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OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: Response to Public Comments on Draft Ecological Risk Assessment for 7 Anticoagulant Rodenticides

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This memorandum provides the Environmental Fate and Effects Division's (EFED) responses to public comments on the draft ecological risk assessment (DRA) for seven anticoagulant rodenticides (ARs)[1]. These include the first-generation anticoagulants (FGARs) warfarin, diphacinone, and chlorophacinone; and the second-generation anticoagulants (SGARs) brodifacoum, bromadiolone, difenacoum, and difethialone. See **Table 1** below.

The DRA was posted for a 60-day public comment period from May 4 to July 6, 2020 in the public docket EPA-HQ-OPP-2015-0768, at www.regulations.gov.

[1] Seven Anticoagulant Rodenticides: Draft Ecological Risk Assessment for Registration Review. DP 453282. March 17, 2020.

Table 1. Anticoagulant rodenticides included in the 3/17/2020 grouped DRA	
Chemical (PC code)	***Registration Review Docket***
First generation anticoagulant rodenticides	
Chlorophacinone (067707)	EPA-HQ-OPP-2015-0778
Diphacinone (067701)	EPA-HQ-OPP-2015-0777
Warfarin (086002)	EPA-HQ-OPP-2015-0481
Second generation anticoagulant rodenticides	
Brodifacoum (112701)	EPA-HQ-OPP-2015-0767
Bromadiolone (112001)	EPA-HQ-OPP-2015-0768
Difenacoum (119901)	EPA-HQ-OPP-2015-0769
Difethialone (128967)	EPA-HQ-OPP-2015-0770

Commenter: Animal and Plant Health Inspection Service (APHIS), U.S. Department of Agriculture (USDA)

APHIS Comment: USDA APHIS supports the continued registration of the various rodenticides evaluated during this registration review process. Many of these products have important conservation uses in addressing invasive mice and rat populations on islands, as well as other uses important to protecting agriculture and human health. USDA APHIS will continue to work with the EPA to maintain regulatory compliance for the above-listed products it has registered with the Agency.

> **EFED Response:** EPA recognizes that the APHIS registrations are used in support of conservation efforts in consultation with the U.S. Fish and Wildlife Service, and that APHIS takes appropriate measures to safeguard protected species while using diphacinone and brodifacoum for this purpose. EPA anticipates that the relatively controlled nature of the island rat eradication programs will offer valuable insights into the effects of ARs on listed species.

Commenter: Office of Pest Management Policy (OPMP), USDA

OPMP Comment: The 2008 Risk Mitigation Decision for Ten Rodenticides (RMD) also limited broadcast applications of the FGARs chlorophacinone and diphacinone to certain non-residential uses. Floating bait stations with chlorophacinone are allowed only to control muskrats in California and may only be purchased through agricultural commissioners. For agricultural use, certain site-specific mitigations can further reduce exposure to wildlife. For example, elevating bait stations can eliminate access to bait for many protected mammal species, such as kangaroo rats and the Tulare grasshopper mouse, which are not usually associated with climbing trees.

> **EFED Response:** EPA welcomes OPMP's suggestions for Best Management Practices (BMPs) (e.g., elevated bait stations), if they can be shown to offer greater protection for wildlife than current label instructions. CalDPR has shared specifications for both a modified and elevated bait station mitigation intended to reduce take to listed species. Other California mitigations are documented in the PRESCRIBE database (https://calpip.cdpr.ca.gov/county.cfm).

OPMP Comment: USDA encourages EPA to continue to examine efficacy of prior mitigations, and to consider the importance of rodenticide uses when developing any additional mitigations. Particularly, USDA appreciates that EPA acknowledges that the FGARs chlorophacinone and diphacinone account for only 13.6% of reported incidents that were rated as 'highly probable', 'probable', and 'possible', despite their potentially riskier use pattern. It is unclear from the data provided in the anticoagulant and non-anticoagulant risk assessments how many incident reports were associated with legal uses, or how many were associated with residential uses compared to agricultural or commercial. Additional characterization of incidents may provide insight into which use patterns are more frequently associated with incidents.

> **EFED Response**: EPA will continue to monitor the effectiveness of the 2008 RMD mitigations. It is difficult to associate particular incidents with specific use patterns, especially when carcasses are found at a distance from actual use sites, as in this case. While chlorophacinone and

diphacinone accounted for only approximately 13.6% of reported incidents, it is difficult to interpret this observation given that a vast majority of incidents that occur are not reported to EPA.

Commenter: Hacco, a Neogen company

Hacco Comment: We note that MRID 50951801, Diphacinone Technical Grade Earthworm (*Eisenia fetida*) 28-Day Sub Chronic Toxicity Limit Test was submitted after generation of the draft risk assessment and request that it be included in the final risk assessment.

> **EFED Response:** A Data Evaluation Record (DER) for this study will be prepared and made available to the commenter and posted to the docket at www.regulations.gov. The data will be considered in any future risk assessment for diphacinone.

Hacco Comment: On page 63 of the risk assessment, it is stated that "insects such as ants or cockroaches are sometimes attracted to the bait and may feed on it or transport it outside of the bait boxes where they, as well as the bait particles, may be consumed by insectivorous wildlife." What data is available to demonstrate this path of exposure? The statement is made but no data is cited as a clear line to support this as a viable exposure pathway.

> **EFED Response:** This route of exposure was identified through a combination of bioaccumulation data, data showing low toxicity to invertebrates and incidents in insectivorous birds. It has also been documented by M. De L. Brooke et al., Persistence of brodifacoum in cockroach and woodlice: Implications for secondary poisoning during rodent eradications, Ecotoxicology and Environmental Safety 97 (2013) 183–188, and L.H. Booth et al., Toxicity and residues of brodifacoum in snails and earthworms, DOC SCIENCE INTERNAL SERIES 143, Department of Conservation PO Box 10-420 Wellington, New Zealand.

Commenter: Syngenta Crop Protection, LLC

Reference: Page 41; 7.1 Overall Process; Paragraph 3: "In this assessment, risk to birds and mammals will be quantified through assessing AR levels in non-target taxa through the consumption of bait based on both one-day consumption and consumption over six days."
Syngenta Comment:
EPA presumes that birds and mammals - other than those targeted, i.e., commensal rodents - can be exposed via direct consumption of the bait for all uses, including uses that require tamper resistant bait stations. Wildlife, especially birds, are unlikely to be directly exposed to brodifacoum contained in tamper-resistant bait stations that are required for brodifacoum-based formulations.

In previous responses to comments (EPA-HQ-OPP-2015-0767-0043), EFED noted that "though bait boxes will certainly limit direct exposure to the bait contained within them for larger birds and mammals unable to enter the boxes, there is no guarantee that bait particles will not be removed and transported outside of these stations by targeted or non-targeted organisms, such as insects

or small reptiles that enter the bait stations and then leave."

> **EFED Response:** The bait stations required by the 2008 RMD were intended, in part, to limit exposure of wildlife, including birds, to anticoagulant rodenticides, but were not expected to reduce exposure to zero. EPA's analysis of ecological incident data shows that birds continue to be exposed, but EPA cannot determine the exposure route or routes with certainty. Table 6-9 in the draft risk assessments lists the bird species involved in incidents. Many of these species are not predators of small mammals (e.g., geese, ducks, doves, gulls, turkeys, etc.) thus it is suspected that their exposure was via other routes, including direct dietary consumption. This could include consumption of tolerant invertebrates (e.g., maggots) from carcasses.

Reference: Page 41; 7.1 Overall Process; Paragraph 3: "The chronic risk to birds via secondary exposure will be quantified for chlorophacinone. A reproductive study on chlorophacinone will be used to qualitatively estimate lowest-observed-adverse-effect concentrations (LOAEC), using 5-day dietary LC50 data on the other 6 ARs."

Syngenta Comment:

Syngenta appreciates that the Agency has allowed a waiver for the avian reproduction study for brodifacoum. However, it appears that the Agency still considers the avian reproduction endpoint important for the risk assessment even though it is based on an exposure that is not relevant for wildlife secondary exposure to anticoagulant rodenticides.

Syngenta questions whether avian reproduction studies provide any value for the ecological risk assessment given that:

- The current guidance requires birds to be exposed continuously for several weeks, which is not representative of actual exposure to birds (especially raptors); and
- The practical difficulties of long-term administration of anticoagulants, would likely result in failure to meet the guideline requirements.

> **EFED Response:** EPA has agreed to waive avian reproduction studies for the remaining anticoagulant rodenticides, recognizing the difficulties involved in such studies, and has stated its intention to instead use the ACR as documented on p. 64-65 of the DRA. EPA's conclusion is that reproductive effects in birds are likely, given documented exposures and estimated LOAECs. However, any additional data directly bearing on reproductive outcomes (eggs laid, eggs hatched, 14-day survivorship, etc.) in birds or other taxa would be welcome.

Reference: Page 64, Paragraph 1: "Estimation of Avian Chronic LOAEC for Several ARs."

Syngenta Comment:

As avian reproduction endpoints for brodifacoum have not been determined, a LOAEC for brodifacoum was estimated using the brodifacoum LC50 and the chlorophacinone equation: 2.7 mg a.i./kg-diet / 1792 = 0.0015 mg a.i./kg-diet. The EPA acknowledges that there is uncertainty in applying the chlorophacinone ACR to the other anticoagulant rodenticides, including brodifacoum. In addition, Syngenta requests the use of the difenacoum ACR of 1,155 in lieu of the chlorophacinone ACR for estimating the brodifacoum LOAEC. As a SGAR, difenacoum may be a more appropriate surrogate for brodifacoum than chlorophacinone (i.e., a first generation anticoagulant rodenticide FGAR) given the

differences noted in both toxicity and persistence (i.e., bioaccumulation) in tissues between the SGARs and FGARs. Although the difference in the estimated brodifacoum LOAEC may appear negligible (i.e., 0.0023 compared to 0.0015), the ratio of exposure to effect level value for brodifacoum (i.e., Table 9-18 in the Ecological Risk Assessment) would be 11,291 as opposed to the current value of 13,000 estimated using the chlorophacinone ACR.

However, as noted previously, Syngenta questions the relevance of the guideline avian reproduction endpoint in a risk assessment for wildlife secondary exposure to anticoagulant rodenticides.

> **EFED Response:** EPA recognizes the difficulty of performing avian reproduction studies with anticoagulant rodenticides, thus the proposal to use an ACR. EPA will consider Syngenta's comments when conducting future risk assessments, however reproduction effects in birds are considered likely given documented exposures. Also, EPA believes its ACR analysis is correct in the current assessment, and that an exposure-to-effect ratio of 11,291 will not lead to different conclusion than a ratio of 13,000 in any future assessment.

Reference: Page 5; General Conclusions from the Incident Analysis; Paragraph 3: "The reported incident data show an apparent increase in wildlife exposure and deaths. This may be attributed to greater effort in seeking out incidents, especially in California. The report cited herein was the result of a formal petition by an NGO. The data presented in this assessment therefore do not necessarily represent an increase in incidents, but instead show that upon closer examination, incidents continue and have apparently not decreased."

Syngenta Comment:

Syngenta agrees with the view that the trends in the incident data may be attributed to greater effort in seeking out incidents and is heavily weighted toward California (51% of reported incidents) which has active monitoring versus other States. As mentioned by the Agency (p. 63), "incident reporting is not standardized and is potentially subject to error in reporting" and "should be interpreted with caution." In addition, the incident data reported tends to be biased towards distressed/deceased animals or animals suspected of being exposed. This likely resulted in a greater probability of a detection with a higher tissue concentration than in wildlife populations as a whole.

Like all incident reporting, data reported by wildlife agencies are not specifically collected to support a regulatory risk assessment. Without clearly designed monitoring studies that establish a baseline exposure of non-target wildlife, it is extremely difficult to determine whether the incident data represent an overall change in exposure and subsequent unacceptable risk to wildlife populations.

> **EFED Response**: EPA recognizes that it is not certain that the nation-wide effects of the 2008 RMD can be discerned from the incident data that has been reported to date. As a result, EPA concluded that there was no apparent decrease in incidents, although it is not concluded that the 2008 RMD was ineffective in this regard. EPA expects that trends in the incident data reflected in states with robust monitoring programs such as California and New York would also

be observed in other states if a sufficient monitoring effort were made. EPA agrees that off-label use could potentially confound the overall exposure assessment on a local level.

Commenter: Liphatech

Liphatech Comment: Instead of relying on incident data and laboratory toxicity studies as the Draft Risk Assessment does, we recommend the Agency adopt a broader approach that incorporates the best available information from additional sources, and prioritizes filling in the data gaps to address the following list of questions:

1. How can wildlife populations be sampled for rodenticide exposure and effects using standardized and statistically robust methods?
    a. What proportion of a population is being exposed?
    b. What proportion of exposed individuals are compromised?
    c. How do the AR compounds differ in their probability of detection?
2. How do application methods differ in both the likelihood and magnitude of exposure?
3. How accurately do toxicity results from small groups of taxonomically distant surrogate species in laboratory studies predict the effects in wild populations of different species?
4. How should tissue residue values be interpreted?
5. How can the effects of ARs be distinguished from those of other anthropogenic chemicals and stressors?
6. What are the causal mechanisms linking exposure to sublethal and reproductive effects?

> **EFED Response**: The Overview document (EPA, 2004) describes OPP's methods for ecological risk assessment. These methods rely mainly on laboratory toxicity testing, exposure modeling, and characterization of risks from the comparison of toxicity endpoints and estimated exposures. Monitoring data, including wildlife incidents, are used to document actual exposures and the resulting adverse effects. The questions that Liphatech poses are commonly addressed in OPP's FIFRA risk assessments (e.g., questions 2, 3, and 4). Data relevant to questions 1a and 1b are also available in open literature, wherein animals are evaluated for AR toxicosis; however, these data often come from deceased animals or populations of animals in clinics which may not be fully representative of the total population in an area. Detection of ARs depends on analytical methods, their half-lives in environmental compartments and body tissues, and time since exposure (question 1c). Question 5 is outside the bounds of a typical FIFRA assessment, however it is recognized that certain natural substances have anticoagulant properties (for example, sweet clover disease in cattle). Sublethal and reproduction effects are linked to exposure through the general weakening effects of hemorrhages, if they are not fatal (question 6).

Liphatech Comment: The incident data from the Agency's Incident Data System (IDS), the California Department of Pesticide Regulation's (CDPR) 2018 Investigation Report, the Kentucky Department of Fish and Wildlife Resources' analysis of barn owl carcasses, and the analysis of raptors admitted to a Massachusetts wildlife clinic do not provide data on the rates of exposure for wildlife populations. An exposure rate would be the number of animals testing positive, including both symptomatic and asymptomatic individuals, expressed as a proportion of an index representative of the total population.

Incidents involving endangered species, such as the San Joaquin kit fox, should be evaluated separately to identify and address how exposure is occurring to individuals. The incidents listed in Table 6-9 for seabirds, shorebirds, and New Zealand species, and all those listed in Table 6-11, occurred during island eradications, which primarily apply bait by aerial broadcast. The island conservation uses were explicitly exempted by the 2008 RMD and should be removed from consideration in the Final Risk Assessment.

> **EFED Response**: EFED agrees that is difficult to interpret the wildlife incident data, including sampling bias, rates of exposure, and the discernment of trends. This is why the data were interpreted qualitatively as indicating no "apparent decrease" in the number of incidents, but that incidents were continuing. More robust, statistically sound monitoring programs are expensive and difficult to carry out, and so would likely have to be funded by industry. Incidents associated with listed species, such as the San Joaquin kit fox, may be considered in species specific risk assessments, e.g., biological evaluations. EPA is aware of the island rat eradication programs, and may look to their results as indicative of a more controlled experiment, and their use to benefit listed species, as well as possible mitigation strategies.

Liphatech Comment: Wildlife may be exposed to anticoagulant rodenticides through a number of pathways, which vary considerably in their complexity. Constructing an exposure pathway requires accurate information about the source of the rodenticide, each species' diet and foraging behavior, and the prevalence of exposure within each species' population. A limitation of the current state of knowledge for exposure pathways is that the studies conducted are qualitative, and therefore unable to predict the likelihood of exposure for individuals (which is needed for endangered species), the proportion of a population that is exposed, and the effect on survivorship or other demographic parameters as a result of the exposure. Quantitative data from field studies are urgently needed to develop probabilistic models of exposure and effects.

Substantial progress is being made on employing new approaches to detect nontarget exposure and quantify the effects of applied rodenticide that travels through specific routes to each nontarget species. Studies using cameras and direct visual observations provide documentation of nontarget species' interactions with bait or the target species at or near the source of the rodenticide application. This information is being used to identify Best Management Practices tailored for different application methods and specific to habitats and nontarget species. One such example is elevating bait stations off the ground when targeting roof rats, a simple measure that excludes native nontarget rodents from entering.

> **EFED Response:** EFED appreciates the suggestions to improve documentation and measurement of exposure pathways. Such field studies are beyond the scope of a FIFRA risk assessment, although the research goals would greatly help to understand actual risks. EPA also welcomes Liphatech's suggestions for BMPs (e.g., elevated bait stations for roof rats), if they can be shown to offer greater protection for wildlife than current label instructions.

Liphatech Comment: The toxicity values of the anticoagulant compounds have been derived from laboratory studies with only a few species. These domestic strains of birds and mammals serve as

surrogates for a broad range of taxa. The accuracy of using toxicity values to predict the effects of exposure on individuals and populations of wildlife needs to be assessed because susceptibility to the anticoagulants varies substantially between individuals and species. Results from toxicity studies can be inconsistent even among test groups of the same species conducted under identical conditions. Furthermore, the exposure method can produce different results (oral gavage of technical a.i. vs dietary exposure) and the composition of diets in the wild can affect the absorption of and response to an ingested dose. A thorough review of the issues associated with laboratory toxicity studies can be found in Rattner and Mastrota (Chapter 3 in 'Anticoagulant Rodenticides and Wildlife' (van den Brink et al., Eds., 2017)).

> **EFED response:** EPA routinely uses data from two or three bird species (typically mallard duck, bobwhite quail, and a passerine species) to assess the toxicity of a pesticide to avian species in its risk assessments. Because not all individual species can be tested, a surrogate approach is used, extrapolating results from the three test species to all wild bird species. Literature data from other species is used, as available. EPA recognizes the uncertainties in this approach, and routinely accounts for it in risk characterization. Recently, EPA examined the route of administration in its acute avian tests and found that the oral single dose (LD_{50}) was generally more sensitive than the 5-day dietary test (LC_{50}) with the notable exception of the SGARs.

Liphatech Comment: The methods for estimating the risk from cumulative exposure make multiple assumptions that, while being conservative, likely result in values that may not be representative for most exposures in the wild. The accuracy of the estimate would be increased by incorporating a pharmacokinetic approach.

> **EFED Response**: EPA's approach to "cumulative" exposure (in this context, repeated exposure to a single compound over time) for the anticoagulant rodenticides is the same as in the previous risk assessment, supporting the 2008 RMD, and its conservative nature is acknowledged. EPA would welcome additional data on liver half-life, body burden, metabolism and excretion rates. EPA would also be interested in an applicable pharmacokinetic model, if it were helpful in suggesting mitigation strategies.

Liphatech Comment: Chronic risk to birds was estimated using two reproductive toxicity studies, one with chlorophacinone on the mallard duck (*Anas platyrhynchos*), and the other with difenacoum on the Japanese quail (*Coturnix coturnix japonica*). Both of these are proprietary studies submitted by registrants that are not available for review. The Draft RA states that a reduction in the mean 14-day survivor weights in the reproductive toxicity study with chlorophacinone on mallard ducks was used to establish the LOAEC. This value may not provide an accurate prediction of the effects of chronic exposure across taxonomic groups in the wild.

> **EFED Response**: As noted previously, EPA routinely uses data from two or three bird species (typically mallard duck, bobwhite quail, and a passerine species) to assess the toxicity of a pesticide to avian species. Because not all individual species can be tested, a surrogate approach is used, extrapolating results from the three test species to all wild bird species. Literature data from other species is used, as available. EPA recognizes the uncertainties in this

approach, and routinely accounts for it in risk characterization. Because avian reproduction data has been waived for the five remaining anticoagulant rodenticides, EPA will use the data it has on chlorophacinone and difenacoum and will extrapolate the results to the entire group of FGARs and SGARs.

Liphatech Comment: We agree with the Agency's statement that the biological evaluations for the ARs will require greater certainty with respect to the level of exposure associated with reproductive effects to make effects determinations and to set the action area for endangered species. Identifying studies that provide this information should be a high priority for discussions between the Agency, the U.S. Fish and Wildlife Service, registrants, researchers, and other stakeholders.

EFED Response: EPA would welcome any data that would help to better assess risks to reproduction in birds.

Liphatech Comment: We note the Draft RA's use of a limited selection of literature and urge the Agency to review the much larger body of relevant literature available (e.g., recent publications, and the book on Anticoagulant Rodenticides and Wildlife (van den Brink et al., Eds., 2017)).

EFED Response: EPA's risk assessment was focused on wildlife incidents and avian reproduction, the major areas of uncertainty relevant to risk management of these anticoagulant rodenticides. The general risk profile for these anticoagulant rodenticides has already been established in prior EPA risk assessments. Thus, not all literature was relevant to this assessment. However, the cited publication does touch (pp. 100, 103) on the differential toxicity and metabolism of the many enantiomers of several of the SGARs, which may be an avenue for reduction of harm to wildlife. This would require submission of reformulated rodenticides as new active ingredients with the less toxic, less persistent enantiomers enriched; this is considered the most promising route of future mitigation to reduce the adverse effects of SGARs.

Liphatech Comment: We also recommend that the Agency conduct its own review and analysis of the material used by CDPR in its 2018 investigation. CDPR's analysis calls attention to the assertion in Serieys et al. (2018) that a high proportion of individuals (62%) with no detectable levels of ARs in blood were in fact 'false negatives' based on the higher detectability of the ARs in liver vs. blood. CDPR expresses concern over this issue, which was not disclosed by the authors in their 2015 publication.

EFED Response: EPA thanks the commenter for bringing the "false negative" issue to our attention. Caveats for each study were noted in our open literature review summary (OLRS). EPA used the CDPR analysis at face value in the FIFRA risk assessment.

Liphatech Comment: The link between AR exposure and immune dysfunction in bobcats has not been independently validated, and conflicting results have been published by USDA researchers who were unable to produce immunosuppressant effects in domestic cats (*Felis catus*) in a laboratory study with brodifacoum (Kopanke et al. 2018). The authors of this study raise a number of arguments that the association between mange and AR exposure has not been proven and should be considered correlative. The effects of exposure to other anthropogenic chemicals and stressors known to cause

immunosuppressant effects were not thoroughly assessed. The inconsistent findings and conclusions from this group of studies highlights the need for much more research in this area.

> **EFED Response**: EPA thanks the commenter for bringing this issue to our attention. The association of AR exposure and mange in wild cats falls into the category of sublethal effects, rather than EPA's apical effects endpoints (survival, growth, reproduction), and thus does not figure quantitatively in the FIFRA assessment.

Commenter: Responsible Industry for a Sound Environment (RISE)

RISE Comment: Certain exposure data calculations, which appear to be errors resulting from copying or transposing data from various sources, are off by several orders of magnitude. Revisiting these calculations will provide a more accurate exposure picture. We recommend the 2004 Erickson data, which is of sufficient quality as one resource for revising and refining the calculations. (Erickson, W.; Urban, D. Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: A Comparative Approach; U.S Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC, 2004.)

> **EFED Response:** EFED obtained formulas for calculation of exposure from our own past risk assessments. EFED also re-ran those calculations to ensure that the same results were found. EFED would appreciate any specific example of calculations which may be in error from the commenter.

RISE Comment: It is unclear why incidents from island eradication efforts are included in this risk assessment and more explanation would be helpful as well as providing an opportunity for refinement. These applications are unique and unusual, and while essential for protecting species and fragile island ecosystems, are not representative of regular, labeled use patterns.

> **EFED Response:** EPA recognizes that the APHIS registrations are used in support of conservation efforts in consultation with the U.S. Fish and Wildlife Service. APHIS takes appropriate measures to safeguard protected species while using diphacinone and brodifacoum for this purpose. Therefore, these incidents were included in EPA's analysis because they constitute an approved, controlled use of these rodenticides. They also offer a unique situation where these chemicals are used, and there is systematic monitoring afterwards to give insight into the ecological risks and secondary exposure.

RISE Comment: Relative to chronic toxicity to birds, we believe EPA's consideration of the following information would refine this portion of the risk assessment for most, if not all, of the rodenticides under review:

- All bait that is used outdoors and above ground is required to be placed in tamper-resistant bait stations that are designed to exclude non-rodent animals;
- Bait stations represent a point-source of exposure (not a broadcast application) that limits not only the size of birds that could enter the stations but also the amount of bait that could be

consumed as the bait stations contain limited quantities of bait;
• The design of bait stations and form of the bait selected can minimize access, so that even a small bird that could potentially enter a bait station would not likely stay in the station long enough to access much (if any) bait;
• Labels which permit bait to be used outdoors include risk mitigation language that limits the potential exposure to non-target animals (e.g. collecting and disposing of dead rodents); and
• Even in the unlikely event of accidental non-target exposure, it is highly unrealistic this would be a repeated occurrence which would lead to chronic exposure.

> **EFED Response:** Reproduction effects in birds are possible, given the exposures and body burdens documented in the wildlife incident reports. Bait stations are intended to limit exposure, but it cannot be precluded, especially when considering secondary exposure. EPA has agreed to waive avian reproduction studies for the remaining anticoagulant rodenticides, recognizing the difficulties involved in such studies, and has stated its intention to instead use the ACR as documented on p. 64-65 of the DRA. For secondary exposure, a chronic exposure is possible due to the persistence of the chemicals in target animals and fact that the bait is likely to be present (for primary consumption) for prolonged periods of time at different locations.

Commenter: Center for Biological Diversity (CBD)

CBD Comment: As part of the registration review process for all nine rodenticide active ingredients EPA must complete the Endangered Species Act ("ESA") consultation process, incorporate all of the necessary factors into the registration review evaluations, require that the registrant provide all necessary data and studies, account for real-world scenarios of pesticide use, and assess the enhanced toxicity of pesticide mixtures.

> **EFED Response:** EPA agrees that, where appropriate, the Agency will conduct an assessment for federally listed species. EPA and CBD partially settled a lawsuit (*Center for Biological Diversity v. EPA*, Case No. 3:11-cv-00293 (N.D. Cal.) that includes dates for EPA to conduct Biological Evaluations for four rodenticides (brodifacoum, bromadiolone, warfarin, and zinc phosphide). Under this settlement, these BEs are currently scheduled to be finalized in 2024. Three of these chemicals (brodifacoum, bromadiolone, and warfarin) are anticoagulant rodenticides.

CBD Comment: In order for the EPA to have the substantial evidence necessary to register a pesticide it must assure that it analyzes all of the appropriate factors and does not fail to consider an important unreasonable adverse impact. The factors that EPA should analyze include the following, at a minimum:
a. effects on species listed as protected under the ESA and their critical habitat,
b. effects on pollinators and other beneficial insects, including indirect effects,
c. effects on human health or environmental safety concerning endocrine disruption, and
d. any additive, cumulative or synergistic effects of the use of this pesticide.

> **EFED Response:** Issue (a) will be addressed in the upcoming Biological Evaluations for brodifacoum, bromadiolone, and warfarin. Issue (b) will be prioritized in the context of all other pesticides that need to be tested for pollinator effects, including insecticides. However, pollinator exposure is deemed unlikely given the use patterns. Issue (c) was addressed in the

human health risk assessment from OPP's Health Effects Division. Issue (d) has been partly addressed in the wildlife incidents analysis section of the 2020 DRA, in that it was documented that exposure to multiple ARs does in fact happen frequently, and results in mortality.

CBD Comment: The EPA must take into account real-world scenarios. The EPA often claims that it is acting conservatively by using the maximum labeled use rates when estimating exposure to plants and animals. These upper-level exposure scenarios, however, do not take into account real-world scenarios for pesticide use that commonly occur, such as accidental spills and illegal uses of the pesticide. An assumption of 100 percent label compliance underestimates risk and is unsupported by data.

EFED Response: EPA recognizes that off-label uses of the ARs do occur. Such uses cannot be assessed quantitatively due to the lack of label instructions and lack of usage survey data. However, the wildlife incident data presented in the DRA accounts for both legal and illegal usage of the ARs. Since the regulatory action is based on labels registered under FIFRA, the risk assessment focuses on registered uses of pesticides. Because off-label uses are not legal, they are not part of the regulatory action, and are not included in the assessments. There are enforcement mechanisms to address off-label uses

CBD Comment: The EPA must assess the enhanced toxicity of pesticide mixtures. The protocol that is currently being used to identify claims of synergy and place restrictions on pesticide use is a step above how the agency has utilized synergy data in the past, yet many steps in the process appear arbitrary and poorly executed. Therefore, we have outlined the steps that the EPA must take to ensure that its process for evaluating pesticide synergy is scientifically robust, defensible and compliant with FIFRA. Current rodenticide assessments are carried out on individual compounds and fail to acknowledge that the second-generation anticoagulants (as well as some of the first generation anticoagulants) act on the same receptors as they bioaccumulate in the animal making their impact additive.

EFED Response: The procedure for identifying synergistic effects that CBD cites is intended for new FIFRA section 3 registrations, not the registration review process. That said, the DRA for the ARs does document that wildlife are commonly exposed to multiple ARs, as demonstrated by residue analysis of carcasses. EPA expects that the combined effect of multiple ARs will be additive, not synergistic, because of the common mode of action. The overall risk picture would not be changed by such an analysis.

CBD Comment: Sublethal Effects of Second Generation Anticoagulants Contribute to Wildlife Deaths. Even if exposed wildlife survive after anticoagulant rodenticide intoxication, the animal still may suffer possible disruptions in vital physiological processes. Analysis by the California Department of Pesticide Regulation of SGAR exposure to non-target wildlife "found evidence of possible population-level impacts among non-target wildlife in California due to statistically significant associations with SGAR exposure and sublethal impacts."

ESA Listed Species Are Frequently Poisoned and Killed by SGARs. The pervasive nature of SGARs in the environment and food chain lead to lethal and sub-lethal harm to endangered species. As noted by state

and federal wildlife officials SGARs "can cause take, including mortality, which could have 'substantial population level effects' on an endangered species that is 'in danger of extinction.'"

> **EFED Response:** EPA is aware of CDPR's conclusions regarding population-level impacts. The forthcoming ESA BEs will consider sublethal effects as appropriate when making effects determinations. (See answer to first CBD comment).

Commenter: Raptors are The Solution

Raptors Are The Solution, a project of Earth Island Institute based in Berkeley, California, respectfully requests that the EPA not re-register any diphacinone or chlorophacinone products because of the ecological risk they pose, including both direct and indirect mortality in wildlife.

Comment 1. Diphacinone is toxic, and misapplication can lead to mortality in field settings even for "low-risk" species.

> **EFED Response**: Agreed. EPA is considering further mitigations to deal with this issue.

Comment 2. Diphacinone exposure, and thus the potential consequences thereof, is often overshadowed by second-generation compound detection in liver tissue.

> **EFED Response**: SGARs do appear to be most prevalent in carcasses. Proposed mitigations will seek to reduce harm from all seven anticoagulant rodenticides.

Comment 3. Diphacinone circulating in blood is linked with sublethal immune consequences [in] bobcats and humans.

Comment 4. Chronic exposure to rodenticides (including diphacinone) is pervasive, and the cumulative, sublethal effects are linked with notoedric mange parasitism in bobcats.

Comment 5. Indandione chlorophacinone is linked with increased mortality to a pathogen stressor in other species.

Comment 6. Diphacinone exposure can occur before an individual is born and indandione (diphacinone) compounds have reproductive consequences.

> **EFED Response to Comments 3 - 6**: FIFRA ecological risk assessments are conducted on the basis of apical endpoints (mortality, growth, and reproduction). Prenatal effects are accounted for in guideline reproduction studies used in EPA risk assessments.