UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

Statement of Reasons and Factual Basis for

Notice Intent to Cancel Registrations of, and Notice of Denial of Applications for,

Certain Rodenticide Bait Products

January 29, 2013

This document provides the reasons and factual basis for the U.S. Environmental Protection Agency's (EPA's) Notice of Intent to Cancel the registrations of twelve rodenticide bait products and EPA's Notice of Denial of registration applications of two rodenticide bait products, as required by 40 CFR §164.21(a).

EPA has determined that all of these rodenticide products cause, or would cause, unreasonable adverse effects on the environment because they are sold for residential consumer use in controlling commensal rodents in and around buildings in forms and for means of placement that do not adequately protect against access by children, companion and domesticated animals, and non-target wildlife. EPA bases this determination on data and other information showing that these products cause, or would cause, unreasonable risks to children, companion and domesticated animals, and non-target wildlife.[1]

[1] The risk assessments that form the basis for the denials of registration are essentially the same as those that form the basis for the cancellations. In order to make the remainder of this document somewhat easier to read, EPA will generally dispense with "or would cause" and similar phrases that specifically pertain to the products that have not been introduced into commerce. However, note that the discussion that follows concerning the risks and benefits of the 12 registered products also applies to the two products subject to the denials of registration.

Further, EPA has determined that eight of the twelve registered rodenticide products also cause unreasonable adverse effects on the environment because they contain the active ingredients brodifacoum or difethialone and are sold for residential consumer use, as do the two products subject to denial. EPA bases this determination primarily on data and other information showing that these products cause unreasonable adverse effects to non-target wildlife. EPA is therefore issuing a Notice of Intent to Cancel pursuant to section 6(b) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and Notice of Denial pursuant to section 3(c)(6) of FIFRA. This document provides the reasons and factual basis for the Agency's actions. Although each of the products at issue differs in some respects from the others, the reasons and factual basis for cancellation or denial articulated here apply to each of the products, except as expressly noted. Please see FRL-9377-7 for the Notice of Intent to Cancel Registrations of, and Notice of Denial of Applications for, Certain Rodenticide Bait Products (hereinafter "NOIC"). The NOIC and other documents supporting the NOIC, including this document, are available through www.regulations.gov in docket number EPA-HQ-OPP-2013-0049.

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I. Regulatory History

Many pesticides were originally registered well before EPA came into existence or before EPA identified a complete set of data requirements sufficient to allow it to determine whether new pesticides met the standard for registration. In 1972, Congress therefore directed EPA to assess all existing pesticides to determine whether they would qualify for the new standard of registration adopted in the 1972 amendments to FIFRA. This process of assessing existing pesticides against current standards is known as "reregistration". In1988, Congress established a formal five-phase process for EPA to use in conducting a comprehensive review of all products registered before November 1, 1984 to determine whether these products had satisfied all applicable data requirements and the registration criteria of FIFRA section 3(c)(5). See FIFRA section 4(a), 7 U.S.C. § 136a-1(a).

Shortly after passage of the 1988 amendments to FIFRA, EPA began the Section 4 reregistration process for products registered for control of commensal rodents (i.e., house mice (*Mus musculus*), Norway rats (*Rattus norvegicus*), and roof rats (*Rattus rattus*)). These commensal rodents typically live in close association with humans, and are often found in and around homes as well as commercial establishments (Brooks, 1973; Timm 1994). The active ingredients in rodenticide products registered in the US to control commensal rodents include a variety of anticoagulants and three chemicals with other, more rapid modes of action (bromethalin, cholecalciferol, and zinc phosphide). The anticoagulants are commonly classed as first generation anticoagulant rodenticides (FGARs) or second generation anticoagulant rodenticides (SGARs). SGARs were developed, in part, to control rodents that were tolerant of the previously developed FGARs (e.g., Hadler and Shadbolt, 1975; Dubock and Kaukeinen,

1978; Marsh, et al, 1980). FGARs currently registered in the US include: chlorophacinone, diphacinone, and warfarin. SGARs registered in the US include brodifacoum, difenacoum, difethialone, and bromadiolone. [2]

In 1991, EPA issued a Reregistration Eligibility Decision (RED) for rodenticide products containing the active ingredient warfarin. In July 1998, after making comprehensive reassessments of data relating to the use and effects of the remaining commensal rodenticide products subject to reregistration, EPA issued two REDs addressing seven different active ingredients that previously had been registered for rodent control in both agricultural and residential settings. 63 FR 48729, September 11, 1998. The "Rodenticide Cluster RED" contained eligibility decisions for the ingredients brodifacoum, bromadiolone, chlorophacinone, diphacinone, bromethalin, and pival (a FGAR for which all registrations now are canceled). The "Zinc Phosphide RED" addressed reregistration issues for the ingredient zinc phosphide. In these 1998 REDs, EPA issued FIFRA section 4(g)(2)(A) determinations that certain rodenticide products would not be eligible for reregistration unless their registrants adopted certain risk mitigation measures to reduce the risks they posed to human health and the environment.

While the 1998 REDs identified certain measures intended to reduce children's exposure as necessary in order for the rodenticides to be eligible for reregistration, EPA also stated at that time that "new, safer rodenticide use technology" was needed to further reduce child and pet exposures. Rodenticide Cluster RED at viii. EPA announced that it would form a stakeholder group to "discuss means of significantly reducing exposures to children and pets" and to

[2] The second generation anticoagulants, difethialone and difenacoum, and the acute toxin cholecalciferol, were first registered after November 1, 1984, and therefore were not subject to reregistration.

"develop workable mitigation measures to adequately protect children from accidental rodenticide exposures." Id. at viii and 112. The group's objectives included discussing long-term risk reduction measures and "decid[ing] on specific timing and other issues associated with bait dyes [and] bittering agents." Reregistration Eligibility Decision for Zinc Phosphide (July 1998). In 1999, EPA formed the Rodenticide Stakeholders Workgroup (RSW) as a subcommittee of the federally-chartered advisory group, the Pesticide Program Dialogue Committee (the "PPDC").[3] The RSW included members from EPA, the US Consumer Product Safety Commission, the US Department of Agriculture, the District of Columbia Department of Health, Maryland Public Interest Research Group, the California Department of Food and Agriculture, the State of Maine, the Children's National Medical Center, the Association of Poison Control Centers, the National Pest Control Association, and several registrants of rodenticide products.

The findings and recommendations of the RSW are contained in the November 15, 2000 report, Recommendations for Managing Rodenticide Exposures to Children in the Home. EPA adopted those recommendations in a 2001 amendment to the REDs. 66 Fed. Reg. 59,425. One of the recommendations adopted by EPA was to rescind the 1998 RED determination that registrants should add a bitter taste (via a bittering agent) and an indicator dye to rodenticide bait products registered for use in and around homes or at other sites where children might encounter them. An environmental group successfully challenged EPA's 2001 rescission of the bittering agent requirement, and a district court remanded it to EPA. *West Harlem Env. Action v. EPA*, 380 F. Supp. 2d 289, 294-295 (S.D.N.Y. 2005).

[3] The PPDC is the principal stakeholder advisory body to EPA's Office of Pesticide Programs and was established pursuant to the Federal Advisory Committee Act.

EPA's concerns regarding the effects of rodenticides on non-target wildlife also continued after issuing the 1998 REDs, leading the Agency to conclude that further evaluation of the ecological risks of rodenticides was necessary. As part of this work, the Agency developed a comparative ecological assessment for nine[4] rodenticide active ingredients. Between October 1999 and December 2001, the comparative risk assessment was drafted by Agency scientists, received both internal and external peer review as well as review by the Rodenticide Registrant Task Force. Based on input from these reviews, the comparative risk assessment was revised. There were two public comment periods in 2003 and 2004 and the Agency reviewed and responded to the public comments and revised the risk assessment based upon those comments.

In September 2004, the Agency opened Phase 5 of the reregistration public participation process by publishing the revised comparative ecological risk assessment, which incorporated new ecological incident data and reflected revisions made in response to public comments on the preliminary version of the assessment.[5] Along with the revised ecological assessment, EPA also published a document discussing the benefits associated with rodenticide products and EPA's preliminary position on appropriate risk reduction options. EPA accepted public comments on those documents through January 2005.

In January 2007, EPA issued a Proposed Risk Mitigation Decision for public comment. Based on an evaluation of the ecological risks associated with the use of rodenticide bait products containing these nine active ingredients, and consideration of the public health and other important benefits of the use of commensal rodenticide baits, EPA proposed to classify all

[4] The active ingredient difenacoum was first registered in the U.S. in 2007 and therefore, was not included in the Comparative Analysis or the 2007 Proposed Risk Mitigation.

[5] The public process for reregistration is described in 69 Fed.Reg. 26819 (May 14, 2004).

such bait products containing the SGAR active ingredients brodifacoum, bromadiolone, and difethialone as restricted-use pesticides, which "would limit their use to certified applicators who have had sufficient training to know when to use the products and how to use them in order to limit risks [and] would result in marked overall reduction in exposure to and adverse effects from those compounds." 2007 Proposed Risk Mitigation Decision at 4. Further, to decrease the possibility of children's exposure to any rodenticide products used in homes, EPA proposed requiring that all commensal rodenticide bait products available for sale to consumers be sold only in tamper-resistant bait stations with solid bait blocks as the only permissible bait form.

EPA took comment on the proposed mitigation measures for 120 days and received extensive comments from a wide range of stakeholders. During this comment period, the Rodenticide Registrant Task Force surveyed their constituents. The survey indicated that in 2004, there were 105 million bait placements and in 2005, the number had increased to 115 million bait placements distributed on the consumer market. Based on anecdotal evidence from several sources, EPA believed that the majority of products sold on the consumer market contained brodifacoum and difethialone. Brodifacoum also was implicated in a high percentage of reported non-target wildlife incidents. EPA concluded that if the lower toxicity and less persistent active ingredients replaced the higher toxicity and more persistent active ingredients for a portion of this market, there would be significant reduction in the adverse effects to non-target wildlife. Based on the restrictions some municipalities place on restricted-use pesticides and concerns about imposing additional regulatory burdens on the poultry, livestock and pest control operator industries, and recognizing the importance of SGARs to these industries, EPA decided to employ sale and distribution limitations – rather than restricted-use classification – to

accomplish the same purpose of reducing the use of SGARs in settings where the risks outweigh the benefits (most residential consumer uses).

On May 28, 2008, in response to the district court's remand order, EPA issued the "Risk Mitigation Decision for Ten Rodenticides" (RMD).[6] The RMD explained EPA's section 4(g)(2)(A) conclusions about the reregistration eligibility of rodenticides containing any of ten listed active ingredients. Among other things, EPA stated that rodenticide baits sold to residential consumers must be packaged in a bait station designed to prevent children, domestic animals and non-target wildlife from being able to come into contact with bait. RMD at 17-18. EPA also stated that rodenticides containing SGARs pose significant risks to wildlife and the environment, and that rodenticides containing those compounds should only be sold to pest control professionals (i.e., governmental, commercial, and agricultural users)—not residential consumers—and then only with additional risk mitigation measures. *Id.* EPA stated that unless a rodenticide product incorporates the risk mitigation measures listed in the RMD, it "would present unreasonable risks inconsistent with FIFRA" and therefore should not remain registered. RMD at 15.

The May 28, 2008, RMD announced EPA's conclusions about rodenticide safety and signaled EPA's intentions for the future completion of the reregistration process, but did not change the legal status of any rodenticide product. Recognizing that design and production of bait stations conforming to the RMD requirements would take some time, EPA did not attempt to

[6] The RMD did not reinstate either the bittering agent or indicator dye requirement for a number of reasons. After review of all the available information, EPA concluded that, among other things, neither bittering agents nor indicator dyes would provide risk reduction comparable to a bait station requirement, because neither prevents exposure. At best, bittering agents might reduce consumption, and indicator dyes might provide a signal of an exposure event.

immediately remove from the market rodenticides that did not incorporate the specified mitigation measures. Instead, EPA asked registrants to adopt those mitigation measures voluntarily, on a schedule that would allow registrants until June 4, 2011 to convert their products. RMD at 26.

By June 4, 2011, most rodenticide registrants had voluntarily amended their registrations or replaced them with new registrations meeting the risk mitigation goals of the RMD, thereby significantly reducing rodenticide risks. Today, only twelve rodenticide products, all produced by Reckitt Benckiser, Inc., fail to meet the risk mitigation goals of the RMD. As set forth in this document, EPA intends to achieve the necessary risk reduction identified in the RMD by cancelling and denying the registrations of these remaining Reckitt-Benckiser rodenticide products that do not include mitigation measures sufficient to prevent unreasonable risks to man and the environment.

Since the issuance of the RMD, EPA has received a number of applications for registration of new commensal rodenticide products intended for the general consumer market. Most of these applications meet the risk management goals of the RMD and those products have been registered, but some have not. On February 4, 2011, EPA notified Reckitt Benckiser, Inc. (Reckitt Benckiser), of deficiencies in applications for two products (designated as 3282-RNL and 3282-RNU), and offered Reckitt 75 days to correct those deficiencies. Reckitt Benckiser's April 19, 2011 response indicated that additional data to support their application would be submitted no later than May 20, 2011. Reckitt Benckiser's May 20, 2011, letter offered several arguments supporting the applications, and provided revised draft labels that would prohibit outdoor use. Because these products do not meet the risk management goals of the RMD, EPA

is formally denying the applications for registration of those products.

Certain rodenticide registrants who have disagreed with the Agency's positions regarding rodenticides have challenged aspects of the Agency's actions in two court cases; however, neither case has addressed the merits of the scientific, economic, and policy questions at issue in this cancellation proceeding. *See generally*, *Reckitt Benckiser, Inc. v. Jackson*, 762 F. Supp. 2d 34, 46 (D.D.C. 2011)(concerning the scope of EPA's authority to pursue enforcement action in lieu of a cancellation proceeding), and *Woodstream Corp. v. Jackson*, 845 F.Supp.2d 174 (D.D.C 2012) (concerning EPA's authority to place certain conditions on pesticide registrations).

II. Scope of Intended Cancellation and Denials

For the reasons set forth in Sections III and IV, below, EPA has determined that certain registered rodenticide bait products, when used in accordance with widespread and commonly recognized practice, generally cause unreasonable adverse effects on humans and the environment. Accordingly, EPA intends to cancel the registrations of the following pesticide products:

Table 1. Pesticide Products Subject to the Notice of Intent to Cancel.

Product	EPA Reg. No.	Registrant	Active Ingredient	Deficiency
D-Con Concentrate Kills Rats & Mice	3282-3	Reckitt Benckiser, Inc.	Warfarin	Consumer product in a powder form[7] and packaged without a protective bait station
D-Con Ready Mixed Kills Rats & Mice	3282-4	Reckitt Benckiser, Inc.	Warfarin	Consumer product in a pelleted form and packaged without a protective bait station
D-Con Mouse Prufe Kills Mice	3282-9	Reckitt Benckiser, Inc.	Warfarin	Consumer product in a pelleted form and packaged without a protective bait station
D-Con Pellets Kills Rats & Mice	3282-15	Reckitt Benckiser, Inc.	Warfarin	Consumer product in a pelleted form and packaged without a protective bait station
D-Con Mouse Prufe II	3282-65	Reckitt Benckiser, Inc.	Brodifacoum	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con Pellets Generation II	3282-66	Reckitt Benckiser, Inc.	Brodifacoum	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con Bait Pellets II	3282-74	Reckitt Benckiser, Inc.	Brodifacoum	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con Ready Mixed Generation II	3282-81	Reckitt Benckiser, Inc.	Brodifacoum	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con Mouse-Prufe III	3282-85	Reckitt Benckiser, Inc.	Difethialone	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con Bait Pellets III	3282-86	Reckitt Benckiser, Inc.	Difethialone	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con II Ready Mix Baitbits III	3282-87	Reckitt Benckiser, Inc.	Difethialone	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR
D-Con Bait Packs III	3282-88	Reckitt Benckiser, Inc.	Difethialone	Consumer product: 1) in a pelleted form and packaged without a protective bait station, and 2) containing a SGAR

[7] EPA Reg. No. 3282-3 is not itself a rodenticide bait, but rather, a general use rodenticide concentrate bearing label directions requiring that the user mix it with suitable bait materials before placement. Accordingly, this product shares the same risks as the other products, plus the additional risks associated with the characteristics and use of a pesticide concentrate.

For the same reasons, EPA intends to deny applications for registration of the following pesticide products:

Table 2. Pesticide Product Applications Subject to Denial.

Product	EPA Application No.	Registrant	Active Ingredient	Deficiency
D-Con Bait Station XV Kills Mice	3282-RNU	Reckitt Benckiser Inc.	Brodifacoum	Consumer product containing an SGAR
D-Con Bait Station XVI Kills Mice	3282-RNL	Reckitt Benckiser Inc.	Brodifacoum	Consumer product containing an SGAR

In the RMD, EPA identified a number of mitigation measures that, if adopted, would make existing rodenticides eligible for reregistration. EPA is now proposing to cancel the rodenticide products identified above based on two of the most significant mitigation measures identified in the RMD: Removing SGARs from residential consumer products, and assuring that rodenticides available to residential consumers include bait stations designed to prevent children, domestic animals and non-target wildlife from being able to come into contact with the bait. Although the mitigation measures identified in the RMD are designed to act in concert, with each measure contributing towards safer outcomes, the bait station requirement is expected to protect children, domestic animals and non-target wildlife from exposures to commensal rodenticides generally, while the exclusion of SGARs from the homeowner market is expected to reduce environmental loading of SGARs and thereby reduce secondary poisonings among non-target wildlife. As currently labeled and sold, each of the rodenticide products identified above causes unreasonable risks to man or the environment owing to the lack of one or both of these mitigation measures. Individual products may also fail to meet the FIFRA registration criteria for other reasons. In order to focus a hearing on the most critical risk mitigation issues, the proposed

cancellations and the denials are based only on the presence of SGARs in products marketed for general consumer use in controlling commensal rodents in and around buildings, and/or on the rodenticide products being in forms that do not adequately protect against access by children, companion and domesticated animals, and non-target wildlife.

EPA is proposing to cancel the registration of twelve rodenticide products sold in the general consumer market, and deny the applications for registration of two additional such products. The scope of this action is very narrow. Commercial, agricultural and professional users (including public health officials, pest control operators (PCOs), and other occupational applicators) are not affected because they are not significant users of the products identified in the NOIC and will continue to have access to the same types of rodenticide products that they had prior to June 4, 2011. Residential consumers will see a different mix of rodenticide products that conform to the RMD on retail store shelves, but will continue to find effective rodenticide products at prices comparable to those that EPA proposes to cancel. Since its inception, EPA has been concerned that children, pets, and non-target wildlife are being unnecessarily exposed to rodenticides. This concern was expressed in Pesticide Registration (PR) Notice 83-5, setting criteria for “tamper-proof” bait stations nearly 30 years ago. That notice was followed 11 years later by PR Notice 94-7, which updated PR Notice 83-5 with label text intended to increase compliance with requirements to use bait stations if bait placements were to be made in areas within the reach of children, pets, domestic animals, and/or non-target wildlife. Most of the children and pet incident concerns are occurring in and around homes, despite mandatory label statements requiring use in tamper-resistant (or tamper-proof) bait stations where placements otherwise would be accessible to children, domestic animals, and/or non-target wildlife. These incidents can be significantly reduced if rodenticide products sold on the general consumer

market include bait stations designed to prevent children, domestic animals and non-target wildlife from being able to come into contact with bait, rather than relying on consumers to separately purchase and use such bait stations. Further, based on the reported incidents of wildlife exposures to rodenticides, EPA has determined that it is appropriate to limit use of products containing the more toxic and persistent anticoagulants brodifacoum and difethialone. EPA has determined that the risks of use by residential consumers of rodenticides containing brodifacoum and difethialone outweigh the benefits of such use. There are over 30 alternative rodenticide products registered for sale in the general consumer market that can provide effective rodent control, that fully conform to the RMD, and that meet the no unreasonable adverse effects on the environment standard of FIFRA. In addition, residential consumers also have access to mechanical control methods as well as the services of PCOs who will continue to have access to a broader range of products.

The NOIC includes only rodenticides intended to control the commensal rodents: the Norway (brown or sewer) rat, the roof (black or ship) rat, and the house mouse. Control of these commensal rodents in sewers, in and around commercial buildings, and in connection with agricultural and food processing establishments will not be affected by the proposed cancellations, because the products EPA proposes to cancel are marketed to general consumers in small sizes unlikely to be used by professional, commercial or agricultural users. Products registered for the control of other types of rodents are also outside the scope of the NOIC.

In making the determination that the products subject to the NOIC do not meet the FIFRA registration criteria, EPA has relied upon evidence and analyses demonstrating significant exposure to children, domestic animals, and non-target wildlife from the use of consumer use rodenticide products which are not protected in bait stations designed to prevent

children, domestic animals and non-target wildlife from being able to come into contact with bait. For four of the products EPA proposes to cancel and the two applications EPA is denying, this determination additionally relies upon the substantial and well documented risks to non-target wildlife from primary and secondary exposures to the active ingredients brodifacoum and difethialone. EPA also considered evidence and analyses relating to the benefits of continued use of the rodenticide products identified in the NOIC, and has determined that, based on the availability of adequate and affordable alternative rodenticide products and methods of commensal rodent control, the benefits linked specifically to the products identified in the NOIC are, at best, minimal. However, given the potential for exposure these products pose to children, coupled with risks to domestic animals and wildlife in the absence of further mitigation, EPA believes that this cancellation action would be warranted even if the anticipated costs of rodent control as a result of this action were somewhat greater than EPA has estimated. Accordingly, EPA is issuing a Notice of Intent to Cancel and a Notice of Denial of registrations of the consumer-use commensal rodenticide products listed in above. See FRL-9377-7 for the NOIC. The NOIC and other documents supporting the NOIC, including this document, are available through www.regulations.gov in docket number EPA-HQ-OPP-2013-0049.

III. Risks Associated with Exposure to Rodenticide Products Subject to the NOIC (Humans, Domestic Animals, and Non-target Wildlife)

A. Effects on Mammals and Birds

Rodenticides are designed to kill mammals, and so their effects on humans, birds, and non-target mammals are qualitatively the same as their effects on target pests, unlike other pesticides such as herbicides and certain insecticides where adverse effects on mammals are

often different in nature than their effects on target pests. Rodenticides can be divided into three broad classes in terms of their effects: FGARs, SGARs, and non-anticoagulants. The non-anticoagulant rodenticides work in different ways to cause death. Each of these is discussed below:

- The FGARs, such as chlorophacinone, diphacinone, diphacinone sodium salt, warfarin, and warfarin sodium salt, disrupt the production in the liver of vitamin K dependent blood-clotting factors II (prothrombin), VII, IX, and X, interfering with blood clotting and causing hemorrhages. Due to the long half-lives of the vitamin K-dependent clotting factors, the anticoagulant effect does not result in rodent mortality until after several days of ingestion. The onset of lengthened prothrombin time (PT) from a toxic dose may occur within 24 hours, and reach a maximum in 36-72 hours at a dose much lower than the dose that can cause hemorrhage (Reigart J.R. et.al, 1999). These agents also increase permeability of capillaries throughout the body, leading to widespread internal hemorrhage.
- The SGARs such as brodifacoum, bromadiolone, difenacoum, and difethialone are more toxic than FGARs and are more likely to cause lethal effects to rodents that consume the amount of bait equivalent to a single night's feeding. These chemicals block the formation of the active form of vitamin K in the same manner as warfarin and warfarin sodium; however, SGARs have much longer half-lives in the body (Batten and Bratt, 1990). Similar to the FGARs, the toxic effects of these agents usually begin several days after ingestion, because of the long half-life of the coagulation factors.

Three other active ingredients that are not anticoagulants are registered for use as rodenticides, although only one – bromethalin – is registered for use against the commensal

rodents that are at issue in this action. Each of the non-anticoagulants has a distinct mode of action:

- Bromethalin causes decreased production of adenosine-5'-triphosphate (ATP) in the cells of the central nervous system by uncoupling oxidative phosphorylation in the mitochondria. Low levels of ATP reduce the efficiency of the enzyme Na/K ATPase, leading to increased intracellular sodium levels. This in turn draws more water into neuronal cells (cerebral edema) and increases intracranial pressure which can be lethal. Symptoms and signs of cerebral edema include headache, dizziness, nausea numbness, weakness, loss of coordination or balance, altered level of consciousness, respiratory depression, seizures, and death.
- Cholecalciferol increases calcium absorption from food, and mobilizes calcium from bone which leads to hypercalcemia (increased calcium levels in blood). Hypercalcemia can cause formation of calcium crystals in internal organs such as blood vessels, kidneys, stomach wall and lungs (Chavhan S.G., et.al, 2011). Abnormal heart conduction and irregular heartbeats can also occur since the heart tissue is sensitive to changes in blood calcium levels. Symptoms and signs of cholecalciferol poisoning may include fatigue, weakness, nausea, anorexia, headache and irregular heartbeats (Goldfrank et.al, 2010). Acute renal tubular injury due to hypercalcemia may cause excessive urination, increased water intake, protein in urine and increased blood urea levels. Prolonged hypercalcemia may eventually cause kidney failure due to formation of kidney stones and calcium deposition in kidney tissues.

- Zinc phosphide can quickly produce toxic phosphine gas when it comes in contact with acids or water. Phosphine is thought to produce toxicity by blocking cytochrome oxidase and, inhibiting oxidative phosphorylation which may lead to cell death (Perry H.E., 1998). Most of the tissue damage can occur in liver, kidneys and heart. Patients may present with symptoms such as, severe gastrointestinal irritation, nausea, vomiting (with fishy odor), chills, tightness of chest, difficulty in breathing and cough (from pulmonary edema). Development of liver failure can cause jaundice and excessive hemorrhage. Symptoms such as delirium, convulsions and coma from toxic encephalopathy were reported. Renal tubular damage and renal failure can occur. A common cause of death is from ventricular arrhythmias and shock due to myocardial damage (Reigart J.R., 1999).

B. Characterization of Hazard to Human Health

The products subject to the NOIC each contain one of three rodenticide active ingredients: warfarin, brodifacoum, and difethialone. Warfarin is a FGAR; brodifacoum and difethialone are SGARs that are very similar in structure to each other. Bromethalin is not an anticoagulant but an uncoupler of oxidative phosphorylation whose effects are manifested as cerebral edema. The symptoms of anticoagulant poisoning can be treated with vitamin K_1, although the SGARs may require repeated administration over many days or weeks, transfusion with fresh frozen plasma, and clotting factor therapy (e.g., recombinant activated factor VII). There is no specific antidote for bromethalin poisoning, however clinicians and veterinarians can treat the symptoms of bromethalin toxicity in the same manner as other toxins causing cerebral edema, such as aspirin and ibuprofen. Treatment, if needed, typically lasts for several hours, depending on the level of exposure.

Anticoagulant rodenticides block the production of active vitamin K which is essential for the synthesis of several clotting factors. The first sign of anticoagulant poisoning is an increase in the time it takes blood to clot (prothrombin time), although this would only be observed through tests in a medical facility. Because it takes time for the body's ordinary metabolic processes to clear vitamin K-dependent clotting factors from the blood, changes in prothrombin time resulting from an anticoagulant's inhibition of the replenishment of those factors would not be apparent until 24 hours or more after exposure. Significant adverse effects begin 2-3 days after exposure, and include easy bruising and bleeding from almost any tissue such as gums, nose, urinary tract, gastrointestinal tract, etc. Patients may also have symptoms of anemia, including fatigue and dyspnea on exertion. In severe cases, there is massive loss of blood leading to shock and death. Symptoms resulting from FGAR exposure are likely to pass within 24 hours with treatment; symptoms of SGAR exposure could persist for months, even with treatment.

A fourth active ingredient, bromethalin, is also relevant to the Agency's cancellation decision, inasmuch as that decision is based on the comparative risks of the products subject to the NOIC and the registered, available alternative rodenticide products. Bromethalin is not an anticoagulant and produces no unique or definitive symptoms, but instead produces the same constellation of potential symptoms as other uncouplers of oxidative phosphorylation. At low doses, a poisoned individual might exhibit fever, vomiting, dizziness, mental confusion or dullness. At higher doses, as cerebrospinal pressure increases, there may be indications of weakness in limb strength. Very high doses can cause general paralysis or convulsions, and ultimately death. These effects are likely to become manifest within 2 to 8 hours, and the sublethal effects pass within 1 to 4 days.

The acute toxicity of each of the four rodenticides is discussed briefly below with the focus being on acute toxicity values and other relevant parameters reported in the studies.

Warfarin. Warfarin is a FGAR. The acute oral LD_{50} for warfarin in rats is reported as 3 mg/kg (males only) (Gaines, T. B. 1969).[8] Another source indicates there is considerable variability in reported rat LD_{50}s for warfarin: "Reported oral LD_{50} values for warfarin in rats vary by a considerable magnitude. Values of 11 mg/kg body weight (Lund, 1982), 58 mg/kg body weight (Thomson, 1988) and 58 mg/kg (female) and 323 mg/kg (male) (Hagan & Radomski, 1953) have been reported." (http://www.inchem.org/documents/ehc/ehc/ehc175.htm). Another study reports a large difference between the acute toxicity of warfarin to male and female rats with the LD_{50} for males reported to be between 450 and 680 mg/kg and the LD_{50} for females reported as between 5 and 10 mg/kg (MRID 00143093).

Brodifacoum. Brodifacoum is a SGAR. The oral (gavage) LD_{50} of brodifacoum in rats is 0.42 mg/kg in males and 0.56 mg/kg in females. There were no mortalities or signs of toxicity in male and female rats at a dose of 0.25 mg/kg (MRID 42687501). 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 liver half-life for brodifacoum is long – up to 350 days (MRID 42007502).

[8] The LD_{50} is the median lethal dose, which is the quantity of a toxin that is estimated to kill half the members of an exposed population.

Difethialone. Difethialone is a SGAR. Difethialone and brodifacoum have similar structures, differing only in the hetero atom in the coumarin ring. Like brodifacoum, difethialone has a long half-life in the body. The estimated half life of difethialone in rat liver from a single oral dose at 0.5 mg/kg is 175 days for males and 98 days for females (MRID 42065010). In an acute lethality study, the oral (gavage) LD_{50} of difethialone in rats was 0.55 mg/kg (males) and 0.58 mg/kg ((females) (MRID 40268903). Animals died in 4-8 days with symptoms of anticoagulant toxicity. There were no deaths for either males or females at 0.4 mg/kg, indicating a very steep dose response curve. There was a second acute lethality study in rats (MRID 40268903) in which 0/10 rats died at 0.4 mg/kg and 10/10 rats died at 0.8 mg/kg. The two acute studies are consistent with each other and support an LD_{50} value of 0.55 mg/kg for acute lethality of difethialone in rats.

Bromethalin. Bromethalin is not an anticoagulant but an uncoupler of oxidative phosporylation in which the the most apparent manifestation of toxicity involves the central nervous system. The oral LD_{50} in rats for bromethalin is reported as 3.2 mg/kg (males), 2.1 mg/kg (females) and 2.6 mg/kg (combined males and females) (MRID 44775101). Another study (MRID 00241521) lists the LD_{50} for females as 9.1 mg/kg and the LD_{50} for males as 10.7 mg/kg.

EPA routinely characterizes the risk to humans posed by pesticides with uses in or around the home. An important part of a residential assessment is consideration of potential “incidental oral” exposure. The incidental oral assessment seeks to determine the exposure and risks to young children who may ingest pesticide by putting their hands in their mouths after touching objects bearing pesticide residues (hand to mouth activity), or by mouthing an object with pesticide residue on it, or by picking up and eating solid particles of pesticide applied in and around the home.

EPA has developed a quantitative approach to evaluating whether a pesticide poses risks to those who might be exposed as a consequence of pesticide uses. Using available toxicity data and other information such as physical and chemical properties of the pesticide, and activity patterns of potentially exposed persons, EPA estimates a level of exposure that would not cause harm (referred to in this analysis as the "exposure level of concern"), and compares that level to the amount of exposure people would get as a consequence of pesticide use. If the estimated exposure exceeds the exposure level of concern, the use of the pesticide poses risks that may or may not be unreasonable, depending on the benefits of the use. EPA uses a similar logic in determining whether dietary risks are of concern when evaluating exposure to pesticides in food under section 408 of the Federal Food, Drug and Cosmetic Act (FFDCA), although in that context, the safety of the exposure is considered independently of any pesticidal benefits.

EPA relies primarily on toxicity studies conducted with laboratory animals to derive exposure levels of concern for pesticide active ingredients. First, EPA examines all of the available hazard studies and identifies the most sensitive toxic effect caused by a pesticide for the route and duration of exposure that matches the proposed exposure scenario. For rodenticides, EPA is primarily concerned about the hazards of a single instance of oral exposure. The only acute oral exposure studies available for the subject rodenticides are acute LD_{50} studies. Acute LD_{50} studies are not designed to identify sublethal toxic effects, but instead, to determine the amount of exposure that will cause death to 50% of the test animals after a single exposure. Because most chemicals cause adverse effects at dose levels well below the median lethal dosage, EPA typically would base a human health risk assessment on toxicity effects that occur at dosages lower than the acute LD_{50}. However, in the absence of a more appropriate toxicity data, the acute oral LD_{50} studies were used as the effect of concern for this assessment.

To derive an exposure level of concern, EPA typically divides the point of departure (i.e., the exposure level that corresponds to the toxic effect of concern, here the acute oral LD_{50}) by appropriate uncertainty factors. The uncertainty factors are intended to account for possible differences in sensitivity between humans and laboratory animals, for differences between humans, and in this case, to account for the likelihood of sublethal adverse effects. Using these uncertainty factors, EPA identifies a level of exposure that, with reasonable certainty, would not cause harm to humans because the difference between predicted exposures and the levels that cause adverse effects is large enough that no harm would reasonably be expected. It should be noted that an exposure at a level above the exposure level of concern may not elicit any discernible symptoms, depending on the nature of the effect, the amount of the exposure and the sensitivity of the individual person. To address the possibility that the pesticide may generally be more toxic to humans than animals and the possibility that variations in human sensitivity may be greater than seen in the test animals, the Agency usually applies uncertainty factors of at least 100, meaning that in order to be presumed safe, an exposure should be at least 100 times lower than the toxicity endpoint. Often, EPA applies additional uncertainty factors to account for the limitations of the toxicity database including the absence of a “no observed adverse effect level” (NOAEL).

Owing to the paucity of data on sublethal effects of the subject rodenticides, EPA cannot confidently establish exposure levels of concern for acute human exposure to the subject rodenticides. However, if EPA had a complete toxicity database with appropriate studies of sublethal effects with clearly established NOAELs, EPA would apply to that endpoint an uncertainty factor of at least 100 (i.e., a level of concern 100 times lower than the NOAEL) for each active ingredient to account for interspecies and intraspecies variability. If EPA had all the

same studies, but the study showing the most sensitive toxic effect failed to establish a NOAEL, EPA would, in all likelihood, use an uncertainty factor of 1000. In the present case, all of these uncertainties are present, and moreover, the acute toxicity effect of concern (death) is severe and its relationship to sublethal acute adverse effects is unknown. In view of these uncertainties, EPA is unable to say with confidence that there is any finite level of exposure to the subject rodenticides that can be considered reasonably likely to cause no harm. Nevertheless, with the caveat that this undoubtedly understates the risks of sublethal adverse effects, Table 3 below shows the LD_{50} values for each of the rodenticides and what the exposure level of concern would be if EPA applied an uncertainty factor of 1000 to derive a level of concern based on rat LD_{50}s.

Table 3. Surrogate Exposure Level of Concern

Rodenticide	LD_{50} (mg/kg)	Provisional Uncertainty Factor	Surrogate Exposure Level of Concern (mg/kg)
Warfarin	3 mg/kg	1000	0.003 mg/kg
Brodifacoum	0.42 mg/kg	1000	0.00042 mg/kg
Difethialone	0.55 mg/kg	1000	0.00055 mg/kg
Bromethalin	2.6 mg/kg	1000	0.0026 mg/kg

After deriving an exposure level of concern, EPA would estimate potential exposure of different population groups. As is evident from human poisoning and suspected poisoning events, and corroborated by studies of children's behavior, young children will pick up and put small amounts of food-like material into their mouths. In the 1998 Rodenticide Cluster RED, EPA had cited a poison specialist's estimate that a child weighing 10 kg would consume approximately 5 grams of rodenticide bait in one bite (less than a quarter of an ounce). In the current analysis, EPA's estimate of the potential exposure to children eating a single, 5-gram bite of rodenticide bait containing any of the active ingredients at issue greatly exceeds possible safe

levels, without even considering potential sublethal effects. Table 4 below shows how the estimated child exposure from taking one bite of rodenticide bait compares to the surrogate exposure levels of concern for each of the subject rodenticides.

Table 4. Surrogate Exposure Level of Concern for 5 gm Rodenticide Bait.

Rodenticide	% active ingredient in a bait product	Rodenticide ingested in a 5 gm bite of bait by a 10 kg child	Surrogate Exposure Level of Concern (UF = 1000)
Warfarin	0.025%[9]	0.13 mg/kg	0.003 mg/kg
Brodifacoum	0.005%	0.025 mg/kg	0.00042 mg/kg
Difethialone	0.0025%	0.0125 mg/kg	0.00055 mg/kg
Bromethalin	0.01%	0.05 mg/kg	0.0026 mg/kg

This quantitative analysis based on animal toxicity data is consistent with information from reports of incidents of human poisonings. Children who have accidentally ingested quantities of the subject rodenticides have displayed symptoms that are consistent with exposure to toxic levels of these compounds. Symptoms for the anticoagulants include hematological effects such as bruising, and bleeding from gums, nose and other tissues. Symptoms from bromethalin poisoning may include fever, dizziness, dullness, and tremors.

Anticoagulant poisonings present additional risks: Even initially asymptomatic children may experience a period of increased risk of excessive bleeding following exposure to anticoagulant rodenticides. Accidental ingestion of anticoagulants can lead to coagulopathy (impairment of the body's ability to stop bleeding) in a child; although the child is initially asymptomatic they have the potential to bleed excessively (internally or externally) if they

[9] One warfarin product subject to cancellation (EPA Reg. No. 3282-9) contains 0.054% active ingredient.

experience bodily trauma while their ability to stop bleeding is impaired. This potential is not limited to easily recognized locations. Bleeding can take place within a less easily recognized location, such as the brain.

In sum, EPA's analysis shows that, unless use and exposure patterns are changed, children could easily ingest quantities of the subject rodenticides that would contain sufficient amounts of active ingredient to exceed levels that EPA would consider safe. Consequently, EPA could not conclude that exposure to the subject rodenticides was reasonably certain not to cause harm. EPA fully appreciates that rodenticides are governed by the FIFRA risk-benefit standard rather than the FFDCA reasonable certainty of no harm standard, and that any hearing on the NOIC must consider the benefits of rodenticide use against the risks of such use. Nevertheless, the FFDCA criteria for unsafe exposures to pesticides in food provide a meaningful benchmark: If Congress would not allow these levels of pesticide exposure in food – no matter how beneficial the pesticide use might be to agricultural producers – it is reasonable to infer that children should not suffer the same levels of exposures through other routes absent important countervailing benefits.

The rodenticide active ingredients in products subject to the NOIC are man-made chemicals designed to kill rodents and are highly toxic to all mammals. Consequently, the nature and extent of their effects in humans has not been studied in detail. Much of the available information on their potential risk to humans and domestic animals comes from the numerous reported incidents detailing the frequent exposure of children to rodenticides, and observations of the serious consequences to companion animals exposed to rodenticides. These incidents are discussed in the next sections.

1. Sources of Human Incident Data

EPA generally relies on toxicity studies conducted on animals and exposure information based on the pesticide's use pattern when registering a pesticide. After a pesticide is registered, however, human observational data about the effects and exposure of registered pesticides may be collected and analyzed. In assessing the risks of products subject to the NOIC, EPA analyzed human observational data, or incidents, from the following sources: summary data from the American Association of Poison Control Centers (AAPCC), human incident (poisoning) data from such sources as OPP's Incident Data System (IDS) database, National Institute for Occupational Safety and Health (NIOSH) Sentinel Event Notification System for Occupational Risks (SENSOR), the EPA-sponsored National Pesticide Information Center (NPIC), California's Pesticide Incident Surveillance Program (PISP), and additional review of the open literature.

Incident data can provide important information about actual real-world exposures and risks associated with pesticide products. Incident data are collected systematically, but differently, by a number of organizations. The databases used by the Agency differ with respect to such issues as coverage, certainty/confidence, fields/parameters reported, and usability. These five pesticide incident data sources in combination with additional data from the open literature provide useful content and historical perspective. Various other comparable sources of data are available (e.g. the Bureau of Labor Statistics, emergency room outpatient surveillance, etc.) but are believed to be of limited additional utility and were not relied upon for the development of this document. Information from all 5 databases and open literature is provided in the Rodenticides Tier II: Review of Human Incidents, November 1, 2011 Memorandum.

In regard to children's exposures to household products such as rodenticide baits, the AAPCC reports are the most applicable and complete, and are therefore the focus of this discussion. By looking across the data sources which were used, the Agency is confident that the data are adequate and appropriate for discerning trends and patterns in incident poisonings associated with the following rodenticides used for commensal rodent control in bait form: brodifacoum, bromadiolone, bromethalin, chlorophacinone, cholecalciferol, difethialone, diphacinone, diphacinone sodium salt, warfarin, warfarin sodium salt, and zinc phosphide. Although these incident reporting databases can provide important information regarding the frequency, distribution and severity of adverse effects, they are far from comprehensive. EPA estimates that only one quarter of the total number of pesticide poisoning incidents are reported to the AAPCC or state counterparts. (Blondell and Spann, 06/03/1999, D256673).

The AAPCCis a non-profit, national organization founded in 1958 that represents the poison control centers of the United States and the interests of poison prevention and treatment of poisoning. All of the calls to a poison control center are answered by a medical professional trained to answer questions about poisons. Additionally, AAPCC reports provide clearly summarized information on pesticide incidents within the context of other poisoning events. AAPCC produces an annual summary report giving statistics and information on all the poisonings reported to poison control centers in a calendar year. AAPCC ranks the severity of human exposure incidents as follows:

- Death,
- Major – symptoms are life-threatening or result in residual disability or disfigurement (coma, cardiovascular instability, repeated seizures),

- Moderate – symptoms are more pronounced, prolonged, or more of a systemic nature than minor symptoms with no residual disability. Usually some form or treatment is indicated (high fever, disorientation),
- Minor – symptoms are minimal with no residual disability (skin irritation, drowsiness, mild gastrointestinal symptoms), or
- None – patient developed no symptoms as a result of exposure.

2. Observed Human Exposures and Resultant Health Effects

a. Prevalence

When looking across human incident data sources, as well as the open literature, rodenticides are found to be involved in numerous reported incidents, especially those involving children less than 6 years old. While all the sources (IDS, NPIC, PISP, NIOSH SENSOR) demonstrated that humans are being exposed to rodenticides, it is most evident in the Agency's examination of the AAPCC rodenticide data from 1999 to 2009. The 1999-2009 AAPCC data showed that on average 17,000 human exposures to rodenticides were reported annually. Approximately 85% (i.e., approximately 15,000 per year) of these 17,000 exposures occurred to children under 6 years old over the 11 year period analyzed (Table 5).[10] Approximately 16% of all reported exposures to pesticides in the AAPCC data are related to rodenticide exposure. Approximately 26% of all reported pesticide exposures among children under 6 in the AAPCC data are related to rodenticide exposure. Out of all reported pesticide-related exposure incidents to children under 6 years old, for all pesticides, approximately 26% of the exposures are due to

[10] It should be noted that there has been a decrease over a number of years and the in 2010 there were 10,966 incidents reported to AAPCC occurring to children under 6 years old for all rodenticides (there were 406 bromethalin incidents, 8966 SGAR incidents, and 210 FGAR incidents).

rodenticides. Although incident data generally do not specify which products were the subject of the reported exposures, very few, if any, rodenticide products marketed to general consumers during this timeframe included bait stations intended to prevent children's exposure.

Table 5. AAPCC Reported Pesticide Exposure Incidents Involving Children <6 years old by Pesticide Category from 1999-2009

Pesticide Category	Total reported exposure incidents	Number of reported incidents involving children <6 years old	% Reported pesticide incidents that involved children
Disinfectants	224,578	122,868	55%
Fungicides	14,308	3,593	25%
Herbicides	101,832	26,774	26%
Insecticides	474,149	192,745	41%
Organophosphates	84,931	24,877	29%
Other pesticides	150,196	98,309	65%
Rodenticides	195,263	166,250	85%

While certain AAPCC data are publicly available through 2010, EPA purchased access to the raw data and ancillary information for the years 1999 to 2005. More detailed analysis of AAPCC raw data from 1999 to 2005 of the children's exposures to rodenticides, demonstrates that approximately 3,686 children less than 6 years old were treated at a health care facility for the seven year period analyzed. The analysis also demonstrates that on average for this seven year period approximately 128 cases per year (or 1%) of the exposures to children result in a medical outcome classified by the AAPCC as minor, moderate or major. Also, of all pesticide-related cases involving children less than 6 years old from 1999 to 2005, approximately 39% of those seen in a health care facility are related to rodenticide exposure and 13% of hospitalization cases are related to rodenticide exposure. Fortunately, no deaths to children under 6 years old have been reported in these AAPCC data from 1999 to 2010.

b. Circumstances

Incidents involving children appear to result primarily from their picking up unprotected baits in the home. These incidents may result from failure to follow label directions to keep bait away from children, though in some cases, baits might have been moved by rodents from appropriate placement locations. In some cases, it appears that parents underestimated children's abilities to access places where rodenticides were applied. In other cases, it appears that the exposed children were visiting a different environment (such as grandparents, friends, or neighbors) and their parent or guardian was unaware that the baits were accessible. Most incidents involving rodenticide exposures among adults appear to be due to suicide or malicious intent. Accidental exposures, although rare, occasionally occur for adults.

c. Resultant effects

The majority of the rodenticide exposures reported to AAPCC did not result in significant symptoms based on those cases which received follow up to determine medical outcome. However, given the high number of children exposed to rodenticides, the small percentage experiencing significant symptoms is still a matter of concern, both for the symptoms themselves and (in the case of anticoagulants) on account of the risk of excessive bleeding (internally or externally) in response to subsequent trauma while their ability to stop bleeding is impaired. Moreover, while exposures to rodenticides generally result in no detected clinical signs in children, the Agency believes that the number of non-symptomatic exposure incidents is unacceptably high because of the social and other costs (medical care, worry) associated with evaluating and treating children who might have been exposed.

Although most symptomatic exposures do not result in lasting harm, severe outcomes from human exposures to rodenticides do occur. The AAPCC data from 1999-2005 indicates that, compared to other pesticide exposures, rodenticide exposures are much more likely to receive medical treatment, accounting for 39% of all pesticide-related cases seen in a health care facility and 13% of all hospitalized cases involving children less than 6 years old. From 1999-2005, 894 cases were reported having minor, moderate, or major effects (Table 6). For cases reporting moderate or major effects, the most common effect reported was hematological, 37% and 55% respectively. These symptoms are likely a result from anticoagulant rodenticides' abilities to interfere with blood clotting and are likely the result of rodenticide exposure.

Table 6. AAPCC Reported Exposure Symptoms for Symptomatic Children Less Than 6 Exposed to Rodenticide from 1999-2005

Level of Effect	Total Exposures	Reported Exposure Symptoms*							
		Neuro-logical	***Ocular***	***Renal***	***Respir-atory***	***Misc.***	***Dermal***	***GI***	***Hemat-ological***
Minor effect	727	15 (2%)	17 (2%)	0	20 (3%)	180 (25%)	18 (2%)	277 (38%)	36(5%)
Moderate effect	147	7 (5%)	1 (1%)	4 (3%)	2 (1%)	22 (15%)	8 (5%)	34 (23%)	55 (37%)
Major effect	20	1 (5%)	0	0	2 (10%)	5 (25%)	2 (10%)	4 (20%)	11 (55%)

* The categories are not mutually exclusive (i.e. a person could report both a neurological and renal symptom). No cardiovascular symptoms were reported.

3. Comparison of SGAR and Bromethalin Poisonings

Whether a particular exposure is to an anticoagulant or a bromethalin rodenticide is of significantly less importance to human health than whether the exposure occurs in the first place. EPA is concerned about both SGAR and bromethalin poisonings and believes that packaging rodenticide bait products in tamper-resistant bait stations will result in dramatic reductions in

exposures. In comparing bromethalin to the SGARs, animal acute toxicity data indicate that one bite of bromethalin bait is one third as toxic as one bite of brodifacoum bait (an SGAR),[11] and bromethalin clears from the body more quickly than the SGARs. Table 7 compares the toxicological properties of bromethalin and brodifacoum, one of the SGARs.

Table 7. Comparative properties of consumer products containing bromethalin and brodifacoum for rat and mouse control

Property	**Bromethalin**	**Brodifacoum**
Formulations - % active ingredient	0.010%	0.005%
mg active ingredient consumed per 5 gm bite	0.5	0.25
dose to a 10 kg child (mg/kg/bite)	0.05	0.025
Acute lethality - Rat oral LD_{50} (mg/kg)	2.6	0.42 (male)
MOE based on rat LD_{50}	52	17
Rat LD_{50} expressed as a human equivalent dose (mg/kg)	0.65	0.10
MOE based on human equivalent LD_{50}	13	4.2
Ounces of bait containing the HED LD_{50}	2.3	0.7
Estimated human acute lethality (mg/kg)	0.33	0.25 (est.)
MOE based on case studies	6.6	10
Ounces of bait containing a lethal dose	1.2	1.8
Repeated dose toxicity - study	90 day subchronic	developmental
- species	rat, dog	rabbit
- NOAEL mg/kg/day	0.025	0.002
- LOAEL mg/kg/day	0.125	0.005
MOE based on rept. dose NOAEL	0.5	0.08
Plasma half-life	5.6 days (rat)	16 -36 days (human)
Range (time) of anticoagulant action	N/A	51 days - 8 months
Time to onset of clinical effects	6.5-8 hours	24-36 hours

[11] This determination is based on the assumption that "one bite" is 5 grams of bait, which contains either 0.025 mg of brodifacoum or 0.05 mg bromethalin. The predicted dose of 0.05 mg bromethalin produces a margin of exposure (MOE) of 52, based on the acute oral LD50s in the rat (2.6 mg/kg). For brodifacoum, the MOE based on a rat LD50 is 17.

a. Incident Data

Incident data presented in the American Association of Poison Control Centers National Poison Data System (AAPCC-NPDS) for 1993 through 2005 show 4,271 total calls reporting exposure to bromethalin for children less than six years of age. Only eleven of the 4,271 incidents with bromethalin were classified as "moderate" and none were classified as "major." Over the same time period, there were a total of 173,262 SGAR exposures, of which AAPCC classified 269 as moderate and 29 as major incidents. When evaluating differences in these incident counts during the period analyzed, it is important to recognize that many more units of SGAR baits were sold and used than were bromethalin baits. But assuming that users are equally likely to call a poison control center in the event of an exposure incident, regardless of what active ingredient the rodenticide contains, the rate of non-minor incidents involving a particular chemical per 10,000 calls relating to that chemical can provide a useful basis for comparison of the likelihoods of non-minor incidents. For bromethalin, the rate of non-minor incidents was 26 per 10,000 exposure calls, while for SGARs, the rate of non-minor incidents was 17 per 10,000 exposure calls. Because the difference is not statistically significant, these incident reports support a conclusion that bromethalin exposures are not significantly more likely to result in non-minor incidents than are SGAR exposures.

The small number of moderate incidents and the absence of major incidents for bromethalin in the AAPCC-NPDS data are consistent with the results of animal studies that suggest that ingestion of 5 grams of bromethalin bait is unlikely to cause adverse effects in a 10 kilogram (22 pound) child.[12]

[12] In two 90-day sub-chronic studies with bromethalin in the rat (MRID 43582102) and dog (MRID 43582101), there

b. Exposure and Treatment

Neither bromethalin nor the anticoagulants produce symptoms that would serve to immediately alert a parent who is unaware that his or her child has ingested a rodenticide. If a toxic dose is ingested, bromethalin will, within hours of ingestion, cause non-specific symptoms including fever, dizziness, and, depending on the amount consumed, tremors. A toxic dose of an anticoagulant causes somewhat more distinctive bruising and bleeding (including blood in urine, bleeding from the nose and gums, coughing blood and, depending on the amount consumed, bleeding into the joints and brain), but those symptoms do not appear until several days after ingestion. Thus, neither type of rodenticide (i.e., either anticoagulant or bromethalin) is more likely than the other to produce symptoms that would alert parents or health care workers of a rodenticide poisoning within the critical first hours when gastric decontamination could be an effective treatment. Sufficiently high exposures to both bromethalin and the anticoagulants (particularly the SGARs) have the potential to result in patients being admitted to intensive care units at considerable harm and expense to the patient. Because the persistent SGARs are metabolized more slowly by the body, compared to bromethalin, and due to the different mode of toxic action, SGARs result in longer-term medical effects and necessitate longer treatment regimes, at greater costs to the patient.

Bromethalin poisonings are treatable, and do not present greater concerns or difficulties than treatment of anticoagulant rodenticide poisonings. Although emergency room physicians are more likely to have treated an anticoagulant poisoning than a bromethalin poisoning in recent

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were no effects in either the rat or dog after 90 days of continuous daily exposure to bromethalin at a dose of 0.025 mg/kg/day. For comparison, the No Observed Adverse Effects Level (NOAEL) for maternal effects in a rabbit developmental study with brodifacoum was 0.002 mg/kg/day (MRIDs 00052442 and 40307201).

years, specific experience with bromethalin is not important to successful treatment. Like aspirin, indomethacin and ibuprofen, bromethalin is an uncoupler of oxidative phosphorylation, and clinicians are experienced in the appropriate emergency care for exposure to other common chemical substances that act in the same way as bromethalin and require the same treatment. Uncoupling of electron transport is a reversible effect. Once the uncoupler is removed from the system, normal mitochondrial respiration resumes. Transient effects associated with the uncoupling are not associated with long term neurological damage.

Regardless of the rodenticide at issue, treatment outcomes are likely to be better when the symptoms are linked to a rodenticide exposure event, and in particular when the identity of the specific product or active ingredient is known. Initial emergency room treatment for known ingestion of a toxic dose of either type of rodenticide would, however, be the same. In both cases, physicians would work to limit the quantity absorbed by gastric decontamination, and administration of activated charcoal. However, the opportunity for decontamination is short (2 hours or less), and after that, treatment methods diverge. In SGAR poisoning cases where bleeding is evident, the patient would be treated with repeated doses of vitamin K and, depending on the severity of the bleeding, fresh frozen plasma and clotting factor therapy such as recombinant activated factor VII therapy. In bromethalin cases, the patients would be treated for symptoms such as fever and dizziness and, in severe cases with cerebral edema and increased intracranial pressure, treatment would include osmotic diuretics and steroids. In cases where exposure is unknown or uncertain, neither type of rodenticide (i.e., anticoagulant or bromethalin) is more likely than the other to produce symptoms that would alert parents or health care workers of a rodenticide poisoning within the critical first hours when gastric decontamination could be an effective treatment.

Although Vitamin K treatment can compensate for reduced levels of active vitamin K resulting from anticoagulant poisoning, a prolonged treatment regime may be necessary because of the long half-lives of the SGARs.[13] Coagulopathy, a reduction in the blood's ability to clot when there is bleeding, can last for several months while the anticoagulant is cleared from the body. Patients will often need repeated vitamin K treatments, based on prothrombin time and hemoglobin level determinations. Clinical effects from severe bromethalin poisonings are typically present for a shorter period of time as compared with the SGARs. Data from AAPCC-NPDS indicate that for the 9 bromethalin incidents mentioned previously, the duration of clinical effects was from 2 to 8 hours, and the incident reports do not indicate any lasting effects.

Every child's exposure event is of concern, because any time a child can access rodenticide bait, there is the potential for the child to swallow some or all of it. A single 5 gram bite (less than a quarter of an ounce) of any rodenticide bait would result in a pesticide exposure that greatly exceeds levels considered safe as a dietary exposure for a child weighing 10 kg, and the quantity of active ingredient contained in a single placement of any of the rodenticides subject to the NOIC is sufficient to cause adverse health effects. Symptomatic exposures – diagnosed or undiagnosed – are a matter of concern, both for the symptoms themselves and (in the case of anticoagulants) on account of the risk of excessive bleeding (internally or externally) in response to subsequent trauma while their ability to stop bleeding is impaired. In addition to concerns about the actual health impacts of exposure of children to any rodenticide, the Agency

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[13] Bromethalin half-life is 5.6 days (MRID 000146583). SGAR half-lives range from 11-170 days: brodifacoum half-life is 16-36 days (Blood, Vol76. 1990: pp 2555-2559; bromadiolone half-life is 8-170 days (biphasic) http://www.inchem.org/documents/pds/pds/pest88_e.htm; difenacoum half-life is 11-42 days http://toxwiki.wikispaces.com/Anticoagulant+Rodenticides_Oral._logPs are 8.5 (brodifacoum, an SGAR) and 4.26 (bromethalin) Rodenticide Cluster RED (1998).

is mindful of both the potential medical costs associated with children's exposure to rodenticides in the home and the anxiety to parents (and perhaps children as well) caused by the exposure of children to poisons in the home.

C. Characterization of Hazard to Domestic Animals

Rodenticides are highly toxic to mammals and birds, and have much the same effects on domestic animals as they do on humans and on target mammals, as discussed above. Species may differ somewhat in sensitivity to particular rodenticides; however, in the absence of reliable data on relative sensitivities, it is reasonable to presume that all vertebrate pet species are highly vulnerable to all rodenticides.

1. Sources of Domestic Animal Incident Data

EPA generally relies on toxicity studies conducted on laboratory animals and exposure information relevant to the pesticide's use pattern when initially registering a pesticide. After a pesticide is registered; however, observational data about the effects and exposure of registered pesticides may be collected and analyzed. In assessing the risks of products subject to the NOIC, pet observational data, or incidents, from the following sources were analyzed:

- Information from the National Animal Poison Control Center (APCC), the Pet Poison Helpline, and the open literature.
- OPP's Incident Data System (IDS) database,
- The EPA-sponsored National Pesticide Information Center (NPIC),

Animal Poison Control Center and Pet Poison Helpline

The American Society for the Prevention of Cruelty to Animals (ASPCA) Animal Poison Control Center (APCC) is a 24 hours a day, 365 days a year resource for animal poison-related emergencies. Calls to the APCC are triaged by specially trained veterinary toxicologists. The Pet Poison Helpline, another poison reporting center which is available throughout the U.S., Canada and the Caribbean, is managed by veterinary specialists who also help triage animal poisoning events. The veterinary specialists include board-certified veterinary internal medicine emergency critical care specialists, and veterinary toxicologists.

OPP Incident Data System (IDS)

The OPP IDS database of pet exposure information includes reports of alleged incidents from various sources, including FIFRA Section 6(a)(2) reports from registrants and reports from other environmental agencies and individual consumers. The IDS exposure severity types for domestic animals, as defined by 40 CFR 159.184, are as follows:

- DA – Death – if the domestic animal died or was euthanized;
- DB – Major – if the domestic animal exhibited or was alleged to have exhibited symptoms which may have been life-threatening or resulted in residual disability;
- DC – Moderate – if the domestic animal exhibited or was alleged to have exhibited symptoms which are more pronounced, more prolonged or of a more systemic nature than minor symptoms and included some treatment and return to pre-exposure state;
- DD – Minor – if the domestic animal was alleged to have exhibited symptoms, but they were minimally bothersome and resolved rapidly;
- DE – Unknown – if symptoms are unknown or not specified.[14]

[14] Some exposures are classified as "D" in IDS, which is a classification used before 1998 (at which point reporting requirements were updated) or used to indicate the severity is undetermined; as the focus of this assessment is on incidents occurring in 1999 or later, we assume all "D" exposures are "DE" and have undetermined severity.

National Pesticide Information Center (NPIC)

NPIC is a cooperative effort between Oregon State University and EPA which is funded by EPA to serve as a source of objective, science-based pesticide information and respond to inquiries from the public and to incidents. NPIC receives approximately 25,000 calls per year, with about 4000 of these being related to pesticide exposure incidents. NPIC collects the information about the incidents and records that information in a database. NPIC is a source of national incident information; but generally receives fewer reports than IDS. Regardless, NPIC can provide an additional source of incident information. Unlike IDS, incidents reported to NPIC are assigned a certainty classification, which helps ascertain whether the exposure and reported outcome are related.

2. Observed Domestic Animal Exposure and Resultant Health Effects

a. Prevalence

The American Society for the Prevention of Cruelty to Animals (ASPCA) Animal Poison Control Center (APCC) website identifies the top ten pet toxicants of 2010 based on the number of calls received. Out of the approximately 167,000 phone calls about pet exposures they received during 2010, rodenticides were listed as the third most frequent reason for calls to the APCC (after human medications and insecticides). Another 24-hour hotline, the Pet Poison Helpline, in 2009 identified rodenticides as the third most common class of toxicants involved in dog poisonings (after chocolate and insect bait stations) and the fourth most common class of toxicants involved in cat poisonings (after lilies, canine permethrin insecticides and household cleaners).

Both the IDS and NPIC data indicate that the number of reported incidents of pet exposure to rodenticides is increasing over time. However, different rodenticides are associated

with this increase in the different databases.

IDS reports that the number of reported pet exposures involving FGARs and non-anticoagulant rodenticides was relatively stable from 1999 to 2009, whereas reported exposures involving SGARs (chiefly bromadiolone) increased over time, from approximately 200 per year to approximately 1400 per year, primarily in the moderate, minor and unknown outcome categories. The overall upward trend may be a result of increased usage or increased reporting, rather than an increase in the likelihood that use of a product results in an incident.

By contrast, NPIC reports that the number of reported pet exposures involving FGARs and SGARs was relatively stable from 1999 to 2010, whereas reported exposures involving non-anticoagulants (chiefly zinc phosphide) increased over time, from approximately 5 per year to approximately 180 per year. To the extent that this increase is associated with use of zinc phosphide, it is not relevant to the proposed cancellation because zinc phosphide is not registered for commensal rodent control in and around homes. The only zinc phosphide products registered for general consumer use are for mole and pocket gopher control, and must be manually applied below ground to maximize exposure to target species, which minimizes exposure to non-target animals.

b. Circumstances

The narrative information available regarding these incidents and EPA's review of the scientific literature indicate that many pets gain access to baits placed in and around homes. EPA believes the main reason these incidents are occurring is because rodenticide baits are being placed in areas accessible to pets without use of pet-resistant bait stations required by the products' labels.

c. Resultant effects

The IDS data reflect that, although most rodenticide incidents appear to result in lower severity outcomes, there were a substantial number of fatalities (1209) and major outcomes (565) from 1999 to 2009. These numbers indicate that rodenticides cause, on average, about 160 severe (death or major effect) domestic animal incidents every year. EPA believes that the IDS data are likely to significantly underestimate the number of incidents that actually occur because many incidents go unreported.

The IDS data also allow rodenticide active ingredients to be ranked according to the severity of domestic animal incidents reported. Although the data may be influenced by market share, focusing on those exposures resulting in severe outcomes provides an indication of the hazard of a particular active ingredient. The rodenticide with the highest number of incidents ranked DA (death) and DB (major) over the period 1999-2010 was brodifacoum (710 incidents), followed by bromadiolone (355), bromethalin (292) and diphacinone and its sodium salt (262). Together, the SGARs brodifacoum and bromadiolone accounted for 60% of the major and fatal domestic animal incidents (DA+DB) attributed to rodenticides.

Comparing the major and fatal incidents (DA+DB) per active ingredient as a percentage of total incidents for that same active ingredient provides a way to judge whether a particular active ingredient is more or less likely to cause serious adverse effects (i.e., major or fatal incidents) than another. For example, 22% of reported exposures to brodifacoum result in a pet death or major incident, but only 8% of reported exposures to bromadiolone result in a death or major incident, indicating that brodifacoum exposures are more likely to cause severe consequences than bromadiolone exposures.

Table 8: IDS - Rodenticides as a Percentage of Severe Outcomes, 1999-2009			
Rodenticide	**Category**	**Percentage of Death + Major Incidents out of Total Exposure Count**	**Total Exposure Count**
Diphacinone and diphacinone, sodium salt	First generation anticoagulant	22%	1,192
Warfarin and warfarin, sodium salt		22%	151
Chlorophacinone		21%	29
Brodifacoum	Second generation anticoagulant	22%	3,229
Bromadiolone		8%	4,661
Difethialone		13%	144
Difenacoum		27%	11
Bromethalin	Non-anticoagulant	12%	2,460
Zinc phosphide		18%	258
Cholecalciferol		23%	209

The incident data show that all rodenticides have caused death or major adverse health effects to pets. Although this analysis shows some differences in the likelihood of death or major outcomes for the different rodenticides, large percentages of pets exposed to a rodenticide are likely to experience severe outcomes, regardless of the category or identity of the rodenticide. Use of bait stations that meet EPA's criteria for pet resistance would reduce the frequency of pet exposures to rodenticides. Although such products have been available in the commercial and agricultural pest-control markets for nearly 30 years, they were virtually absent from consumer-oriented markets until the June 4, 2011, RMD compliance date.

D. Characterization of Hazard to Non-Target Wildlife

This discussion summarizes the ecological risk concerns that form part of the basis of EPA's decision to cancel and deny registrations for the commensal rodent control products identified above in the NOIC. EPA has updated its previous risk assessment findings conducted in support of the May 2008 RMD through the application of additional effects and exposure data,

use of additional exposure modeling, and quantitative risk assessment techniques for the four rodenticide active ingredients (brodifacoum, difethialone, warfarin and bromethalin) contained in products subject to the NOIC and for two rodenticides (chlorophacinone and diphacinone) that are potential alternatives to brodifacoum and difethialone in the consumer rodenticide market.

Rodenticide baits are intended to be lethal to rodents and a few other small mammals, but the active ingredients are not selective to target species. All mammals and birds are vulnerable to adverse effects, including mortality, from rodenticides, although different species and individuals may have differing sensitivities. Rodenticide exposures and mortalities have been documented for mammals and birds that are primary and secondary consumers.

1. Routes of exposure

For the purpose of the ecological risk assessment, primary exposure was defined as consumption of rodenticide treated bait by non-target organism. Use of rodenticide baits around structures is likely to result in primary exposures among non-target wildlife. Many factors influence which non-target animals might be exposed directly to baits. For instance, birds and mammals that are attracted to seeds and grains may consume grain-based rodenticide baits and baits in forms similar to seeds and grains. Some non-target animals will readily consume rodenticide baits that have a block form. Incident reports document rodenticide exposures among a number of species that are likely to be primary consumers of bait, including quail, turkeys, squirrels, opossums, raccoons, skunks, and deer.

Secondary consumers were defined for purposes of the ecological risk assessment as those animals that prey upon or scavenge primary consumers of bait. Rodenticide baits pose potential secondary poisoning risks, because predators and scavengers are likely to be attracted

to dead or dying rats, mice, and poisoned non-target animals. Incident reports document rodenticide exposures among a number of secondary consumer species including larger mammals such as bobcats and foxes, and numerous bird species such as hawks, eagles and owls. Omnivores were considered as both primary and secondary consumers for this analysis.

EPA is concerned with both the primary and secondary risks to birds and non-target mammals from exposure to the commensal rodent control products subject to the NOIC. This concern is based upon consideration of several lines of evidence, including (1) an assessment of the risks to non-target animals associated with primary exposure to rodenticides; (2) an assessment of the risks of non-target animals through secondary exposure to rodenticides, including an evaluation using probabilistic risk assessment techniques; (3) an evaluation of available feeding studies as they relate to secondary exposure risks; and (4) an evaluation of reported wildlife incidents as they relate to primary and secondary mortality events for non-target species in a variety of land use settings, including urban, suburban, and rural settings.

Table 9 provides a summary of EPA's conclusions on primary and secondary risks for each chemical based on an analysis of the above lines of evidence. Across all lines of evidence, the evaluated data suggest that all assessed chemicals pose risk to wildlife that exceeds levels of concern. For birds, brodifacoum and difethialone stand out as posing the greatest potential for adverse effects. Bromethalin also exhibits a high potential for adverse effects to birds, although the relatively short blood half-life and the tendency of animals to stop eating bait after consuming a toxic dose of bromethalin reduces the potential for secondary exposure. For mammals, the ranking of relative chemical risk is similar; however, there is much less differentiation in risk among the chemicals as might be expected given that rodenticides were

developed with the goal of mammal mortality. For the individual lines of evidence, EPA concludes the following:

a. Primary Exposure Risk

- Brodifacoum and difethialone are more toxic to birds and mammals than are warfarin, chlorophacinone, diphacinone, and bromethalin; however, the toxicity differences between chemicals are much more pronounced for birds.

- For primary exposure to birds, all or a majority of lines of evidence (i.e., results of the deterministic risk assessments, days required to consume the bait equivalent of an LD50, and quantity of bait required to consume an LD50) for brodifacoum, difethialone, and bromethalin indicate that birds are likely to be adversely affected if they directly consume bait. For both bait concentrations of warfarin (0.025 and 0.054%), the deterministic risk assessment indicates that some weight classes of birds are likely to be adversely affected if they directly consume bait; however, the additional lines of evidence indicate that the required feeding times and bait consumption quantities are greater than for brodifacoum, difethialone, and bromethalin. For chlorophacinone and diphacinone, the analysis suggests that birds do have the potential to be adversely affected following primary consumption of bait, but the estimated days of feeding on bait to reach an LD_{50} (ranging from 16 to >365 days) are much greater than for the other evaluated rodenticides.

- For primary exposure to mammals, all or a majority of lines of evidence for all evaluated rodenticides suggest that mammals are likely to be adversely affected if they directly consume bait.

- Analysis of the available reported wildlife incidents indicated that for both birds and mammals, consumption of bait does occur resulting in mortality across a majority of the

chemicals. The most notable exception is bromethalin, as only a few incidents were reported; however, bromethalin is not often included in tissue residue analyses.

b. Secondary Exposure Risk

For secondary exposure to birds, all lines of evidence (i.e., results of the deterministic risk assessments, quantity of contaminated mice or rats in diet required to consume the equivalent of an LD50, results of a limited probabilistic analysis, and results of available secondary feeding studies) indicate that birds are likely to be adversely affected by brodifacoum if birds consume contaminated prey (incident data confirms that birds have been adversely affected by consuming contaminated prey). Similar conclusions can be made for difethialone: the predominance of the evidence is that difethialone adversely affects birds if they consume contaminated prey, but a few exposure scenarios (larger birds consuming prey with low contamination levels) are less likely to result in adverse effects than is the case for brodifacoum. Evidence that predators or scavenger may be adversely affected by secondary exposure to warfarin, chlorophacinone, diphacinone, and bromethalin is equivocal, suggesting that risks may be dependent on the sensitivity of individual species or a rodenticide's potential for accumulation in prey animals.

For secondary exposure to mammals, all lines of evidence indicate that mammals are likely to be adversely affected if exposed to contaminated prey (incident data confirms that mammals have been adversely affected by consuming contaminated prey) for brodifacoum. Bait containing difethialone, bait containing the higher concentration of warfarin (0.054%), and bait containing bromethalin also may adversely affect mammals that consume contaminated prey; but a few exposure scenarios are less likely to result in adverse effects than in the case of brodifacoum. Also, bromethalin appears to have lower potential to accumulate and be retained

in prey relative to the other assessed chemicals, which reduces the secondary exposure potential.

Analysis of the available reported wildlife incidents indicated that for both birds and mammals, consumption of bait does occur resulting in mortality across a majority of the chemicals. The most notable exception is bromethalin, as no secondary exposure incidents were reported; however, bromethalin is not often included in tissue residue analyses.

Table 9. Ecological risk conclusions from all lines of evidence

Chemical	RQs and Opportunity for Exposure		Incident Data			Overall Conclusion	
	Primary Risk	Secondary Risk	Primary	Secondary	Urban/ Suburban	Primary	Secondary
Birds							
Brodifacoum	All lines	All lines	All lines	All lines	All lines	All lines	All lines
Difethialone	All lines	Predominant	No data	All lines	All lines	All lines	Predominant
Warfarin (0.025%)	Equivocal	Equivocal	All lines	All lines	All lines	Equivocal	Equivocal
Warfarin (0.054%)	Equivocal	Equivocal	All lines	All lines	All lines	Equivocal	Equivocal
Chlorophacinone	Equivocal	Little	All lines	All lines	All lines	Equivocal	Equivocal
Diphacinone	Little	Equivocal	All lines	All lines	All lines	Equivocal	Equivocal
Bromethalin	Predominant	Equivocal	No data	No data	No data	Predominant	Equivocal
Mammals							
Brodifacoum	All lines	All lines	All lines	All lines	All lines	All lines	All lines
Difethialone	All lines	Predominant	All lines	All lines	All lines	All lines	Predominant
Warfarin (0.025%)	All lines	Equivocal	All lines	No data	No data	All lines	Equivocal
Warfarin (0.054%)	All lines	Predominant	All lines	No data	No data	All lines	Predominant
Chlorophacinone	Predominant	Equivocal	All lines	All lines	All lines	Predominant	Equivocal
Diphacinone	All lines	Equivocal	All lines	All lines	All lines	All lines	Equivocal
Bromethalin	All lines	Predominant	All lines	No data	No data	All lines	Predominant

"All Lines" = All lines of evidence suggest risk exceeds concern levels and effects are likely to occur
"Predominant" = The predominance of the evidence is that the chemical causes adverse effects, but a few exposure scenarios are less likely to result in those adverse effects.
"Equivocal" = Equivocal evidence that risk exceeds concern levels and effects are likely to occur
"Little" = Little evidence that risk exceeds concern levels or that effects are likely to occur

2. EPA's Deterministic Assessment Approach

In conducting both the primary and secondary risk assessments, EPA utilized several independent lines of evidence to determine whether and to what extent the commensal rodenticides at issue in this proceeding adversely affect non-target wildlife. These lines of evidence include the following:

- Risk quotients (RQs),
- Evaluation of primary and secondary exposure studies,
- Measures to determine the feasibility of an effect occurring, and
- Incident data.

The RQ is briefly described in this section, and other lines of evidence evaluated in this assessment are described in greater detail in subsequent sections. The RQ is a unitless value that is the ratio of exposure to the toxicity endpoint. For example, in the context of acute avian risk estimates (e.g., mortality), an RQ of 1 would mean that non-target birds may be exposed in the environment to an amount of the pesticide that would be expected to result in 50% mortality based upon laboratory tests (specifically, the LD_{50} dose). EPA compares RQs to the Agency's levels of concern ("LOC") for non-target species. The LOC represents the exposure levels at which, in EPA's judgment, a pesticide has the potential to cause risks of concern to non-target organisms. Thus, when the RQ for a pesticide exceeds the LOC for a particular category of non-target species, the Agency believes there is a risk of concern for species in that category. In this assessment, risk quotients were compared with the acute level of concern that EPA regularly uses in assessing risks to non-target wildlife generally (LOC = 0.5). Additional levels of concern may also be used to evaluate potential risks to species listed as threatened or endangered (LOC = 0.1); however, for simplicity, this analysis only used the LOC of 0.5. Therefore,

conclusions made with respect to the LOC of 0.5 may not apply to listed species.

Because this deterministic assessment is intended to serve as a screening tool for identifying a potential for adverse effects, it is somewhat limited and conservative by design. As a result, EPA does not believe that the RQs derived in this assessment can be used as a precise measure of the magnitude of effects that will occur, but rather serve as tools for addressing whether or not a chemical poses a risk to assessed animals at a level of concern to the Agency. As a result, direct comparisons between chemicals on the basis of RQs can be misleading. Therefore, in this assessment, the Agency also uses other lines of evidence to characterize the relative risks of the rodenticides that are subject to the NOIC and the alternatives considered here, as described in succeeding sections.

a. Primary Exposure and Risk

i. Methodology

For the purpose of this assessment, primary exposure is defined as non-target organism consumption of rodenticide treated bait. Primary exposure risk is influenced by factors including toxicity, toxicokinetics (chemical absorption, distribution and elimination in the body), concentration of active ingredient in the bait, and availability of bait for consumption. For each of the evaluated chemicals, risk was assessed in several ways. RQs were calculated assuming:

- Single day dose-based exposure to bait, based on allometric equations that allow for differentiation among taxa and body size, is compared to acute oral LD_{50} toxicity values;
- Six day dose-based exposure to bait, based on metabolism rate in the body and allometric equations that allow for differentiation among taxa and body size, is compared to acute oral LD_{50} toxicity values; and

- Diet-based exposure, based on the concentration of rodenticide active ingredient in bait, is compared to acute dietary LC_{50} values.

Further lines of evidence were evaluated, including:

- An analysis of the number of days of bait consumption required to reach the median lethal dose of rodenticide;
- The amount of bait individuals would need to consume in order to accumulate the median lethal dose; and
- Incident data.

For the single-day dose-based exposure method, exposure was calculated by dividing the dose (in milligrams of active ingredient) by the body weight (in kilograms) of the consuming individual for three standard weight classes of birds and mammals. Allometric equations that relate food consumption to body weight (Wildlife Exposures Handbook, USEPA 1993) were used to determine potential exposures for typical birds and mammals of varying sizes. Allometric equations were used for the generic bird and mammal. In addition, allometric equations for passeriform birds and rodent mammals were also used as these would best approximate those individuals with high potential for consuming bait and they would give conservative exposure estimates. Animal exposure was determined based on daily food intake rates (dry weight), assuming 100% of their diet consisted of dry bait. It was assumed for this assessment that the form of the bait would not influence rate of intake or total intake.

Weight-adjusted LD_{50} values for birds and mammals were used as the measure of toxicity to non-target species. The toxicity values selected for this assessment for birds were the most

sensitive LD_{50} values available for Northern bobwhite quail (*Colinus virginianus*) or mallard duck *(Anas platyrhynchos*). The toxicity values selected for this assessment for mammals were the most sensitive LD_{50} values available for the Norway rat (*Rattus norvegicus*). For this assessment, EPA used standard bird (bobwhite quail and mallard duck) and mammal (Norway rat) test species to estimate weight-adjusted LD_{50} values for non-target animals. Although there are numerous studies addressing the toxicity of one or more rodenticides in a wide variety of non-target species, these standard test species are the only ones for which studies are available on all of the rodenticides of interest. Therefore, in order to provide a uniform basis of comparison between rodenticides, EPA's analysis focused on these standard test species. However, this method may be less conservative if other non-target species are more sensitive to rodenticide exposure than are the standard test species.

Scaling factors were used to modify the available avian and mammalian toxicity data to account for differences in sensitivity between animals of different body weights. For example, when using the default scaling factor, smaller birds are estimated to be more sensitive compared to larger birds. Scaling factors, derived from Mineau *et al*. (1996) for birds are used in this assessment, which is consistent with the Agency's terrestrial animal risk assessment model T-REX v.1.4.1 (U.S. EPA 2008). A chemical-specific scaling factor was available for brodifacoum (0.76) from Mineau *et al*. (1996), and for all other chemicals where such a specific value is unavailable, the default scaling factor (1.15) was used to adjust the avian LD_{50}s. Using additional data, Mineau *et al*. (2001) provided an alternative scaling factor for brodifacoum (0.88) and a chemical-specific scaling factor for chlorophacinone (-0.53). Mammalian weight-adjusted LD_{50} values were calculated using the "body weight ^{¾}" adjustment (USEPA 1995, 2011). EPA's assessment for primary exposure and risk utilized default weight classes of birds

(small (20 g), medium (100 g), and large (1000 g)), and mammals (small (15 g), medium (35 g), and large (1000 g)). These are the standard bird and mammal body weights used in by EPA for ecological risk assessments (T-REX version 1.4.1, U.S. EPA 2008).

The six day dose-based exposure assessment utilized the same toxicity information discussed above, but in this assessment RQs were calculated by estimating body burden based on the assumption that bait was consumed exclusively for six days. Body burden concentrations (milligram active ingredient per kilogram body weight [mg a.i./kg-bwt]) were based on feeding rates and elimination rates from liver half-life estimates.

For the diet-based primary exposure assessment, EPA evaluated the concentration of a.i. in the bait and the dietary $LC_{50.}$ The LC_{50} (mg a.i./kg-diet) is obtained from 5-day exposure dietary toxicity studies. RQs are calculated as a ratio of a.i. concentration and the LC_{50}. Risk results that agree between this method and the multiple day accumulated dose method described above provide an enhanced degree of confidence in risk conclusions for a given chemical.

As noted above, EPA also evaluated further lines of evidence, including an analysis of the number of days of bait consumption required to reach the median lethal dose of rodenticide and the mass of bait animals would need to consume in order to reach the median lethal dose, and incident data. The first line of evidence involved calculation of the number of days it would take an individual non-target bird or mammal (assuming the standard body weights described above) to reach the LD_{50} through consuming 100% of its daily diet as bait. The second line of evidence involved calculating the amount of bait that would need to be consumed to be equivalent to the $LD_{50.}$ These additional lines of evidence represent useful tools for comparing risks among chemicals. The greatest concerns for non-target primary risk are with those pesticides for which little feeding time or only a small amount of treated material is necessary for

mortality to occur. Mortality to non-target primary consumers becomes less likely when consistent feeding or large amounts of consumption are necessary over a protracted period of time to cause death.

ii. Risk Characterization

Variation in toxicity among the chemicals and sensitivity across taxonomic groups, species, and exposure methods are evident when examining the available toxicity endpoints (Figures 1-4). Generalized conclusions based on the available acute oral (LD_{50}) studies are: (1) mammals are more sensitive to these rodenticides than are birds; (2) there is a larger variation in toxicity to rodenticides for birds than there is for mammals; (3) within a chemical, significant variation is present among species and/or laboratories; (4) for birds, an approximate toxicity ranking is brodifacoum and difethialone, followed by bromethalin, followed by warfarin, chlorophacinone, and diphacinone; and (5) for mammals, an approximate toxicity ranking is brodifacoum and difethialone, followed by bromethalin, warfarin, chlorophacinone, and diphacinone.

Although fewer toxicity endpoints are available for the acute dietary (LC_{50}) studies, the general conclusions are similar: (1) mammals are more sensitive than birds; (2) there is a larger variation in toxicity to rodenticides for birds than there is for mammals; (3) within a chemical, significant variation is present among species and/or laboratories; (4) for birds, an approximate toxicity ranking is brodifacoum and difethialone, followed by bromethalin, warfarin, chlorophacinone, and diphacinone; and (5) for mammals, the central tendencies and ranges in toxicity appear very similar across all chemicals for which data are available.

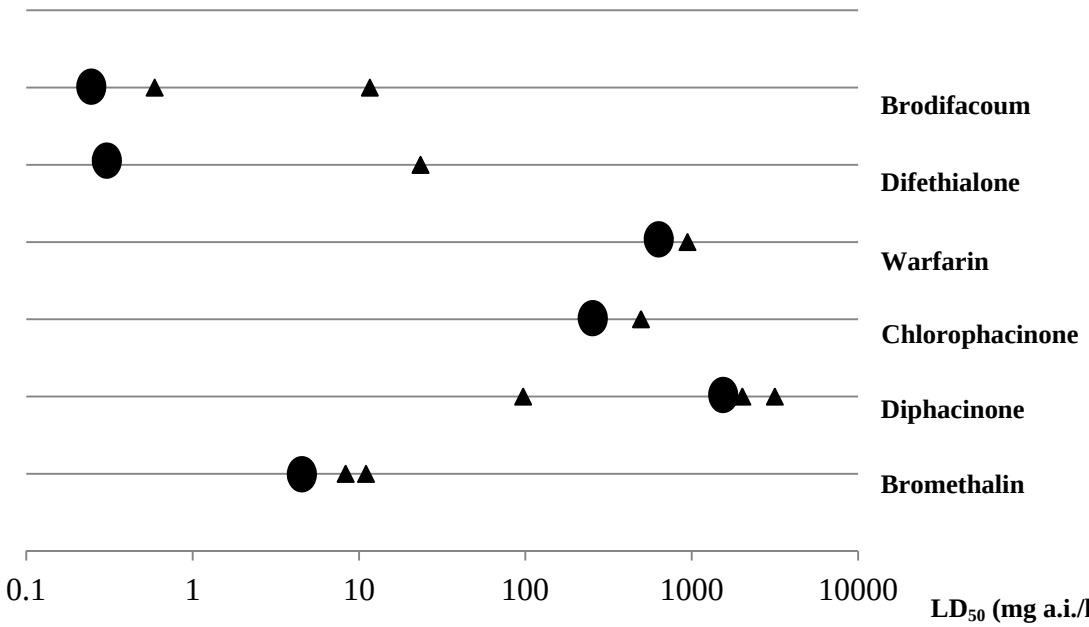

Figure 1. Avian acute oral LD_{50} (mg a.i./kg-bwt) values for all evaluated chemicals. Only toxicity values obtained using the technical material were included. Circles represent the lowest toxicity value obtained from a standard test species (bobwhite quail or mallard duck); these values were used for RQ calculation. Triangles represent toxicity values obtained from non-standard test species or less sensitive standard test species.

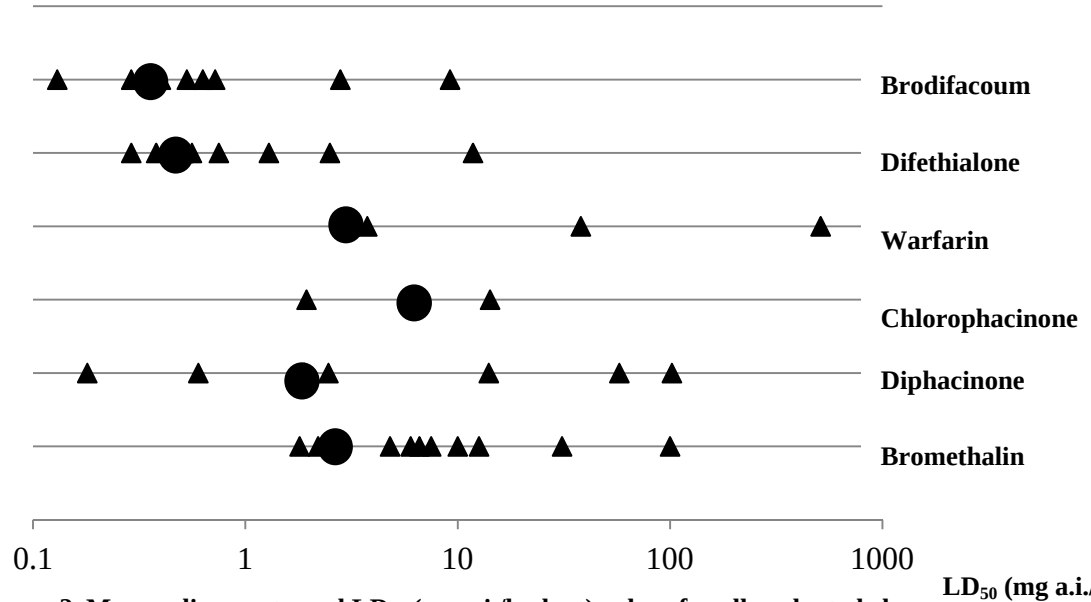

Figure 2. Mammalian acute oral LD_{50} (mg a.i./kg-bwt) values for all evaluated chemicals. Only toxicity values obtained using the technical material were included. Circles represent the lowest toxicity value obtained from a standard test species (laboratory rat); these values were used for RQ calculation. Triangles represent toxicity values obtained from non-standard test species or less sensitive standard test species

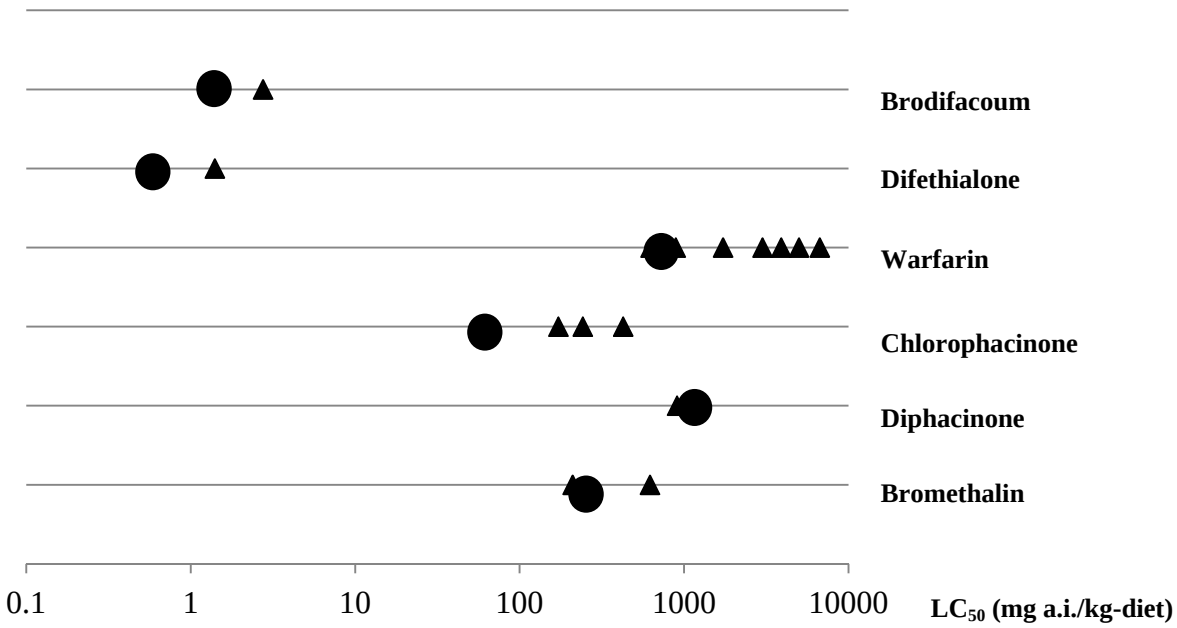

Figure 3. Avian acute dietary LC_{50} (mg a.i./kg-diet) values for all evaluated chemicals. Only toxicity values obtained using the technical material were included. Circles represent the lowest toxicity value obtained from a standard test species (bobwhite quail or mallard duck); these values were used for RQ calculation. Triangles represent toxicity values non-standard test species or less sensitive standard test species

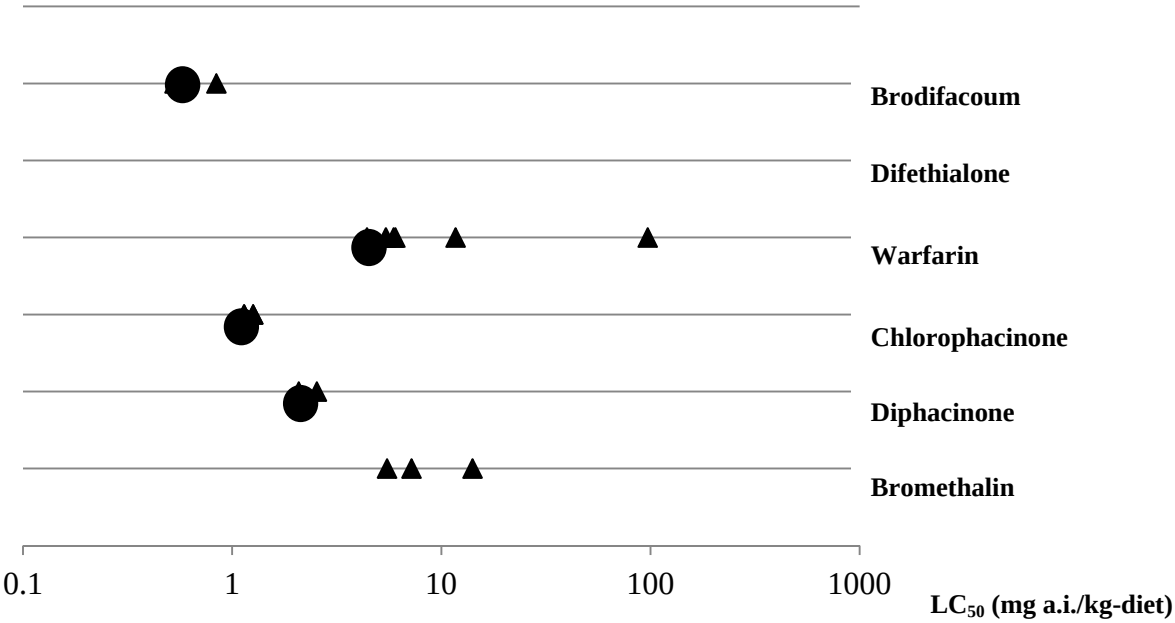

Figure 4. Mammalian acute dietary LC_{50} (mg a.i./kg-diet) values for all evaluated chemicals. Only toxicity values obtained using the technical material were included. Circles represent the lowest toxicity value obtained from a standard test species (laboratory rat); these values were used for RQ calculation. Triangles represent toxicity values non-standard test species or less sensitive standard test species. No data were available for difethialone; data for bromethalin were not acceptable for RQ calculation.

The risks identified by the deterministic analyses and the other lines of evidence for each of the rodenticides considered in the EPA assessment are characterized below. Tables 10 and 11 include the RQs for primary exposures of birds and mammals (respectively) to rodenticides. These tables also include the estimated number of days required to reach the LD_{50} through 100% consumption of bait and the mass of bait to be consumed for an individual to reach the LD_{50}.

Table 10. Bird risk assessment: primary exposure of passerine birds to bait.

		Body weights (g)	Second Generation Anticoagulants		First Generation Anticoagulants				Non-anti-coagulant
			Brodifacoum	Difethialone	Warfarin (0.025%)	Warfarin (0.054%)	Chlorophacinone	Diphacinone	Bromethalin
Risk Quotients	**Single day dose RQ**	**20**	**20***	**30***	0.23	**0.50***	0.07	0.01	**7.8***
		100	**23***	**18***	0.14	0.31	0.04	0.01	**4.8***
		1000	**28***	**9.2***	0.07	0.16	0.02	<0.01	**2.4***
	Six day dose RQ	**20**	**120***	**170***	**1.4***	**2.9***	0.40	0.05	**NA**
		100	**140***	**100***	**0.84***	**1.8***	0.25	0.03	**NA**
		1000	**170***	**52***	0.42	**0.91***	0.12	0.01	**NA**
	Dietary RQ	NA	**38***	**45***	0.40	**0.86***	**0.89***	0.06	0.48
Additional lines of evidence	**Days to consume sufficient bait to reach the LD_{50}**	**20**	<1	<1	4-5	1-2	16-17	>365	<1
		100	<1	<1	7-8	3-4	30-31	>365	<1
		1000	<1	<1	14-15	6-7	117-118	>365	<1
	Grams bait consumed to reach the LD_{50}	**20**	<1	<1	25	10	86	>1800	<1
		100	<1	1.1	160	80	620	>7300	4.2
		1000	5	15	2100	990	17000	>52000	59

NA = not applicable ND = no data * RQ exceeds acute risk LOC = 0.50

Table 11. Mammal risk assessment: primary exposure of rodents to bait.

		Body weights (g)	Second Generation Anticoagulants		First Generation Anticoagulants				Non-anti-coagulant
			Brodifacoum	Difethialone	Warfarin (0.025%)	Warfarin (0.054%)	Chlorophacinone	Diphacinone	Bromethalin
Risk Quotients	Single day dose RQ	15	**9.9***	**4.3***	**8.4***	**18***	**0.82***	**2.0***	**5.1***
		35	**8.5***	**3.7***	**7.1***	**15***	**0.70***	**1.7***	**4.4***
		1000	**4.6***	**2.0***	**3.8***	**8.3***	0.38	**0.90***	**2.4***
	Six day dose RQ	15	**59***	**24***	**49***	**110***	**4.7***	**12***	**NA**
		35	**51***	**21***	**42***	**90***	**4.0***	**9.9***	**NA**
		1000	**27***	**11***	**22***	**48***	**2.1***	**5.3***	**NA**
	Dietary RQ	NA	**94***	ND	**57***	**120***	**44***	**22***	**ND**
Additional lines of evidence	Days to consume sufficient bait to reach the LD_{50}	15	<1	<1	<1	<1	1-2	<1	<1
		35	<1	<1	<1	<1	1-2	<1	<1
		1000	<1	<1	<1	<1	2-3	<1	<1
	Grams bait consumed to reach the LD_{50}	15	<1	<1	<1	<1	6	1.1	<1
		35	<1	1.3	<1	<1	9	2.1	1.1
		1000	6.7	16	8.0	3.7	61	25	13

NA = not applicable ND = no data * RQ exceeds acute risk LOC = 0.50

RQs exceed the LOC for all mammals exposed to brodifacoum and difethialone. These pesticide active ingredients were developed to kill rodents; they pose a lethal primary risk to non-target small mammals that eat bait containing either of these rodenticides. However, the quantitative assessment also demonstrates that bait containing these two rodenticides constitutes a primary exposure risk concern for larger mammals as well as all avian size classes – that is, species that are plainly not the intended targets of these products. This conclusion is consistent across all primary exposure risk analyses performed (single oral dose, six-day accumulated dose, dietary concentration and the feeding period- lethality assessment). EPA's analysis indicates birds and mammals could attain a lethal dose (LD_{50}) of either brodifacoum or difethialone upon feeding for less than one day on treated bait. The brevity of feeding required to reach a potentially lethal exposure represents an increased opportunity (relative to all other rodenticides assessed) for non-target animals – especially birds -- to chance upon bait and consume a lethal dose of either brodifacoum or difethialone.

Warfarin, as expected for all rodenticides, also demonstrates a primary exposure risk concern to small mammals. The assessment of warfarin also indicates a risk to large mammals for all assessment methods employed as well. EPA's analysis indicates that feeding on treated bait for less than a day is sufficient to attain a lethal dose in all evaluated size classes of mammals, suggesting a similar opportunity, relative to brodifacoum and difethialone, for non-target mammals to chance upon treated bait and consume a lethal dose. In contrast to brodifacoum and difethialone, warfarin's primary exposure risk for birds is limited to small passeriformes and other medium sized birds. While a single day dose risk assessment suggests only a risk to small passeriformes from the highest concentration formulation, accounting for the potential for multiple day accumulation on a dose basis expands the concerns to include

passeriformes and other small and medium sized birds at all formulation concentrations assessed. The dietary assessment does not consider body weight as a determinant factor. However, this assessment method still predicts a risk concern at the highest formulation concentration. EPA estimates that birds would attain a lethal warfarin dose after 1 to 7 days of feeding (0.054% warfarin bait) or after 4-15 days of feeding (0.025% warfarin bait). This finding suggests that, for birds there is less of an opportunity for consuming a lethal dose of warfarin by chance when compared with brodifacoum and difethialone, since it would generally require multiple days of feeding on warfarin treated bait to reach a lethal dose in birds.

For bromethalin, as can be expected for a relatively fast acting compound (target mortality occurs 1 to 7 days after initial exposure, Pitt *et al*. 2011, and registrant-submitted studies), acute risk concern levels are exceeded for all mammalian size classes feeding on treated bait regardless of the assessment method EPA employed. In addition, bromethalin exceeds risk concern levels in all assessment methodologies with the exception of the dietary exposure methodology. EPA's analysis indicates that less than a single day's feeding on bromethalin bait is sufficient to attain a lethal dose in birds and mammals, suggesting (again like brodifacoum and difethialone) adverse effects to non-target wildlife are likely from primary exposure events with treated bait.

Two anticoagulant alternatives, chlorophacinone and diphacinone, also present primary exposure risk concerns for nearly all mammal sizes assessed using all primary exposure assessment methods (however, large rodents, greater than 1000 g, consuming chlorophacinone bait for one day are not expected to experience risks of concern). EPA's analysis indicates that <1 day (diphacinone) and <1 to 3 days (chlorophacinone) of feeding on bait are sufficient to attain the median lethal dose in mammals. These periods are not materially different from the

other rodenticides with respect to the opportunity for non-target mammals to chance upon and ingest a lethal dose of treated bait. In contrast to mammals, primary avian risk is below concern levels for these two compounds. This finding may be due to a limitation in the analysis of primary exposure models which had them terminating at six days (i.e., longer exposure periods might provide sufficient exposure to bait for adverse accumulation to occur). However, the analysis indicates that, unlike brodifacoum and difethialone, a very consistent and protracted feeding period for either diphacinone or chlorophacinone is required to attain a lethal dose in birds (i.e., daily feedings over weeks to months).

b. Secondary Exposure and Risk

The toxicity of each of the rodenticides and a variety of factors concerning their fate and effects in biological systems influence their potential for risk to secondary consumers, i.e., non-target wildlife that may ingest living or dead animals that have consumed rodenticide bait. These characteristics can be compared to predict the rodenticides' relative potential for such secondary risk. The elimination rate, potential to accumulate within body tissues, time to death, and toxicity to both primary and secondary consumers influence exposure and risk.

A compound that is rapidly metabolized or excreted from a primary consumer likely results in a lesser secondary risk to non-target predators and scavengers than one that accumulates with repeated exposure, even if repeated exposure occurs weeks or months after initial exposure (Eason and Murphy 2000). Compounds that more rapidly clear from the body are less likely to pose secondary risk because the rodenticide is less able to accumulate to a level sufficient to affect a secondary consumer. Time to death also influences the potential for exposure, because compounds that kill rapidly would prevent the primary consumer from

continuing to eat bait, thereby consuming a dose that would be toxic to a secondary consumer. Rodenticides that are slower to cause death also prolong the period when contaminated (and potentially more vulnerable) prey are available to predators. The toxicity of the rodenticide to the secondary consumer would also affect the risk of adverse effects that would result from exposure. Based on these characteristics, rodenticides that are eliminated more slowly and have greater potential to accumulate within body tissues, take longer to kill the primary consumer, and have greater toxicity to secondary consumers are expected to present greater secondary exposure risk. Below is an evaluation of the elimination and accumulation potential for each of the assessed chemicals.

i. Accumulation and Elimination

Information available from residue studies in primary consumers indicates that, of the anticoagulants, brodifacoum and difethialone accumulate in body tissues to a greater extent than warfarin, chlorophacinone, and diphacinone. Data from these types of studies are not available for bromethalin, but the opportunity for primary consumers to feed on bromethalin bait and accumulate the rodenticide is limited due to this chemical's rapid mode of action and the likelihood that target animals will stop feeding after a toxic dose is reached (Pitt et al. 2011). In addition, an available secondary feeding study shows that dogs consuming 600 g of bromethalin-contaminated rat meat for 14 days did not show overt signs of bromethalin toxicity. While rats in this study were exposed to one half of the bromethalin found in currently registered bromethalin baits, these data suggest that bromethalin is not likely retained in body tissues in toxicologically significant amounts.

Available toxicokinetic data also indicate that, of the anticoagulants, brodifacoum is more persistent in animal tissue than all of the other rodenticides considered in this assessment. In one

study, brodifacoum was detected in rat livers up to 200 days post exposure to a single oral dose of 0.2 mg a.i./kg (Hawkins et al. 1991), and up to 11.7% was detected in livers of rats after 104 weeks following a single dose of 0.15 mg a.i./kg (Batten and Bratt 1990). Other studies reviewed by the Agency provide further evidence of the long-term retention of brodifacoum in body tissues, and half-lives range up to 307.4 days in liver tissue and 91.7 days in plasma (Vandenbroucke et al. 2008).

The study by Vandenbroucke et al. (2008) shows that difethialone may be much less persistent in the body than brodifacoum, with a liver half-life of 28.5 days and a plasma half-life of 38.9 days.

However, other studies submitted to EPA (Belleville 1986 and 1991, MRID#s 42065010 and 42065009 respectively) indicate that the half-life of difethialone may be several times greater than Vandenbroucke et al (2008). Belleville (1991) calculated a half-life for difethialone of 74 days in liver.

Biological persistence data available for warfarin show variation among the species tested; however, most of the information on tissue retention indicates that it is generally less persistent in the body than brodifacoum and difethialone. A liver half-life of up to 66.8 days has been calculated for warfarin in rats (Vandenbroucke et al. 2008), and other estimates are less than this value. Most data indicate that the plasma half-lives are less than 1 day (Pyrola 1968, Breckenridge et al. 1985, and Eason et al. 1999).

Available data also show that chlorophacinone and diphacinone are more persistent than warfarin, but less persistent than brodifacoum and difethialone. Liver and plasma half-lives for chlorophacinone are 35.4 days and 11.7 days (Vandenbroucke et al. 2008), respectively and a plasma half-life of 0.4 days has also been calculated (Belleville 1991). Half-lives for

diphacinone have been estimated to be shorter in some species (ranging from 3 – 5.43 days), but liver retention times in cattle were determined to be >90 days (Fisher 2006, Fisher et al. 2003, Bullard et al. 1976).

Available data on the non-anticoagulant rodenticide bromethalin suggest that it is rapidly eliminated by the body. While there are no data on the elimination half-life of bromethalin in liver, a metabolism study conducted in rats indicated a plasma half-life of 5.6 days.

Owing to the lack of available whole-body elimination data for all assessed rodenticides, liver half-lives were selected from the range of available data as a conservative representation of whole body elimination in animals consuming bait. If liver half-lives were not available, as in the case of bromethalin, the blood plasma half-life was used. In order to allow for comparisons of half-lives among chemicals, liver half-lives for brodifacoum, difethialone, warfarin, and chlorophacinone from the same study (by Vandenbroucke et al. (2008)) were selected. Although this approach reduces variability due to differences attributed to laboratories, it is not necessarily the most conservative approach. For instance, the liver half-life value for difethialone reported by Vandenbroucke (28 days) is lower than provided in other studies (74 days from Belleville, 1991). Though a liver half-life value is available for diphacinone, it is based on a study on pigs, rather than the rats used in the other studies. There is some indication from the available half-life studies that different species react differently to anticoagulant rodenticides. Therefore, the pig value may overestimate or underestimate the liver half-life of rats for diphacinone. For bromethalin, there are no available data on the liver half-life, so a blood plasma value was used instead. It is uncertain how a blood plasma half-life would differ from the liver half-life for this chemical. The half-lives that were used to estimate doses of each rodenticide in non-target and target animals are provided in Table 12.

Table 12. Elimination half-lives for certain rodenticides based on elimination rates from liver.		
Rodenticide	**Elimination half-life (days)**	**References**
Brodifacoum	307.4	Vandenbroucke et al. 2008
Difethialone	28.5	Vandenbroucke et al. 2008
Warfarin	66.8	Vandenbroucke et al. 2008
Chlorophacinone	35.4	Vandenbroucke et al. 2008
Diphacinone	5.4	Fisher 2006
Bromethalin	5.6*	MRID 0004724
*Value is based on elimination from blood plasma.		

ii. Potential to Accumulate a Lethal Dose

Many of the assessed rodenticides typically cause mortality several days after exposure, which may allow target rodents to feed for several days upon rodenticide bait before dying. Such repeated feeding can lead to doses that far exceed the lethal dose. To compare the extent to which an accumulated dose may exceed the median lethal dose of target animals, EPA calculated estimated doses at the time of death assuming that target rodents continued to consume anticoagulant baits at the same rate until the date when mortality was observed in acute oral toxicity studies. For rodents exposed to baits containing 0.25% warfarin, doses were estimated to be 4 to 94 times the LD_{50} at the time of death. For rodents exposed to chlorophacinone and diphacinone, estimated doses at the time of death ranged from 3 to 13 times the LD_{50}. In contrast, for rodents exposed to brodifacoum and difethialone, estimated doses at the time of death ranged from 9 to 82 times the LD_{50}.[15] This analysis indicates that target rodents that

[15] For rodents exposed to bromethalin, similar calculations would predict estimated doses at the time of death ranging from 2 to 16 times the LD_{50}. However, bromethalin is not expected to result in elevated levels in target rodents because one effect of bromethalin poisoning is that the animals stop feeding soon after attaining a lethal dose.

continue consuming anticoagulant rodenticide bait after reaching a lethal dose may accumulate rodenticide doses that are many times the levels that are sufficient to cause mortality. Elevated residues resulting from repeated consumption of bait poses increased risk for secondary consumers that prey upon poisoned rodents because the secondary consumers receive high doses of rodenticides. Although all anticoagulants present risks that target rodents may bear rodenticide concentrations in excess of the lethal dose, this risk is clearly higher for the SGARs difethialone and brodifacoum.

3. Assessment Based on Calculated Residues in Prey

a. Methodology

Exposure for secondary consumers was estimated by calculating the amount of rodenticide in target rodents (i.e., house mouse and Norway rat) that represent potential prey. As with the primary assessment, EPA's secondary risk assessment estimated exposure using allometric equations of daily food intake from the Wildlife Exposure Factors Handbook (EPA 1993). Rodenticide intake based on consumption of bait by the primary consumers (prey) was calculated for the house mouse (23 g) and Norway rat (485 g). For this analysis, rodenticide accumulation in prey over three different time periods (1, 3 and 6 days) was calculated. These time periods were used as representative time periods that target rodents may survive after the initial daily dose of a pesticide (based on available toxicity studies) and in order to bracket the available data from residue studies submitted to the Agency and reported in open literature. Accumulation was determined based on daily food intake rates for the prey, conservatively assuming 100% of their diet consisted of dry bait. It was assumed that the form of the bait would not influence intake. Based on the assumed weight of the primary consumers, the percent active

ingredient in the bait, and daily food intake, the concentration within the prey animal at the end of a day's feeding was determined. Accumulation of rodenticide within the prey animal over time was calculated using an elimination rate constant based on the liver half-lives for each chemical (described above). This analysis is expected to produce a conservative estimate of exposure.

In addition to the estimates of rodenticide residues in target rodents representing prey of secondary consumers, empirically measured rodenticide concentrations in carcasses of rodents were used to represent potential exposure values for secondary consumers. Although this method of representing concentrations of rodenticides in prey of secondary consumers would be expected to be less conservative than the estimates described in the previous paragraph, both analyses produced similar findings.

Dose-based exposure to secondary consumers was assessed for mammals weighing 50g, 1000g, or 3000g, and birds weighing 100g, 1000g, or 5000g. These weights were selected based on the range of secondary consumers identified in rodenticide incidents in the Environmental Incident Information System (EIIS) database. The generic bird and mammal equations for food intake (Wildlife Exposure Factors Handbook) were used to calculate the daily rodenticide intake for predator/scavenger birds and mammals consuming house mice and Norway rats exposed to rodenticide bait for three or six days. Dose-based RQs were calculated by dividing the dose-based exposure values from the estimated dose by the adjusted LD_{50} values.

In addition, dietary-based RQs were calculated for secondary consumers. This was accomplished by dividing the estimated concentrations of rodenticides in target rodents by the LC_{50} values for birds or mammals.

b. Risk Estimation

Based on acute exposure of predator and scavenger birds to rodenticides accumulated in prey organisms, RQs for brodifacoum and difethialone exceed the Agency's acute LOC regardless of assessed weight class, prey organism consumed, or accumulation scenario. RQs calculated for warfarin, diphacinone, and chlorophacinone do not exceed the acute LOCs for birds, except for small predator and scavenger birds consuming prey exposed to the higher concentration of warfarin (0.054%) bait for six days. The results for bromethalin fall in between the two anticoagulant groups, as bromethalin RQs exceed the acute LOC for all predator and scavenger birds consuming small prey animals (i.e., house mice), but do not exceed the acute LOC for large predator and scavenger mammals consuming large prey animals (i.e., Norway rats). When considering dietary-based exposures of predator and scavenger birds to rodenticides, brodifacoum and difethialone RQs exceed the acute LOC, while warfarin, chlorophacinone, diphacinone, and bromethalin RQs do not exceed the acute LOC. Secondary bird RQs are provided in Table 13. Although warfarin, chlorophacinone, and diphacinone RQs for secondary birds do not exceed the acute LOC, there is uncertainty associated with these values. Available data suggest that some predatory birds may be substantially more sensitive to diphacinone exposure compared to the bobwhite quail and mallard ducks that are the source of the majority of the avian toxicity data. If bobwhite quail and mallard ducks are significantly less sensitive to anticoagulant rodenticides than predatory birds, then the secondary bird RQs calculated for these chemicals may not be conservative.

For predator and scavenger mammals exposed to rodenticides accumulated in prey, RQs for all assessed chemicals exceed the acute LOC, except for predator and scavenger mammals exposed to a three day accumulation of chlorophacinone in large prey animals and small

predators/scavengers exposed to a six day accumulation of chlorophacinone in large prey animals. Dietary-based RQs exceed the acute LOC for all of the assessed rodenticides for which relevant data were available. Dietary toxicity data in mammals are not available for difethialone or bromethalin so these chemicals were not included in this analysis. Secondary exposure RQs for birds are provided in Table 13; secondary exposure RQs for mammals are provided in Table 14.

Table 13. RQs from the bird risk assessment: secondary exposure of predator/scavenger birds to residues in consumed rodents.

		Body weights (g)	Second Generation Anticoagulants		First Generation Anticoagulants				Non-Anti-Coagulant
			Brodifacoum	Difethialone	Warfarin (0.025%)	Warfarin (0.054%)	Chlorophacinone	Diphacinone	Bromethalin
Secondary exposure to carnivores and scavengers	**House mouse consumption: 3 day accumulation in prey RQ**	**100**	**20***	**17***	0.14	0.30	0.04	0.01	**4.1***
		1000	**15***	**5.4***	0.04	0.09	0.01	<0.01	**1.3***
		5000	**13***	**2.4***	0.02	0.04	0.01	<0.01	**0.58***
	Norway rat consumption: 3 day accumulation in prey RQ	**100**	**5.3***	**4.5***	0.04	0.08	0.01	<0.01	**1.1***
		1000	**4.1***	**1.4***	0.01	0.02	<0.01	<0.01	0.34
		5000	**3.4***	**0.64***	0.01	0.01	<0.01	<0.01	0.15
	House mouse consumption: 6 day accumulation in prey RQ	**100**	**39***	**33***	0.27	**0.58***	0.08	0.01	**NA**
		1000	**31***	**10***	0.09	0.19	0.02	<0.01	**NA**
		5000	**16***	**4.7***	0.04	0.08	0.01	<0.01	**NA**
	Norway rat consumption: 6 day accumulation in prey RQ	**100**	**10***	**8.7***	0.07	0.15	0.02	<0.01	**NA**
		1000	**8.1***	**2.8***	0.02	0.05	0.01	<0.01	**NA**
		5000	**6.8***	**1.2***	0.01	0.02	<0.01	<0.01	**NA**
	House mouse consumption: dietary RQ	NA	**18***	**21***	0.19	0.41	0.32	0.02	0.20
	Norway rat consumption: dietary RQ	NA	**4.7***	**5.5***	0.05	0.11	0.09	<0.01	0.05

NA = not applicable ND = no data * RQ exceeds acute risk LOC = 0.50

Table 14. RQs from the mammal risk assessment: secondary exposure of predator/scavenger mammals to residues in consumed rodents.

			Second Generation Anticoagulants		First Generation Anticoagulants				Non-Anti-Coagulant
		Body weights (g)	Brodifacoum	Difethialone	Warfarin (0.025%)	Warfarin (0.054%)	Chloro-phacinone	Dipha-cinone	Bromethalin
Secondary exposure to carnivores and scavengers	House mouse consumption: 3 day accumulation in prey RQ	50	11 *	4.7*	8.8*	19*	0.84*	2.5*	4.3*
		1000	14*	5.9*	11*	24*	1.0*	3.1*	3.5*
		3000	15*	6.4*	12*	26*	1.1*	3.4*	5.8*
	Norway rat consumption: 3 day accumulation in prey RQ	50	2.9*	1.3*	2.3*	5.0*	0.22	0.66*	1.1*
		1000	3.7*	1.6*	2.9*	6.3*	0.27	0.82*	1.4*
		3000	4.0*	1.7*	3.1*	6.8*	0.30	0.89*	1.5*
	House mouse consumption: 6 day accumulation in prey RQ	50	22*	9.2*	17*	37*	1.6*	4.2*	NA
		1000	27*	11*	22*	47*	2.0*	5.2*	NA
		3000	30*	12*	23*	50*	2.2*	5.6*	NA
	Norway rat consumption: 6 day accumulation in prey RQ	50	5.9*	2.4*	4.6*	9.9*	0.43	1.1*	NA
		1000	7.3*	3.0*	5.7*	12*	0.53*	1.4*	NA
		3000	7.9*	3.3*	6.2*	13*	0.58*	1.5*	NA
	House mouse consumption: dietary RQ	NA	45*	ND	27*	58*	20*	10*	ND
	Norway rat consumption: dietary RQ	NA	11*	ND	7.0*	15.23*	5.4*	2.7*	ND

NA = not applicable ND = no data * RQ exceeds acute risk LOC = 0.50

4. Whole Carcass Residue Analysis

a. Methodology

As discussed above, EPA also assessed secondary risks by analyzing residues in test animals that had consumed contaminated carcasses. This analysis differs from the carcass concentration-based risk assessment described previously in that it makes use of measured residues in intoxicated target organisms as a basis for dietary exposure in scavengers and predators. Using actual animal concentrations eliminates some uncertainty associated with bait feeding, absorption, and elimination rates used in the previous assessment. However, alone, this method is limited by the types and magnitude of rodenticide exposure in the prey base (i.e., the animals intoxicated at the primary exposure level). A concordance of risk conclusions made using this method with conclusions based on the previous method allows for more confidence in the risk conclusions overall; however, if the empirically-based RQs calculated in this section do not exceed the LOC, risk cannot necessarily be precluded, especially if the previously estimated RQs do exceed the LOC.

In field and laboratory studies, rodenticide whole-carcass residues were determined in mammals after exposure to bait. Data are available for a variety of small and medium sized mammalian granivores and omnivores exposed to brodifacoum, difethialone, warfarin, chlorophacinone and diphacinone. No such residue data were identified for bromethalin. These measured residue concentrations were also used as the exposure component of the RQ for predators and scavengers in the same manner as the calculated residue values previously described.

b. Risk Estimation

The acute LOC was exceeded for secondary exposure risk to birds for brodifacoum and difethialone; however, RQs for secondary exposure risk to birds exposed to warfarin did not exceed the acute LOC. RQs for secondary exposure risk to birds exposed to chlorophacinone or diphacinone on an acute basis did not exceeded the acute LOC. Carnivore/scavenger mammalian RQs for brodifacoum and difethialone exceeded the acute LOC. For warfarin, chlorophacinone, and diphacinone, RQs did not exceed the acute LOC, as shown in Table 15.

Table 15. Secondary Acute RQs based on a Single-dose of Rodenticide through Consumption of Contaminated Carcasses

Predator	**Birds**			**Mammals**		
Predator Weight Class	**100 g**	**1000 g**	**5000 g**	**50 g**	**1000 g**	**3000 g**
Brodifacoum	**6.4***	**5.0***	**4.2***	**3.6***	**4.5***	**4.8***
Difethialone	**4.6***	**1.5***	**0.66***	**1.4***	**1.8***	**1.9***
Warfarin	< 0.01	< 0.01	< 0.01	0.26	0.32	0.34
Chlorophacinone	< 0.01	< 0.01	< 0.01	0.07	0.08	0.08
Diphacinone	< 0.01	< 0.01	< 0.01	0.19	0.23	0.25
Bolded (*) RQs exceed acute risk LOC (0.5).						

Avian and mammalian RQs based on five-day dietary studies are provided in Table 16. Carnivore and scavenger bird RQs for brodifacoum and difethialone exceeded acute risk LOCs. Warfarin RQs for carnivore and scavenger birds did not exceed any LOCs. RQs for birds exposed to chlorophacinone and diphacinone in their diet do not exceed acute risk LOCs. For carnivore and scavenger mammals, RQs for brodifacoum, warfarin and chlorophacinone exceed the acute risk LOC. There are no available mammalian dietary data for difethialone, bromethalin, or diphacinone.

Table 16. Secondary Dietary RQs based on a 5-day Exposure of Rodenticide through Consumption of Contaminated Carcasses		
	Birds	**Mammals**
Brodifacoum	**5.3***	**13***
Difethialone	**5.5***	ND
Warfarin	< 0.01	**0.67***
Chlorophacinone	0.02	**1.4***
Diphacinone	< 0.01	ND
ND = no data Bolded (*) RQs exceed acute risk LOC (0.5).		

5. Secondary Feeding Studies

Secondary feeding studies address a number of uncertainties associated with the quantitative dose-based risk estimation methods using estimated or empirically based prey-base concentrations estimates of rodenticide. The feeding studies empirically account for primary organism feeding, absorption and elimination uncertainties surrounding the estimated dose-based assessment. They also account for uncertainties associated with biological availability of rodenticide from consumed prey and assumptions of predator/scavenger sensitivity to the rodenticide which are present in both of the dose-based risk estimation methods. Concordance between risk conclusions between all three methods constitutes enhanced confidence in the overall risk conclusions made for predators and scavenging wildlife.

Concerns for secondary risks with brodifacoum are supported by available data from secondary toxicity studies showing mortality in 63% of predator/scavenger birds and 42% of predator/scavenger mammals fed brodifacoum contaminated target organisms. No secondary feeding data are available for difethialone.

In the case of warfarin, mammalian secondary feeding studies involving mammal predators/scavengers show mixed results and for some species the differences extended to a

dose-dependent response. No mortalities were observed in raccoons and European ferrets (no dose dependency and bait concentrations equal to or higher than levels found in US registered products). Other studies showed mortalities in mink, least weasels and dogs, although the results often involved few test organisms. Avian secondary feeding studies of warfarin involved testing of four species. In three of the four species tested there was no observed mortality. Interestingly, the results from feeding tests do not completely parallel the results of the quantitative secondary risk assessment where risks were expected for small birds exposed to prey contaminated with higher concentrations of warfarin bait. For example no mortality was observed in the feeding studies with black-billed magpies (~170 g bodyweight) while the risk assessment suggests a concern for a 100 gram bird. Conversely, mortality results were mixed in larger birds of similar weights (death in barn owls but not in tawny owls both ~400-500 g body weight). These discrepancies suggest that allometric relationships for predicting effects of warfarin toxicity may incompletely explain the factors contributing to species sensitivity variability.

Bromethalin secondary feeding studies are limited to a single case. In that study involving domestic dogs fed intoxicated rats there were no mortalities (n=4). The number of species tested is limited; therefore, there is insufficient evidence from these data alone to make definitive conclusions regarding the accuracy of the secondary quantitative risk assessment results. While these data are not sufficient to make definitive conclusions, they do indicate that bromethalin may not be retained in body tissues in toxicologically significant amounts as discussed previously. No bird feeding studies were available for bromethalin.

Chlorophacinone secondary toxicity results include studies with five mammal species. Mortality responses were variable and ranged from approximately 50 percent to 100 percent of

individuals tested. In one single species, European ferret, different studies yielded highly variable results, ranging from zero to 100 percent mortality. It should be noted again that all these studies involve a low number of test individuals and differences in perceived sensitivity may be as much a product of low number of individuals as from real differences in toxic response across species. Avian feeding studies with chlorophacinone span 10 species with a wide range of bodyweights (170 to 4400 g). In no cases were mortalities observed. This finding is consistent with the secondary risk assessment.

Diphacinone secondary feeding data span studies from seven mammal species. The effects range from 0 to 100 percent mortality. Of particular note is the study involving actual secondary feeding with rats. This study is of note because (1) the secondary exposure risk assessment used a rat acute toxicity endpoint as a surrogate for predators and scavengers and (2) the assumed prey item concentrations in the risk assessment were 10 to 20 times higher than tested in the feeding study. The feeding study with rats yielded a 50 percent mortality response under conditions of similar toxicity and lower exposure than modeled conditions showing risk. Looking back on the quantitative risk results, substituting the modeled diphacinone dietary concentrations with the actual concentrations used in the feeding study would still trigger secondary acute risk concerns. These results are considered supportive of the secondary risk assessment with mammals. Avian feeding studies with diphacinone span five species of varying bodyweights. In three species there were no mortalities, consistent with the secondary risk assessment results. In the case of two owl species, mortalities were observed contrary to what the risk assessment results suggested. As discussed earlier, the toxicity endpoint relied upon in the risk assessment may underestimate the sensitivity of raptoral species to this chemical.

6. Estimation of number of prey animals equal to median lethal dose in secondary animals

As evaluated in the secondary exposure risk assessment, residues were estimated and observed to reach levels in target organisms that, when consumed by predators and scavengers can result in death. When considering those risks among the assessed rodenticides it is important to consider the likelihood of predators and scavengers encountering enough intoxicated target prey to reach potential lethal doses. Furthering the evaluation of secondary exposure of rodenticides are the results of analyses of the number of individual target organisms necessary for dietary consumption to achieve a lethal dose in predators and scavengers. The fewer the number of intoxicated target organisms necessary to reach a lethal dose, the less efficiently and intently a predator or scavenger must locate and consume these organisms to reach lethal body burdens. The analysis considered different bodyweights of predator/scavengers consuming either rats or mice which have ingested bait for a single day or up to six days. Again, compounds that can present a lethal dose to predators and scavengers after consumption of target organisms with only a single day of exposure are likely to represent greater opportunities for lethal secondary exposure events than those which require multiple days of target organism exposure.

Analyses were conducted to determine the number of rodenticide-intoxicated target organism a predator/scavenger mammal would need to consume in order to trigger lethal incidents (Table 17). Based on these analyses, every size predator/scavenger mammal exposed to brodifacoum through consumption of rats would only need to consume a fraction of a single target organism to reach lethal endpoint exposures, even if the rat fed on brodifacoum bait for just one day. Comparing brodifacoum results for predator/scavenger mammals to other assessed

rodenticides does not reveal a marked difference among the chemicals. Owing to their smaller size, consumption of brodifacoum intoxicated mice must be slightly more intensive for the predator/scavengers to reach lethal endpoint exposure (<1 to 5 organisms) as compared to rats. These results are not atypical of the results for difethialone, warfarin and bromethalin assessed rodenticides. However, the amount of brodifacoum that must be consumed to reach lethal exposure is substantially lower than diphacinone and chlorophacinone.

Table 17. Secondary Exposure to Predator and Scavenger Mammals: Number of animals consumed to reach the LD_{50}

	Body Weights (g)	Brodif-acoum	Difeth-ialone	Warfarin (0.025%)	Warfarin (0.054%)	Chloro-phacinone	Dipha-cinone	Brometh -alin
1-Day Accumulation in Prey								
House Mice	**100**	<1	<1	<1	<1	3	<1	<1
	1000	2	5	3	1	27	8	5
	5000	5	11	6	3	60	18	11
Norway Rats	**100**	<1	<1	<1	<1	<1	<1	<1
	1000	<1	<1	<1	<1	5	1	<1
	5000	<1	2	1	<1	11	3	2
6-Day Accumulation in Prey*								
House Mice	**50**	<1	<1	<1	<1	<1	<1	<1
	1000	<1	<1	<1	<1	5	2	2
	3000	<1	2	<1	<1	11	4	4
Norway Rats	**50**	<1	<1	<1	<1	<1	<1	<1
	1000	<1	<1	<1	<1	<1	<1	<1
	3000	<1	<1	<1	<1	2	<1	<1

* For bromethalin, numbers are based on 3-day accumulation in prey

Similar analyses were conducted to determine the target organism numbers necessary to trigger lethal incidents in scavenger/predator birds (Table 18). Brodifacoum results show consumption of only a fraction of an intoxicated rat, regardless of rat exposure duration, is needed to reach lethal endpoint exposures in all bird sizes modeled. These results with brodifacoum are similar to results with difethialone, but are greater for the other assessed

rodenticides, particularly for warfarin. Because house mice are much smaller than Norway rats, avian predators or scavengers generally must ingest more house mice than Norway rats in order to attain a lethal dose, but ingestion of only <1 to 5 house mice intoxicated by brodifacoum would be sufficient to cause lethal secondary poisoning. With difethialone, consuming less than one intoxicated house mouse would be expected to kill a 100-g avian predator or scavenger, but the numbers of mice needed to kill birds at the 1000-g and 5000-g sizes are somewhat greater with difethialone than brodifacoum. Depending on the size of the predator or scavenger bird, slightly to many times more bromethalin-intoxicated mice would be needed to cause lethal secondary poisoning than would be the case with either of the SGARs brodifacoum or difethialone. However, similar analyses conducted with warfarin, chlorophacinone, and diphacinone reveal that avian predators and scavengers must consume many more intoxicated mice to reach lethal exposure endpoints than is the case with brodifacoum or difethialone. When taken together, these analyses suggests that brodifacoum has a substantially greater opportunity than these other active ingredients to result in lethal incidents following exposure of a predator/scavenger bird to intoxicated target organisms.

Table 18. Secondary Exposure to Predator and Scavenger Birds: Number of animals consumed to reach the LD_{50}

	Body weights (g)	Brodif-acoum	Difeth-ialone	Warfarin (0.025%)	Warfarin (0.054%)	Chloro-phacinone	Dipha-cinone	Brometh-alin
1-Day Accumulation in Prey								
House Mice	**100**	<1	<1	38	18	130	821	1
	1000	2	4	539	249	1836	11602	16
	5000	5	27	3429	1587	11690	73852	104
Norway Rats	**100**	<1	<1	7	3	23	147	<1
	1000	<1	<1	97	45	329	2079	3
	5000	<1	5	614	284	2094	13232	17
6-Day Accumulation in Prey*								
House Mice	**50**	<1	<1	7	3	23	183	<1
	1000	<1	<1	92	43	321	2590	6
	3000	<1	5	586	271	2045	16483	39
Norway Rats	**50**	<1	<1	1	<1	4	33	<1
	1000	<1	<1	17	8	58	464	1
	3000	<1	<1	105	49	366	2953	7

* For bromethalin, numbers are based on 3-day accumulation in prey

7. Probabilistic Analysis

EPA conducted a probabilistic analysis that addressed the two comparative variables of whole body half life and toxicity to inform the level of confidence and explore uncertainty in the likelihood that a randomly selected predator or scavenger birds may achieve a lethal rodenticide dose. This was accomplished using a Monte Carlo simulation with a distribution of possible outcomes that were analyzed to allow for more thorough understanding of the uncertainties associated with the available data. The modeling exercise was performed by varying selected parameters for liver or blood-plasma half-life and the LD50 or LC50. The metric for comparing chemicals was based on probability density functions for percentage of species with RQs above the acute LOC value of 0.5. This represents the likelihood that a bird feeding on prey containing rodenticide could receive a dose of that rodenticide that may pose a risk to the secondary

consumer. Although the results presented below focus on birds at risk through secondary exposure, an equivalent analysis was conducted for predator/scavenger mammals. The probabilistic assessment for mammals at risk through secondary exposure sheds no new light on the issues in the proposed cancellations, as it simply confirms, as did the Agency's deterministic assessment, that rodenticides designed to target mammalian species will be toxic to mammals regardless of whether they are primary or secondary consumers. However, the enhanced toxicity and extended residence time in non-target animals suggests that bioaccumulation potential and resulting secondary poisoning potential of brodifacoum and difethialone are greater relative to the other assessed rodenticides. The probabilistic analysis conducted by EPA is described in more detail in "Probabilistic Analysis Associated with Avian Risks from Exposure to Brodifacoum, Difethialone, Chlorophacinone, Diphacinone, Warfarin, or Bromethalin" (Riley 2013).

Ten thousand RQs were calculated for 100-g, 1000-g, and 5000-g birds consuming mice or rats that are primary consumers of rodenticides based on 10,000 randomly sampled LD50 and half-life values. For each rodenticide, the values in Table 19 provide the percentage of calculated RQs that were above the LOC for birds when toxicity and exposure parameters were randomly sampled. These percentages allow for the comparison of risks among chemicals where larger percentage values suggest a higher likelihood that a randomly selected bird may achieve a lethal dose under the assumptions of this analysis. Based on this analysis, birds have a high likelihood of receiving a dose sufficient to pose a risk of mortality when consuming prey species intoxicated with brodifacoum or difethialone, even after 1 day of accumulation in the prey. However, the likelihood of risk from exposure to difethialone is less than the likelihood of risk from exposure to brodifacoum, especially for large birds consuming intoxicated prey animals.

Relative to the risks of brodifacoum and difethialone, there is a lower likelihood for birds consuming prey contaminated with warfarin to receive a dose sufficient to pose a risk of mortality. Chlorophacinone and diphacinone have a low likelihood of posing a risk of mortality, relative to the other assessed rodenticides. However, it should be noted that sensitive 100-g birds (e.g., American kestrels) feeding on small mammals exposed to diphacinone bait for an extended period of time may be at risk.

For bromethalin, there is a high likelihood of risk exceeding concern levels for small birds consuming small mammals exposed to bromethalin bait for 1 day. However, small birds consuming large prey organisms and larger birds consuming either small or large prey items have a low likelihood of risk exceeding concern levels from exposure to bromethalin. In addition, it is important to note that several factors suggest that bromethalin poses a lower risk to birds from secondary exposure, relative to brodifacoum and difethialone. These factors include: 1) target animals tend to stop feeding after consumption of toxic doses of bromethalin; therefore, they are less likely to carry residue levels in excess of toxic doses; and 2) available data suggests that bromethalin is eliminated quickly from target and non-target animals relative to the other chemicals; therefore, bromethalin levels are not likely to increase after long-term low-dose exposure, like chemicals with longer half-lives.

Table 19. Percentage of Secondary Avian Acute Dose-Based RQs that are Greater than the LOC (0.5)

Prey	Prey Exposure Type	Brodif-acoum	Difeth-ialone	Warfarin (0.025%)	Chloro-phacinone	Dipha-cinone	Brometh-alin
100-g Birds							
house mice	**1 day**	99%	60%	5%	~0%	~0%	95%
	6 days	100%	80%	50%	~0%	~0%	NA
	14 days	100%	85%	75%	~0%	1%	NA
Norway rats	**1 day**	70%	40%	~0%	~0%	~0%	10%
	6 days	100%	65%	10%	~0%	~0%	NA
	14 days	100%	75%	30%	~0%	~0%	NA
1000-g Birds							
house mice	**1 day**	95%	40%	~0%	~0%	~0%	10%
	6 days	100%	65%	15%	~0%	~0%	NA
	14 days	100%	75%	40%	~0%	~0%	NA
Norway rats	**1 day**	60%	25%	~0%	~0%	~0%	~0%
	6 days	100%	50%	~0%	~0%	~0%	NA
	14 days	100%	60%	40%	~0%	~0%	NA
5000-g Birds							
house mice	**1 day**	95%	30%	~0%	~0%	~0%	~0%
	6 days	100%	55%	5%	~0%	~0%	NA
	14 days	100%	65%	15%	~0%	~0%	NA
Norway rats	**1 day**	50%	15%	~0%	~0%	~0%	~0%
	6 days	99%	35%	~0%	~0%	~0%	NA
	14 days	100%	50%	~0%	~0%	~0%	NA

NA- not applicable. Animals consuming bromethalin are not expected to continue feeding on bromethalin bait for six or fourteen days, therefore these numbers were not calculated.

For each rodenticide, the values in Table 20 provide the percentage of calculated dietary-based RQs that exceeded the LOC for birds when toxicity and exposure parameters were randomly sampled. Based on this analysis, birds have a high likelihood of receiving a dose sufficient to pose a risk of mortality when consuming prey species intoxicated with brodifacoum

and difethialone on a dietary basis. For warfarin and chlorophacinone there is little chance of predator/scavenger birds receiving a dose that may pose a risk of mortality, except under high accumulation scenarios. Again, birds feeding on diphacinone and bromethalin contaminated animals have a lower likelihood of exceeding concern levels relative to the other rodenticides evaluated.

Table 20. Percentage of Acute Dietary-Based RQs for Birds that are Greater than the LOC.

Prey Exposure Type	Brodifacoum	Difethialone	Warfarin	Chlorophacinone	Diphacinone	Bromethalin
House Mouse as prey						
1 day	100%	100%	~0%	~0%	~0%	~0%
6 days	100%	100%	1%	15%	~0%	NA
14 days	100%	100%	15%	60%	~0%	NA
Norway Rat as prey						
1 day	95%	50%	~0%	0%	~0%	~0%
6 days	100%	100%	~0%	0%	~0%	NA
14 days	100%	100%	~0%	5%	~0%	NA

NA- not applicable. Animals consuming bromethalin are not expected to continue feeding on bromethalin bait for six or fourteen days.

8. Summary of secondary exposure risks

The assessment of secondary exposure risks for wildlife involved a series of assessment methodologies that encompassed both estimated accumulation of rodenticides in a prey base as well as empirical measurements of rodenticide residues in prey. This assessment concluded that all of the assessed rodenticides pose a risk of mortality to predator and scavenger mammals via secondary exposure. In addition, some of the rodenticides pose a risk of mortality to predator and scavenger birds via secondary exposure. Based on the analysis of the number of prey

organisms that would have to be consumed in order for predators and scavengers to receive an LD_{50} dose and the probabilistic analysis, the following conclusions can be made for risk to birds:

- Brodifacoum and difethialone pose greater secondary exposure risk to birds relative to the other chemicals assessed regardless of exposure scenario.
- Bromethalin may pose secondary exposure risk to certain sensitive species (*i.e.*, small birds consuming small prey animals); however, potential for secondary risk is somewhat limited due to the lower likelihood of continuous feeding of prey after reaching a lethal threshold and rapid mortality observed in primary feeding studies with bromethalin. Risks to small birds consuming large prey animals and risks to medium and large birds consuming small or large prey animals are substantially lower than for brodifacoum and difethialone.
- Warfarin may pose risk to certain sensitive species, especially under high accumulation scenarios; however, the likelihood of secondary exposure to exceed the LOC for warfarin is substantially lower than for brodifacoum and difethialone.
- Diphacinone does not have a high likelihood of triggering secondary risk concerns regardless of accumulation scenario assessed. However, results of the probabilistic analysis indicate that there is a possibility that the most sensitive smaller secondary avian consumers modeled may be at risk from diphacinone poisoning under the highest accumulation scenario. Secondary exposure risks for diphacinone are substantially lower than for brodifacoum and difethialone.
- For chlorophacinone, results for the acute dose-based exposure scenarios demonstrate a low likelihood of secondary exposure concerns. However, results of the probabilistic assessment conducted for dietary-based exposure indicate that chlorophacinone may have

a greater likelihood of posing risk to predator/scavenger birds under the higher accumulation scenarios than the one-day accumulation scenario. While these results represent a departure from the other analyses, the likelihood of secondary exposure risk for chlorophacinone is still substantially lower than for brodifacoum and difethialone.

9. Incident Findings Related to Primary & Secondary Risk Analyses

The quantitative risk assessment does not evaluate the actual potential for wildlife to come into contact with treated bait; it simply evaluates the consequences of exposure. To determine if any documented adverse effects have been reported, indicating complete exposure pathways, EPA looks to available incident and exposure information from a variety of sources, including state and local governments and pesticide registrants. The majority of available reported incidents for the rodenticides assessed are included in EPA's Environmental Incident Information System (Version 2.1) EIIS. EPA believes these data offer strong support for the conclusion that residential use of rodenticides in urban/suburban and rural areas provide complete exposure pathways for a variety of wildlife, and that both primary and secondary exposures can cause mortality in non-target wildlife. Table 21 presents the total number of reported incidents associated with each of the rodenticides considered in EPA's assessment. Where possible, EPA distinguished between incidents resulting from primary and secondary exposures. Additional details on these incidents are tabulated in Compilation of Rodenticide Wildlife Mortality Incidents Reported Between 1971-2012 (EPA 2013).

Table 21. Total Number of Wildlife Incidents by Rodenticide Active Ingredient and Exposure Type, Occurring between 1971 and 2012.

Rodenticide Active Ingredient	Exposure Type						Total	
	Primary		Secondary		Unknown			
Brodifacoum	72		202		39		313	
	Birds 4	Mammals 68	Birds 176	Mammals 26	Birds 21	Mammals 18	Birds 201	Mammals 112
Difethialone	1		5		0		7	
	Birds 0	Mammals 1	Birds 5	Mammals 1	Birds 0	Mammals 0	Birds 5	Mammals 2
Chlorophacinone	6		5		3		14	
	Birds 3	Mammals 3	Birds 3	Mammals 2	Birds 1	Mammals 2	Birds 7	Mammals 7
Diphacinone	11		9		1		21	
	Birds 1	Mammals 10	Birds 5	Mammals 4	Birds 0	Mammals 1	Birds 6	Mammals 15
Warfarin	6		5		0		11	
	Birds 1	Mammals 5	Birds 5	Mammals 0	Birds 0	Mammals 0	Birds 6	Mammals 5
Bromethalin	2		0		0		2	
	Birds 0	Mammals 2	Birds 0	Mammals 0	Birds 0	Mammals 0	Birds 0	Mammals 2
Totals	**98**		**227**		**43**		**368**	
	Birds 9	**Mammals 89**	**Birds 194**	**Mammals 33**	**Birds 22**	**Mammals 21**	**Birds 225**	**Mammals 143**

* Incident counts exclude incidents with certainty levels of "unrelated" and "unlikely," incidents known to be associated with intentional misuse, and incidents associated with other active ingredients.

In evaluating EPA's incident database for rodenticides, it is important to understand that reported incidents likely represent only a fraction of the incidents that have occurred. Because of the delay between consumption of a lethal dose and death associated with the anticoagulant rodenticides considered in this analysis (all assessed rodenticides except bromethalin), the deaths of animals killed by these rodenticides typically occur at a distance, both spatially and temporally, from the site where the rodenticide was used. As a result, the cause of death generally is not obvious to persons finding animals killed by these rodenticides. Only when the mortality is reported to an authority, typically a state fish and wildlife office, and that agency conducts an investigation into the cause of death is an incident likely to be linked to

rodenticide exposure. The investigating state agency may then take tissue samples from the animal, normally from the liver, and have laboratory analyses performed to screen for the presence of various rodenticides, as well as various other pesticides. Only when the residue analysis finds one or more rodenticides in the tissue of the dead animal does the incident become diagnosed as a suspected or confirmed rodenticide incident. Because the linkage between wildlife mortalities and exposure to the rodenticides subject to the NOIC depends on thorough investigations, including residue analysis of tissue samples, incident reporting rates vary greatly from state to state and likely depend largely on whether the state has the personnel and resources to conduct and report investigations. Only two states, New York and California, have had programs that have systematically analyzed and reported wildlife mortality incidents, and thus are responsible for the majority of known rodenticide incidents. Many states have never reported any wildlife mortality incidents related to rodenticides. Given these considerations, and the fact that most dead or dying animals are never seen by humans, EPA believes the vast majority of wildlife incidents from exposure to rodenticides go unreported. The general character of the reported incidents for each chemical are briefly discussed below.

Notwithstanding the likely extent of underreporting of wildlife incidents, the available data support the quantitative risk assessment's conclusion that both primary and secondary exposure to brodifacoum poses lethal risk to a variety of sizes of mammals and birds. Mortality incidents likely to have resulted from primary exposure to brodifacoum include non-target mammalian wildlife ranging in size from chipmunks to white-tailed deer. This range is consistent with the size classes predicted to be at risk from brodifacoum in EPA's analysis above. For birds, mortality incidents likely to have resulted from primary exposure to brodifacoum involved species ranging in size from robins to geese, again consistent with the risk model predictions.

Incidents representing likely secondary exposure of mammals to brodifacoum range from kit foxes to mountain lions, consistent with the modeled size classes predicted to be at risk from brodifacoum in EPA's analysis above. Between 1971 and 2012, there were 176 total incidents of bird mortality attributed to secondary exposure to brodifacoum. For birds, incidents likely to have resulted from secondary exposure involve a variety of raptors, again consistent with the risk model predictions for larger birds. These incidents occurred in urban/suburban and rural habitats. In summary, incident data indicate that both primary and secondary exposures to brodifacoum are likely to cause mortalities among non-target wildlife in rural, suburban, and urban environments.

The incident data set for difethialone is much more limited than that for brodifacoum. Analysis of the toxicity and retention time of difethialone indicates that it is toxicologically similar to brodifacoum, suggesting that the small number of reported incidents for this ingredient could be due to the relatively low use of difethialone or to other factors not related to the intrinsic risk of the chemical. Nevertheless, one lethal incident apparently resulting from direct exposure to difethialone treated bait has been reported, involving Key deer in a suburban environment. Lethal exposures such as this incident are consistent with the conclusions of the mammalian primary exposure risk assessment. Although there are no reported incidents involving bird species and primary exposure to difethialone, the absence of reported incidents neither supports nor refutes the findings of the avian primary exposure risk assessment. Lethal incidents involving predatory birds and mammals and difethialone have been reported, consistent with the conclusions of the mammalian and avian secondary exposure risk assessments. All the reported difethialone incidents are associated with urban/suburban areas.

Warfarin incidents involving non-target wildlife generally parallel the findings of the quantitative risk assessment for primary exposure to this chemical in that primary exposure incidents have been reported, confirming that exposure pathways are complete. No incidents of secondary poisonings to non-target mammals have been reported for warfarin; however, reported incidents of birds exposed to warfarin include a variety of raptoral species presumed to be secondary consumers. These secondary exposure incidents are consistent with the quantitative secondary risk assessment and are in partial agreement with the available secondary feeding toxicity studies (warfarin secondary feeding studies showed mixed results as described in the Risk Estimation Section). Incident data indicate that secondary exposure to warfarin can cause mortalities among non-target wildlife in rural, suburban and urban environments.

The incident data set for primary exposure of animals to bromethalin is limited to two reported mortality incidents of small mammals. This limited information is consistent with a quantitative risk assessment that indicates a risk to small mammals exposed to treated bait, yet provides little support for the risk assessment predictions for larger mammals. There are no reported incidents involving bird species that appear to have resulted from primary exposure to bromethalin-treated bait, and no incidents involving either mammals or bird species that appear to have resulted from secondary exposure. Incidents involving this chemical may be under reported because, as discussed in the incident section of the ecological risk assessment, bromethalin is not commonly assayed for in investigations of wildlife mortality incidents. Thus, the lack of reported secondary exposure incidents involving bromethalin can neither support nor refute conclusions of the mammalian and avian secondary risk assessments.

There are few reported incidents where there is high certainty that mammal mortalities resulted from primary exposure to chlorophacinone bait. Reports of mortalities in squirrels

(Central Park, New York) are in agreement with the primary exposure risk assessment predictions for small mammals. No larger mammal incidents attributable to primary exposure to this chemical have been reported. An incident report where a bird (California quail in an orchard) is likely to have received a lethal dose of chlorophacinone through primary exposure suggests the possibility that chlorophacinone presents greater primary exposure risk to birds than indicated in the primary exposure risk assessment. Chlorophacinone incidents of high certainty involving likely secondary exposures of mammals and birds are also scarce, but include reports of mortalities in wild felids (bobcats) and raptors (red-tailed hawk). The mammal incidents are consistent with the secondary exposure risk assessment findings. The bird incident, however, is inconsistent with the secondary exposure risk assessment, which did not predict secondary exposure risk to birds. It is possible that raptors may be more sensitive to both chlorophacinone and diphacinone than the test species employed in the risk assessment. If the chlorophacinone secondary exposure risk assessment were adjusted for this possible increased sensitivity in raptors by assuming a 20-fold increase in sensitivity, as has been observed for diphacinone (Rattner *et al.*, 2011), then the conclusions of the dietary subacute portions of the secondary exposure risk assessment would then be consistent with reported incidents. However, the incident report would still be inconsistent with the single oral dose risk assessment. On balance, incidents indicate that chlorophacinone may cause secondary lethalities to birds, but because of attendant uncertainties inherent in incident data interpretation, they do not necessarily refute the conclusion of the risk assessments that chlorophacinone presents negligible risk to birds, and they are consistent with the conclusion that the secondary risks of chlorophacinone are considerably less than those of brodifacoum and difethialone.

The diphacinone incident data set for mammals with primary exposure is similar to that for chlorophacinone in that four incidents involved poisoning of squirrels in urban/suburban settings, but is different in that incidents have also been reported of large mammals being poisoned (two incidents of mortality of white-tailed deer in New York). The reported incidents are consistent with the prediction of the risk assessment of risk to small mammals from primary exposure. Diphacinone incidents of high certainty involving mammals and birds of likely secondary exposure are limited but include reports of mortalities in wild canids, mustilids and felids (fox, coyote, raccoon, and mountain lion) and raptors (snowy and barred owls, red-tailed hawk). The mammal incidents are consistent with the secondary exposure risk assessment findings. The bird incidents are inconsistent with the modeling portions of secondary exposure risk assessment, which did not predict significant secondary risk to birds, but are consistent with available feeding studies, especially for owls. If the diphacinone secondary exposure risk assessment were adjusted for the possible increased sensitivity in raptors, the secondary risk conclusions would still yield risk quotients below concern levels. On balance, incidents indicate that diphacinone may cause secondary lethalities to birds, but because of attendant uncertainties inherent in incident data interpretation, those incidents do not necessarily refute the conclusion of the risk assessments that diphacinone presents negligible risk to birds, and they are consistent with the conclusion that the secondary risks of diphacinone are considerably less than those of brodifacoum and difethialone.

a. Implications for Risk Mitigation

The proposed cancellations would limit the availability of brodifacoum and difethialone in ways expected to limit their use in urban and suburban areas to commercial and professional users. This change in the availability and use of brodifacoum and difethialone will reduce the

potential for wildlife to encounter these rodenticides, because residential consumers have been responsible for a large proportion of the use of these chemicals. As the quantitative risk assessment concludes, these two rodenticides present greater risk to non-target species – particularly to birds – than other rodenticides registered for general consumer use against commensal rodents. The incident reports support the quantitative risk assessment finding that bromethalin, chlorophacinone, diphacinone and warfarin present considerably less risk of primary and secondary poisoning than brodifacoum and difethialone. While the use of tamper resistant bait stations could effectively mitigate primary exposure to birds and larger mammals for all rodenticides, secondary poisoning would remain a concern for wildlife that consumes commensal mice and rats or other primary consumers that enter and consume bait from stations sized to accommodate commensal rats and/or house mice. In this regard, brodifacoum and difethialone present a greater risk of secondary poisoning when compared to other commensal rodenticides. Limiting sales of brodifacoum and difethialone in the consumer market is expected to cause most consumers to turn to one of the other available rodenticides or to use alternative mechanical controls, thereby reducing overall use of -- and wildlife exposure to -- brodifacoum and difethialone. While the replacement compounds may still present some risk of secondary poisoning, EPA believes that this change will greatly reduce the risk of adverse effects to non-target wildlife.

The NOIC also proposes the cancellation of certain consumer commensal rodent control products because they are not sold in or with bait stations reasonably anticipated not to release rodenticide bait. Although labels of these products currently require consumers to use tamper resistant bait stations if bait is placed where it would otherwise be accessible to non-target wildlife, it is readily apparent that such label requirements have been unsuccessful in preventing

harmful exposures to non-target animals. EPA expects that eliminating from the general consumer market all commensal rodenticides except for those sold in or with bait stations will reduce rodenticide exposures among birds and among non-target mammals larger than target rodents. As bait stations are optimized for the body sizes of either house mice or Norway and roof rats, larger mammals are physically limited by the station portal size preventing them from reaching the bait within, and most birds will not enter a small, confined space. Bait stations also reduce rodenticide risks to predators: Reducing the number and types of prey species likely to be contaminated with rodenticides should reduce the proportion of rodenticide-contaminated prey in a predator's diet and reduce the total quantity of a rodenticide available to the predator.

Moreover, limiting the availability of bait forms such as pellets, granules, grain and meal is likely to reduce the spatial extent of bait dispersal across the landscape. Bait in forms such as pellets, granules, grain and meal is easily scattered, offering non-target wildlife increased opportunities for rodenticide exposure when compared with a more focally placed bait station. Limiting access to rodenticide baits in the form of pellets, granules, grain and meal is likely to reduce bait scattering, resulting in a reduction of encounters of wildlife directly with rodenticides. This may be especially significant for chemicals such as brodifacoum, difethialone, bromethalin and warfarin where only a few feeding episodes are sufficient to cause mortality. Measures that make rodenticide baits less available to non-target wildlife that are primary consumers are also likely to result in a reduction of predatory and scavenger wildlife encounters with intoxicated prey species, because the number and range of affected prey species should be reduced if less scattered bait is available.

Although the proposed cancellations will not limit use of bait forms such as pellets, granules, grain and meal by professional, commercial and agricultural users, it is EPA's belief

that such users (including persons who routinely apply pesticides as a minor part of their job, as well as full-time pesticide applicators) are more likely to choose a method of pest control appropriate for the specific circumstances, more likely to have reusable tamper-resistant bait stations, more likely to appreciate the consequences and liability of pesticide misuse, and in most cases acutely sensitive to the economic consequences of overuse. For these reasons, EPA believes that pesticides generally pose less risk when applied by professional, commercial and agricultural users than when applied by the general public. In the case of rodenticides containing brodifacoum and difethialone (active ingredients that are not registered for field uses, except for certain restricted use products registered to USDA/APHIS for very limited island conservation uses by or under the supervision of agencies of the U.S. government), EPA believes that this difference is significant enough to warrant taking steps to limit access to these products to professional, commercial and agricultural users.

b. Endangered Species Considerations for Rodenticide Active Ingredients

The Agency has concluded that the rodenticides subject to the NOIC pose risks of concern to non-target wildlife. By extension, these chemicals would also pose risks of direct effects to federally listed threatened and endangered species and designated critical habitat. Further, potential indirect effects to any species dependent upon a species that experiences effects from use of rodenticide active ingredients cannot be precluded based on the deterministic ecological risk assessment. These findings are based solely on EPA's deterministic assessment and, because they do not take into account such factors as whether the species would be expected to be exposed to rodenticide active ingredients, do not in themselves constitute "may affect" findings under the Endangered Species Act. EPA previously consulted with the Fish and Wildlife

Service (the Service) under the Endangered Species Act on certain uses of rodenticides, and in 1993, as part of that consultation, the Service issued a biological opinion finding that a number of rodenticides, including several addressed and analyzed in this action, will likely jeopardize a number of animal species. (A more recent biological opinion and consultations regarding the prairie dog bait products Rozol and Kaput-D are not applicable here, as those products are not registered for use against commensal rodents.) EPA has not in large measure implemented recommended measures provided in that 1993 opinion, but in March 2005, initiated informal consultation. That informal consultation for products containing one of the nine rodenticide active ingredients registered for commensal rodents at that time was for the purpose of obtaining technical assistance in identifying the full suite of listed species that may be affected by the full range of uses of these products, to determine whether further, formal consultation would be necessary and if so, to explore possible mitigation relative to specific species that may be affected. Several reported incidents have involved Federally listed threatened and endangered species, for example the San Joaquin kit fox and northern spotted owl. In addition, reported incidents include the bald eagle, which is protected under the Bald and Golden Eagle Act. Although the action EPA is taking in the NOIC will likely reduce risks to a number of protected species, this action is not intended to resolve the need for mitigation to address federally listed and other protected species. If EPA determines, as a result of its own further assessment, or through consultation with the Service, that additional restrictions on use are necessary to address adverse impacts to listed and other protected species or designated critical habitat, EPA may initiate other appropriate action to address such impacts.

IV. Benefits

FIFRA requires that, when determining whether a non-dietary pesticide use causes unreasonable adverse effects, EPA must take into account the economic, social and environmental costs and benefits of the pesticide use. This sense of the term "benefit" is therefore different from its use in a benefit – cost analysis. In the FIFRA context, the benefits of the rodenticide products that EPA proposes to cancel are equivalent to the impacts of cancellation on their users. The impacts of cancelling certain products are also representative of the foregone benefits of denying registration to products of similar nature. EPA examined several potential impacts of the proposed cancellation of the rodenticide products identified in the NOIC, including:

- Whether residential consumers can achieve similar levels of control over rodent infestations.
- Whether it may take longer for residential consumers to achieve control of their rodent problems.
- Whether the cost of rodent control, including non-monetary costs, may increase.
- Whether the proposed cancellations will increase resistance to anticoagulant rodenticides.

Overall, EPA concludes that cancellation of products subject to this NOIC will not result in the loss of a residential consumer's ability to control commensal rodents nor increase the time required to control commensal rodents. Residential consumers will still have a wide variety of options for rodent control, including several non-chemical options as well as multiple rodenticide active ingredients. The performance of all commensal rodent control measures can vary widely according to external environmental conditions, state of the residence, and the behavior of individual rodents, but there is no evidence that SGARs consistently out-perform all other active

ingredients, or that unprotected bait consistently out-performs bait in bait stations, regardless of circumstances. Residential consumers who would otherwise use a product subject to the NOIC may experience a slight increase in the cost of house mouse control, of about $0.25 per placement or in the range of $1.50 to $3.00 per infestation. Cost increases such as these are unlikely to induce consumers who would use rodenticides to switch to non-chemical measures. Currently, rat control products that conform to the RMD and are available on the market are $7.00 to $8.00 more expensive per placement ($42 to $48 for a minor infestation) than the products proposed to be cancelled. However, since the issuance of the RMD, registrants have been able to develop technologies for producing RMD-conforming house mouse products at substantially lower cost than was seen in 2008. Thus, it is possible that prices for conforming rat products will similarly decline. At the moment, the increase in cost may induce some residential consumers to use lower-cost, mechanical control options, but these measures would entail some additional non-monetary costs, such as disposing of dead rats (although the labels of the products subject to cancellation also require the disposal of dead rodents if found). These cost impacts arise because of the requirement that bait be contained in bait stations; the choice of active ingredient does not affect the per-unit cost or the cost of control. The additional cost is generally less than two percent of the monthly non-housing income for a family of three at the poverty line, and a considerably smaller proportion for the majority of residential consumers.

When comparing these costs against the expected risk reduction, EPA regards these cost increases as only affecting those residential consumers who do not use rodenticides where children, pets or non-target wildlife might gain access. For other residential consumers, products with included, RMD-conforming bait stations are likely to provide a cost savings relative to the costs of obtaining products subject to the NOIC plus the tamper-resistant bait stations (which are

unlikely to be available at the same retail establishment) necessary for use consistent with those products' existing labels.

The following sections provide an overview of the methodology used in EPA's impact assessment, target pests, the use and advantages of the rodenticide products EPA intends to cancel and their alternatives, and expected impacts on households that would be affected by the proposed cancellation.

A. Methodology

EPA's impact analysis (Cook and Hill, 2011) explored the potential impacts incurred by households currently using products EPA proposes to cancel; specifically, rodenticides marketed to residential consumers containing SGARs and/or unprotected bait, *i.e.*, not confined to a bait station reasonably anticipated not to release rodenticide bait. The analysis distinguishes between impacts on consumers treating for mice and for rats and also on consumers facing a single or sporadic infestation and those facing chronic or repeated infestations. Chronic infestations may occur in situations where rodent populations are particularly high due to favorable external environmental conditions such as readily available food and shelter. Examples include urban environments where food refuse (e.g., restaurant and residential waste) collects and rural areas where there may be readily available food (e.g., fields or livestock feed) and harborage (barns or natural sites). In these situations, sanitation and exclusion are difficult and infestations can be prolonged and recurring.

To assess the impacts of the proposed cancellations, EPA identified the target rodents and how the products are used. The Agency then identified available alternatives and compared their performance in terms of ability and time needed to achieve control of an infestation. EPA also compared other factors that may be considered advantageous or disadvantageous, such ease of

use and disposition of carcasses, and compared control costs. Finally, these factors formed the basis for EPA's conclusions about the most likely alternatives to the products proposed for cancellation and the impacts of cancellation.

B. Target pests and use of rodent control measures

The products subject to the NOIC bear label claims for control of one or more of three commensal rodents: the house mouse, Norway rat, and roof rat. The house mouse is by far the most common of these rodent pests. Of households reporting seeing signs of rodents, 86 percent reported signs of mice, nine percent reported signs of rats, and another five percent could not identify the rodent (Census Bureau, 2011). Most rat problems in the United States are likely to be Norway rats, as the roof rat appears limited to Hawaii and relatively warm and coastal areas in the contiguous 48 states (Marsh, 1994). Options to control these pests include various rodenticides, non-chemical methods such as snap traps and glue boards, and professional pest control operators (PCOs).

According to the American Housing Survey (Census Bureau, 2011), slightly more than six percent of U.S. households reported having seen signs of a rodent in the three months that preceded the survey. Extrapolating over the whole year suggests that as much as 25 percent of U.S. households could see rodent signs. This is likely an overestimate of affected households since, as noted above, some households face chronic or recurring problems. Market survey data (IRI, 2012b) indicate that rodenticides account for approximately 30 percent of sales, by unit, of rodent control products, with mechanical traps accounting for almost 40 percent of the market and glue boards for the remaining 30 percent. If 25 percent of households treat for rodents each year and 30 percent of those households choose rodenticides, then about 7.5 percent of all households would use rodenticides each year.

Residential consumers with commensal rat problems may, in general, choose different control options than those with house mouse problems. It seems likely, for example, that someone with a commensal rat problem would be more likely to call a professional pest control service than someone with a house mouse problem, but specific data are not available. Rodenticides can, in general, be used to target either mice or rats although bait stations for mice would typically be too small for rats to enter. Results of a market survey indicate that nearly 90 percent of rodenticide sales in the residential consumer market were for the elimination of house mice (Kline & Company, 2006). EPA's review of annual production data for 2007 and 2008 supports this figure: EPA estimates that over 95 percent of commensal rodenticide bait sold is in products intended for use against house mice. Glue boards come in different sizes; market data from 2010 (IRI, 2010) indicate that mouse-sized glue boards account for almost 88 percent of sales. However, as the larger, rat-sized boards are also capable of entrapping house mice, it is possible that some users of large-size glue board are actually targeting mice. Snap traps are sized specifically to catch either mice or rats, and sales data indicate only two percent of the sales for these products are for rat-sized units (IRI, 2010). Together these data indicate that 90 percent or more of rodent control problems involve house mice. Given that only 7 percent of residences have rodent problems, these data imply that less than one percent of US residents face problems with commensal rats.

A summary of market survey data for the year ending in July, 2012, indicate that SGAR pellets are the dominant form of mouse baits with just over 65 percent of the market (IRI, 2012a). Single-use, disposable bait stations, which primarily contain bromethalin, account for about 12 percent of the market, while refillable bait stations, also mostly with bromethalin, account for 15 percent. The remaining portion of the market comprises various other forms

including baits of various active ingredients and forms (e.g., blocks) not in stations and a few bait stations containing SGARs such as bromadiolone. EPA has recently conducted an informal check of available products which suggest that products targeting rats are more likely to be SGARs in block form than in pellet form. Some blocks contain bromethalin or an FGAR such as diphacinone. A disposable bait station containing bromethalin was recently registered for rat control. However, data on sales or use of recently registered products are not yet available.

C. Usage Patterns

Rodenticides are formulated in baits designed to be sufficiently appealing to rodents that even marginal feeders will return and eat enough to reach a lethal dose. Regardless of form (e.g., block or pellet, unprotected or in stations), the locations and amounts of bait placements will essentially be the same. Labels for commensal rodenticides, including those proposed for cancellation, direct users to place bait in the areas where the rodents are active, typically along walls or other likely routes of travel. When used to control house mice, these labels typically direct that bait placements be made at intervals of 8 to 12 feet. When used to control commensal rats, these labels typically direct that bait placements are to be spaced 15 to 30 feet apart. All products subject to the NOIC bear labels that require that placements that would be accessible to children, pets, domestic animals and/or non-target wildlife must be in tamper-resistant bait stations. With one exception, all products subject to the NOIC bear labels that require the user to check the condition of the bait after placement, replenish consumed bait, and collect and dispose of unused bait and dead rodents.[16] Directions for use for non-chemical methods like snap traps

[16] EPA Reg. No. 3282-3 does not require collection and disposal of unused baits, although it does require that users check perishable baits daily, and replace contaminated or spoiled bait immediately. The requirement to treat for rats for at least 10 days, and to treat for mice for at least 15 days, is effectively a replenishment requirement.

and glue boards also call for placements in similar locations.

Not all target rodents will begin to feed on bait immediately. Two or more weeks may be required to kill all rodents in an infestation, regardless of the active ingredient in the rodenticide used. The longer treatment times are more likely where food items other than the bait are available to the rodents. From the time target rodents begin feeding on them, anticoagulant rodenticides take at least three to five days to kill their first victims, and two or more weeks to kill all of the rodents that will ultimately be taken. The acute rodenticide bromethalin typically causes death within two days from the onset of feeding, although it may take a few more days for some lethally exposed individuals to die. Thus, under good conditions (especially lack of alternate food sources), a successful rodenticide baiting program will typically last from one to several weeks. Because it is difficult to determine how many rodents are present in a residential infestation, it is prudent for users to continually monitor for fresh signs of rodents during the course of control operations – regardless of the method of control – and continue baiting until new evidence of rodent activity is no longer detected.

Effective use of rodenticides depends on a number of factors including the size and complexity of the infested area and the size of the infestation. Use of multiple bait placements will increase the likelihood that rodents will find them and consume a lethal dose of rodenticide. To characterize the likely range of use, EPA evaluated scenarios for minor and major infestations, reflecting smaller and larger numbers of rodents and areas to be treated. By minor infestation, EPA means several individual rodents, which is the most common scenario. Rodents will typically take up residence near a supply of food (e.g., kitchen cupboards or pantry) where, despite their nocturnal habits, they will be noticed either by their movement, by the consumption of food, or by their droppings. A major infestation might occur if rodents find a food source that

is rarely disturbed, such as a large supply of pet food in a basement, and can establish a sizable population (e.g., a half dozen or more individuals with active breeding) before being observed. Such an infestation would be relatively uncommon, especially with rats. EPA also evaluated one-time infestation and repeated infestations in each of these scenarios. Repeated infestations may occur because environmental conditions in areas adjacent to the residential unit support large rodent populations. Examples of such areas are urban alleys with trash receptacles filled with food waste from nearby restaurants and rural settings where livestock feed provides an abundant food supply for rodents. EPA has no data on the frequency of recurring infestations, but it is likely to vary widely. Many households may observe a seasonal pattern where rodents seek shelter in late fall and winter. Major infestations in occupied residences are likely to be rare because most residents will observe signs and take action before a sizable population is established.

For purposes of comparison, EPA assumed that a user would make six bait placements (e.g., a block, packet, or baited station) in the case of a minor infestation of rodents, and 12 placements for a major infestation of rodents. These assumptions are based on university agricultural extension agencies and government recommendations for homeowners to control rodents (CDC 2010; Pierce 1993; Koehler and Kern, 2008; Hovanic et al., 2010; Illinois Department of Public Health undated), which EPA is confident will not underestimate use. The number of placements encompasses a variety of situations where bait placements are used both spatially and sequentially. For example, six placements could represent a case where the user sets three placements around the kitchen area and replaces each one time as the bait is consumed.

D. Alternatives to Products Proposed to be Cancelled

The anticipated effects of the cancellations proposed in the NOIC are the removal from the general consumer market, and from residential consumer use, of rodenticide bait products where the bait is not protected in a bait station meeting the criteria announced in the RMD, and rodenticide bait products containing SGARs. EPA concludes that the proposed cancellations will not impair the ability of residential consumers to control commensal rodents, because the alternative control methods discussed below remain available.

1. House Mouse Control Products

a. Rodenticides

There are currently more than 30 rodenticide products that conform to the RMD registered for general consumer use against commensal rodents. A regularly updated list of RMD-conforming consumer use products appears at http://www.epa.gov/pesticides/mice-and-rats/rodent-bait-station.html. All are registered for use against house mice, despite the fact that the names of several products only mention rats. These currently registered, RMD-conforming products each use one of three different active ingredients (bromethalin, chlorophacinone, and diphacinone). At least four of these products contain refillable bait stations with replacement bait blocks, and the rest consist of bait in single-use, disposable bait stations.

The bait components of these products meet the efficacy testing requirements that EPA has established for registration of commensal rodenticide baits under FIFRA. In order to demonstrate the effectiveness of a rodenticide active ingredient, EPA requires (1) acute oral toxicity testing with wild-type rodents of the targeted species; (2) laboratory efficacy screening of one or more bait formulations with wild-type rodents of the targeted species; (3) indoor and outdoor field efficacy trials involving the targeted species in actual use situations in different

regions of the U.S.[17] In addition to these requirements for registering an new active ingredient for controlling commensal rodents, each new bait formulation must be screened for effectiveness in laboratory efficacy tests. These tests are not designed to rank the efficacy of the various rodenticide products, but instead to establish whether each product meets the efficacy threshold that EPA considers necessary to support registration.

According to market research (IRI, 2012a), RMD-conforming products currently make up about 27 percent of the market for mouse rodenticides. EPA's informal check of products and prices, conducted in the fall of 2011, suggests that most of the available RMD-conforming products contain the active ingredient bromethalin, which is not an anticoagulant. Like most SGARs, bromethalin products are formulated such that a mouse could consume a lethal dose in a single feeding. A mouse consuming bromethalin will typically die in two to three days (Corrigan, 1997), a period that is somewhat shorter than the three to five days typical of SGARs. The major difference in performance is that a mouse will stop feeding once it consumes a lethal dose of bromethalin; in that respect, less bromethalin bait is needed to control an infestation than anticoagulant bait because each individual mouse consumes less bromethalin bait before it dies.

The rest of the RMD-conforming products currently available contain chlorophacinone or diphacinone, which are FGARs. They are less acutely toxic than SGARs and often require a mouse to feed multiple times over several nights before it will obtain a lethal dose. In studies, however, the time to death is approximately the same for FGARs as for SGARs (Dubock and Kaukeinen, 1978; Kaukeinen and Rampaud, 1986; Pitt, *et al.*, 2011; Witmer, 2007a,b). The need for multiple feedings may suggest that the user would have to make greater effort to maintain fresh bait and reduce the availability of other food options in comparison to SGARs or

[17] General guidance for the design of such studies appears on pages 307-310 of Subdivision G of EPA's Pesticide Assessment Guidelines, Office of Pesticides and Toxic Substances, Washington, DC, 1982.

bromethalin. In practice, however, the difference is likely minimal, because the amount of bait applied (assuming use in accordance with label directions) is more than the amount likely to be consumed in one night by the number of house mice in typical infestations. Infestations are likely to consist of more than one house mouse, and users cannot be sure that all individuals will take bait on the first night regardless of what rodenticide product is used. As a result, most labels for all types of commensal rodenticides direct users to continue to provide fresh bait and sanitation for ten days or more.

In a review of the literature, Clapperton (2006) found several studies demonstrating that block baits were preferred and several others showing that pellets or meals were preferred. Prescott (2011) reported that bait-block formulations from many countries tended not to be accepted as well as pelleted baits when tested under similar conditions. However, these reports do not address whether the products subject to the NOIC perform better than the registered, RMD-conforming alternatives. Kaukeinin and Marsh (2009) report that improved manufacturing processes and EPA's bait-specific efficacy data requirements have led to the production in the U.S. of bait blocks that are highly palatable to commensal rats and mice. EPA requires that all commensal rodenticide bait forms (e.g., pellets, meals, pastes, powders, block baits) meet the same efficacy criteria for registration for use in and around residences (Jacobs, 2011). There is no basis for presuming that certain bait forms offer faster control or a higher degree of control.

Protective bait stations do not appear to affect the acceptance of bait by mice (e.g., Kaukeinin and Marsh, 2009). In fact, protective bait stations may provide several advantages over the use of uncontained bait. They may protect bait from dust and moisture, thereby keeping the bait palatable longer. They provide mice with a protected place to feed leading to greater

consumption and a higher likelihood of obtaining a lethal dose (Vantassel *et al.*, 2006; Corrigan, 1997). Blocks anchored in bait stations will not be moved and cached by individual mice, and thus are more likely to remain available for consumption by the whole mouse population. Although bait station size may prevent placement in some locations, many recently registered bait station products are approximately the same size as the cardboard box in which one of the best-selling commensal rodenticides is applied, D-Con Mouse Proof II, EPA Reg. No. 3282-65. Although some may argue for the desirability of being able to toss a packet of pellets or loose blocks in wall crevices or attic spaces, such placement would not increase the level or speed of control of house mice because they forage for human and pet food where it is stored or spilled. Such places are typically in living areas, which consequently, are the most appropriate locations for placing any rodenticide (or any trap) intended to control a house mouse infestation. House mice tend to move through living spaces along walls and behind appliances, places where bait stations can easily be placed. Moreover, placement in wall voids or other places from which bait cannot be checked or retrieved is not allowed under the use directions on the labels of any of the products subject to the NOIC. Tossing baits where they cannot be monitored or retrieved precludes compliance with label directions to monitor bait consumption and to collect and dispose of uneaten bait. Inability to do so can result in inefficient rodent control and insect infestations.

On the basis of these considerations, EPA concludes that residential consumers will be able to achieve essentially the same level of control of house mouse infestations, within essentially the same time frame, and with essentially the same level of effort, using other currently registered rodenticide products that conform to the RMD as they would with products subject to this NOIC.

b. Non-chemical Methods

The most common forms of non-chemical control methods are snap traps and glue boards. Other non-chemical control methods (e.g., live traps, devices that electrocute mice) are also marketed, however, EPA's alternatives analysis focused on the more commonly used lethal measures: snap traps and glue traps.

Snap traps have a long history of use, are an effective way to control mice and have a number of advantages over rodenticides. Snap traps are relatively inexpensive and they may be reused. In most cases, death is essentially instantaneous. Some disadvantages include the time and effort of baiting and setting the traps and, once sprung, a trap will not work until reset. The user must dispose of the dead mouse, which may be an unpleasant task (although users of rodenticides are also required to dispose of dead rodents if they find them). On the other hand, the presence of the dead mouse offers a concrete measure of success, and enables the user to dispose of the carcass immediately, thus avoiding odor from decomposing mice, which can be a non-monetary cost associated with the use of rodenticides. Because snap traps can be deployed with different food items or other attractive objects, they may be more effective than rodenticide baits in situations where other available food sources cannot be eliminated.

Glue boards have a sticky substance to catch and hold rodents that run across them. Some consumers may like the ease of glue boards, as there are no triggers or baits to set, and as trapped rodents can be disposed along with the used trap. Glue traps may be useful to kill snap trap-wary mice and are sometimes used in conjunction with snap traps (Illinois Department of Public Health, undated). However, dampness, dust, and even temperature extremes will diminish the efficacy of the glue boards (Illinois Department of Public Health, undated). Since rodents trapped on glue boards do not die quickly, they can use their urine, feces, and fur to

escape (Corrigan 1997). Rodents have been observed to use paper, dirt, or leaves to essentially create bridges over the sticky surfaces (Corrigan 1997). The Centers for Disease Control does not recommend glue boards because often the trapped rodents are not dead when users collect the used glue boards, thereby increasing the potential for disease transmission or rodent bites (CDC 2010). Despite these apparent drawbacks, glue boards account for about 30 percent of the rodent control market (IRI, 2012b.)

In summary, snap traps and glue boards are commonly used and both provide similar levels of control as rodenticides within a similar time frame. In comparison to rodenticides, there may be some non-monetary costs associated with their use, *e.g.*, the effort to bait snap traps and monitoring of and disposal of dead or dying rodents from snap traps or glue boards. Considering the Centers for Disease Controls' concerns about glue boards, EPA concludes that snap traps are the most appropriate alternative to rodenticides.

c. Professional Pest Control Operators

Many residential consumers routinely rely on professional pest control operators (PCOs) to treat their homes for rodents and other pests, even though PCO services are more expensive than do-it-yourself pest control. Products routinely used by PCOs are not subject to the NOIC, therefore consumers currently using PCO services will not be impacted by this action. According to a market survey, 56 percent of PCOs use rodenticides as their primary method of control for their residential accounts, 24 percent use mechanical traps, and 16 percent use glue boards (Curl, 2012).[18] There is a similar distribution across commercial accounts, which

[18] A recent survey indicates that 100 percent of PCOs use tamper proof bait stations for exterior rodenticide applications (the survey did not ask about indoor applications), so it is clear that PCOs have access to, and regularly use, tamper proof bait stations. This same survey also indicates that 79 percent of PCOs use rodenticides in bait

includes apartment buildings and condominiums. The SGAR bromadiolone is the rodenticide most commonly used by PCOs, accounting for about 45 percent of PCO rodenticide use (measured by expenditures), and difethialone accounted for about 20 percent of PCO rodenticide use, with all other rodenticides combining to account for the remaining 35 percent (Curl, 2012). The source of these market data did not distinguish between mouse and rat control.

2. Rat Control Products

a. Rodenticides

Currently, there are only three rodenticide products that conform to the RMD registered for general consumer use against commensal rats. Two of these products are baits in single-use, disposable bait stations and one consists of a refillable bait station and multiple bait block refills. The RMD-conforming consumer use products are listed at http://www.epa.gov/pesticides/mice-and-rats/rodent-bait-station.html. All of these products contain bromethalin, which, as discussed above, is an acute rodenticide. Each product is formulated so that a rat may consume a lethal dose in a single night's feeding. The rat will generally cease feeding at that time and die in two to three days. Thus, the typical time to death is shorter than those typical of anticoagulants.

There are currently no RMD-compliant FGAR products currently registered for residential consumer use in controlling commensal rats, but there are no apparent impediments to the adaptation of currently registered bait block formulations containing FGARs for use in bait stations that conform to the RMD and are sized appropriately for baiting commensal rats. As noted in the discussion of mouse control products, feeding on FGARs over several nights might

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stations for residential rodent control sometimes, often, or all the time, and 13 percent use loose baits for residential rodent control sometimes, often, or all the time. The survey clearly supports an inference that use of bait stations is widespread among PCOs. ASPCRO/NPMA, Rodenticide Use Survey of Pest Management Professionals, 2013.

be necessary for a rat to obtain a lethal dose. Time to death with FGARs, however, is similar to that of SGARs.

Blocks are an effective bait form for rat control, as evidenced by their widespread use by PCOs and public health programs. Bait blocks are not novel pest management tools and they are the preferred bait form of professional applicators in residential settings (Lublinkhof 2011). Bait blocks have been on the residential consumer markets as far back as the late 1980s. EPA's informal check of products and prices also found more examples of block baits than pelleted baits among products marketed to general consumers for commensal rat control. Of course, many pellet forms are likely marketed for both rat and mouse control. As discussed above, EPA requires both block and pelleted commensal rodent baits to meet the same criteria in efficacy screening tests (except for bait blocks limited by labeling to use exclusively in wet or damp areas), so there is no basis for presuming that pelleted or meal baits offer faster control or a higher degree of control.

Unlike house mice, which tend to explore new items, commensal rats tend to avoid new objects (Timm, 1994; Corrigan, 2001). Such "neophobia", defined as "new object reaction …consists of avoiding an unfamiliar object in familiar surroundings." (Barnett, 1958) includes a reluctance to enter a station to consume bait, and is affected by a broad array of factors. Although neophobia can delay an individual rat's entry into a bait station and consumption of bait, it is unlikely that it will noticeably affect either the ability or time to control a rat infestation.

Bait-stations have been employed in effective urban rat control projects for many years, and have also been used in successful eradications of commensal rats from offshore islands, indicating that satisfactory levels of control can be achieved using bait stations. For several

decades, pesticides registered for use to control commensal rodents have had label statements requiring use in tamper-resistant (or tamper-proof) bait stations where placements otherwise would be accessible to children, pets, domestic animals, and/or non-target wildlife, and commercial and professional users generally achieve effective rodent control while complying with this requirement.

There are several reasons supporting EPA's conclusion that the bait station requirement will not noticeably increase the time required for control of a residential rat problem. First, rats' tendency to avoid new objects is not confined to bait stations. The introduction of a new bait block or packet of pellets into the rats' environment is also likely to induce some neophobia. Second, most rats will explore a new bait station after a few days (Corrigan, 2001). This potential delay is small relative to the variation in time to mortality of an individual rat and the variation in the time to control an infestation. Third, entering a container of some sort would not be a new behavior for rats that are accustomed to entering boxes and cans containing food leftovers or buckets and bins of animal feed. Moreover, each rat that enters and leaves a bait station safely leaves behind scent clues that diminish neophobia of other rats. Fourth, rats will not likely be fully accustomed to a human-occupied residence before the resident notices their presence and takes action. In such circumstances, rats may not perceive a bait station as new relative to other features of their environment.

Achieving control of an infestation using rodenticide baits without bait stations (such as the products proposed to be cancelled) will generally take ten days to two weeks, and in some cases considerably longer. It can take several days for all of the rodents to find the bait placements; it can take multiple days for a rat to consume a lethal dose (even of those baits formulated to deliver a lethal dose in a single night's feeding), and there can be differences of

several days in the length of time between consumption of a lethal dose and death. The potential variation in these factors for an individual rat is far greater than the potential variation in time between acceptance of bait in a bait station and acceptance of unprotected bait, and this difference is even more pronounced for a group of several rats considered collectively. Given the long and highly variable treatment period needed to achieve control of an infestation even without bait stations, neophobia associated with use of a bait station is unlikely to lead to a noticeable extension of the treatment period. Note, too, that many of the alternative rodenticides currently registered all contain bromethalin, which typically kills one to three days faster than anticoagulants. Finally, for bait placements in areas accessible to children, pets, domestic animals and/or nontarget wildlife, use of RMD-conforming bait stations is not likely to lead to an increase in treatment duration in comparison with use of the tamper-resistant bait stations already required by the labels of the products subject to the NOIC. In conclusion, available rodenticides with RMD-conforming bait stations for rats will perform similarly to the products subject to the NOIC in terms of level of control, the time to achieve control, and the effort required of the user.

b. Non-chemical Methods

As with house mice, non-chemical control methods include snap traps and glue boards as well as other devices. Data are not available to discern the relative market shares of various methods in the control of rats, which is a relatively small proportion of the rodent problems among residential consumers.

Snap traps for rats are distinctly larger than snap traps for mice, and owing to their size, they are unlikely to kill mice. Only about two percent of all snap traps sold are rat-sized (IRI, 2010, via Bell Labs). Since about ten percent of households reporting identifiable signs of rodents report rats, it appears that consumers with rat problems are either more likely to hire

PCOs or less likely to use snap traps than are those with mouse problems. It is reasonable to think that the perceived disadvantages of snap traps, including the effort of baiting and disposing of dead rats, are relatively larger than for rats than for mice. One advantage of traps – the likelihood of locating and disposing of the carcass – is also relatively larger for rats, as the odors of decomposing rats are more powerful and longer-lasting than those of mice. Regardless of the relative weights attached to these advantages and disadvantages, traps are an effective means of control and could address a residential infestation in a similar time frame as would rodenticides.

Glue boards, like snap traps, are sold in sizes appropriate for catching commensal rats. According to market research, approximately 13 percent of glue board sales are of rat-sized products. Unlike snap traps, however, the larger rat-sized glue boards also could be used to catch mice. As with snap traps, it is reasonable to think that the advantages and disadvantages of glue boards, especially disposing of a trapped – but not necessarily dead – rat, are relatively higher for rats than for mice. In terms of performance, however, extensive use of glue boards by PCOs suggests that glue boards are an effective form of control.

As with any rodenticides, the performance of non-chemical methods for rat control will be subject to the wariness that characterizes the behavior of individual rats. Thus, the level of control and the time to achieve control with non-chemical methods will likely be similar to that obtained with rodenticides. As with mouse control, non-chemical methods may require more effort on the part of the user to bait snap traps and to dispose of rats.

c. Professional Pest Control Operators

The market data available to EPA concerning PCO rodent control activities do not distinguish between treatments for rats versus mice. Treatments for commercial accounts, which include apartment buildings or condominiums, are for control of both rodents, along with other

pests (Curl, 2012). Treatments for residential accounts are typically for mice (Curl, 2012), but this may simply reflect the fact that about 90 percent of rodent problems involve mice (Census Bureau, 2011). It is reasonable to think that reliance on PCOs is relatively higher among households with rat problems than with mice. Products typically used by PCOs are not subject to the NOIC, so PCOs and consumers currently using such services will not be affected by the proposed cancellations. It is also worth noting that most PCOs report that they routinely use bait stations when using rodenticides in residences (ASPCRO/NPMA 2013).

E. Impacts of Cancellation on Residential Consumers

Based on the information present in IV.4., EPA concludes that the cancellation of the products identified in the NOIC will not significantly impact either the level of rodent control that residential consumers will obtain or the length of time it takes to achieve control. Since this action does not affect products typically used by professional users (e.g., PCOs, commercial and agricultural users, government agencies), there will be no impact on such users, or on others who rely on their services. The impact on consumers will likely be limited to any change in the cost of control due to differences in the cost of compliant products relative to non-compliant products. Impacts will include any incremental change in monetary expenditures as well as any non-monetary costs such as an increase in the effort needed to use an alternative method or to dispose of carcasses.

This section summarizes EPA's analysis comparing control costs of rodenticides that would be cancelled to the control costs using available alternatives (Cook and Hill, 2011). This analysis addresses commensal mouse and rat control across a range of situations differing in the size of the infestation (minor or major) and the frequency of infestation (one-time or repeated) as described in IV.3.

1. Incremental costs of house mouse control

Overall, EPA expects that incremental costs of using RMD-conforming rodenticide products for mouse control in lieu of products proposed to be cancelled will be small. The rodenticide active ingredient used does not appear to significantly affect the price of rodenticide products, so the incremental cost of the proposed cancellations will be driven by the RMD bait station criteria. EPA obtained summary data from a national market survey covering the 52 weeks ending July 8, 2012 (IRI, 2012a), showing average prices weighted by quantity sold. The cost per placement for rodenticide products that include disposable bait stations for mice was $1.63 while the cost per placement for SGAR pellet products (the product type that accounts for a majority of sales of mouse control products) was $1.66, suggesting that consumers would face no incremental costs associated with the cancellation of the registrations of pelleted products.

In a 2011 analysis of both mouse and rat products then on the market, EPA identified differences in the average price of RMD-conforming and non-conforming products that would indicate a cost increase for a one-time infestation ranging from around $2.00 for a minor infestation to as much as $12.00 for a major infestation (Cook and Hill, 2011). Using pellet products of the type that accounted for a majority of sales of mouse control products as the baseline, EPA's 2011 analysis indicated that most residential consumers would be expected to see an average increase in cost of $1.50 in a minor infestation and $3.00 in a major infestation, or $0.25 per placement with the use of rodenticide products that include disposable or single use bait stations. These price data were based on a check of local sources and national chains with internet pricing and represent simple averages of prices.

In situations where infestations are expected to recur, residential consumers may find it less expensive to buy rodenticides in larger quantities of 16 to 28 placements per package.

EPA's check of stores found a per placement price of about $0.75. The average cost of rodenticide products that include reusable bait stations, which provide a bait station and six to eight blocks, implies a per-placement cost of less than $1.00. More recent information from the market survey indicates a cost per placement for products that include reusable bait stations of about $0.90 (IRI, 2012a), but did not provide a price for bait blocks that might be purchased in quantities of 16 to 28 placements per package. Using these figures, the incremental cost associated with reusable bait stations is about $0.15 to $0.25 per placement, similar to the one-time infestation scenario.

In conclusion, market survey data suggest that for house mouse control there is no difference between the cost of products proposed to be cancelled and registered rodenticides that conform to the RMD. Data generated by EPA suggest that consumers may face a cost increase of about $0.25 per placement or an additional cost of $1.50 for a minor infestation to about $3.00 more to control a major infestation. Costs per infestation would be similar regardless of the frequency at which the infestation occurs. This very modest increase in price is not likely to induce any changes in consumer behavior. If a consumer would typically use one of the products proposed to be cancelled, such as a SGAR in pellet form, the incremental cost of using an alternative rodenticide in a bait station would not likely induce him or her to purchase a non-chemical method instead. Thus, EPA does not anticipate an increase in the use of snap traps or glue boards by consumers treating for house mice. Again, mice account for approximately 90 percent of commensal rodent problems in U.S. households.

It is worth noting that the house mouse control market has undergone considerable changes in recent years. When the RMD was announced in 2008, few rodenticides were available in ready-to-use bait stations, despite a long-standing requirement on labels that tamper

resistant bait stations be used where children, pets or non-target wildlife could otherwise have access to the bait. Stand-alone, reusable, tamper-resistant bait stations were very expensive and available mainly through vendors catering to professional users. Since the RMD, however, several manufacturers have developed rodenticide products with single-use and reusable bait stations that are similar in price to unprotected baits.

2. Incremental costs of commensal rat control

As with mouse control products, the choice of active ingredient used does not appear to significantly affect the price. For residential consumers treating for commensal rat infestations, EPA's 2011 analysis indicated that incremental costs of using alternative rodenticide products with single-use bait stations for rats instead of products proposed to be cancelled would be about $8.00 per placement. For a one-time problem, this implies a cost increase ranging from $46 in a minor infestation to $92 in a major infestation. Note that rat problems are relatively rare, comprising about ten percent of rodent problems annually, and that major infestations would be exceedingly rare because the infestation would have to go untreated for some time in order for a population to become established. See the discussion in IV.3. EPA does not have market data for rodenticide products intended to control rats as it does for rodenticides intended to control house mice.

The incremental cost per treatment is similar for situations regarding repeated infestations. Stand-alone, reusable, tamper-resistant bait stations are very expensive and available mainly through vendors catering to professional users. A new rodenticide product containing a rat-sized, reusable bait station was registered in October 2012 and may soon be available in retail outlets, but the price of the product is presently unknown. Improving technology rapidly has led to decreases in the price of mouse-sized bait stations and the same

could happen for rat control products. Compared to the purchase of small quantities of rat bait blocks, EPA's informal check of prices (Cook and Hill, 2011) indicates that purchases of rat bait blocks in large quantities do not substantially lower the per-placement cost, and hence produce little change in the cost of treatment or the incremental cost of using disposable stations for repeated infestations.

The estimated increase in the cost of commensal rat control products as a result of the proposed cancellations could induce consumers to seek other rat control options. Snap traps, according to EPA's informal check of prices, average $2.00 to $2.25 more per placement than the products proposed to be canceled (Cook and Hill, 2011). Glue boards average about $1.00 more per placement than the products proposed to be canceled. Thus, control of a minor rat infestation is estimated to increase in cost by about $6.00 more with glue boards and $12.00 more with snap traps. Snap traps are recommended by the CDC, but glue boards are not. There are non-monetary costs associated with the use of both types of traps (i.e., regular monitoring and resetting, disposal of dead rodents, possibly the dispatching of rats trapped but not killed). The disposal of dead rats, however, may be less of a disadvantage than with mice because the decomposing bodies of poisoned rats are likely to give off strong and unpleasant odors for a prolonged time, and poisoned rodents may be difficult to locate and recover.

For repeated infestations, snap traps are reusable, suggesting an overall per-infestation cost similar to or lower than the rodenticide products proposed to be cancelled.

In conclusion, the limited number and higher cost of RMD-conforming rat control products will result in incremental costs of addressing a rat infestation ranging from $46 in a minor infestation to $92 in a major infestation, or $8 per placement. Only a small proportion of residential consumers are expected to incur these costs, however, as commensal rats make up

about ten percent of residential rodent problems and only a portion of those problems would typically be addressed with rodenticide products proposed to be cancelled. Use of snap traps or glue boards, rather than RMD-compliant rodenticides, would result in a lower incremental cost of rat control, but may entail additional non-monetary costs.

3. Socio-Economic Equity Assessment

Changes in the per-unit cost of rodent control do not completely describe the impacts that may arise from the proposed cancellations. To place the estimated incremental cost in context, EPA has considered how the proposed cancellations would affect households that are at the poverty threshold. This concern is not only that these households have less income with which to purchase rodent control products, but also that, as according to the U.S. Census Bureau's American Housing Survey (Census Bureau, 2011), households below the poverty-threshold have a greater likelihood of rodent problems. The AHS reports that about 14 percent of U.S. households are below the poverty line, but they account for almost 20 percent of households observing signs of rodents.

To assess the per household impacts of cancellation, EPA compared the incremental costs, as presented in the previous section, likely to result from the proposed cancellations to household disposable income (i.e., excluding housing costs) at the poverty threshold. The poverty-threshold income varies depending on household size; this analysis used the income threshold for a three-person household as a reference, which is considered the average size household in the United States (Census Bureau, 2012). The poverty threshold is higher for larger household, thus the analysis is also representative of larger household at the poverty line. Monthly income rather than annual income was considered for two reasons. First, many low income households may lack savings or other methods for spreading the cost of rodent control

across time and will have to pay for it from immediate cash resources. Second, some households will face recurring rodent control costs rather than one-time or annual costs. The Census Bureau (2012) reports that households at or below the poverty line spend 42 percent of income on housing. Thus, for this analysis, EPA calculates monthly disposable income at $900.

For house mouse control, the average incremental costs for consumers using RMD-conforming rodenticide products instead of products proposed to be cancelled ranges from zero to two percent of monthly non-housing income at the poverty threshold. For commensal rat control, incremental costs for consumers at the poverty threshold range from five percent of monthly non-housing income in a minor infestation to 11 percent in a major infestation if they use the RMD-conforming rodenticides that are currently available. Use of glue boards or snap traps would result in incremental costs of one percent or over three percent of monthly non-housing income, respectively, plus non-monetary costs associated with the effort to set and monitor traps and dispose of dead or trapped rats.

Again, because those low income households facing rodent problems overwhelmingly have mouse problems (88% of rodent infestations are mice, per Census Bureau, 2011), it is expected that impacts on most low-income residential consumers will be equivalent to zero to two percent of monthly non-housing income. Moreover, because less than ten percent of low income households report having seen signs of rodents within the preceding three month period, it is a small proportion of low income households that would be subject to this burden.

It is also worth repeating here that if these households have, or are visited by, young children (or pets), they already should be using bait station products and the potential cost of the cancellation action on these users should not be relevant to the cancellation decision. In fact, by making bait stations more easily available (and possibly cheaper as they become more available),

the cancellation action may actually economically benefit lower income households with young children.

F. Potential for Resistance

EPA considered the risks of increased resistance to anticoagulant rodenticide products due to the proposed cancellation of certain consumer-oriented products containing SGARs and concluded that the risks are minimal. Resistance refers to genetic changes in a rodent population as a result of tolerant individuals being more likely to reproduce and pass that trait on to subsequent generations, as a result of rodenticides removing large portions of susceptible individuals. EPA recognizes that there is the potential for rodents to develop resistance to anticoagulants, as there is with most pest-pesticide combinations. However, residential consumer use of the conforming anticoagulant rodenticides will not be so widespread, frequent, and repetitive that enough anticoagulant tolerant individuals will be selected to result in a resistant population.

First, relatively few residential consumers face rodent problems. Current housing statistics show that only six percent of U.S. households report seeing rodent signs in the preceding 3 months (Census Bureau, 2011). With such a low percentage of households observing rodent signs nationwide at any one time, and given the widespread distribution of rodents, few sites are subject to widespread, frequent, and repetitive use of rodent control in general.

Second, rodenticides as a whole make up a relatively small proportion of residential control products. Market data indicate that traps account for about 70% of retail sales of rodent control products, with rodenticides account for the remaining 30% of sales (IRI, 2012b). And after SGARs are removed from the residential consumer market, the 30% of residential

consumer rodent control that relies upon rodenticides appears likely to be divided between rodenticides containing active ingredients with two very different modes of action: FGARs and bromethalin.

Finally, residential consumers are not the only persons controlling rodents. Some households will hire professional applicators who can utilize additional products, including SGARs. The external rodent populations from which residential infestations arise are also subject to control by commercial applicators and public health officials using SGARs. These personnel, along with natural predators, will exert their own selection pressures on rodent populations, further diminishing the likelihood of an anticoagulant tolerant individual surviving treatment by a residential consumer altering the genetic makeup of the rodent population.

Considering the lack of selection pressure resulting from the activities of residential consumers treating their own premises, EPA concludes that cancellation of the products identified in the NOIC presents, at most, a minimal risk of increasing the frequency of resistance-conferring alleles within U.S. populations of commensal rodents, even in areas with chronic rodent problems.

V. Conclusions Regarding Whether Subject Rodenticide Products Meet the FIFRA Registration Criteria

Despite mandatory label statements requiring use in tamper-resistant (or tamper-proof) bait stations where placements otherwise would be accessible to children, domestic animals, and/or non-target wildlife, each of these groups experience significant rodenticide exposures that cause risks of adverse effects. The rodenticide products identified in the NOIC (and listed in Tables 1 and 2 of this document) present significantly greater risks to domestic animals and non-target wildlife than other rodenticide products registered for the same uses, owing to various

factors. Chief among these factors are the presence of the active ingredients brodifacoum and difethialone and/or the absence of a bait station conforming to the criteria of the RMD in products registered for general consumer use in the control of commensal rodents. The exposures to children and risks to the environment caused by the rodenticide products identified in this document are unreasonable because they are avoidable through the use of alternative products that are effective and affordable.

A. Cancellation and Denial of Registrations of Rodenticides Containing Brodifacoum and Difethialone and Intended for Residential Consumer Use.

1. Effective alternatives to brodifacoum and difethialone are available.

All active ingredients and all or nearly all bait formulations containing them that are registered for use to control commensal rodents have met the applicable criteria for registration that EPA has established under FIFRA, including data requirements addressing the effectiveness of the products against wild-type rodents of the target species. Products containing bromethalin and FGARs rodenticides have been registered based on reliable studies demonstrating satisfactory effectiveness against target rodents. EPA concludes that cancellation of products subject to the NOIC will not cause residential consumers to lose the ability to control commensal rodents and will not increase the time required to control commensal rodents. Currently registered rodenticide products that contain bromethalin or FGARs, when used in combination with prudent sanitation and exclusion measures, are effective for general consumer use for the control of commensal rodents in and around buildings.

2. Alternatives to brodifacoum and difethialone are affordable.

The rodenticide active ingredient used does not appear to significantly affect the price of rodenticide products, so the replacement of products containing the active ingredients brodifacoum and difethialone with products containing other active ingredients will not increase the price of rodenticides. Inasmuch as residential consumers will be able to achieve essentially the same level of control of rodent infestations, within essentially the same time frame, and with essentially the same level of effort, using other currently registered rodenticide products, the cancellation of products containing the active ingredients brodifacoum and difethialone will not measurably increase the cost of rodent control.

3. *Residential consumer use of brodifacoum and difethialone causes adverse effects to non-target wildlife that could be avoided.*

Rodenticides that accumulate in rodents in quantities greatly exceeding the dose needed to kill the target pest, or that accumulate in predators and scavengers that consume target rodents, pose greater risks to non-target wildlife than rodenticides that do so to a lesser degree. Available toxicokinetic data indicate that the SGARs brodifacoum and difethialone are much more persistent in animal tissue than the FGARs chlorophacinone, diphacinone and warfarin. The available information on bromethalin supports a conclusion that it is rapidly eliminated from the body. These findings concur with the results of wildlife monitoring studies (analysis of animals that died from causes unknown or unrelated to rodenticide poisoning), which show that accumulation of brodifacoum residues is prevalent in many species of avian and mammalian predators and scavengers. Accumulation of difethialone also appears to be fairly prevalent in some areas, especially when considering the relatively low usage of this rodenticide in the United States. Species in which widespread accumulation of anticoagulant rodenticides in liver

tissue has been observed include owls, hawks, vultures, mustelids, bobcats, and mountain lions. Notably, rodenticides were detected in 100% of the great horned owls tested in one study in central Massachusetts and 100% of mountain lions tested in a study in southern California. Inasmuch as products containing brodifacoum and difethialone are only registered for use against commensal rodents in and around buildings and are not registered for field uses or use against other rodent species, all non-target wildlife exposures to brodifacoum and difethialone are believed to result from commensal rodent products registered for use in and around buildings.[19] Cancellation of brodifacoum and difethialone products sold to residential consumers is expected to reduce environmental loading of these highly toxic and persistent chemicals and to thereby reduce secondary poisonings among non-target wildlife. Information from several lines of evidence (i.e., predictions from toxicity and metabolism studies, whole carcass residue studies, secondary feeding studies, wildlife incident reports) indicate that brodifacoum and difethialone accumulate in body tissues to a greater extent, and persist for a longer time, than do warfarin, chlorophacinone, diphacinone, and bromethalin. The high retention of brodifacoum and difethialone in the tissue of prey animals, combined with the high toxicity of these chemicals, presents significant risks of secondary exposure to non-target predators and scavengers. Moreover, the potential for target rodents to consume a lethal dose of brodifacoum or difethialone in one night's feeding, and then to continue to consume additional bait for 3 or more additional days, can result in rodents with brodifacoum and difethialone body burdens well in excess of the dose lethal to the target pest, and in many cases in excess of the lethal dose for non-target predators and scavengers.

[19] Minor exceptions are restricted use products registered to the U.S.D.A. Animal and Plant Health Inspection Service for its use in eliminating non-native rodents from islands where they are disrupting the ecosystem. "Field uses" refers to uses in crop land, non-crop areas, ditch banks, river banks, gullies, irrigation ditches, railroad tracks, fence lines, buffer strips, garbage dumps, landfills, orchards, and rangelands.

Wildlife incident data support the quantitative risk assessment's conclusion that secondary exposure to brodifacoum poses lethal risk to predator and scavenger mammals and birds. The incident data set for difethialone is much more limited than that for brodifacoum, which is not surprising given difethialone's lower extent of use in the United States. However, analysis of the toxicity and retention time of difethialone indicates that its risks to predators and scavengers are more similar to those posed by brodifacoum than by warfarin, chlorophacinone, diphacinone, and bromethalin. Therefore, the lack of reported incidents involving difethialone may well be due to the low use of difethialone or to other factors not related to risk.

All the rodenticides subject to the NOIC present primary poisoning risks to non-target vertebrates. Primary poisoning risk for large non-target mammals and for birds can effectively be eliminated through the use of tamper resistant bait stations. However, the secondary exposure risk to predators and scavengers cannot be adequately addressed through use of bait stations alone. Risks of secondary poisoning are greater for products containing the SGARs brodifacoum or difethialone than for those containing warfarin, chlorophacinone, diphacinone, or bromethalin. Brodifacoum and (to a lesser extent) difethialone have been widely used by residential consumers, and residential consumer use may contribute significantly to brodifacoum and difethialone poisonings in non-target wildlife. Limiting availability of these chemicals in the consumer market will likely cause consumers who would otherwise buy brodifacoum and difethialone products to buy other rodenticides, thereby reducing use and environmental loading of brodifacoum and difethialone – and hence, secondary exposure risks to non-target wildlife. While switching to alternative rodenticides will not completely eliminate secondary exposure risks, EPA believes that these risks to wildlife will be significantly reduced if brodifacoum and

difethialone are not available to residential consumers but are limited to the professional, commercial and agricultural (structural only) markets.

4. Conclusion.

Non-target wildlife exposed to rodenticides containing brodifacoum or difethialone experience significant adverse effects. These adverse effects occur despite label statements requiring use in tamper-resistant bait stations where placements otherwise would be accessible to non-target wildlife. Brodifacoum and difethialone present greater risks to non-target wildlife than other rodenticides because they persist longer in the bodies of predators and scavengers, who may attain a lethal dose by consuming rodents that individually contain less than the dose that would be lethal to the secondary consumer. Brodifacoum and difethialone also present greater risks to non-target wildlife than other rodenticides because target rodents can continue to consume bait for several days after attaining a lethal dose, increasing their toxicity to predators and scavengers. Products containing brodifacoum and difethialone are only registered for use against commensal rodents in and around buildings. Significant numbers of incidents of secondary rodenticide poisonings of non-target wildlife involving brodifacoum and difethialone occur in urban and suburban areas, suggesting that use of products containing brodifacoum and difethialone in these areas pose significant risk to non-target wildlife.

These adverse effects could be substantially reduced if the quantity of brodifacoum and difethialone introduced in to the environment were reduced. Registered rodenticide products containing other active ingredients can provide essentially the same level of control of rodent infestations, within essentially the same time frame, and with essentially the same level of effort, at essentially the same cost, and without the higher risks associated with brodifacoum and difethialone.

Inasmuch as rodenticides containing the active ingredients bromethalin, chlorophacinone, diphacinone, and warfarin are effective, affordable, and cause significantly less risk to the environment, EPA concludes that the risks caused by residential consumer use of rodenticide products containing brodifacoum or difethialone active ingredients cause risks that are unreasonable. Accordingly, the following rodenticide products registered for general consumer use for the control of commensal rodents in and around buildings should be cancelled:

D- MOUSE PRUFE II, EPA Reg. No. 3282-65 (brodifacoum)

D- PELLETS GENERATION II, EPA Reg. No. 3282-66 (brodifacoum)

D- BAIT PELLETS II, EPA Reg. No. 3282-74 (brodifacoum)

D- READY MIXED GENERATION II, EPA Reg. No. 3282-81 (brodifacoum)

D- MOUSE-PRUFE III, EPA Reg. No. 3282-85 (difethialone)

D- BAIT PELLETS III, EPA Reg. No. 3282-86 (difethialone)

D- II READY MIX BAITBITS III, EPA Reg. No. 3282-87 (difethialone)

D- BAIT PACKS III, EPA Reg. No. 3282-88 (difethialone)

In addition, EPA denies applications for registration of the following products:

D-CON BAIT STATION XV KILLS MICE, EPA Application No. 3282-RNU (brodifacoum)

D-CON BAIT STATION XV KILLS MICE, EPA Application No. 3282-RNL (brodifacoum)

EPA denies these applications on account of the same risk concerns that are the basis for the cancellation of the products described above, and in addition, notes that because no one is currently relying on these unregistered products for rodent control, denial of these registrations does not cause any impacts to consumers. Nor does denial result in any loss of future benefits that are not available through other registered products that do not cause unreasonable adverse effects.

B. Cancellation and Denial of Registration of Rodenticides Intended for Residential Consumer Use In Controlling Commensal Rodents In and Around Buildings In Forms That Do Not Adequately Protect Against Access By Children, Companion And Domesticated Animals, And Non-Target Wildlife.

Rodenticide baits are directly accessible to children, domestic animals and non-target wildlife, unless the baits are placed where children, domestic animals and non-target wildlife cannot reach them or unless the baits are enclosed in bait stations that effectively prevent access by organisms larger than the target pests. In practice, it is difficult to place rodenticides in or around residential structures in places where children, domestic animals and non-target wildlife cannot reach them. Even if rodenticides are initially well placed, rodents often move unsecured, small-particle baits (e.g., pellets, granules, grain, meal) to other locations, which may be readily accessible to children, domestic animals and non-target wildlife.

The labels of each of the rodenticide products subject to the NOIC prohibit placement where children, domestic animals and non-target wildlife can reach them, unless they are enclosed in bait stations that qualify as tamper resistant. Although such bait stations exist, they are marketed primarily to commercial users, and they are seldom, if ever, available for purchase in retail stores where residential consumers typically purchase rodenticides. Consequentially, the widespread and commonly recognized practice of residential consumers has been to apply rodenticides without tamper resistant bait stations, in locations that in many instances fall short of label requirements prohibiting placement where children, domestic animals and non-target wildlife can reach them. That practice is becoming less common as registrants introduce new RMD-conforming products, but it likely continues unabated among purchasers of the products

subject to the NOIC. Although some residential consumers might purchase tamper resistant bait stations from the companies that supply them to commercial users, EPA believes that the number who do so is negligible in comparison to the number who do not. Moreover, the products subject to the NOIC are not designed or expected to fit securely in such third-party bait stations.

The primary exposures of children, domestic animals, and non-target wildlife to rodenticides, and the resultant risks, can be substantially reduced if the bait is contained in a bait station that meets the standards of the RMD. The RMD describes four types of bait stations varying in terms of resistance to children, dogs, and weather:

- **Tier 1** - Tamper-Resistant and Weather-Resistant: These bait stations are resistant to weather and to tampering by children and dogs. Tier I bait stations meet the tamper resistance and weather resistance standards set forth in Pesticide Registration Notice 94-7, and have also satisfactorily demonstrated the ability to isolate bait from children and dogs in laboratory testing conforming to EPA protocols.

- **Tier 2** - Tamper-Resistant (but not weather resistant): Tier 2 bait stations have satisfactorily demonstrated the ability to isolate bait from children and dogs in laboratory testing conforming to EPA protocols. Tier 2 bait stations have not met weather resistance standards; therefore, rodenticide bait products that include Tier 2 bait stations must be labeled for indoor use only.

- **Tier 3** – Tamper-Resistant for Children Only: Tier 3 bait stations have satisfactorily demonstrated the ability to isolate bait from children in laboratory testing conforming to EPA protocols. Tier 3 bait stations have not demonstrated the ability to isolate bait from dogs and have not met weather resistance standards; therefore, rodenticide bait products that include Tier 3 bait stations must be labeled for indoor use only and to prohibit placement where the product is accessible to domestic animals and/or non-target wildlife.

- **Tier 4** - Tamper-Resistance Unknown: Tier 4 bait stations have not been demonstrated to meet the testing standards required of the higher tiers, but must be made of a material of sufficient rigidity such that the station is not easily crushed or opened by a child less

than 6 years of age, not easily chewed by target rodents, and not reasonably anticipated to release rodenticide bait except for bait removed by target rodents and minor quantities of crumbs created by target rodents. Rodenticide bait products that include Tier 4 bait stations must be labeled for indoor use only and to prohibit placement where the product is accessible to children, domestic animals and/or non-target wildlife.

1. Rodenticides in bait stations that meet the standards of the RMD are effective alternatives to rodenticides without bait stations.

In order to be registered in the U.S. for use in and around residences and other buildings, rodenticide baits – whether formulated as blocks, pellets, meal, etc. – must meet the same criteria in laboratory efficacy trials. Rodenticide products purchased by professional applicators (including public health officials, pest control operators (PCOs), and other occupational applicators) are overwhelmingly in block form (Lublinkhof 2012). There is no basis for presuming that pelleted or meal baits offer faster control or a higher degree of control.

Bait-stations are widely used by professional applicators and effective rodent control has been achieved using bait stations in a wide variety of circumstances (Kaukeinen and Marsh 2009). For several decades, pesticides registered for use to control commensal rodents have had label statements requiring use in tamper-resistant (or tamper-proof) bait stations where placements otherwise would be accessible to children, pets, domestic animals, and/or non-target wildlife, and commercial and professional users generally achieve effective rodent control while complying with this requirement. Some rodents (particularly Norway rats) are wary of any new objects in their environments, and may avoid a newly introduced bait station for a period of time, however, the delay in initial entry is small compared to the variability in the other factors affecting the length of the treatment period needed to achieve control of an infestation even

without bait stations. Consequently, any delay in entry is unlikely to cause an measureable increase in the time required to control a rat infestation.

2. Rodenticides in bait stations that meet the standards of the RMD are affordable alternatives to rodenticides without bait stations.

Most residential consumers will not be affected by the proposed removal of rodenticides without bait stations from the residential consumer market, because most residential consumers use mechanical methods of control, which will not be affected by the proposed cancellations. Likewise, residential consumers who prefer to use rodent control services provided by professional and commercial applicators will not be affected by the proposed cancellations. Professional users (e.g., PCOs, commercial users, property managers, public health officials) generally have access to tamper-resistant bait stations (required by existing rodenticide labels for use outdoors and where placements otherwise would be accessible to children, domestic animals, and/or non-target wildlife) and will continue to have access to many registered rodenticides intended for use in those bait stations, and in addition, will continue to have access to rodenticides formulated as pellets, granules, grains, and meal if special circumstances might warrant their use. Inasmuch as these professional users will not be affected by the cancellations, neither will residential consumers who rely on their services.

The only users likely to be affected by the proposed cancellations are those residential consumers who purchase and use rodenticides for control of commensal rodents in and around buildings, and who prefer one or more of the products subject to the NOIC. Most such residential consumers are likely to experience only modest cost increases as a consequence of the proposed cancellation of rodenticide products registered for the control of commensal rodents in and around buildings products without bait stations conforming to the RMD criteria, because

there are multiple alternative rodenticide products conforming to the RMD and marketed at prices comparable to those of the products EPA proposes to cancel. And to the extent that these households have, or are visited by, young children and/or pets, they are already required to be using products in bait stations and the potential cost impact of the cancellation action on these users should not be relevant to the cancellation decision. Moreover, by making bait stations more easily available (and possibly cheaper as they become more available), the cancellation action may actually economically benefit lower income households with young children.

For residential consumers currently using rodenticide products that do not conform to the RMD to control mice, data from a recent national market survey shows the cost per placement for rodenticide products that include disposable bait stations for mice was $1.63 while the cost per placement for pellet products was $1.66, suggesting that consumers would face no incremental costs associated with the cancellation of the registrations of pelleted products (IRI, 2012a). For the much smaller number of residential consumers attempting to control rats (approximately10% of the consumer rodenticide market), the data suggest that some cost increases are likely. EPA estimates that the change in costs resulting from the proposed cancellations will range from $46 in a minor infestation to up to $92 in a major infestation. EPA has compared these changes in costs against monthly non-housing income for a family at the poverty threshold. For mouse control, incremental costs for control of a minor infestation would range from zero to two percent of monthly non-housing income at the poverty threshold. For rat control, incremental costs for consumers at the poverty threshold range from five percent of monthly non-housing income in a minor infestation to 11 percent in a major infestation. Because those low income households facing rodent problems overwhelmingly have mouse problems (88% of rodent infestations are mice, per Census Bureau, 2011), it is expected that impacts on

most low-income residential consumers will be equivalent to zero to two percent of monthly non-housing income. Moreover, because less than ten percent of low income households report having seen signs of rodents within the preceding three month period, it is a small proportion of low income households that would be subject to this burden.

Finally, in considering whether the risks posed by these rodenticide products are unreasonable, EPA does not believe it appropriate to attribute any significance to potential cost increases for consumers who are currently using the products subject to the NOIC in violation of their label requirements, i.e., in circumstances where children, domestic animals, or non-target wildlife can get access to the product. Such uses present unreasonable risks and cannot reasonably be viewed as benefits to society that would be lost as a result of the cancellations.

3. Rodenticides without bait stations cause adverse effects to children, non-target wildlife and domesticated and companion animals that could be avoided.

Bait stations that conform to the standards of the RMD are designed to prevent children, domestic animals and non-target wildlife from being able to come into contact with rodenticides. The rodenticide products proposed for cancellation lack significant engineering controls against contact by children, domestic animals and non-target wildlife, and therefore rely on users to only place the rodenticides where they would not be accessible to children, domestic animals, and/or non-target wildlife in order to prevent exposure and ingestion of rodenticides. Use of a bait station that substantially reduces exposure to the bait plainly poses less risk to children, domestic animals and non-target wildlife risk than presentations that allow direct contact with the bait.

Many thousands of incidents of children being exposed to rodenticides have been reported. Although most exposures generally result in no clinical harm, these events are not risk-

free and should not be taken lightly. The high numbers of reports of exposed children are of concern because every exposure event presents the possibility of significant adverse health effects. Approximately 85% of the rodenticide exposures reported to AAPCC involved children under 6 years old (i.e., approximately 15,000 per year during the period1999-2009; approximately 11,000 in 2010). These incidents may have resulted from failure to follow label directions to keep bait away from children, though in some cases, baits might have been moved by rodents from appropriate placement locations. In some cases, it appears that parents underestimated children's abilities to access places where rodenticides were applied. In other cases, it appears that the exposed children were visiting a different environment (such as grandparents, friends, or neighbors) and their parent or guardian was unaware that the baits were accessible. Every child's exposure event is of concern, because any time a child can access rodenticide bait, there is the potential for the child to swallow an amount sufficient to cause adverse effects.

Of the rodenticide incidents to reported to AAPCC from 1999 to 2005, approximately one percent of exposed children (an average of 128 cases per year) experienced a medical outcome classified by AAPCC as minor, moderate or major. Such symptomatic exposures – diagnosed or undiagnosed – are a matter of concern, both for the symptoms themselves and (in the case of anticoagulants) on account of the risk of excessive bleeding (internally or externally) in response to subsequent trauma. The adverse health consequences of these symptomatic exposures could be prevented through the use of tamper resistant bait stations, as could the social and economic costs that arise from addressing children's asymptomatic exposures to rodenticides, including economic costs to health care facilities and poison control hotlines, and social and economic costs to the families whose children are exposed.

EPA's analysis shows that, unless use and exposure patterns are changed, children could easily ingest quantities of the subject rodenticides that would contain sufficient amounts of active ingredient to exceed levels that EPA would consider safe. A single 5 gram bite (less than a quarter of an ounce) of any of the rodenticide baits subject to the NOIC would result in a pesticide exposure that greatly exceeds levels considered safe as a dietary exposure for a child weighing 10 kg, and the quantity of active ingredient contained in a single placement of rodenticide baits subject to the NOIC is sufficient to cause adverse health effects. Consequently, EPA could not conclude that exposure to the subject rodenticides was reasonably certain not to cause harm. EPA fully appreciates that the rodenticide products at issue are governed by the FIFRA risk-benefit standard rather than the FFDCA reasonable certainty of no harm standard, and that any hearing on the NOIC must consider the benefits of rodenticide use against the risks of such use. Nevertheless, the FFDCA criteria for unsafe exposures to pesticides in food provide a meaningful benchmark: If Congress would not allow these levels of pesticide exposure in food – no matter how beneficial the pesticide use might be to agricultural producers – it is reasonable to infer that children should not suffer the same levels of exposures through other routes absent important countervailing benefits.

Rodenticides are implicated in numerous reported accidental poisonings of domestic animals, which have the potential to result in death and other severe outcomes that have required veterinary care. In 2010, APCC identified rodenticides as the third most likely cause of pet poisonings and the Pet Poison Helpline identified rodenticides as the third most common toxin involved in dog poisonings and the fourth most common toxin involved in cat poisonings. OPP's IDS identifies two rodenticides (brodifacoum and bromadiolone) in the top 20 pesticides most likely associated with a domestic animal fatality. OPP's IDS indicates that in recent years

there are about 2000 reported incidents per year of domestic animals exposed to rodenticides. Many of these exposures result in severe outcomes -- on average 14% result in death or a major outcome -- which may necessitate veterinary care. The IDS data indicate that about 160 severe (death or major effect) domestic animal incidents attributable to rodenticides are reported every year, which EPA believes significantly underestimates the actual number of incidents.

The various lines of evidence evaluated by EPA have led the Agency to conclude that risks to non-target wildlife from all the rodenticides addressed in the NOIC are significant. There is little question that non-target wildlife are being exposed to rodenticide bait products. Incident reports and exposure studies make clear that a wide range of mammalian and avian wildlife can come into contact with the rodenticides from primary exposure, and these primary consumers can put predator and scavenger species at risk of secondary exposure. EPA's quantitative assessment and the incident data provide evidence that rodenticide exposure causes non-target wildlife deaths. Although many non-target wildlife species avoid areas of human habitation, significant numbers of incidents of both primary and secondary rodenticide poisonings of non-target wildlife occur in urban and suburban areas. These data suggest that residential and commercial uses of rodenticides for commensal rodent control pose significant risk to non-target wildlife.

Moreover, regardless of collection location, autopsies and biopsies of predatory and scavenging wildlife routinely show accumulation of rodenticide residues in liver tissue of numerous predatory and scavenging wildlife species, including owls, eagles, hawks, vultures, mustelids, bobcats, and mountain lions. Numerous monitoring studies conducted throughout the United States have found SGARs present in over 85% of individuals of one or more species studied. The prevalence of SGARs in wildlife regardless of location of collection indicates that

rodenticides used in and around buildings for control of commensal rodents (the only lawful uses of SGARs) affect predatory and scavenging wildlife everywhere.

Bait stations conforming to the RMD can prevent primary exposures to birds and to mammals larger than mice and rats by preventing them from direct access to the bait. While bait stations cannot prevent secondary exposures to intoxicated prey, bait stations can ensure that fewer intoxicated birds and mammals are available as prey.

4. Conclusion.

The rodenticides subject to the NOIC are poisonous to all mammals and birds. Exposure to these rodenticides is widespread among children, domestic animals, and non-target wildlife. If rodenticides continue to be available in the residential consumer market without bait stations, these exposures are likely to continue.

Bait stations conforming to the RMD criteria can significantly reduce rodenticide exposures among children, domestic animals, and non-target wildlife, compared to products without bait stations conforming to the RMD criteria. EPA has determined that control of commensal rodents in and around buildings by residential consumers can be satisfactorily accomplished with rodenticides protected by bait stations. For many years, labels for commensal rodenticides have required that baits used where children, domestic animals, and non-target wildlife might be exposed must be placed in tamper-resistant bait stations. Registered rodenticide products that include bait stations that meet the RMD criteria are now available on the market at costs comparable to the rodenticide products subject to the NOIC, and, when used in combination with prudent sanitation and exclusion measures, are effective for the control of commensal rodents in and around buildings.

Inasmuch as rodenticides in bait stations that meet the standards of the RMD are available, effective, affordable, and cause significantly less risk to man or the environment, rodenticide products intended to control commensal rodents in and around structures and marketed for general consumer use cause unreasonable risks unless they include a bait station that meets the standards of the RMD. Accordingly, EPA proposes to cancel the following rodenticide products registered for the control of commensal rodents in and around buildings products without bait stations conforming to the RMD criteria:

D-CON CONCENTRATE KILLS RATS & MICE, EPA Reg. No. 3282-3 (warfarin)

D- READY MIXED KILLS RATS & MICE, EPA Reg. No. 3282-4 (warfarin)

D- MOUSE PRUFE KILLS MICE, EPA Reg. No. 3282-9 (warfarin)

D- PELLETS KILLS RATS & MICE, EPA Reg. No. 3282-15 (warfarin)

D- MOUSE PRUFE II, EPA Reg. No. 3282-65 (brodifacoum)

D- PELLETS GENERATION II, EPA Reg. No. 3282-66 (brodifacoum)

D- BAIT PELLETS II, EPA Reg. No. 3282-74 (brodifacoum)

D- READY MIXED GENERATION II, EPA Reg. No. 3282-81 (brodifacoum)

D- MOUSE-PRUFE III, EPA Reg. No. 3282-85 (difethialone)

D- BAIT PELLETS III, EPA Reg. No. 3282-86 (difethialone)

D- II READY MIX BAITBITS III, EPA Reg. No. 3282-87 (difethialone)

D- BAIT PACKS III, EPA Reg. No. 3282-88 (difethialone)

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VI. Citations

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