the active ingredient(s) in the product is derived exclusively from purchased, registered pesticide products containing the active ingredient(s). EPA has concluded, as an exercise of its discretion, that it normally will not suspend the registration of a product which would qualify and continue to qualify for the generic data exemption in section 3(c)(2)(D) of FIFRA. To qualify, all of the following requirements must be met:

a. The active ingredient(s) in your registered product must be present solely because of incorporation of another registered product which contains the subject active ingredient(s) and is purchased from a source not connected with you; and,

b. every registrant who is the ultimate source of the active ingredient(s) in your product subject to this DCI must be in compliance with the requirements of this Notice and must remain in compliance; and

c. you must have provided to EPA an accurate and current "Confidential Statement of Formula" for each of your products to which this Notice applies.

To apply for the Generic Data Exemption you must submit a completed Data Call-In Response Form, Attachment 2 and all supporting documentation. The Generic Data Exemption is item number 6a on the Data Call-In Response Form. If you claim a generic data exemption you are not required to complete the Requirements Status and Registrant's Response Form. Generic Data Exemption cannot be selected as an option for product specific data.

If you are granted a Generic Data Exemption, you rely on the efforts of other persons to provide the Agency with the required data. If the registrant(s) who have committed to generate and submit the required data fail to take

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appropriate steps to meet the requirements or are no longer in compliance with this Data Call-In Notice, the Agency will consider that both they and you are not in compliance and will normally initiate proceedings to suspend the registrations of both your and their product(s), unless you commit to submit and do submit the required data within the specified time. In such cases the Agency generally will not grant a time extension for submitting the data.

4. Satisfying the Data Requirements of this Notice - There are various options available to satisfy the data requirements of this Notice. These options are discussed in Section III-C of this Notice and comprise options 1 through 6 on the Requirements Status and Registrant's Response Form and option 6b and 7 on the Data Call-In Response Form. If you choose option 6b or 7, you must submit both forms as well as any other information/data pertaining to the option chosen to address the data requirement.

5. Request for Data Waivers. Data waivers are discussed in Section III-D of this Notice and are covered by options 8 and 9 on the Requirements Status and Registrant's Response Form. If you choose one of these options, you must submit both forms as well as any other information/data pertaining to the option chosen to address the data requirement.

C. SATISFYING THE DATA REQUIREMENTS OF THIS NOTICE

If you acknowledge on the Data Call-In Response Form that you agree to satisfy the data requirements (i.e. you select option 6b and/or 7), then you must select one of the six options on the Requirements Status and Registrant's Response Form related to data production for each data requirement. Your option selection should be entered under item number 9, "Registrant Response." The six options related to data production are the first six options discussed under item 9 in the instructions for completing the Requirements Status and Registrant's Response Form. These six options are listed immediately below with information in parentheses to guide registrants to additional instructions provided in this Section. The options are:

1. I will generate and submit data within the specified time frame (Developing Data),

2. I have entered into an agreement with one or more registrants to develop data jointly (Cost Sharing),

3. I have made offers to cost-share (Offers to Cost Share),

4. I am submitting an existing study that has not been submitted previously to the Agency by anyone (Submitting an Existing Study),

5. I am submitting or citing data to upgrade a study classified by EPA as partially acceptable and upgradeable (Upgrading a Study),

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6. I am citing an existing study that EPA has classified as acceptable or an existing study that has been submitted but not reviewed by the Agency (Citing an Existing Study).

Option 1, Developing Data --

If you choose to develop the required data it must be in conformance with Agency deadlines and with other Agency requirements as referenced herein and in the attachments. All data generated and submitted must comply with the Good Laboratory Practice (GLP) rule (40 CFR Part 160), be conducted according to the Pesticide Assessment Guidelines (PAG), and be in conformance with the requirements of PR Notice 86-5. In addition, certain studies require Agency approval of test protocols in advance of study initiation. Those studies for which a protocol must be submitted have been identified in the Requirements Status and Registrant's Response Form and/or footnotes to the form. If you wish to use a protocol which differs from the options discussed in Section II-C of this Notice, you must submit a detailed description of the proposed protocol and your reason for wishing to use it. The Agency may choose to reject a protocol not specified in Section II-C. If the Agency rejects your protocol you will be notified in writing, however, you should be aware that rejection of a proposed protocol will not be a basis for extending the deadline for submission of data.

A progress report must be submitted for each study within 90 days from the date you are required to commit to generate or undertake some other means to address that study requirement, such as making an offer to cost-share or agreeing to share in the cost of developing that study. A 90-day progress report must be submitted for all studies. This 90-day progress report must include the date the study was or will be initiated and, for studies to be started within 12 months of commitment, the name and address of the laboratory(ies) or individuals who are or will be conducting the study.

In addition, if the time frame for submission of a final report is more than 1 year, interim reports must be submitted at 12 month intervals from the date you are required to commit to generate or otherwise address the requirement for the study. In addition to the other information specified in the preceding paragraph, at a minimum, a brief description of current activity on and the status of the study must be included as well as a full description of any problems encountered since the last progress report.

The time frames in the Requirements Status and Registrant's Response Form are the time frames that the Agency is allowing for the submission of completed study reports or protocols. The noted deadlines run from the date of the receipt of this Notice by the registrant. If the data are not submitted by the deadline, each registrant is subject to receipt of a Notice of Intent to Suspend the affected registration(s).

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If you cannot submit the data/reports to the Agency in the time required by this Notice and intend to seek additional time to meet the requirement(s), you must submit a request to the Agency which includes: (1) a detailed description of the expected difficulty and (2) a proposed schedule including alternative dates for meeting such requirements on a step-by-step basis. You must explain any technical or laboratory difficulties and provide documentation from the laboratory performing the testing. While EPA is considering your request, the original deadline remains. The Agency will respond to your request in writing. If EPA does not grant your request, the original deadline remains. Normally, extensions can be requested only in cases of extraordinary testing problems beyond the expectation or control of the registrant. Extensions will not be given in submitting the 90-day responses. Extensions will not be considered if the request for extension is not made in a timely fashion; in no event shall an extension request be considered if it is submitted at or after the lapse of the subject deadline.

Option 2, Agreement to Share in Cost to Develop Data --

If you choose to enter into an agreement to share in the cost of producing the required data but will not be submitting the data yourself, you must provide the name of the registrant who will be submitting the data. You must also provide EPA with documentary evidence that an agreement has been formed. Such evidence may be your letter offering to join in an agreement and the other registrant's acceptance of your offer, or a written statement by the parties that an agreement exists. The agreement to produce the data need not specify all of the terms of the final arrangement between the parties or the mechanism to resolve the terms. Section 3(c)(2)(B) provides that if the parties cannot resolve the terms of the agreement they may resolve their differences through binding arbitration.

Option 3, Offer to Share in the Cost of Data Development --

If you have made an offer to pay in an attempt to enter into an agreement or amend an existing agreement to meet the requirements of this Notice and have been unsuccessful, you may request EPA (by selecting this option) to exercise its discretion not to suspend your registration(s), although you do not comply with the data submission requirements of this Notice. EPA has determined that as a general policy, absent other relevant considerations, it will not suspend the registration of a product of a registrant who has in good faith sought and continues to seek to enter into a joint data development/cost sharing program, but the other registrant(s) developing the data has refused to accept your offer. To qualify for this option, you must submit documentation to the Agency proving that you have made an offer to another registrant (who has an obligation to submit data) to share in the burden of developing that data.

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You must also submit to the Agency a completed EPA Form 8570-32, Certification of Offer to Cost Share in the Development of Data. In addition, you must demonstrate that the other registrant to whom the offer was made has not accepted your offer to enter into a cost sharing agreement by including a copy of your offer and proof of the other registrant's receipt of that offer (such as a certified mail receipt). Your offer must, in addition to anything else, offer to share in the burden of producing the data upon terms to be agreed or failing agreement to be bound by binding arbitration as provided by FIFRA section 3(c)(2)(B)(iii) and must not qualify this offer. The other registrant must also inform EPA of its election of an option to develop and submit the data required by this Notice by submitting a Data Call-In Response Form and a Requirements Status and Registrant's Response Form committing to develop and submit the data required by this Notice.

In order for you to avoid suspension under this option, you may not withdraw your offer to share in the burdens of developing the data. In addition, the other registrant must fulfill its commitment to develop and submit the data as required by this Notice. If the other registrant fails to develop the data or for some other reason is subject to suspension, your registration as well as that of the other registrant will normally be subject to initiation of suspension proceedings, unless you commit to submit, and do submit the required data in the specified time frame. In such cases, the Agency generally will not grant a time extension for submitting the data.

Option 4, Submitting an Existing Study --

If you choose to submit an existing study in response to this Notice, you must determine that the study satisfies the requirements imposed by this Notice. You may only submit a study that has not been previously submitted to the Agency or previously cited by anyone. Existing studies are studies which predate issuance of this Notice. Do not use this option if you are submitting data to upgrade a study. (See Option 5).

You should be aware that if the Agency determines that the study is not acceptable, the Agency will require you to comply with this Notice, normally without an extension of the required date of submission. The Agency may determine at any time that a study is not valid and needs to be repeated.

To meet the requirements of the DCI Notice for submitting an existing study, all of the following three criteria must be clearly met:

a. You must certify at the time that the existing study is submitted that the raw data and specimens from the study are available for audit and review and you must identify where they are available. This must

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be done in accordance with the requirements of the Good Laboratory Practice (GLP) regulation, 40 CFR Part 160. As stated in 40 CFR 160.3(7) " *raw data* means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the exact copy or exact transcript may be substituted for the original source as raw data. *Raw data* may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments." The term "specimens", according to 40 CFR 160.3(7), means "any material derived from a test system for examination or analysis."

b. Health and safety studies completed after May 1984 must also contain all GLP-required quality assurance and quality control information, pursuant to the requirements of 40 CFR Part 160. Registrants must also certify at the time of submitting the existing study that such GLP information is available for post-May 1984 studies by including an appropriate statement on or attached to the study signed by an authorized official or representative of the registrant.

c. You must certify that each study fulfills the acceptance criteria for the Guideline relevant to the study provided in the FIFRA Accelerated Reregistration Phase 3 Technical Guidance and that the study has been conducted according to the Pesticide Assessment Guidelines (PAG) or meets the purpose of the PAG (both available from NTIS). A study not conducted according to the PAG may be submitted to the Agency for consideration if the registrant believes that the study clearly meets the purpose of the PAG. The registrant is referred to 40 CFR 158.70 which states the Agency's policy regarding acceptable protocols. If you wish to submit the study, you must, in addition to certifying that the purposes of the PAG are met by the study, clearly articulate the rationale why you believe the study meets the purpose of the PAG, including copies of any supporting information or data. It has been the Agency's experience that studies completed prior to January 1970 rarely satisfied the purpose of the PAG and that necessary raw data are usually not available for such studies.

If you submit an existing study, you must certify that the study meets all requirements of the criteria outlined above.

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If EPA has previously reviewed a protocol for a study you are submitting, you must identify any action taken by the Agency on the protocol and must indicate, as part of your certification, the manner in which all Agency comments, concerns, or issues were addressed in the final protocol and study.

If you know of a study pertaining to any requirement in this Notice which does not meet the criteria outlined above but does contain factual information regarding unreasonable adverse effects, you must notify the Agency of such a study. If such a study is in the Agency's files, you need only cite it along with the notification. If not in the Agency's files, you must submit a summary and copies as required by PR Notice 86-5.

Option 5, Upgrading a Study --

If a study has been classified as partially acceptable and upgradeable, you may submit data to upgrade that study. The Agency will review the data submitted and determine if the requirement is satisfied. If the Agency decides the requirement is not satisfied, you may still be required to submit new data normally without any time extension. Deficient, but upgradeable studies will normally be classified as supplemental. However, it is important to note that not all studies classified as supplemental are upgradeable. If you have questions regarding the classification of a study or whether a study may be upgraded, call or write the contact person listed in Attachment 1. If you submit data to upgrade an existing study you must satisfy or supply information to correct all deficiencies in the study identified by EPA. You must provide a clearly articulated rationale of how the deficiencies have been remedied or corrected and why the study should be rated as acceptable to EPA. Your submission must also specify the MRID number(s) of the study which you are attempting to upgrade and must be in conformance with PR Notice 86-5.

Do not submit additional data for the purpose of upgrading a study classified as unacceptable and determined by the Agency as not capable of being upgraded.

This option should also be used to cite data that has been previously submitted to upgrade a study, but has not yet been reviewed by the Agency. You must provide the MRID number of the data submission as well as the MRID number of the study being upgraded.

The criteria for submitting an existing study, as specified in Option 4 above, apply to all data submissions intended to upgrade studies. Additionally your submission of data intended to upgrade studies must be accompanied by a

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certification that you comply with each of those criteria as well as a certification regarding protocol compliance with Agency requirements.

Option 6, Citing Existing Studies --

If you choose to cite a study that has been previously submitted to EPA, that study must have been previously classified by EPA as acceptable or it must be a study which has not yet been reviewed by the Agency. Acceptable toxicology studies generally will have been classified as "core-guideline" or "core minimum." For ecological effects studies, the classification generally would be a rating of "core." For all other disciplines the classification would be "acceptable." With respect to any studies for which you wish to select this option you must provide the MRID number of the study you are citing and, if the study has been reviewed by the Agency, you must provide the Agency's classification of the study.

If you are citing a study of which you are not the original data submitter, you must submit a completed copy of EPA Forms 8570-34 and 8570-35, Certification with Respect to Citation of Data, and Data Matrix.

D. REQUESTS FOR DATA WAIVERS

There are two types of data waiver responses to this Notice. The first is a request for a low volume/minor use waiver and the second is a waiver request based on your belief that the data requirement(s) are inapplicable and do not apply to your product.

1. Low Volume/Minor Use Waiver -- Option 8 on the Requirements Status and Registrant's Response Form. Section 3(c)(2)(A) of FIFRA requires EPA to consider the appropriateness of requiring data for low volume, minor use pesticides. In implementing this provision EPA considers as low volume pesticides only those active ingredient(s) whose total production volume for all pesticide registrants is small. In determining whether to grant a low volume, minor use waiver the Agency will consider the extent, pattern and volume of use, the economic incentive to conduct the testing, the importance of the pesticide, and the exposure and risk from use of the pesticide. If an active ingredient(s) is used for both high volume and low volume uses, a low volume exemption will not be approved. If all uses of an active ingredient(s) are low volume and the combined volumes for all uses are also low, then an exemption may be granted, depending on review of other information outlined below. An exemption will not be granted if any registrant of the active ingredient(s) elects to conduct the testing. Any registrant receiving a low volume minor use waiver must remain within the sales figures in their forecast supporting the waiver request in order to remain qualified for such waiver. If granted a waiver, a registrant will be required, as a condition of the waiver, to submit annual sales reports. The Agency will respond to requests for waivers in writing.

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To apply for a low volume, minor use waiver, you must submit the following information, as applicable to your product(s), as part of your 90-day response to this Notice:

a. Total company sales (pounds and dollars) of all registered product(s) containing the active ingredient(s). If applicable to the active ingredient(s), include foreign sales for those products that are not registered in this country but are applied to sugar (cane or beet), coffee, bananas, cocoa, and other such crops. Present the above information by year for each of the past five years.

b. Provide an estimate of the sales (pounds and dollars) of the active ingredient(s) for each major use site. Present the above information by year for each of the past five years.

c. Total direct production cost of product(s) containing the active ingredient(s) by year for the past five years. Include information on raw material cost, direct labor cost, advertising, sales and marketing, and any other significant costs listed separately.

d. Total indirect production cost (e.g. plant overhead, amortized plant and equipment) charged to product(s) containing the active ingredient(s) by year for the past five years. Exclude all non-recurring costs that were directly related to the active ingredient(s), such as costs of initial registration and any data development.

e. A list of each data requirement for which you seek a waiver. Indicate the type of waiver sought and the estimated cost to you (listed separately for each data requirement and associated test) of conducting the testing needed to fulfill each of these data requirements.

f. A list of each data requirement for which you are not seeking any waiver and the estimated cost to you (listed separately for each data requirement and associated test) of conducting the testing needed to fulfill each of these data requirements.

g. For each of the next ten years, a year-by-year forecast of company sales (pounds and dollars) of the active ingredient(s), direct production costs of product(s) containing the active ingredient(s) (following the parameters in item c above), indirect production costs of product(s) containing the active ingredient(s) (following the parameters in item d above), and costs of data development pertaining to the active ingredient(s).

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h. A description of the importance and unique benefits of the active ingredient(s) to users. Discuss the use patterns and the effectiveness of the active ingredient(s) relative to registered alternative chemicals and non-chemical control strategies. Focus on benefits unique to the active ingredient(s), providing information that is as quantitative as possible. If you do not have quantitative data upon which to base your estimates, then present the reasoning used to derive your estimates. To assist the Agency in determining the degree of importance of the active ingredient(s) in terms of its benefits, you should provide information on any of the following factors, as applicable to your product(s):

(1) documentation of the usefulness of the active ingredient(s) in Integrated Pest Management, (b) description of the beneficial impacts on the environment of use of the active ingredient(s), as opposed to its registered alternatives, (c) information on the breakdown of the active ingredient(s) after use and on its persistence in the environment, and (d) description of its usefulness against a pest(s) of public health significance.

Failure to submit sufficient information for the Agency to make a determination regarding a request for a low volume minor use waiver will result in denial of the request for a waiver.

2. Request for Waiver of Data --Option 9 on the Requirements Status and Registrant's Response Form. This option may be used if you believe that a particular data requirement should not apply because the corresponding use is no longer registered or the requirement is inappropriate. You must submit a rationale explaining why you believe the data requirements should not apply. You must also submit the current label(s) of your product(s) and, if a current copy of your Confidential Statement of Formula is not already on file you must submit a current copy.

You will be informed of the Agency's decision in writing. If the Agency determines that the data requirements of this Notice do not apply to your product(s), you will not be required to supply the data pursuant to section 3(c)(2)(B). If EPA determines that the data are required for your product(s), you must choose a method of meeting the requirements of this Notice within the time frame provided by this Notice. Within 30 days of your receipt of the Agency's written decision, you must submit a revised Requirements Status and Registrant's Response Form indicating the option chosen.

IV. CONSEQUENCES OF FAILURE TO COMPLY WITH THIS NOTICE

A. NOTICE OF INTENT TO SUSPEND

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The Agency may issue a Notice of Intent to Suspend products subject to this Notice due to failure by a registrant to comply with the requirements of this Data Call-In Notice, pursuant to FIFRA section 3(c)(2)(B). Events which may be the basis for issuance of a Notice of Intent to Suspend include, but are not limited to, the following:

1. Failure to respond as required by this Notice within 90 days of your receipt of this Notice.

2. Failure to submit on the required schedule an acceptable proposed or final protocol when such is required to be submitted to the Agency for review.

3. Failure to submit on the required schedule an adequate progress report on a study as required by this Notice.

4. Failure to submit on the required schedule acceptable data as required by this Notice.

5. Failure to take a required action or submit adequate information pertaining to any option chosen to address the data requirements (e.g., any required action or information pertaining to submission or citation of existing studies or offers, arrangements, or arbitration on the sharing of costs or the formation of Task Forces, failure to comply with the terms of an agreement or arbitration concerning joint data development or failure to comply with any terms of a data waiver).

6. Failure to submit supportable certifications as to the conditions of submitted studies, as required by Section III-C of this Notice.

7. Withdrawal of an offer to share in the cost of developing required data.

8. Failure of the registrant to whom you have tendered an offer to share in the cost of developing data and provided proof of the registrant's receipt of such offer, or failure of a registrant on whom you rely for a generic data exemption either to:

   a. inform EPA of intent to develop and submit the data required by this Notice on a Data Call-In Response Form and a Requirements Status and Registrant's Response Form; or,

   b. fulfill the commitment to develop and submit the data as required by this Notice; or,

   c. otherwise take appropriate steps to meet the requirements stated in this Notice, unless you commit to submit and do submit the required data in the specified time frame.

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9. Failure to take any required or appropriate steps, not mentioned above, at any time following the issuance of this Notice.

B. BASIS FOR DETERMINATION THAT SUBMITTED STUDY IS UNACCEPTABLE

The Agency may determine that a study (even if submitted within the required time) is unacceptable and constitutes a basis for issuance of a Notice of Intent to Suspend. The grounds for suspension include, but are not limited to, failure to meet any of the following:

1. EPA requirements specified in the Data Call-In Notice or other documents incorporated by reference (including, as applicable, EPA Pesticide Assessment Guidelines, Data Reporting Guidelines, and GeneTox Health Effects Test Guidelines) regarding the design, conduct, and reporting of required studies. Such requirements include, but are not limited to, those relating to test material, test procedures, selection of species, number of animals, sex and distribution of animals, dose and effect levels to be tested or attained, duration of test, and, as applicable, Good Laboratory Practices.

2. EPA requirements regarding the submission of protocols, including the incorporation of any changes required by the Agency following review.

3. EPA requirements regarding the reporting of data, including the manner of reporting, the completeness of results, and the adequacy of any required supporting (or raw) data, including, but not limited to, requirements referenced or included in this Notice or contained in PR 86-5. All studies must be submitted in the form of a final report; a preliminary report will not be considered to fulfill the submission requirement.

C. EXISTING STOCKS OF SUSPENDED OR CANCELLED PRODUCTS

EPA has statutory authority to permit continued sale, distribution and use of existing stocks of a pesticide product which has been suspended or cancelled if doing so would be consistent with the purposes of the Federal Insecticide, Fungicide, and Rodenticide Act.

The Agency has determined that such disposition by registrants of existing stocks for a suspended registration when a section 3(c)(2)(B) data request is outstanding would generally not be consistent with the Act's purposes. Accordingly, the Agency anticipates granting registrants permission to sell, distribute, or use existing stocks of suspended product(s) only in exceptional circumstances. If you believe such disposition of existing stocks of your product(s) which may be suspended for failure to comply with this Notice should be permitted, you have the burden of clearly

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demonstrating to EPA that granting such permission would be consistent with the Act. You must also explain why an "existing stocks" provision is necessary, including a statement of the quantity of existing stocks and your estimate of the time required for their sale, distribution, and use. Unless you meet this burden the Agency will not consider any request pertaining to the continued sale, distribution, or use of your existing stocks after suspension.

If you request a voluntary cancellation of your product(s) as a response to this Notice and your product is in full compliance with all Agency requirements, you will have, under most circumstances, one year from the date your 90 day response to this Notice is due, to sell, distribute, or use existing stocks. Normally, the Agency will allow persons other than the registrant such as independent distributors, retailers and end users to sell, distribute or use such existing stocks until the stocks are exhausted. Any sale, distribution or use of stocks of voluntarily cancelled products containing an active ingredient(s) for which the Agency has particular risk concerns will be determined on case-by-case basis.

Requests for voluntary cancellation received after the 90 day response period required by this Notice will not result in the Agency granting any additional time to sell, distribute, or use existing stocks beyond a year from the date the 90 day response was due unless you demonstrate to the Agency that you are in full compliance with all Agency requirements, including the requirements of this Notice. For example, if you decide to voluntarily cancel your registration six months before a 3 year study is scheduled to be submitted, all progress reports and other information necessary to establish that you have been conducting the study in an acceptable and good faith manner must have been submitted to the Agency, before EPA will consider granting an existing stocks provision.

SECTION V. REGISTRANTS' OBLIGATION TO REPORT POSSIBLE UNREASONABLE ADVERSE EFFECTS

Registrants are reminded that FIFRA section 6(a)(2) states that if at any time after a pesticide is registered a registrant has additional factual information regarding unreasonable adverse effects on the environment by the pesticide, the registrant shall submit the information to the Agency. Registrants must notify the Agency of any factual information they have, from whatever source, including but not limited to interim or preliminary results of studies, regarding unreasonable adverse effects on man or the environment. This requirement continues as long as the products are registered by the Agency.

SECTION VI. INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding the requirements and procedures established by this Notice, call the contact person listed in Attachment 1, the Data Call-In Chemical Status Sheet.

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All responses to this Notice (other than voluntary cancellation requests and generic data exemption claims) must include a completed Data Call-In Response Form (Attachment 2) and a completed Requirements Status and Registrant's Response Form (Attachment 3) and any other documents required by this Notice, and should be submitted to the contact person identified in Attachment 1. If the voluntary cancellation or generic data exemption option is chosen, only the Data Call-In Response Form need be submitted.

The Office of Compliance (OC) of the Office of Enforcement and Compliance Assurance (OECA), EPA, will be monitoring the data being generated in response to this Notice.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
Reregistration Division

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RODENTICIDE CLUSTER DATA CALL-IN CHEMICAL STATUS SHEET

INTRODUCTION

You have been sent this Generic Data Call-In Notice because you have product(s) containing one or more rodenticides.

This Generic Data Call-In Chemical Status Sheet, contains an overview of data required by this notice, and point of contact for inquiries pertaining to the reregistration of the rodenticides. This attachment is to be used in conjunction with (1) the Generic Data Call-In Notice, (2) the Generic Data Call-In Response Form (Attachment 2), (3) the Requirements Status and Registrant's Form (Attachment 2), (4) a list of registrants receiving this DCI (Attachment 4), (5) the EPA Acceptance Criteria (Attachment 5), and (6) the Cost Share and Data Compensation Forms in replying to this rodenticide Generic Data Call In (Attachment F). Instructions and guidance accompany each form.

DATA REQUIRED BY THIS NOTICE

The additional data requirements needed to complete the generic database for each of the rodenticide cluster active ingredients are contained in the Requirements Status and Registrant's Response, Attachment C. The Agency has concluded that additional product chemistry data on the rodenticides are needed. These data are needed to fully complete the reregistration of all eligible rodenticide cluster products.

INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding the generic data requirements and procedures established by this Notice, please contact Dennis Deziel at (703) 308-8180.

All responsades to this Notice for the generic data requirements should be submitted to:

Dennis Deziel, Chemical Review Manager
Reregistration Branch I
Special Review and Registration Division (H7508W)
Office of Pesticiafde Programs
U.S. Environmental Protection Agency
Washington, D.C. 20460
RE: **Rodenticide**

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SPECIFIC INSTRUCTIONS FOR THE GENERIC DATA CALL-IN RESPONSE FORM

This Form is designed to be used to respond to call-ins for generic and product specific data for the purpose of reregistering pesticides under the Federal Insecticide Fungicide and Rodenticide Act. Fill out this form each time you are responding to a data call-in for which EPA has sent you the form entitled "Requirements Status and Registrant's Response."

Items 1-4 will have been preprinted on the form Items 5 through 7 must be completed by the registrant as appropriate Items 8 through 11 must be completed by the registrant before submitting a response to the Agency.

Public reporting burden for this collection of information is estimated to average 15 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggesting for reducing this burden, to Chief, Information Policy Branch, PM-223, U S Environmental Protection Agency, 401 M St, S W, Washington, D C 20460; and to the Office of Management and Budget, Paperwork Reduction Project 2070-0107, Washington, D C 20503.

INSTRUCTIONS

Item 1. This item identifies your company name, number and address.

Item 2. This item identifies the ease number, ease name, EPA chemical number and chemical name.

Item 3. This item identifies the date and type of data call-in.

Item 4. This item identifies the EPA product registrations relevant to the data call-in. Please note that you are also responsible for informing the Agency of your response regarding any product that you believe may be covered by this data call-in but that is not listed by the Agency in Item 4. You must bring any such apparent omission to the Agency's attention within the period required for submission of this response form.

Item 5. Cheek this item for each product registration you wish to cancel voluntarily. If a registration number is listed for a product for which you previously requested voluntary cancellation, indicate in Item 5 the date of that request. You do not need to complete any item on the Requirements Status and Registrant's Response Form for any product that is voluntarily cancelled.

Item 6a. Check this item if this data call-in is for generic data as indicated in Item 3 and if you are eligible for a Generic Data Exemption for the chemical listed in Item 2 and used in the subject product. By electing this

exemption, you agree to the terms and conditions of a Generic Data Exemption as explained in the Data Call-In Notice.

If you are eligible for or claim a Generic Data Exemption, enter the EPA registration Number of each registered source of that active ingredient that you use in your product.

Typically, if you purchase an EPA-registered product from one or more other producers (who, with respect to the incorporated product, are in compliance with this and-any other outstanding Data Call-In Notice), and incorporate that product into all your products, you may complete this item for all products listed on this form If, however, you produce the active ingredient yourself, or use any unregistered product (regardless of the fact that some of your sources are registered), you may not claim a Generic Data Exemption and you may not select this item.

Item 6b. Check this Item if the data call-in is a generic data call-in as indicated in Item 3 and if you are agreeing to satisfy the generic data requirements of this data call-in. Attach the Requirements Status and Registrant's Response Form that indicates how you will satisfy those requirements.

Item 7a. Check this item if this call-in if a data call-in as indicated in Item 3 for a manufacturing use product (MUP), and if your product is a manufacturing use product for which you agree to supply product-specific data. Attach the Requirements Status and Registrants' Response Form that indicates how you will satisfy those requirements.

Item 7b. Check this item if this call-in is a data call-in for an end use product (EUP) as indicated in Item 3 and if your product is an end use product for which you agree to supply product-specific data. Attach the Requirements Status and Registrant's Response Form that indicates how you will satisfy those requirements.

Item 8. This certification statement must be signed by an authorized representative of your company and the person signing must include his/her title. Additional pages used in your response must be initialled and dated in the space provided for the certification.

Item 9. Enter the date of signature.

Item 10. Enter the name of the person EPA should contact with questions regarding your response.

Item 11. Enter the phone number of your company contact.

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b. Diphacinone, and Salts

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c. Brodifacoum

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d. Bromadiolone

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e. Bromethalin

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SPECIFIC INSTRUCTIONS FOR COMPLETING THE REQUIREMENTS STATUS AND REGISTRANTS RESPONSE FORM

Generic Data

This form is designed to be used for registrants to respond to call-in- for generic and product-specific data as part of EPA's reregistration program under the Federal Insecticide Fungicide and Rodenticide Act. Although the form is the same for both product specific and generic data, instructions for completing the forms differ slightly. Specifically, options for satisfying product specific data requirements do not include (1) deletion of uses or (2) request for a low volume/minor use waiver. These instructions are for completion of generic data requirements.

EPA has developed this form individually for each data call-in addressed to each registrant, and has preprinted this form with a number of items. DO NOT use this form for any other active ingredient.

Items 1 through 8 (inclusive) will have been preprinted on the form. You must complete all other items on this form by typing or printing legibly.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggesting for reducing this burden, to Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, D.C. 20460; and to the Office of Management and Budget, Paperwork Reduction Project 2070-0107, Washington, D.C. 20503.

INSTRUCTIONS

Item 1. This item identifies your company name, number, and address.

Item 2. This item identifies the case number, case name, EPA chemical number and chemical name.

Item 3. This item identifies the date and type of data call-in.

Item 4. This item identifies the guideline reference numbers of studies required to support the product(s) being reregistered. These guidelines, in addition to requirements specified in the Data Call-In Notice, govern the conduct of the required studies.

Item 5. This item identifies the study title associated with the guideline reference number and whether protocols and 1, 2, or 3-year progress reports are required to be

submitted in connection with the study. As noted in Section III of the Data Call-In Notice, 90-day progress reports are required for all studies.

If an asterisk appears in Item 5, EPA has attached information relevant to this guideline reference number to the Requirements Status and Registrant's Response Form.

Item 6. This item identifies the code associated with the use pattern of the pesticide. A brief description of each code follows:

A.	Terrestrial food
B.	Terrestrial feed
C.	Terrestrial non-food
D.	Aquatic food
E.	Aquatic non-food outdoor
F.	Aquatic non-food industrial
G.	Aquatic non-food residential
H.	Greenhouse food
I.	Greenhouse non-food crop
J.	Forestry
K.	Residential
L.	Indoor food
M.	Indoor non-food
N.	Indoor medical
O.	Indoor residential

Item 7. This item identifies the code assigned to the substance that must be used for testing. A brief description of each code follows.

EP	End-Use Product
MP	Manufacturing-Use Product
MP/TGAI	Manufacturing-Use Product and Technical Grade Active Ingredient
PAI	Pure Active Ingredient
PAI/M	Pure Active Ingredient and Metabolites
PAI/PAIRA	Pure Active Ingredient or Pure Active Ingredient Radiolabelled
PAIRA	Pure Active Ingredient Radiolabelled
PAIRA/M	Pure Active Ingredient Radiolabelled and Metabolites
PAIRA/PM	Pure Active Ingredient Radiolabelled and Plant Metabolites
TEP	Typical End-Use Product
TEP _ *	Typical End-Use Product, Percent Active Ingredient Specified
TEP/MET	Typical End-Use Product and Metabolites
TEP/PAI/M	Typical End-Use Product or Pure Active Ingredient and Metabolites

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TGAI/PAIRA	Technical Grade Active Ingredient or Pure Active Ingredient Radiolabelled
TGAI	Technical Grade Active Ingredient
TGAI/TEP	Technical Grade Active Ingredient or Typical End-Use Product
TGAI/PAI	Technical Grade Active Ingredient or Pure Active Ingredient
MET	Metabolites
IMP	Impurities
DEGR	Degradates

*See: guideline comment

Item 8. This item identifies the time frame allowed for submission of the study or protocol identified in item 2. The time frame runs from the date **of your** receipt of the Data Call-In Notice.

Item 9. Enter the appropriate Response Code or Codes to show how you intend to comply with each data requirement. Brief descriptions of each code follow. The Data Call-In Notice contains a fuller description of each of these options.

1. (Developing Data) I will conduct a new study and submit it within the time frames specified in item 8 above. By indicating that I have chosen this option, I certify that I will comply with all the requirements pertaining to the conditions for submittal of this study as outlined in the Data Call-In Notice and that I will provide the protocol and progress reports required in item 5 above.

2. (Agreement to Cost Share) I have entered into an agreement with one or more registrants to develop data jointly. By indicating that I have chosen this option, I certify that I will comply with all the requirements pertaining to sharing in the cost of developing data as outlined in the Data Call-ln Notice.

3. (Offer to Cost Share) I have made an offer to enter into an agreement with one or more registrants to develop data jointly. I am submitting a copy of the form "Certification of Offer to Cost Share in the Development of Data" that describes this offer/agreement. By indicating that I have chosen this option, I certify that I will comply with all the requirements pertaining to making an offer to share in the cost of developing data as outlined in the Data Call-In Notice.

4. (Submitting Existing Data) I am submitting an existing study that has never before been submitted to EPA. By indicating that I have chosen this option, I certify that this study meets all the requirements pertaining to the conditions for submittal of existing data outlined in the Data Call-In Notice and I have attached the needed supporting information along with this response.

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5. (Upgrading a Study) I am submitting or citing data to upgrade a study that EPA has classified as partially acceptable and potentially upgradeable. By indicating that I have chosen this option, I certify that I have met all the requirements pertaining to the conditions for submitting or citing existing data to upgrade a study described in the Data Call-In Notice. I am indicating on attached correspondence the Master Record Identification Number (MRID) that EPA has assigned to the data that I am citing as well as the MRID of the study I am attempting to upgrade.

6. (Citing a Study) I am citing an existing study that has been previously classified by EPA as acceptable, core, core minimum, or a study that has not yet been reviewed by the Agency. I am providing the Agency's classification of the study.

7. (Deleting Uses) I am attaching an application for amendment to my registration deleting the uses for which the data are required.

8. (Low Volume/Minor Use Waiver Request) I have read the statements concerning low volume-minor use data waivers in the Data Call-In Notice and I request a low-volume minor use waiver of the data requirement. I am attaching a detailed justification to support this waiver request including, among other things, all information required to support the request. I understand that, unless modified by the Agency in writing, the data requirement as stated in the Notice governs.

9. (Request for Waiver of Data) I have read the statements concerning data waivers other than low volume minor-use data waivers in the Data Call-In Notice and I request a waiver of the data requirement. I am attaching an identification of the basis for this waiver and a detailed justification to support this waiver request. The justification includes, among other things, all information required to support the request. I understand that, unless modified by the Agency in writing, the data requirement as stated in the Notice governs.

Item 10. This item must be signed by an authorized representative of your company. The person signing must include his/her title, and must initial and date all other pages of this form.

Item 11. Enter the date of signature.

Item 12. Enter the name of the person EPA should contact with questions regarding your response.

Item 13. Enter the phone number of your company contact.

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Attachment 4. List of Registrant(s) sent this DCI (Insert)

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

DATA CALL-IN NOTICE

CERTIFIED MAIL

Dear Sir or Madam:

This Notice requires you and other registrants of pesticide products containing the active ingredient identified in Attachment 1 of this Notice, the Data Call-In Chemical Status Sheet, to submit certain product specific data as noted herein to the U.S. Environmental Protection Agency (EPA, the Agency). These data are necessary to maintain the continued registration of your product(s) containing this active ingredient. Within 90 days after you receive this Notice you must respond as set forth in Section III below. Your response must state:

1. How you will comply with the requirements set forth in this Notice and its Attachments A through G; or

2. Why you believe you are exempt from the requirements listed in this Notice and in Attachment 3, Requirements Status and Registrant's Response Form, (see section III-B); or

3. Why you believe EPA should not require your submission of product specific data in the manner specified by this Notice (see section III-D).

If you do not respond to this Notice, or if you do not satisfy EPA that you will comply with its requirements or should be exempt or excused from doing so, then the registration of your product(s) subject to this Notice will be subject to suspension. We have provided a list of all of your products subject to this Notice in Attachment 2, Data Call-In Response Form, as well as a list of all registrants who were sent this Notice (Attachment 6).

The authority for this Notice is section 3(c)(2)(B) of the Federal Insecticide, Fungicide and Rodenticide Act as amended (FIFRA), 7 U.S.C. section 136a(c)(2)(B). Collection of this information is authorized under the Paperwork Reduction Act by OMB Approval No. 2070-0107 (expiration date 12-31-99).

This Notice is divided into six sections and seven Attachments. The Notice itself contains information and instructions applicable to all Data Call-In Notices. The Attachments contain specific chemical information and instructions. The six sections of the Notice are:

Section I - Why You Are Receiving This Notice
Section II - Data Required By This Notice
Section III - Compliance With Requirements Of This Notice
Section IV - Consequences Of Failure To Comply With This Notice
Section V - Registrants' Obligation To Report Possible Unreasonable Adverse Effects
Section VI - Inquiries And Responses To This Notice

The Attachments to this Notice are:

1 - Data Call-In Chemical Status Sheet
2 - Product-Specific Data Call-In Response Form
3 - Requirements Status and Registrant's Response Form
4 - EPA Batching of End-Use Products for Meeting Acute Toxicology Data Requirements for Reregistration
5 - EPA Acceptance Criteria
6 - List of Registrants Receiving This Notice
7 - Cost Share and Data Compensation Forms, and Product Specific Data Report Form

SECTION I. WHY YOU ARE RECEIVING THIS NOTICE

The Agency has reviewed existing data for this active ingredient and reevaluated the data needed to support continued registration of the subject active ingredient. The Agency has concluded that the only additional data necessary are product specific data. No additional generic data requirements are being imposed. You have been sent this Notice because you have product(s) containing the subject active ingredient.

SECTION II. DATA REQUIRED BY THIS NOTICE

II-A. DATA REQUIRED

The product specific data required by this Notice are specified in Attachment 3, Requirements Status and Registrant's Response Form. Depending on the results of the studies required in this Notice, additional testing may be required.

II-B. SCHEDULE FOR SUBMISSION OF DATA

You are required to submit the data or otherwise satisfy the data requirements specified in Attachment 3, Requirements Status and Registrant's Response Form, within the time frames provided.

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II-C. TESTING PROTOCOL

All studies required under this Notice must be conducted in accordance with test standards outlined in the Pesticide Assessment Guidelines for those studies for which guidelines have been established.

These EPA Guidelines are available from the National Technical Information Service (NTIS), Attn: Order Desk, 5285 Port Royal Road, Springfield, Va 22161 (tel: 703-487-4650).

Protocols approved by the Organization for Economic Cooperation and Development (OECD) are also acceptable if the OECD-recommended test standards conform to those specified in the Pesticide Data Requirements regulation (40 CFR § 158.70). When using the OECD protocols, they should be modified as appropriate so that the data generated by the study will satisfy the requirements of 40 CFR § 158. Normally, the Agency will not extend deadlines for complying with data requirements when the studies were not conducted in accordance with acceptable standards. The OECD protocols are available from OECD, 1750 Pennsylvania Avenue N.W., Washington, D.C. 20006.

All new studies and proposed protocols submitted in response to this Data Call-In Notice must be in accordance with Good Laboratory Practices [40 CFR Part 160.3(a)(6)].

II-D. REGISTRANTS RECEIVING PREVIOUS SECTION 3(c)(2)(B) NOTICES ISSUED BY THE AGENCY

Unless otherwise noted herein, this Data Call-In does not in any way supersede or change the requirements of any previous Data Call-In(s), or any other agreements entered into with the Agency pertaining to such prior Notice. Registrants must comply with the requirements of all Notices to avoid issuance of a Notice of Intent to Suspend their affected products.

SECTION III. COMPLIANCE WITH REQUIREMENTS OF THIS NOTICE

III-A. SCHEDULE FOR RESPONDING TO THE AGENCY

The appropriate responses initially required by this Notice for product specific data must be submitted to the Agency within 90 days after your receipt of this Notice. Failure to adequately respond to this Notice within 90 days of your receipt will be a basis for issuing a Notice of Intent to Suspend (NOIS) affecting your products. This and other bases for issuance of NOIS due to failure to comply with this Notice are presented in Section IV-A and IV-B.

III-B. OPTIONS FOR RESPONDING TO THE AGENCY

The options for responding to this Notice for product specific data are: (a) voluntary cancellation, (b) agree to satisfy the product specific data requirements imposed by this notice or (c) request a data waiver(s).

A discussion of how to respond if you chose the Voluntary Cancellation option is presented below. A discussion of the various options available for satisfying the product specific

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data requirements of this Notice is contained in Section III-C. A discussion of options relating to requests for data waivers is contained in Section III-D.

There are two forms that accompany this Notice of which, depending upon your response, one or both must be used in your response to the Agency. These forms are the Data-Call-In Response Form, and the Requirements Status and Registrant's Response Form, Attachment 2 and Attachment 3. The Data Call-In Response Form must be submitted as part of every response to this Notice. In addition, one copy of the Requirements Status and Registrant's Response Form must be submitted for each product listed on the Data Call-In Response Form unless the voluntary cancellation option is selected or unless the product is identical to another (refer to the instructions for completing the Data Call-In Response Form in Attachment 2). Please note that the company's authorized representative is required to sign the first page of the Data Call-In Response Form and Requirements Status and Registrant's Response Form (if this form is required) and initial any subsequent pages. The forms contain separate detailed instructions on the response options. Do not alter the printed material. If you have questions or need assistance in preparing your response, call or write the contact person(s) identified in Attachment 1.

1. Voluntary Cancellation - You may avoid the requirements of this Notice by requesting voluntary cancellation of your product(s) containing the active ingredient that is the subject of this Notice. If you wish to voluntarily cancel your product, you must submit a completed Data Call-In Response Form, indicating your election of this option. Voluntary cancellation is item number 5 on the Data Call-In Response Form. If you choose this option, this is the only form that you are required to complete.

If you chose to voluntarily cancel your product, further sale and distribution of your product after the effective date of cancellation must be in accordance with the Existing Stocks provisions of this Notice which are contained in Section IV-C.

2. Satisfying the Product Specific Data Requirements of this Notice There are various options available to satisfy the product specific data requirements of this Notice. These options are discussed in Section III-C of this Notice and comprise options 1 through 6 on the Requirements Status and Registrant's Response Form and item numbers 7a and 7b on the Data Call-In Response Form. Deletion of a use(s) and the low volume/minor use option are not valid options for fulfilling product specific data requirements.

3. Request for Product Specific Data Waivers. Waivers for product specific data are discussed in Section III-D of this Notice and are covered by option 7 on the Requirements Status and Registrant's Response Form. If you choose one of these options, you must submit both forms as well as any other information/data pertaining to the option chosen to address the data requirement.

III-C SATISFYING THE DATA REQUIREMENTS OF THIS NOTICE

If you acknowledge on the Data Call-In Response Form that you agree to satisfy the product specific data requirements (i.e. you select item number 7a or 7b), then you must select one of the six options on the Requirements Status and Registrant's Response Form related to data production for each data requirement. Your option selection should be entered under item

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number 9, "Registrant Response." The six options related to data production are the first six options discussed under item 9 in the instructions for completing the Requirements Status and Registrant's Response Form. These six options are listed immediately below with information in parentheses to guide registrants to additional instructions provided in this Section. The options are:

(1) I will generate and submit data within the specified time frame (Developing Data)
(2) I have entered into an agreement with one or more registrants to develop data jointly (Cost Sharing)
(3) I have made offers to cost-share (Offers to Cost Share)
(4) I am submitting an existing study that has not been submitted previously to the Agency by anyone (Submitting an Existing Study)
(5) I am submitting or citing data to upgrade a study classified by EPA as partially acceptable and upgradeable (Upgrading a Study)
(6) I am citing an existing study that EPA has classified as acceptable or an existing study that has been submitted but not reviewed by the Agency (Citing an Existing Study)

Option 1, Developing Data -- If you choose to develop the required data it must be in conformance with Agency deadlines and with other Agency requirements as referenced herein and in the attachments. All data generated and submitted must comply with the Good Laboratory Practice (GLP) rule (40 CFR Part 160), be conducted according to the Pesticide Assessment Guidelines (PAG), and be in conformance with the requirements of PR Notice 86-5.

The time frames in the Requirements Status and Registrant's Response Form are the time frames that the Agency is allowing for the submission of completed study reports. The noted deadlines run from the date of the receipt of this Notice by the registrant. If the data are not submitted by the deadline, each registrant is subject to receipt of a Notice of Intent to Suspend the affected registration(s).

If you cannot submit the data/reports to the Agency in the time required by this Notice and intend to seek additional time to meet the requirements(s), you must submit a request to the Agency which includes: (1) a detailed description of the expected difficulty and (2) a proposed schedule including alternative dates for meeting such requirements on a step-by-step basis. You must explain any technical or laboratory difficulties and provide documentation from the laboratory performing the testing. While EPA is considering your request, the original deadline remains. The Agency will respond to your request in writing. If EPA does not grant your request, the original deadline remains. Normally, extensions can be requested only in cases of extraordinary testing problems beyond the expectation or control of the registrant. Extensions will not be given in submitting the 90-day responses. Extensions will not be considered if the request for extension is not made in a timely fashion; in no event shall an extension request be considered if it is submitted at or after the lapse of the subject deadline.

Option 2, Agreement to Share in Cost to Develop Data -- Registrants may only choose this option for acute toxicity data and certain efficacy data and only if EPA has indicated in the attached data tables that your product and at least one other product are similar for purposes of depending on the same data. If this is the case, data may be generated for just one of the

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products in the group. The registration number of the product for which data will be submitted must be noted in the agreement to cost share by the registrant selecting this option. If you choose to enter into an agreement to share in the cost of producing the required data but will not be submitting the data yourself, you must provide the name of the registrant who will be submitting the data. You must also provide EPA with documentary evidence that an agreement has been formed. Such evidence may be your letter offering to join in an agreement and the other registrant's acceptance of your offer, or a written statement by the parties that an agreement exists. The agreement to produce the data need not specify all of the terms of the final arrangement between the parties or the mechanism to resolve the terms. Section 3(c)(2)(B) provides that if the parties cannot resolve the terms of the agreement they may resolve their differences through binding arbitration.

Option 3, Offer to Share in the Cost of Data Development -- This option only applies to acute toxicity and certain efficacy data as described in option 2 above. If you have made an offer to pay in an attempt to enter into an agreement or amend an existing agreement to meet the requirements of this Notice and have been unsuccessful, you may request EPA (by selecting this option) to exercise its discretion not to suspend your registration(s), although you do not comply with the data submission requirements of this Notice. EPA has determined that as a general policy, absent other relevant considerations, it will not suspend the registration of a product of a registrant who has in good faith sought and continues to seek to enter into a joint data development/cost sharing program, but the other registrant(s) developing the data has refused to accept your offer. To qualify for this option, you must submit documentation to the Agency proving that you have made an offer to another registrant (who has an obligation to submit data) to share in the burden of developing that data. You must also submit to the Agency a completed EPA Form 8570-32, Certification of Offer to Cost Share in the Development of Data, Attachment 7. In addition, you must demonstrate that the other registrant to whom the offer was made has not accepted your offer to enter into a cost sharing agreement by including a copy of your offer and proof of the other registrant's receipt of that offer (such as a certified mail receipt). Your offer must, in addition to anything else, offer to share in the burden of producing the data upon terms to be agreed or failing agreement to be bound by binding arbitration as provided by FIFRA section 3(c)(2)(B)(iii) and must not qualify this offer. The other registrant must also inform EPA of its election of an option to develop and submit the data required by this Notice by submitting a Data Call-In Response Form and a Requirements Status and Registrant's Response Form committing to develop and submit the data required by this Notice.

In order for you to avoid suspension under this option, you may not withdraw your offer to share in the burdens of developing the data. In addition, the other registrant must fulfill its commitment to develop and submit the data as required by this Notice. If the other registrant fails to develop the data or for some other reason is subject to suspension, your registration as well as that of the other registrant will normally be subject to initiation of suspension proceedings, unless you commit to submit, and do submit the required data in the specified time frame. In such cases, the Agency generally will not grant a time extension for submitting the data.

Option 4, Submitting an Existing Study -- If you choose to submit an existing study in response to this Notice, you must determine that the study satisfies the requirements imposed by this Notice. You may only submit a study that has not been previously submitted to the Agency

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or previously cited by anyone. Existing studies are studies which predate issuance of this Notice. Do not use this option if you are submitting data to upgrade a study. (See Option 5).

You should be aware that if the Agency determines that the study is not acceptable, the Agency will require you to comply with this Notice, normally without an extension of the required date of submission. The Agency may determine at any time that a study is not valid and needs to be repeated.

To meet the requirements of the DCI Notice for submitting an existing study, all of the following three criteria must be clearly met:

a. You must certify at the time that the existing study is submitted that the raw data and specimens from the study are available for audit and review and you must identify where they are available. This must be done in accordance with the requirements of the Good Laboratory Practice (GLP) regulation, 40 CFR Part 160. As stated in 40 CFR 160.3(j) " 'raw data' means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the exact copy or exact transcript may be substituted for the original source as raw data. 'Raw data' may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments." The term "specimens", according to 40 CFR 160.3(k), means "any material derived from a test system for examination or analysis."

b. Health and safety studies completed after May 1984 must also contain all GLP-required quality assurance and quality control information, pursuant to the requirements of 40 CFR Part 160. Registrants must also certify at the time of submitting the existing study that such GLP information is available for post-May 1984 studies by including an appropriate statement on or attached to the study signed by an authorized official or representative of the registrant.

c. You must certify that each study fulfills the acceptance criteria for the Guideline relevant to the study provided in the FIFRA Accelerated Reregistration Phase 3 Technical Guidance and that the study has been conducted according to the Pesticide Assessment Guidelines (PAG) or meets the purpose of the PAG (both available from NTIS). A study not conducted according to the PAG may be submitted to the Agency for consideration if the registrant believes that the study clearly meets the purpose of the PAG. The registrant is referred to 40 CFR 158.70 which states the Agency's policy regarding acceptable protocols. If you wish to submit the study, you must, in addition to certifying that the purposes of the PAG are met by the study, clearly articulate the rationale why you believe the study meets the purpose of the PAG, including copies of any supporting information or data. It has been the Agency's experience that studies completed

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prior to January 1970 rarely satisfied the purpose of the PAG and that necessary raw data are usually not available for such studies.

If you submit an existing study, you must certify that the study meets all requirements of the criteria outlined above.

If you know of a study pertaining to any requirement in this Notice which does not meet the criteria outlined above but does contain factual information regarding unreasonable adverse effects, you must notify the Agency of such a study. If such study is in the Agency's files, you need only cite it along with the notification. If not in the Agency's files, you must submit a summary and copies as required by PR Notice 86-5.

Option 5, Upgrading a Study -- If a study has been classified as partially acceptable and upgradeable, you may submit data to upgrade that study. The Agency will review the data submitted and determine if the requirement is satisfied. If the Agency decides the requirement is not satisfied, you may still be required to submit new data normally without any time extension. Deficient, but upgradeable studies will normally be classified as supplemental. However, it is important to note that not all studies classified as supplemental are upgradeable. If you have questions regarding the classification of a study or whether a study may be upgraded, call or write the contact person listed in Attachment 1. If you submit data to upgrade an existing study you must satisfy or supply information to correct all deficiencies in the study identified by EPA. You must provide a clearly articulated rationale of how the deficiencies have been remedied or corrected and why the study should be rated as acceptable to EPA. Your submission must also specify the MRID number(s) of the study which you are attempting to upgrade and must be in conformance with PR Notice 86-5.

Do not submit additional data for the purpose of upgrading a study classified as unacceptable and determined by the Agency as not capable of being upgraded.

This option should also be used to cite data that has been previously submitted to upgrade a study, but has not yet been reviewed by the Agency. You must provide the MRID number of the data submission as well as the MRID number of the study being upgraded.

The criteria for submitting an existing study, as specified in Option 4 above, apply to all data submissions intended to upgrade studies. Additionally your submission of data intended to upgrade studies must be accompanied by a certification that you comply with each of those criteria as well as a certification regarding protocol compliance with Agency requirements.

Option 6, Citing Existing Studies -- If you choose to cite a study that has been previously submitted to EPA, that study must have been previously classified by EPA as acceptable or it must be a study which has not yet been reviewed by the Agency. Acceptable toxicology studies generally will have been classified as "core-guideline" or "core minimum." For all other disciplines the classification would be "acceptable." With respect to any studies for which you wish to select this option you must provide the MRID number of the study you are citing and, if the study has been reviewed by the Agency, you must provide the Agency's classification of the study.

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If you are citing a study of which you are not the original data submitter, you must submit a completed copy of EPA Forms 8570-34 and 8570-35, Certification with Respect to Citation of Data, and Data Matrix.

Registrants who select one of the above 6 options must meet all of the requirements described in the instructions for completing the Data Call-In Response Form and the Requirements Status and Registrant's Response Form, as appropriate.

III-D REQUESTS FOR DATA WAIVERS

If you request a waiver for product specific data because you believe it is inappropriate, you must attach a complete justification for the request, including technical reasons, data and references to relevant EPA regulations, guidelines or policies. (Note: any supplemental data must be submitted in the format required by PR Notice 86-5). This will be the only opportunity to state the reasons or provide information in support of your request. If the Agency approves your waiver request, you will not be required to supply the data pursuant to section 3(c)(2)(B) of FIFRA. If the Agency denies your waiver request, you must choose an option for meeting the data requirements of this Notice within 30 days of the receipt of the Agency's decision. You must indicate and submit the option chosen on the Requirements Status and Registrant's Response Form. Product specific data requirements for product chemistry, acute toxicity and efficacy (where appropriate) are required for all products and the Agency would grant a waiver only under extraordinary circumstances. You should also be aware that submitting a waiver request will not automatically extend the due date for the study in question. Waiver requests submitted without adequate supporting rationale will be denied and the original due date will remain in force.

IV. CONSEQUENCES OF FAILURE TO COMPLY WITH THIS NOTICE

IV-A NOTICE OF INTENT TO SUSPEND

The Agency may issue a Notice of Intent to Suspend products subject to this Notice due to failure by a registrant to comply with the requirements of this Data Call-In Notice, pursuant to FIFRA section 3(c)(2)(B). Events which may be the basis for issuance of a Notice of Intent to Suspend include, but are not limited to, the following:

1. Failure to respond as required by this Notice within 90 days of your receipt of this Notice.
2. Failure to submit on the required schedule an acceptable proposed or final protocol when such is required to be submitted to the Agency for review.
3. Failure to submit on the required schedule an adequate progress report on a study as required by this Notice.
4. Failure to submit on the required schedule acceptable data as required by this Notice.

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5. Failure to take a required action or submit adequate information pertaining to any option chosen to address the data requirements (e.g., any required action or information pertaining to submission or citation of existing studies or offers, arrangements, or arbitration on the sharing of costs or the formation of Task Forces, failure to comply with the terms of an agreement or arbitration concerning joint data development or failure to comply with any terms of a data waiver).

6. Failure to submit supportable certifications as to the conditions of submitted studies, as required by Section III-C of this Notice.

7. Withdrawal of an offer to share in the cost of developing required data.

8. Failure of the registrant to whom you have tendered an offer to share in the cost of developing data and provided proof of the registrant's receipt of such offer or failure of a registrant on whom you rely for a generic data exemption either to:

   a. inform EPA of intent to develop and submit the data required by this Notice on a Data Call-In Response Form and a Requirements Status and Registrant's Response Form;

   b. fulfill the commitment to develop and submit the data as required by this Notice; or

   c. otherwise take appropriate steps to meet the requirements stated in this Notice, unless you commit to submit and do submit the required data in the specified time frame.

9. Failure to take any required or appropriate steps, not mentioned above, at any time following the issuance of this Notice.

IV-B. BASIS FOR DETERMINATION THAT SUBMITTED STUDY IS UNACCEPTABLE

The Agency may determine that a study (even if submitted within the required time) is unacceptable and constitutes a basis for issuance of a Notice of Intent to Suspend. The grounds for suspension include, but are not limited to, failure to meet any of the following:

1. EPA requirements specified in the Data Call-In Notice or other documents incorporated by reference (including, as applicable, EPA Pesticide Assessment Guidelines, Data Reporting Guidelines, and GeneTox Health Effects Test Guidelines) regarding the design, conduct, and reporting of required studies. Such requirements include, but are not limited to, those relating to test material, test procedures, selection of species, number of animals, sex and distribution of animals, dose and effect levels to be tested or attained, duration of test, and, as applicable, Good Laboratory Practices.

2. EPA requirements regarding the submission of protocols, including the incorporation of any changes required by the Agency following review.

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3. EPA requirements regarding the reporting of data, including the manner of reporting, the completeness of results, and the adequacy of any required supporting (or raw) data, including, but not limited to, requirements referenced or included in this Notice or contained in PR 86-5. All studies must be submitted in the form of a final report; a preliminary report will not be considered to fulfill the submission requirement.

IV-C EXISTING STOCKS OF SUSPENDED OR CANCELLED PRODUCTS

EPA has statutory authority to permit continued sale, distribution and use of existing stocks of a pesticide product which has been suspended or cancelled if doing so would be consistent with the purposes of the Act.

The Agency has determined that such disposition by registrants of existing stocks for a suspended registration when a section 3(c)(2)(B) data request is outstanding would generally not be consistent with the Act's purposes. Accordingly, the Agency anticipates granting registrants permission to sell, distribute, or use existing stocks of suspended product(s) only in exceptional circumstances. If you believe such disposition of existing stocks of your product(s) which may be suspended for failure to comply with this Notice should be permitted, you have the burden of clearly demonstrating to EPA that granting such permission would be consistent with the Act. You must also explain why an "existing stocks" provision is necessary, including a statement of the quantity of existing stocks and your estimate of the time required for their sale, distribution, and use. Unless you meet this burden the Agency will not consider any request pertaining to the continued sale, distribution, or use of your existing stocks after suspension.

If you request a voluntary cancellation of your product(s) as a response to this Notice and your product is in full compliance with all Agency requirements, you will have, under most circumstances, one year from the date your 90 day response to this Notice is due, to sell, distribute, or use existing stocks. Normally, the Agency will allow persons other than the registrant such as independent distributors, retailers and end users to sell, distribute or use such existing stocks until the stocks are exhausted. Any sale, distribution or use of stocks of voluntarily cancelled products containing an active ingredient for which the Agency has particular risk concerns will be determined on case-by-case basis.

Requests for voluntary cancellation received after the 90 day response period required by this Notice will not result in the Agency granting any additional time to sell, distribute, or use existing stocks beyond a year from the date the 90 day response was due unless you demonstrate to the Agency that you are in full compliance with all Agency requirements, including the requirements of this Notice. For example, if you decide to voluntarily cancel your registration six months before a 3 year study is scheduled to be submitted, all progress reports and other information necessary to establish that you have been conducting the study in an acceptable and good faith manner must have been submitted to the Agency, before EPA will consider granting an existing stocks provision.

SECTION V. REGISTRANTS' OBLIGATION TO REPORT POSSIBLE UNREASONABLE ADVERSE EFFECTS

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Registrants are reminded that FIFRA section 6(a)(2) states that if at any time after a pesticide is registered a registrant has additional factual information regarding unreasonable adverse effects on the environment by the pesticide, the registrant shall submit the information to the Agency. Registrants must notify the Agency of any factual information they have, from whatever source, including but not limited to interim or preliminary results of studies, regarding unreasonable adverse effects on man or the environment. This requirement continues as long as the products are registered by the Agency.

SECTION VI. INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding the requirements and procedures established by this Notice, call the contact person(s) listed in Attachment 1, the Data Call-In Chemical Status Sheet.

All responses to this Notice (other than voluntary cancellation requests and generic data exemption claims) must include a completed Data Call-In Response Form and a completed Requirements Status and Registrant's Response Form (Attachment 2 and Attachment 3 for product specific data) and any other documents required by this Notice, and should be submitted to the contact person(s) identified in Attachment 1. If the voluntary cancellation or generic data exemption option is chosen, only the Data Call-In Response Form need be submitted.

The Office of Compliance Monitoring (OCM) of the Office of Pesticides and Toxic Substances (OPTS), EPA, will be monitoring the data being generated in response to this Notice.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
Reregistration Division

Attachments

1 - Data Call-In Chemical Status Sheet
2 - Product-Specific Data Call-In Response Form
3 - Requirements Status and Registrant's Response Form
4 - EPA Batching of End-Use Products for Meeting Acute Toxicology Data Requirements for Reregistration
5 - EPA Acceptance Criteria
6 - List of Registrants Receiving This Notice
7 - Cost Share and Data Compensation Forms, and Product Specific Data Report Form

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2665 DATA CALL-IN CHEMICAL STATUS SHEET

INTRODUCTION

You have been sent one of the following Product Specific Data Call-In Notices because you have product(s) containing a rodenticide.

This Product Specific Data Call-In Chemical Status Sheet, contains an overview of data required by this notice, and point of contact for inquiries pertaining to the reregistration of the rodenticides. This attachment is to be used in conjunction with (1) the Product Specific Data Call-In Notice, (2) the Product Specific Data Call-In Response Form (Attachment 2), (3) the Requirements Status and Registrant's Form (Attachment 3), (4) EPA's Grouping of End-Use Products for Meeting Acute Toxicology Data Requirement (Attachment 4), (5) the EPA Acceptance Criteria (Attachment 5), (6) a list of registrants receiving this DCI (Attachment 6) and (7) the Cost Share and Data Compensation Forms in replying to your rodenticide Product Specific Data Call-In (Attachment 7). Instructions and guidance accompany each form.

DATA REQUIRED BY THIS NOTICE

The additional data requirements needed to complete the database for the rodenticides are contained in the Requirements Status and Registrant's Response, Attachment 3. The Agency has concluded that additional data on the rodenticides are needed for specific products. These data are required to be submitted to the Agency within the time frame listed. These data are needed to fully complete the reregistration of all eligible rodenticide products.

INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding this product specific data requirements and procedures established by this Notice, please contact Frank Rubis at (703) 308-8184.

All responses to this Notice for the Product Specific data requirements should be submitted to:

Frank Rubis
Chemical Review Manager Team 81
Product Reregistration Branch
Special Review and Reregistration Branch 7508W
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, D.C. 20460

RE: **Rodenticides**

INSTRUCTIONS FOR COMPLETING THE **DATA CALL-IN RESPONSE FORM** FOR **PRODUCT SPECIFIC DATA**

Item 1-4. Already completed by EPA.

Item 5. If you wish to **voluntarily cancel** your product, answer "**yes**." If you choose this option, you will not have to provide the data required by the Data Call-In Notice and you will not have to complete any other forms. Further sale and distribution of your product after the effective date of cancellation must be in accordance with the Existing Stocks provision of the Data Call-In Notice (Section IV-C).

Item 6. Not applicable since this form calls in product specific data only. However, if your product is **identical** to another product and you qualify for a **data exemption**, you must respond with "**yes**" to Item 7a (MUP) or 7B (EUP) on this form, provide the **EPA registration numbers of your source(s)**; you would **not** complete the "Requirements Status and Registrant's Response" form. Examples of such products include **repackaged** products and **Special Local Needs (Section 24c)** products which are identical to federally registered products.

Item 7a. For each **manufacturing use product** (MUP) for which you wish to maintain registration, you must agree to satisfy the data requirements by responding "**yes**."

Item 7b. For each **end use product** (EUP) for which you wish to maintain registration, you must agree to satisfy the data requirements by responding "**yes**." If you are requesting a **data waiver**, answer "**yes**" here; in addition, on the "Requirements Status and Registrant's Response" form under Item 9, you must respond with **Option 7** (Waiver Request) for each study for which you are requesting a waiver. See Item 6 with regard to identical products and data exemptions.

Items 8-11. Self-explanatory.

NOTE: You may provide **additional information** that does not fit on this form in a signed letter that accompanies this form. For example, you may wish to report that your product has already been transferred to another company or that you have already voluntarily canceled this product. For these cases, please supply all relevant details so that EPA can ensure that its records are correct.

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INSTRUCTIONS FOR COMPLETING THE **REQUIREMENTS STATUS AND REGISTRANT'S RESPONSE FORM** FOR **PRODUCT SPECIFIC DATA**

Item 1-3 Completed by EPA. Note the **unique identifier number** assigned by EPA in Item 3. This number **must be used in the transmittal document for any data submissions** in response to this Data Call-In Notice.

Item 4. The guideline reference numbers of studies required to support the product's continued registration are identified. These guidelines, in addition to the requirements specified in the Notice, govern the conduct of the required studies. Note that series 61 and 62 in product chemistry are now listed under 40 CFR 158.155 through 158.180, Subpart C.

Item 5. The study title associated with the guideline reference number is identified.

Item 6. The use pattern(s) of the pesticide associated with the product specific requirements is (are) identified. For most product specific data requirements, all use patterns are covered by the data requirements. In the case of efficacy data, the required studies only pertain to products which have the use sites and/or pests indicated.

Item 7. The substance to be tested is identified by EPA. For product specific data, the product as formulated for sale and distribution is the test substance, except in rare cases.

Item 8. The due date for submission of each study is identified. It is normally based on **8 months after issuance of the Reregistration Eligibility Document** unless EPA determines that a longer time period is necessary.

Item 9. **Enter only one of the following response codes for each data requirement to show how you intend to comply with the data requirements listed in this table.** Fuller descriptions of each option are contained in the Data Call-In Notice.

1. I will generate and submit data by the specified due date (**Developing Data**). By indicating that I have chosen this option, I certify that I will comply with all the requirements pertaining to the conditions for submittal of this study as outlined in the Data Call-In Notice. By the specified due date, I will also submit: (1) a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

2. I have entered into an agreement with one or more registrants to develop data jointly (**Cost Sharing**). I am submitting a **copy of this agreement**. I understand that this option is available **only** for acute toxicity or certain efficacy data and **only** if EPA indicates in an attachment to this Notice that my product is similar enough to another

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product to qualify for this option. I certify that another party in the agreement is committing to submit or provide the required data; if the required study is not submitted on time, my product may be subject to suspension. By the specified due date, I will also submit: (1) a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

3. I have made offers to share in the cost to develop data (**Offers to Cost Share**). I understand that this option is available **only** for acute toxicity or certain efficacy data and **only** if EPA indicates in an attachment to this Data Call-In Notice that my product is similar enough to another product to qualify for this option. I am submitting **evidence that I have made an offer** to another registrant (who has an obligation to submit data) to share in the cost of that data. I am also submitting a completed "**Certification of Offer to Cost Share in the Development Data" form**. I am including a copy of my offer and proof of the other registrant's receipt of that offer. I am identifying the party which is committing to submit or provide the required data; if the required study is not submitted on time, my product may be subject to suspension. I understand that other terms under Option 3 in the Data Call-In Notice (Section III-C.1.) apply as well. By the specified due date, I will also submit: (1) a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

4. By the specified due date, I will submit an existing study that has not been submitted previously to the Agency by anyone (**Submitting an Existing Study**). I certify that this study will meet all the requirements for submittal of existing data outlined in Option 4 in the Data Call-In Notice (Section III-C.1.) and will meet the attached acceptance criteria (for acute toxicity and product chemistry data). I will attach the needed supporting information along with this response. I also certify that I have determined that this study will fill the data requirement for which I have indicated this choice. By the specified due date, I will also submit a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** to show what data compensation option I have chosen. By the specified due date, I will also submit: (1) a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

5. By the specified due date, I will submit or cite data to upgrade a study classified by the Agency as partially acceptable and upgradable (**Upgrading a Study**). I will submit **evidence of the Agency's review** indicating that the study may be upgraded and what information is required to do so. I will provide the MRID or Accession number of the study at the due date. I understand that the conditions for this option outlined Option 5 in the Data Call-In Notice (Section III-C.1.) apply. By the specified due date, I will also submit: (1) a completed "**Certification With Respect**

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To Data Compensation Requirements" form (EPA Form 8570-29) and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

6. By the specified due date, I will cite an existing study that the Agency has classified as acceptable or an existing study that has been submitted but not reviewed by the Agency (**Citing an Existing Study**). If I am citing another registrant's study, I understand that this option is available **only** for acute toxicity or certain efficacy data and **only** if the cited study was conducted on my product, an identical product or a product which EPA has "grouped" with one or more other products for purposes of depending on the same data. I may also choose this option if I am citing my own data. In either case, I will provide the **MRID or Accession number(s)** for the cited data on a "Product Specific Data Report" form or in a similar format. By the specified due date, I will also submit: (1) a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

7. I request a waiver for this study because it is inappropriate for my product (**Waiver Request**). I am attaching a complete justification for this request, including technical reasons, data and references to relevant EPA regulations, guidelines or policies. [Note: any supplemental data must be submitted in the format required by P.R. Notice 86-5]. I understand that this is my **only** opportunity to state the reasons or provide information in support of my request. If the Agency approves my waiver request, I will **not** be required to supply the data pursuant to Section 3(c)(2)(B) of FIFRA. If the Agency denies my waiver request, I **must choose** a method of meeting the data requirements of this Notice by the due date stated by this Notice. In this case, I must, within **30 days** of my receipt of the Agency's written decision, submit a revised "Requirements Status and Registrant's Response" Form indicating the option chosen. I also understand that the deadline for submission of data as specified by the original data call-in notice will not change. By the specified due date, I will also submit: (1) a completed "**Certification With Respect To Data Compensation Requirements" form (EPA Form 8570-29)** and (2) two completed and signed copies of the **Confidential Statement of Formula (EPA Form 8570-4)**.

Items 10-13. Self-explanatory.

NOTE: You may provide **additional information** that does not fit on this form in a signed letter that accompanies this form. For example, you may wish to report that your product has already been transferred to another company or that you have already voluntarily canceled this product. For these cases, please supply all relevant details so that EPA can ensure that its records are correct.

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EPA'S BATCHING OF PRODUCTS CONTAINING A RODENTICIDE CLUSTER ACTIVE INGREDIENT FOR MEETING REREGISTRATION ACUTE TOXICITY DATA REQUIREMENTS

In an effort to reduce the time, resources and number of animals needed to fulfill the acute toxicity data requirements for reregistration of products containing the active ingredient diphacinone, the Agency has batched products which can be considered similar in terms of acute toxicity. Factors considered in the sorting process include each product's active and inert ingredients (identity, percent composition and biological activity), product form (liquid, paste, solid, etc.), and labeling (e.g., signal word, precautionary labeling, etc.).

Using available information, batching has been accomplished by the process described in the preceding paragraph. Notwithstanding the batching process, the Agency reserves the right to require, at any time, acute toxicity data for an individual product should the need arise.

Registrants of products within a batch may choose to cooperatively generate, submit or cite a single battery of six acute toxicological studies to represent all the products within that batch. The registrant has several options to participate with all or some other registrants, or to deal only their own products within a batch, or to generate all the required acute toxicological studies for each of their own products. If a registrant chooses to generate the data for a batch, he/she must use one of the products within the batch as the test material. If a registrant chooses to rely upon previously submitted acute toxicity data, he/she may do so provided that the data base is complete and valid by today's standards (see acceptance criteria attached), the formulation tested is considered by EPA to be similar for acute toxicity, and the formulation has not been significantly altered since submission and acceptance of the acute toxicity data. TRB must approve any new formulations (that were presented to the Agency after the publication of the RED) before data derived from them can be used to cover other products in a batch. Regardless of whether new data is generated or existing data is referenced, registrants must clearly identify the test material by EPA Registration Number. If more than one confidential statement of formula (CSF) exists for a product, the registrant must indicate the formulation actually tested by identifying the corresponding CSF.

In deciding how to meet the product specific data requirements, registrants must follow the directions given in the Data Call-In Notice and its attachments appended to the RED. The DCI Notice contains two response forms which are to be completed and submitted to the Agency within 90 days of receipt. The first form, "Data Call-In Response," asks whether the registrant will meet the data requirements for each product. The second form, "Requirements Status and Registrant's Response," lists the product specific data required for each product, including the standard six acute toxicity tests. A registrant who wishes to participate in a batch must decide whether he/she will provide the data or depend on someone else to do so. If a registrant supplies the data to support a batch of products, he/she must select one of the following options: Developing Data (Option 1), Submitting an Existing Study (Option 4), Upgrading an Existing Study (Option 5) or Citing an Existing Study (Option 6). If a registrant depends on another's data, he/she must choose among: Cost Sharing (Option 2), Offers to Cost Share (Option 3) or Citing an Existing Study (Option 6). If a registrant does not want to participate in a batch, the choices are Options 1, 4, 5 or 6. However, a registrant should know that choosing not to participate in a batch does

not preclude other registrants in the batch from citing his/her studies and offering to cost share (Option 3) those studies.

Table 1: Batches for the active ingredient diphacinone

Batch	Registration Number	Percent Active Ingredient	Form
1	12455-25	diphacinone … 98%	solid
	61282-1	diphacinone … 98%	solid
	61282-5	diphacinone … 99%	solid
2	56-23	diphacinone … 0.005	solid
	56-41	diphacinone … 0.005	solid
	56-42	diphacinone … 0.005	solid
	56-44	diphacinone … 0.005	solid
	56-57	diphacinone … 0.005	solid
	70-133	diphacinone … 0.005	solid
	70-170	diphacinone … 0.005	solid
	769-653	diphacinone … 0.005	solid
	769-655	diphacinone … 0.005	solid
	769-660	diphacinone … 0.005	solid
	769-669	diphacinone … 0.005	solid
	769-670	diphacinone … 0.005	solid
	769-671	diphacinone … 0.005	solid
	769-787	diphacinone … 0.005	solids
	2393-476	diphacinone … 0.005	solid
	2393-497	diphacinone … 0.005	solid
	2393-498	diphacinone … 0.005	solid
	2393-501	diphacinone … 0.005	solid
	2393-508	diphacinone … 0.005	solid
	3487-26	diphacinone … 0.005	solid
	5887-178	diphacinone … 0.005	solid
	5887-180	diphacinone … 0.005	solid
	5887-181	diphacinone … 0.005	solid
	5887-182	diphacinone … 0.005	solid
	6409-1	diphacinone … 0.005	solid
	7122-32	diphacinone … 0.005	solid
	7122-66	diphacinone … 0.005	solid
	7122-69	diphacinone … 0.005	solid
	11885-12	diphacinone … 0.005	solid
	11885-15	diphacinone … 0.005	solid
	12455-5	diphacinone … 0.005	solid
	12455-14	diphacinone … 0.005	solid
	12455-19	diphacinone … 0.005	solid
	12455-29	diphacinone … 0.005	solid
	12455-67	diphacinone … 0.005	solid
	12455-78	diphacinone … 0.005	solid

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	12455-80	diphacinone	… 0.005	solid
	12455-81	diphacinone	… 0.005	solid
	12455-83	diphacinone	… 0.005	solid
	12455-84	diphacinone	… 0.005	solid
	56637-1	diphacinone	… 0.005	solid
	56637-3	diphacinone	… 0.005	solid
	56637-4	diphacinone	… 0.005	solid
	61282-6	diphacinone	… 0.005	solid
	61282-7	diphacinone	… 0.005	solid
	61282-9	diphacinone	… 0.005	solid
	61282-12	diphacinone	… 0.005	solid
	61282-19	diphacinone	… 0.005	solid
	61282-23	diphacinone	… 0.005	solid
	61282-24	diphacinone	… 0.005	solid
	61282-26	diphacinone	… 0.005	solid
	AZ88001900	diphacinone	… 0.005	solid
	CA78014600	diphacinone	… 0.01	Solid
	CA79002500	diphacinone	… 0.005	solid
	CA89002000	diphacinone	… 0.005	solid
	CA89002100	diphacinone	… 0.005	solid
	CA89002200	diphacinone	… 0.01	solid
2	CT881000100	diphacinone	… 0.005	solid
	CT96000200	diphacinone	… 0.005	solid
	FL78006200	diphacinone	… 0.005	solid
	FL86000300	diphacinone	… 0.005	solid
	FL88001800	diphacinone	… 0.005	solid
	GA95000700	diphacinone	… 0.005	solid
	HI91000400	diphacinone	… 0.005	solid
	HI96000800	diphacinone	… 0.005	solid
	ID82002500	diphacinone	… 0.005	solid
	ID86001800	diphacinone	… 0.005	solid
	ID87002200	diphacinone	… 0.005	solid
	ID96000500	diphacinone	… 0.005	solid
	MA77000100	diphacinone	… 0.005	solid
	MI84001200	diphacinone	… 0.005	solid
	MO97000200	diphacinone	… 0.005	solid
	MT86000300	diphacinone	… 0.005	solid
	NC92001000	diphacinone	… 0.005	solid
	NH76000100	diphacinone	… 0.005	solid
	NV88000800	diphacinone	… 0.005	solid
	OH84000300	diphacinone	… 0.005	solid
	OR76003600	diphacinone	… 0.005	solid
	OR85003800	diphacinone	… 0.005	solid
	PA82001600	diphacinone	… 0.005	solid
	SC96000200	diphacinone	… 0.005	solid

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2	UT87000300	diphacinone	… 0.005	solid
	VA82001500	diphacinone	… 0.005	solid
	VA85000300	diphacinone	… 0.005	solid
	VT86000300	diphacinone	… 0.005	solid
	WA86003300	diphacinone	… 0.005	solid
	WA86003400	diphacinone	… 0.005	solid
	WA92003100	diphacinone	… 0.005	solid
	WV82000500	diphacinone	… 0.005	solid
	WV84000400	diphacinone	… 0.005	solid
	WY88000600	diphacinone	… 0.005	solid
3	769-657	diphacinone	… 0.1	solid
	769-758	diphacinone	… 0.1	solid
	2393-488	diphacinone	… 0.1	solid
	2393-517	diphacinone	… 0.1	solid
	3240-17	diphacinone	… 0.1	solid
	12455-9	diphacinone	… 0.1	solid
	12455-61	diphacinone	… 0.1	solid
	HI91000400	diphacinone	… 0.1	solid
4	12455-56	diphacinone	… 0.2	powder
	61282-8	diphacinone	… 0.2	powder

Table 2 lists the diphacinone product the Agency was unable to batch. This product was not batched because it was not considered to be similar to other products in terms of acute toxicity. The registrant of this product is responsible for meeting the acute toxicity data requirements for it individually. This product may not cite acute toxicity/ irritation data derived from any other products in this RED. The registrant may cite pre-existing data conducted on their individual product if it exists and meets current Agency standards.

Table 2: Unbatched Diphacinone Products

Registration Number	Percent Active Ingredient	
2393-493	diphacinone	… 2.0

Table 3: Batches for the Active Ingredient Chlorophacinone

Batch	Registration Number	Percent Active Ingredient		Form
1	OR78001800	chlorophacinone	… 5.34%	spray
	UT78000600	chlorophacinone	… 5.34%	spray
	WA78006000	chlorophacinone	… 5.34%	spray
	WV77000300	chlorophacinone	… 5.34%	spray
2	7173-113	chlorophacinone	… 0.20%	solid
	7173-172	chlorophacinone	… 0.20%	solid
	UT77000200	chlorophacinone	… 0.28%	solid

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3	56-56	chlorophacinone	… 0.005%	solid
	56-58	chlorophacinone	… 0.005%	solid
	56-69	chlorophacinone	… 0.005%	solid
	56-70	chlorophacinone	… 0.005%	solid
	5042-31	chlorophacinone	… 0.01%	solid
	7173-80	chlorophacinone	… 0.005%	solid
	7173-128	chlorophacinone	… 0.005%	solid
	7173-151	chlorophacinone	… 0.005%	solid
	7173-161	chlorophacinone	… 0.005%	solid
	7173-184	chlorophacinone	… 0.005%	solid
	7173-185	chlorophacinone	… 0.005%	solid
	*7173-190	chlorophacinone	… 0.005%	solid
	AZ77000600	chlorophacinone	… 0.005%	solid
	CA77001500	chlorophacinone	… 0.005%	solid
	CA77049600	chlorophacinone	… 0.005%	solid
	CA77049700	chlorophacinone	… 0.005%	solid
	CA80015900	chlorophacinone	… 0.005%	solid
	CA89002300	chlorophacinone	… 0.005%	solid
	CA89002400	chlorophacinone	… 0.01%	solid
	CA9002500	chlorophacinone	… 0.005%	solid
	CA93002200	chlorophacinone	… 0.01%	solid
	CT94000300	chlorophacinone	… 0.005%	solid
	ID92000300	chlorophacinone	… 0.005%	solid
	ID96001200	chlorophacinone	… 0.005%	solid
	MD78000700	chlorophacinone	… 0.005%	solid
	MI77001400	chlorophacinone	… 0.005%	solid
	MO78000100	chlorophacinone	… 0.005%	solid
	MT91000100	chlorophacinone	… 0.01%	solid
	NC77002000	chlorophacinone	… 0.005%	solid
	NV92000100	chlorophacinone	… 0.005%	solid
	NV93000300	chlorophacinone	… 0.005%	solid
	NY94000700	chlorophacinone	… 0.005%	solid
	OH79001300	chlorophacinone	… 0.005%	solid
	OR78001800	chlorophacinone	… 0.005%	solid
	OR8400480	chlorophacinone	… 0.005%	solid
	OR85000300	chlorophacinone	… 0.005%	solid
	OR92000100	chlorophacinone	… 0.005%	solid
	OR95002000	chlorophacinone	… 0.01%	solid
	OR95002600	chlorophacinone	… 0.005%	solid
	PA80004500	chlorophacinone	… 0.005%	solid
	SC78000200	chlorophacinone	… 0.005%	solid
	UT77000100	chlorophacinone	… 0.005%	solid
	VA77001500	chlorophacinone	… 0.005%	solid

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3	VT76000300	chlorophacinone	… 0.005%	solid
	WA78006100	chlorophacinone	… 0.005%	solid
	WA83002600	chlorophacinone	… 0.01%	solid
	WA84002900	chlorophacinone	… 0.005%	solid
	WA92002200	chlorophacinone	… 0.005%	solid
	WA95004200	chlorophacinone	… 0.005%	solid
	WA95004400	chlorophacinone	… 0.005%	solid
	WV7700050	chlorophacinone	… 0.005%	solid

*Due to the formulation of registration number 7173-190, it is likely that the registrant would be granted a waiver of the acute inhalation toxicity study for this product if one was requested. Registrants of other products that contain substantial amounts of oil or paraffin wax should also request a waiver of the acute inhalation toxicity study for these product(s).

Table 4 lists the products the Agency was unable to batch. These products can not be batched because it was not considered to be similar to other the products in terms of acute toxicity. The registrant of these products is responsible for meeting the acute toxicity data requirements for it individually. This product may not cite acute toxicity/ irritation data derived from any other products in this RED. The registrant may cite pre-existing data conducted on their individual product (or data cited in this RED for the technical product) if it exists and it meets current Agency standards.

Table 4: Unbatched Chlorphacinone Products

Registration Number	Percent Active Ingredient		Product Type
7173-72	chlorophacinone	… 0.28%	mineral oil concentrate
7173-75	chlorophacinone	… 96.03%	technical grade

Due to the probable toxicity of registration number 7173-75, TRB will not allow other less concentrated products (beside other technical products) to bridge acute toxicity data from this technical product.

All of the following 23 products in tables 5,6 and 7 contain only one active, bromadiolone, 3-(3-(4'-bromo-(1,1'-biphenyl)-4-yl)-3-hydroxy-1-phenylpropyl)-4-hydroxy-2H-1-benzopyran-2-one.

Table 5 batches the two technicals. The RED includes data on the acute toxicity of either a pure or a very concentrated version (for acute oral toxicity), already clearly a I at the concentration tested. No further testing of the technicals is required.

Table 5: Batch 1 for the Active Ingredient Bromodialone

EPA Reg. No.	% of Bromadiolone	Formulation Type
7173-174	93.5	Solid
12455-70	96.5	Solid

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Table 6 batches the two Bromadiolone manufacturing use-products, each with approximately the same concentration. It should be possible to bridge these with the technicals.

Table 6: Batch 2 for the Active Ingredient Bromodialone

EPA Reg. No.	% of Bromadiolone	Formulation Type
7173-173	1.07	Solid
12455-31	1.0	Solid

The remaining compounds have the same concentration of bromadiolone (0.005%) and are batched together for acute oral and dermal toxicity purposes. The acute inhalation toxicity is waived as all of these are baits. Product 12455-69 was tested acceptably and may be used to cite data.

Table 7: Batch 3 for the Active Ingredient Bromodialone

EPA Reg. No.	% of Bromadiolone	Formulation Type
602-306	0.005	Solid
602-308	0.005	Solid
602-313	0.005	Solid
7173-171	0.005	Solid
7173-186	0.005	Solid
7173-187	0.005	Solid
7173-188	0.005	Solid
7173-189	0.005	Solid
7173-202	0.005	Solid
7173-208	0.005	Solid
12455-34	0.005	Solid
12455-36	0.005	Solid
12455-68	0.005	Solid
12455-69	0.005	Solid
12455-75	0.005	Solid
12455-76	0.005	Solid
12455-79	0.005	Solid
12455-82	0.005	Solid
12455-86	0.005	Solid

However, the following sub-Batches are together for primary irritation testing purposes. Primary eye and dermal irritation testing needs performing.

Table 8: Batch 4 for the Active Ingredient Bromodialone

EPA Reg. No.	% of Bromadiolone	Formulation Type
602-306	0.005	Solid
602-308	0.005	Solid
602-313	0.005	Solid
7173-171	0.005	Solid

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7173-186	0.005	Solid

Table 9: Batch 5 for the Active Ingredient Bromodialone

EPA REG. NO.	% of Bromadiolone	Formulation Type
7173-187	0.005	Solid
7173-188	0.005	Solid
7173-208	0.005	Solid

The batch below contains 12455-69 which was adequately tested, including primary eye and dermal irritation, acceptable for citing.

Table 10: Batch 6 for the Active Ingredient Bromodialone

EPA REG. NO.	% of Bromadiolone	Formulation Type
12455-34	0.005	Solid
12455-36	0.005	Solid
12455-68	0.005	Solid
12455-69	0.005	Solid
12455-75	0.005	Solid
12455-76	0.005	Solid
12455-79	0.005	Solid
12455-82	0.005	Solid
12455-86	0.005	Solid

All of the following 19 products contain the active ingredient bromethalin (N-methyl-2,4-dinitro-N-(2,4,6-tribromophenyl)-6-(trifluoromethyl)benzeneamine). The HED chapter for the RED indicates the acute toxicity of this active is complete and valid. There are two (2) Manufacturing Use (MU) Products, a 2% solid concentrate and a 1.5% liquid concentrate, which are batched together. The highest concentration Manufacturing Use Product -- 67517-64, is the only product to have been tested, and it has nearly complete toxicity information. Only the dermal sensitization was not performed. The active is not a dermal sensitizer, but the products all have various inerts which may or may not be sensitizers.

These products are all baits and the inerts are primarily food-stuffs. Except for the MU products, all are batched together, and the toxicity ratings for the batch could be bridged from data on the 2% concentrate, along with the conductance of an acceptable dermal sensitization study on 67517-66 or 67517-76. If the dermal sensitization study is positive, more studies may be required.

Table 11: Batching for the Active Ingredient Bromethalin

Batch	EPA Reg. No.	% of Bromethalin	Formulation Type
1	67517-64	2.0	Solid
	67517-65	1.5	Liquid

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2	432-746	0.01	Solid
	432-747	0.01	Solid
	432-748	0.01	Solid
	8845-125	0.01	Solid
	67517-63	0.005	Solid
	67517-66	0.01	Solid
	67517-67	0.01	Solid
	67517-68	0.01	Solid
	67517-69	0.01	Solid
	67517-70	0.01	Solid
	67517-71	0.01	Solid
	67517-72	0.01	Solid
	67517-73	0.01	Solid
	67517-74	0.01	Solid
	67517-75	0.01	Solid
	67517-76	0.01	Solid
	67517-77	0.01	Solid

Table 12: The Batches for the Active Ingredient Brodifacoum

Batch	EPA Reg. No.	Percent Active Ingredient	Form
1	10182-28	brodifacoum … 0.25%	liquid
	10182-384	brodifacoum … 0.25%	liquid
2	3282-65	brodifacoum … 0.005%	solid
	3282-66	brodifacoum … 0.005%	solid
	3282-74	brodifacoum … 0.005%	solid
	3282-79	brodifacoum … 0.005%	solid
	3282-81	brodifacoum … 0.005%	solid
	10182-20	brodifacoum … 0.005%	solid
	10182-21	brodifacoum … 0.005%	solid
	10182-24	brodifacoum … 0.005%	solid
	10182-25	brodifacoum … 0.005%	solid
	10182-26	brodifacoum … 0.005%	solid
	10182-38	brodifacoum … 0.005%	solid
	10182-39	brodifacoum … 0.005%	solid
	10182-40	brodifacoum … 0.005%	solid
	10182-41	brodifacoum … 0.005%	solid
	10182-48	brodifacoum … 0.005%	solid
	10182-60	brodifacoum … 0.005%	solid

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2	10182-61	brodifacoum	… 0.005%	solid
	10182-75	brodifacoum	… 0.005%	solid
	10182-76	brodifacoum	… 0.005%	solid
	10182-93	brodifacoum	… 0.005%	solid
	10182-334	brodifacoum	… 0.005%	solid
	10182-335	brodifacoum	… 0.005%	solid
	10182-336	brodifacoum	… 0.005%	solid
	10182-337	brodifacoum	… 0.005%	solid
	10182-338	brodifacoum	… 0.005%	solid
	10182-339	brodifacoum	… 0.005%	solid
	10182-339	brodifacoum	… 0.005%	solid
	10182-340	brodifacoum	… 0.005%	solid
	10182-341	brodifacoum	… 0.005%	solid
	11715-218	brodifacoum	… 0.005%	solid

Table 13 lists the product the Agency was unable to batch. This product can not be batched because it was not considered to be similar to other the products in terms of acute toxicity. The registrant of this product is responsible for meeting the acute toxicity data requirements for it individually. This product may not cite acute toxicity/ irritation data derived from any other products in this RED. The registrant may cite pre-existing data conducted on their individual product if it exists and it meets current Agency standards.

Table 13: Unbatched Brodifacoum Products

Registration Number	Percent Active Ingredient	
10182-29	brodifacoum	… 90%

Due to the toxicity profile of registration number 10182-29, TRB will not allow other less concentrated products to bridge acute toxicity data from this technical product.

There was only one technical product for pival and the sodium salt of pival each, and no end-use products. As such, the two products covered in this RED could not be placed into batches. These products are placed into the "No Batch" group. The registrant of these two products must cite a *separate* set of acute toxicity data to support each of these products. Table 1 displays the two products covered by this RED.

Table 14: No Batch Group for the Active Ingredient Pival and Sodium Salt

Registration Number	Active Ingredient	
3240-9	pival	… 99.99%
3240-10	pival, sodium salt	… 99.99%

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Cost Share, Data Compensation Forms, Confidential Statement of Formula Form and Instructions

The Confidential Statement of Formula (CSF) Form 8570-4 must be used. Two legible, signed copies of the form are required. Following are basic instructions:

a. All the blocks on the form must be filled in and answered completely.

b. If any block is not applicable, mark it N/A.

c. The CSF must be signed, dated and the telephone number of the responsible party must be provided.

d. All applicable information which is on the product specific data submission must also be reported on the CSF.

e. All weights reported under item 7 must be in pounds per gallon for liquids and pounds per cubic feet for solids.

f. Flashpoint must be in degrees Fahrenheit and flame extension in inches.

g. For all active ingredients, the EPA Registration Numbers for the currently registered source products must be reported under column 12.

h. The Chemical Abstracts Service (CAS) Numbers for all actives and inerts and all common names for the trade names must be reported.

I. For the active ingredients, the percent purity of the source products must be reported under column 10 and must be exactly the same as on the source product's label.

j. All the weights in columns 13.a. and 13.b. must be in pounds, kilograms, or grams. In no case will volumes be accepted. Do not mix English and metric system units (i.e., pounds and kilograms).

k. All the items under column 13.b. must total 100 percent.

1. All items under columns 14.a. and 14.b. for the active ingredients must represent pure active form.

m. The upper and lower certified limits for ail active and inert ingredients must follow the 40 CFR 158.175 instructions. An explanation must be provided if the proposed limits are different than standard certified limits.

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n. When new CSFs are submitted and approved, all previously submitted CSFs become obsolete for that specific formulation.

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Confidential Business Information: Does Not Contain National Security Information (E.O. 12065) Form Approved. OMB No. 2070-0060. Approval Expires 2/28/94

EPA

United States Environmental Protection Agency
Office of Pesticide Programs (TS-767)
Washington, DC 20460

Confidential Statement of Formula

A. ☐ Basic Formulation ☐ Alternate Formulation

B. Page of

See Instructions on Back

1. Name and Address of Applicant/Registrant *(Include ZIP Code)*

2. Name and Address of Producer *(Include ZIP Code)*

3. Product Name

4. Registration No./File Symbol

5. EPA Product Mgr/Team No.

6. Country Where Formulated

7. Pounds/Gal or Bulk Density

8. pH

9. Flash Point/Flame Extension

EPA USE ONLY	10. Components in Formulation *(List as actually introduced into the formulation. Give commonly accepted chemical name, trade name, and CAS number.)*	11. Supplier Name & Address	12. EPA Reg. No.	13. Each Component in Formulation a. Amount	13. b. % by Weight	14. Certified Limits % by Weight a. Upper Limit	14. b. Lower Limit	15. Purpose in Formulation

16. Typed Name of Approving Official

17. Total Weight 100%

18. Signature of Approving Official

19. Title

20. Phone No. *(Include Area Code)*

21. Date

EPA Form 8570-4 (Rev. 12-90) **Previous editions are obsolete.** If you can photocopy this, please submit an additional copy. White - EPA File Copy (original) Yellow - Applicant copy

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United States Environmental Protection Agency
Washington, D.C. 20460

Certification of Offer to Cost Share in the Development of Data

Form Approved
OMB No. 2070-0106, 2070-0057
Approval Expires 3-31-99

Public reporting burden for this collection of information is estimated to average 15 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to, Chief Information Policy Branch, PM-233, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0106), Washington, DC 20503.

Please fill in blanks below:

Company Name	Company Number

Product Name	EPA Reg. No.

I Certify that:

My company is willing to develop and submit the data required by EPA under the authority of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), if necessary. However my company would prefer to enter into an agreement with one or more registrants to develop jointly or share in the cost of developing data.

My firm has offered in writing to enter into such an agreement. That offer was irrevocable and included an an offer to be bound by arbitration decision under section 3(c)(2)(B)(iii) of FIFRA if final agreement on all terms could not be reached otherwise. This offer was made to the following firms on the following date(s):

Name of Firm(s)	Date of Offer

Certification:

I certify that I am duly authorized to represent the company named above, and that the statements that I have made on this form and all attachments therein are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature of Company's Authorized Representative	Date

Name and Title (Please Type or Print)

EPA Form 8570-32 (5/91) Replaces EPA form 8580 which is obselete

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460.

Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Active Ingredient(s) and/or representative test compound(s)	Date
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158)	Product Name

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☐ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (I) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to this address.

DATA MATRIX

Date			EPA Reg No./File Symbol		Page of
Applicant's/Registrant's Name & Address			Product		
Ingredient					
Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]					
Signature			Name and Title		Date

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

PublicFileCopy

US EPA ARCHIVE DOCUMENT

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to this address.

DATA MATRIX

Date	EPA Reg No./File Symbol	Page of
Applicant's/Registrant's Name & Address	Product	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note

Signature	Name and Title	Date

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version. **Agency Internal Use Copy**

INSTRUCTIONS FOR DATA MATRIX

INSTRUCTIONS: Identify all data submitted or cited and all submitters from whom permission has been received or to whom offers to pay have been sent by entering sufficient information in the attached matrix (photocopy and attach additional pages a s necessary). Complete all columns; omission of essential information will delay approval of the registration/reregistration. On each page enter the date, Applicant's/Registrant's name, EPA Registration Number or application file symbol of the product, ingredient, page number, and total number of pages.

The Data Compensation Form entit led "Certification with Respect to Citation of Data" and the Data Matrix will be publicly available, except for the Guideline Reference Number, Guideline Study Name, and MRID Number columns after the registration/reregistration of this product has been gra nted or once this form is received in response to a Data-Call-In Notice. However, the information in the Guideline Reference Number, Guideline Study Name, and MRID Number columns is available through the Freedom of Information Act in association with the EPA Registration Number.

Ingredient: Identify the active ingredient(s) in this product for which data are cited. The active ingredient(s) are to be identified by entering the chemical name and the CAS registry number. Begin a new page for each separate active ingredient for which data are cited. If bridging data from a related chemical or representative test compound are cited, enter the identity of tha t chemical/representative test compound including the EPA Registration Number/File Symbol if appropriate.

If the cite-all method is used for all dat a supporting this particular ingredient, enter "CITE-ALL" in the Guideline Reference Number column and leave the Guideline Study Name column blank. If the cite-all method is used for a particular Guideline Reference Number enter "CITE-ALL" in the MRID Number column on the line for that Guideline Reference Number. In either case, enter all submitters to whom offers to pay have been sent on subsequent lines. [Note: if the selective method of support is used and written authorization (letter of permission) is provided, the individual Guideline Reference Number, Guideline Study Name, and MRID Number columns must still be completed.] Otherwise:

Guideline Reference Number: Enter on separate lines in numerical order the Guideline Reference Numbers from 40 CFR Part 158 for all studies cited to support the registration/reregistration for this ingredient.

Guideline Study Name: For each Guideline Reference Number cited, enter the corresponding Guideline Study Name.

MRID Number: For each individual study cited in support of a Guideline Reference Number and Guideline Study Name, enter the Master Record Identification (MRID) Number listed in the Pesticide Document Management System (PDMS). Enter only one MRID Number on each li ne. Note that more than one MRID Number may be required per Guideline Reference Number. Note: Occasionally a study required to maintain a registration/re registration is not associated with a Guideline Reference Number and Guideline Study Name. In such case, enter the MRID Number(s) for the study(ies).

Submitter: Using the most recent Data Submitters List, identify the Original Data Submitter with their current address for each study cited. The EPA assigned company number or othe r abbreviation may be used. Clearly explain any variations (alternate addresses, data owners not on the Data Submitters List, etc.) in footnotes to this table.

Status: Enter one of the following codes for each study cited, as appropriate:

OWN: I am the Original Data Submitter for this study.

EXC: I have obtained written permission of the Original Data Submitter to cite this exclusive-use study in support of this application.

PER: I have obtained the permission of the Original Data Submitter to use this study in support of this application.

OLD: The study was submitted more than 15 years ago and all periods of compensation have expired.

PL: The study is in the public literature.

PAY: I have notified in writi ng the Original Data Submitter or, if the cite-all method is used, all companies listed in the most current Data Submitters List for this ingredient, and have offered (a) to pay compensation in accordance with FIFRA sections 3(c)(1)(F) and/or 3(c)(2)(B), and (b) to commence negotiations to determine the amount and terms o f compensation, if any, to be paid for the use of the study(ies).

GAP: This Guideline data requirement is a data gap as defined in 40 CFR sections 152.83(a) and 152.96.

FOR: I am taking the formulator's exemption for this ingredient only. Other columns of this line should be marked "NA". However, if this product is to be registered/reregistered for additional uses for which the purchased EPA registered ingredient is not supported, additional data must be submitted or cited here to support those uses.

Note: If additional explanation is needed, enter a footnote number in this column and attach the corresponding explanation.

US EPA ARCHIVE DOCUMENT

United States Environmental Protection Agency
Washington, DC 20460

Form Approved
OMB No. 2070-0107, 2070-0057
Approval Expires 3-31-99

CERTIFICATION WITH RESPECT TO DATA COMPENSATION REQUIREMENTS

Public reporting burden for this collection of information is estimated to average 15 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to, Chief, Regulatory Information Division, Mail Code 2137, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0106), Washington, DC 20503.

Please fill in blanks below.

Company Name	Company Number

Product Name	EPA Reg. No.

I Certify that:

1. For each study cited in support of registration or reregistration under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) that is an exclusive use study, I am the original data submitter, or I have obtained the written permission of the original data submitter to cite that study.

2. That for each study cited in support of registration or reregistration under FIFRA that is NOT an exclusive use study, I am the original data submitter, or I have obtained the written permission of the original data submitter, or I have notified in writing the company(ies) that submitted data I have cited and have offered to: (a) Pay compensation for those data in accordance with sections 3(c)(1)(F) and 3(c)(2)(D) of FIFRA; and (b) Commence negotiation to determine which data are subject to the compensation requirement of FIFRA and the amount of compensation due, if any. The companies I have notified are: (check one)

[ ] The companies who have submitted the studies listed on the back of this form or attached sheets, or indicated on the attached "Requirements Status and Registrants' Response Form,"

3. That I have previously complied with section 3(c)(1)(F) of FIFRA for the studies I have cited in support of registration or reregistration under FIFRA.

Signature	Date

Name and Title (Please Type or Print)

GENERAL OFFER TO PAY: I hereby offer and agree to pay compensation to other persons, with regard to the registration or reregistration of my products, to the extent required by FIFRA section 3(c)(1)(F) and 3(c)(2)(D).

Signature	Date

Name and Title (Please Type or Print)

EPA Form 8570-31 (4-96)

The following is a list of available documents for the Rodenticide Cluster that my further assist you in responding to this Reregistration Eligibility Decision document. These documents may be obtained by the following methods:

Electronic
File format: Portable Document Format (.PDF) Requires Adobe® Acrobat or compatible reader. Electronic copies can be downloaded from the Pesticide Special Review and Reregistration Information System at 703-308-7224. They are available on the Internet using ftp on FTP.EPA.GOV, or using WWW (World Wide Web) on WWW.EPA.GOV., or contact CP Moran at (703)-308-8590.

1. PR Notice 86-5.

2. PR Notice 91-2 (pertains to the Label Ingredient Statement).

3. A full copy of this RED document.

4. A copy of the fact sheet for Cases 2100, 2205, 2755, 2760, 2765, and 2810.

The following documents are part of the Administrative Record for the Rodenticide Cluster RED and may included in the EPA's Office of Pesticide Programs Public Docket. Copies of these documents are not available electronically, but may be obtained by contacting the person listed on the Chemical Status Sheet.

1. Health and Environmental Effects Science Chapters.

2. Detailed Label Usage Information System (LUIS) Report.

The following Agency reference documents are not available electronically, but may be obtained by contacting the person listed on the Chemical Status Sheet of this RED document.

1. The Label Review Manual.

2. EPA Acceptance Criteria

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