



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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

July 17, 2004

Memorandum

Subject: Response to Public Comments on EFED's Risk Assessment: "Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: a Comparative Approach", dated December 19, 2002

To: Laura Parsons, Team Leader
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Through: Tom Bailey, Branch Chief
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EFED has reviewed the public comments submitted on the environmental risk assessment entitled "Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: a Comparative Approach" dated December 19, 2002. Comments were received from 26 respondents, including the Rodenticide Registrants Task Force (RRTF), individual rodenticide registrants, user groups, state agencies, environmental organizations, and a private citizen. Comments addressed data and methodologies, processes, benefits, the lack of an open public process, mitigation issues, and others. EFED is responding to those comments relative to the data and methodologies used in the risk assessment. Some comments are raised by more than one respondent, and these comments were grouped together in this response. A numbered list of respondents has been provided to match their respondents with their comments. Many of the comments by the RRTF and individual registrants simply reiterate their "errors-only" comments provided after the risk

assessment was provided to the registrants in October of 2001. The comparative risk assessment, external peer reviews of the assessment by three qualified experts, errors comments of the RRTF and individual registrants, and EFED's response to those errors comments are available in the Rodenticides EDocket: <http://www.epa.gov/oppsrrd1/rodenticidecluster/index.htm>

Respondents:

1. California Department of Fish and Game (CDFG)
2. New York State Department of Environmental Conservation (NYSDEC)
3. California Environmental Protection Agency, Dept. Pesticide Regulation (DPR)
4. Natural Resources Defense Council (NRDC)
5. Defenders of Wildlife, American Bird Conservancy, Rachel Carson Council, Northwest Coalition for Alternatives to Pesticides, and Steve Sheffield
6. Sierra Foothills Audubon Society (SFAC)
7. Grassroots Coalition
8. Beyond Pesticides
9. Private citizen
10. Rodenticide Registrants Task Force (RRTF)
11. Syngenta
12. Reckitt Benckiser
13. Liphatech
14. Hacco, Inc.
15. Bell Laboratories, Inc.
16. United States Department of Agriculture, Animal and Plant Health Inspection Service (USDA/APHIS)
17. The Zinc Phosphide Consortium (TZPC)
18. California Department of Food and Agriculture (CDFA)
19. Dodson Bros. Pest Control
20. J.C. Ehrlich Co., Inc.
21. County of Kings Department of Agricultural Commissioner
22. Alameda County Health Care Services
23. County of Fresno Department of Agriculture
24. American Farm Bureau Federation, American Institute of Baking, National Food Processors Association, North American Millers Association, Association of Structural Pest Control Regulatory Officials, ConAgra Flour Milling Company, and National Pest Management Association
25. Organization of Kittitas County Timothy Hay Growers & Suppliers
26. McCloud Services

Comment 1: The assessment is not an ecological risk assessment, only an assessment or ranking of hazards. A risk assessment must quantify exposure. EPA's Risk Assessment Guidelines define ecological risk assessment as "a process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors."

[10, 11, 12, 13, 14, 15, 18, 21, 23, 24]

EFED Response to Comment 1: EFED's risk assessment is in accord with the Agency's Guidelines for Ecological Risk Assessment¹. Registrants are correct in noting that the Guidelines state that "*Ecological risk assessment is a process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors*"(PART A, page 1, paragraph 1). However, the Guidelines go on to state that "*Descriptions of the likelihood of adverse effects may range from qualitative judgments to quantitative probabilities. Although risk assessments may include quantitative risk estimates, quantitation of risks is not always possible. It is better to convey conclusions (and associated uncertainties) qualitatively than to ignore them because they are not easily understood or estimated*" (PART A, page 1, paragraph 3). Refining the exposure assessment to establish a quantitative measure of likelihood of exposure and effects would require a much more extensive data set than registrants have submitted for their rodenticides and for the nontarget species potentially at risk. The Agency provided the preliminary risk assessment to rodenticide registrants in October, 2001 and posted it in the EDocket on EPA's website for public comments from January 29 to May 30, 2003. No additional data or relevant information to refine the exposure assessment has been provided by the registrants or other stakeholders. The necessary data have been outlined in a section on "*Uncertainty and Data Needs*" in the refined assessment. Nevertheless, despite the lack of quantifiable data, the existence of substantial incident data along with liver-residue analysis confirms that birds and nontarget mammals are being exposed and adversely affected by applications of rodenticide baits. The fact that numerous species of birds and mammals, including predators and scavengers, have been found exposed to these baits indicates that both primary and secondary exposures are occurring.

EFED's risk conclusions are based on analyses of the available data by a "lines-of-evidence" approach and comparative-analysis modeling. Quantitative estimates of risk are used in both; however, the "lines-of evidence" assessment includes qualitative assessments of secondary risk based on mortality and other adverse effects reported in laboratory and field studies, operational control programs, and incident reports, as well as toxicokinetic data and residue levels reported in primary consumers. This approach is in concert with the Guidelines, which clearly state that professional judgement or other qualitative evaluation techniques are appropriate for ranking

¹ EPA. 1998. Guidelines for Ecological Risk Assessment. EPA/630/R-95/002F, April 1998, Final. 171 pp. <http://www.epa.gov/ncea/ecorsk.htm>

risks using categories such as low, medium, and high when exposure and effects data are limited or are not easily expressed in quantitative terms. A "lines-of-evidence" approach also has been advocated by the Avian Effects Dialogue Group² for helping to interpret a wide variety of information.

EFED also notes that the methodology used is similar to that used in the Agency's "*Comparative Analysis of Acute Risk From Granular Pesticides*" (EPA 1992) and "*A Comparative Analysis of Ecological Risks from Pesticides and Their Use: Background, Methodology, Case Study*" (EPA 1998)³; both were reviewed by a FIFRA Scientific Review Panel. Concerning the latter analysis, the Panel noted the many scientific uncertainties in the method, yet agreed that it was a useful screening tool that provides a rough estimate of relative risk. The Panel made a number of helpful suggestions to improve the utility of the method, most of which are included in the risk assessment.

Comment 2: It cannot be emphasized enough that the number of nontarget rodenticide poisoning cases documented to date are indicative of a much larger problem. In suburban areas, people are not likely to pick up a dead animal and send it to a wildlife pathologist to find out why it died. In rural areas, birds and animals that succumb to rodenticide poisoning are simply not likely to be observed or detected. Small birds especially are not likely to be well represented in incident data. Bell Laboratories, Inc., however, disagrees with the conclusion that many incident victims are not found. [2, 5, 15]

EFED Response to Comment 2: EFED agrees with comments asserting that the number of incidents reported is likely only a small portion of nontarget exposure. In the "*Incident Data: Birds and Nontarget Mammals*" section of the comparative risk assessment, we note that most rodenticide incidents likely go undetected except in those rare instances when a predator carcass happens to be exposed in an open area (e.g., roadside) where it is observed by someone willing to take the time and effort to report it to the proper authorities. In many situations, carcasses might not be detected, death may be attributed to natural mortality, or an incident may not be reported for a variety of reasons, including ignorance, apathy, or failure of authorities to investigate and confirm the cause of death. Even if a carcass is found, a proper evaluation of rodenticide exposure requires necropsy of a dead animal by a wildlife pathologist. Liver tissue be extracted, frozen, and shipped to an analytical laboratory for analysis by high performance liquid chromatography. Because so few anticoagulant screens are conducted, exposure of birds to anticoagulants is likely much more widespread than the number of incidents suggests. Most of the incidents in the EIIS database occurred in New York and California, where state agencies have taken the time, effort, and expense of screening the liver of dead animals suspected to have

² Rymph, B. (ed.). 1994. Assessing Pesticide Impacts on Birds: Final Report of the Avian Effects Dialogue Group, 1988-1993. RESOLVE Center for Environmental Dispute Resolution, Washington, DC. 156 pp.

³ See December 8-9, 1998 <http://www.epa.gov/scipoly/sap/1998/index.htm>

been killed by rodenticides. Few other states appear to do so, although Wisconsin has reported several raptor incidents.

It is inconceivable that New York, California, and Wisconsin are the only states with nontarget exposure, even though they represent over 95% of the avian exposure cases. Rather, we believe this distribution, coupled with active programs in these states, affirms EFED's assessment that smaller birds and nontarget mammals are less likely to be detected and reported to authorities than are larger individuals, such as raptors and canids, and they likely are substantially under represented in the incident database. The difficulty in finding animal carcasses, even if systematic searches are conducted, has been discussed by the Avian Effects Dialogue Group. It is important to note that, regardless of the spatial distribution, the incident data available (more than 300 rodenticide cases) do indicate that a wide variety of birds and nontarget mammals are being exposed to rodenticides, especially brodifacoum. As indicated by the RQ determinations for a 25-g bird in the comparative risk assessment, small birds are potentially at risk if they eat even a single bait pellet of brodifacoum, difethialone, or zinc phosphide. Taken together, we believe these factors make a compelling case for substantial occurrence.

Comment 3: The RRTF has provided data on over-the-counter sales of rodenticides to the general public. The Agency hasn't made use of production data. Many states collect detailed information on use of field rodenticides labeled restricted use. [10, 11, 13, 14, 16, 17]

EFED Response to Comment 3: Adequate information quantifying usage of rodenticide baits is lacking. EPA obtains data on the amount of each product produced annually, but production data provide no information on when, where, or how the product is used and thus provide little relevant information for assessing exposure and risk. The RRTF (Kaukeinen et al. 2000)⁴ provided some limited information on the pounds of active ingredient produced or imported in 1996 and 1997 and the number of container/placement units for 4 of the 9 rodenticides. Usage of the other 5 rodenticides was not addressed. One problem with the information provided is that the RRTF does not distinguish between "containers" and "placement units", although they may differ substantially. According to product labels for brodifacoum and bromadiolone, a placement unit is 3 to 16 oz of bait for rats and 0.25 to 0.50 oz of bait for mice. However, according to rodenticide product catalogs, containers (e.g., 10-lb and 25-lb pails⁵; pails containing up to 80 50-g packs⁶) may contain many placement units. Differences in size among containers and between containers and placement units likely explains the discrepancies in the data provided by the RRTF. For example, both brodifacoum and bromadiolone are formulated

⁴ Kaukeinen, D.E., C.W. Spraggins, and J.F. Hobson. 2000. Risk-benefit considerations in evaluating commensal anticoagulant rodenticide impacts to wildlife. Proc. Vertebr. Pest Conf. 19:245-256

⁵ www.belllabs.com/cgi/products.cgi

⁶ www.hacco.com/2004_Catalog/RodenticideCatalog_2004.pdf

as 0.005% ai food baits solely for commensal rat and mouse control. The data provided by the RRTF for 1996 indicate that 395 lb ai of brodifacoum was formulated into more than 40 million "container/placement units" (i.e., 3 oz bait per container/placement unit), whereas 233 lb ai of bromadiolone was formulated into few more than 275,000 container/placement units (i.e., 271 oz bait per container/placement unit). Such differences also occur for 1997 and for chlorophacinone and diphacinone (see Table 2 in the refined comparative risk assessment). Thus, these data provide little useful information for use in the risk assessment. Refining the exposure assessment would necessitate much better information for each rodenticide, including the amount of bait applied annually and seasonally; geographically by state or region; in field settings versus in and around buildings; in urban versus suburban and rural locales; indoor versus outdoor placements; applications for rats versus those for mice; use by the general public versus that by Certified Applicators; proportion of bait placements made in tamper-resistant bait stations; and, for chlorophacinone and diphacinone, use of 0.005% versus 0.01% ai baits.

Regarding state reporting of rodenticide usage, registrants and other stakeholders had the opportunity to provide any such data they believed would have been useful for the risk assessment [see also EFED Response to Comment 1]. Few states actually have any such reporting to our knowledge, and even the most comprehensive state reports⁷ typically only provide the amount of rodenticide applied per crop without providing any information of the target pest, seasonal use, application method (e.g., broadcast versus bait station), or other such relevant factors. Moreover, homeowners and non-certified applicators do not report pesticide use. We also note that many of the Special Local Needs field products for chlorophacinone and diphacinone have not been labeled restricted use. Therefore, any reporting to date would not reflect use of non-restricted field products and thus could be misleading and inconclusive. The Rodenticide Cluster RED is requiring that all field baits be labeled as restricted use, and labels are currently being revised. However, even for those states that may report use of restricted-use products, there is a lag time in collecting, analyzing, and reporting annual data, and it may be several years before such data become available.

Comment 4: The greatest risk to nontarget wildlife is posed by rodenticides available over-the-counter for essentially unregulated homeowner use. Rodenticides should be classified as restricted use pesticides. [1, 5]

EFED Response to Comment 4: This issue will be addressed during the mitigation phase.

⁷ e.g., California Department of Pesticide Regulation, Pesticide Use Reporting, <http://www.cdpr.ca.gov/docs/pur/purmain.htm>

Comment 5: Rodenticide products should be clearly segregated into indoor and outdoor use categories. Outdoor uses of any kind should be limited to specific situations where use is highly controlled and closely monitored. Other countries (e.g., United Kingdom, New Zealand) have recently placed restrictions on the use of brodifacoum for both field and homeowner use. [1, 2, 3, 5]

EFED Response to Comment 5: This issue will be addressed during the mitigation phase.

Comment 6: The Agency shouldn't draw any conclusions on secondary risks, because studies were of widely differing types, dose regimes, sample sizes, etc. [11, 12]

EFED Response to Comment 6: The rodenticides have been in the reregistration process for more than 10 years to date, and registrants have had ample opportunity to propose any standardized testing for any of the rodenticides. None have done so. Standardized studies for each rodenticide would provide useful comparative information; but, until registrants conduct and submit such studies, EFED must rely on the available data. Some of the available studies were conducted under similar protocols and with the same test species, and some studies (e.g., Mendenhall and Pank 1980)⁸ have tested the same test species under the same test protocol to compare the hazards of different rodenticides. Other studies have used different protocols, test species, and sample sizes. What is readily apparent when examining the variety of data available is that some rodenticides (e.g., brodifacoum) exhibited mortality and other adverse effects in many or most test animals in almost every study, despite the differing protocols and/or test species used in the study. When looking at an individual rodenticide, having a variety of studies with a variety of test species is quite useful and relevant for assessing the hazards of that rodenticide.

EFED also emphasizes that potential secondary risks are not based solely on the secondary-hazards studies. As stated in the introduction to the comparative risk assessment, assessments of potential secondary risk are made based on mortality and other adverse effects reported not only in laboratory studies, but also in field studies and operational control programs, incident reports, toxicokinetic data, and residue levels reported in primary consumers.

Comment 7: Syngenta questions why the Agency wants additional toxicity data with predators and scavengers and asks "Are not these the organisms the Agency is trying to protect?" [11]

EFED Response to Comment 7: As noted in EFED's Response to Comment 6, the Agency has attempted to use the available information as much as possible throughout the assessment. For some rodenticides, there may be insufficient information. For brodifacoum, some hazards information exists in the literature, and we have not asked Syngenta or other brodifacoum registrants for additional hazards studies at this time. However, if registrants believe that a

⁸ Mendenhall, V.M. and L.F. Pank. 1980. Secondary poisoning of owls by anticoagulant rodenticides. *Wildl. Soc. Bull.* 8:311-315

standardized study is necessary to compare risks among rodenticides, or that available data are lacking, then additional testing would be needed.

Comment 8: EPA inappropriately infers risk from exposure. [10]

EFED Response to Comment 8: Risk is a function of both toxicity and exposure, as we have clearly stated in the introduction of the comparative risk assessment. For primary risks, a risk quotient (RQ) is compared to a Level of Concern (LOC). If an RQ is below the LOC, minimal risk is presumed. For example, a presumption of minimal acute primary risk to birds was made for the first-generation anticoagulants, because a small bird could eat many bait pellets and be at little risk of mortality. In this case, we inferred minimal risk from exposure.

Comment 9: The RRTF states that one peer reviewer found the comparative model to be inappropriate. [10]

EFED Response to Comment 9: One of the three expert peer reviewers raised a concern about use of the comparative analysis model as presented in an earlier draft of the risk assessment. EFED has made extensive changes in response to that reviewer's concerns.⁹ We also note that the same reviewer also stated that: *“The bulk of the material in the document addresses the development of the weight of evidence argument. In general this part of the document is well-developed and it is hard to argue with the evident conclusion about each of the nine chemicals. These conclusions are largely implicit in the text since the task of deriving a formal assessment for each chemical is passed over to the decision support analysis. The case about each chemical is thoroughly and logically developed in this part of the document and the document is commendable in showing how the Agency staff have been able to develop the weight of evidence approach as a viable approach to the synthesis of a complex body of evidence.”*

Comment 10: EPA suggests in the risk assessment that risk may be inferred by the existence of incidents. This is inappropriate, scientifically indefensible, and bad science. Elsewhere in their comments, the RRTF states that secondary risk is derived solely from hazards tests. [10]

EFED Response to Comment 10: Rodenticides are very highly toxic to mammals, including nontarget species, and some also are very highly toxic to birds, which are nontarget species. That is confirmed by the primary- and secondary-hazards testing that has been conducted and by findings from field, pen, and operational control programs in which nontarget organisms have been killed. Baits are formulated to kill rodents and other mammals (jackrabbits, mongoose, moles, shrews), and registrants have provided no documentation that baits are selective to the target species. Therefore, exposure to rodenticide baits does involve a degree of risk, although the degree varies among the rodenticides. The existence of substantial incident data (more than

⁹ the expert peer reviews are available in the Rodenticide Cluster EDocket, www.epa.gov/oppsrrd1/rodenticidecluster/index.htm

300 documented cases) along with liver residues provides important support for the assumption that nontarget birds and mammals are exposed and at risk from the use of at least some rodenticides. Death has been attributed to brodifacoum exposure in some individuals having liver-residue levels as low as 0.007 to 0.077 ppm¹⁰. These incidents refute the RRTF's contention that liver-residue levels less than an arbitrary "toxicity threshold" of 0.7 ppm for mortality¹¹. The incidents are discussed in more detail in the section entitled "*Incident Data: Birds and Nontarget Mammals*" in the comparative risk assessment.

Comment 11: When homeowners or applicators are using rodenticides according to label directions, they are placing them in inaccessible areas in and around structures or in tamper-resistant bait stations that greatly limits risk and selectivity of these products. Incident data include dissimilar practices and cannot be directly compared. [11]

EFED Response to Comment 11: Documentation of how homeowners are applying bait and complying with label directions is lacking. The RRTF (Kaukeinen et al. 2000, Anonymous 2001 - see footnotes 4 and 11) argues that many of the documented nontarget incidents are due to misuse, in which case applicators are not baiting according to label directions. A major concern is that most outlets selling rodenticide baits over the counter (e.g, grocery stores, hardware stores) do not sell bait stations, and most homeowners would not know where to find and purchase tamper-resistant bait stations even if they were willing to do so. EFED also questions how outdoor applications for rats and mice can be made in areas accessible only to the target species, and product labels provide no advice on how to do so. Even if properly secured, tamper-resistant bait stations are used, they do not prevent small animals from entering the stations and obtaining bait, nor does the use of bait stations preclude secondary exposure of predators and scavengers. The incident data cited in the risk assessment indicate that nontarget animals are being exposed, and the Animal Poison Control Center reports 2334 cases with rodenticides, particularly brodifacoum (1161 cases), between November 2001 and June 2003¹². Most pet cases involved exposure of dogs. These data seem to indicate that exposure is

¹⁰ e. g., barn owl (0.007 ppm brodifacoum) and red-tailed hawk (0.077 ppm brodifacoum) - Final Report, Diagnostic Services Section, Southeastern Cooperative Wildlife Disease Study, College of Veterinary Medicine, The University of Georgia, Athens, Georgia (Case No. CC246-03, January 5, 2003) and Golden eagle (0.04 ppm brodifacoum) - Hosea et al. (2001, Forensic investigative techniques to identify impacts (primary and secondary) from three groups of pesticides on raptors in California. Pages 38-51 in J. J. Johnston (ed.), Pesticides and Wildlife. American Chemical Society Symposium Series 771

¹¹ Anonymous. 2001. Analysis of the supporting data for EPA's EIS database with respect to rodenticides. Unpubl. report prepared for the Rodenticide Registrants Task Force to EPA by Arcadis Geraghty and Miller, Millersville, MD. 29 pp. and Kaukeinen et al. (2000) [cited in footnote 4 for Comment 3]

¹² S. Hansen (Senior Vice President, Animal Poison Control Center, Urbana, IL) pers. comm. to W. Erickson, EFED

occurring and raise the question whether the rodenticide baits, as currently used, can continue to be used without resulting in nontarget exposure of pets and wildlife.

Comment 12: How was the weight-of-evidence assessment performed? [19, 21, 23]

EFED Response to Comment 12: As stated in the introduction of the comparative risk assessment, risk conclusions are based on two analyses of the available data. One is a comparative ranking of the potential risk based on a comparative-analysis model, and the other is a tabular comparative rating of potential risk based on a “lines-of-evidence” approach. Quantitative estimates of risk are used in both; however, the “lines-of-evidence” assessment includes qualitative assessments of secondary risk based on mortality and other adverse effects reported in laboratory and field studies, operational control programs, and incident reports, as well as toxicokinetic data and residue levels reported in primary consumers. The potential-risk rankings are in accord with the EPA’s Risk Assessment Guidelines, which deem professional judgement or other qualitative evaluation techniques as being appropriate for ranking risks according to categories such as low, medium, and high when exposure and effects data are limited or are not easily expressed in quantitative terms. [see also EFED Response to Comments 1 and 13]

Comment 13: The NYSDEC states that the weight-of-evidence (i.e., lines-of-evidence) methodology used in the risk assessment provides an objective assessment of the various rodenticides. They believe that brodifacoum presents the greatest potential for risk to nontarget birds and mammals, which is consistent with the incident findings of the New York State Wildlife Pathologist¹³. [2]

EFED Response to Comment 13: We agree, and we thank the NYSDEC for providing incident reports for EFED’s Ecological Incidents Information System (EIIS). We also note that the California Department of Pesticide Regulation and the California Department of Fish and Game stated in their comments that they agree with most of the conclusions in the comparative risk assessment as well, particularly for those rodenticides used for commensal control. We also thank the CDFG for providing incident reports from California.

¹³ Stone, W.B., J.C. Okonlewski, and J.R. Stedelin. 1999. Poisoning of wildlife with anticoagulant rodenticides in New York. *J. Wildl. Diseases* 35:187-193 and

Stone, W.B., J.C. Okonlewski, and J.R. Stedelin. 2003. Anticoagulant rodenticides and raptors: recent findings from New York, 1998-2001. *Bull. Environ. Contam. Toxicol.* 70:34-40

Comment 14: EPA wrongly assumes that all rodenticide baits weigh 0.2 g per pellet. [10, 21, 23]

EFED Response to Comment 14: EPA assumes that a typical rat-bait pellets weighs 0.2 g, based on information provided by Syngenta as cited in the refined comparative risk assessment. No other information on pellet or whole-grain size was provided by registrants or other stakeholders during the "errors-only" and "public comment" periods [see also EFED Response to Comment 1]. We did calculate the number of 0.2-g pellets needed to provide an LD50 dose to a bird or nontarget mammal weighing 25 g, 100 g, and 1000 g. However, we realize that some bait pellets or grains may be smaller or larger than the typical rat-bait pellet, and some are formulated as meal or wax blocks. Therefore, we also calculated the amount of bait that would need to be eaten by a bird or nontarget mammal to provide an LD50 dose, and we calculated what percent of the diet that would comprise. The later calculations are independent of pellet or grain size.

Comment 15: The American Society for Prevention of Cruelty to Animals (ASPCA) Poison Control Center has many incidents for pets exposed to rodenticides, especially brodifacoum. EPA should obtain this information. [5]

EFED Response to Comment 15: EFED is aware that the ASPCA Animal Poison Control Center has reported 2334 cases involving 2685 animals from November 01, 2001 to June 16, 2003 (S. Hansen pers comm. to W. Erickson). The number of cases were 1161 for brodifacoum, 511 for bromadiolone, 218 for zinc phosphide, 206 for diphacinone, 66 for bromethalin, 48 each for difethialone and warfarin, 42 for chlorophacinone, and 34 for cholecalciferol. Although adverse effects to pets and other domestic animals are addressed by OPP's Health Effects Division, we believe that these data augment the wildlife incident data in demonstrating that nontarget animals are being exposed to rodenticide baits.

Comment 16: Label language needs to be more precise regarding where and how rodenticides are placed in order to avoid confusion. The label should indicate potential adverse effects. People using rodenticides around their homes need to be aware of how their local domestic-life and wildlife could be harmed or killed as secondary nontarget species. [7]

EFED Response to Comment 16: We appreciate the comments of the Grassroots Coalition regarding the need to improve label language to warn of potential nontarget risks. Label directions and precautionary measures will be dealt with during the mitigation phase.

Comment 17: The risk assessment does not consider individual products. Product characteristics such as pellet or grain size, color, stabilizers, waxes, and others offer some degree of selectivity. [13, 16, 17, 18, 21, 23]

EFED Response to Comment 17: Reregistration is an assessment of the active ingredient. Various properties of individual products that might reduce risks will be considered when mitigation issues are addressed, providing that registrants have provided appropriate data to

support any claims of selectivity. Mitigation issues such as mandatory use of bait stations can also be addressed during this next phase of review.

Comment 18: The available mammalian toxicity data are not sufficient to present a full mortality danger to the various mammalian species. The Agency should require a mammalian acute dietary test. [2, 5]

EFED Response to Comment 18: EFED agrees that additional mammalian-toxicity information would help reduce the uncertainty associated with risk estimation. While EFED can request a wild mammal toxicity test¹⁴, EFED has not previously required this test for rodenticides. Rodenticides are formulated and proven to be toxic to small mammals, and there is no evidence that they are selective to the target species. However, we will consider the value of a wild-mammal toxicity test when determining what additional data would be useful for reducing uncertainties in the assessment.

We have recently located reports of rat dietary tests conducted at EPA's former toxicology laboratory in Beltsville, MD, where McCann et al.(1981)¹⁵ developed a short-term dietary LC50 test for small mammals. They exposed immature albino Norway rats (Wistar strain) to dry diet offered ad libitum and treated with one of 17 chemicals pesticides, mostly organophosphate and carbamate pesticides. The tests consisted of a 5-day acclimation period, a 5-day exposure period, and a post-treatment observation period lasting at least 9 days. Following submission of the paper for publication, testing continued and included brodifacoum, bromadiolone, chlorphacinone, diphacinone, and warfarin. Results of the rodenticide testing were not published, but EFED now has the test reports and has incorporated these data in the risk assessment.

Comment 19: The CDFA notes that uncertainties in the assessment can be addressed by requiring new data where necessary. Such data should include residue data to evaluate secondary exposure, mammalian subchronic toxicity data to evaluate secondary exposure risks to nontarget mammals, and use of avian subacute toxicity or avian reproduction data to evaluate secondary exposure risks to birds. [18]

EFED Response to Comment 19: We agree that additional data would reduce uncertainties in the risk assessment, especially to assess sublethal (e.g., reproductive) effects and to quantify exposure. However, we disagree that avian and mammalian reproduction data can be used to

¹⁴ 40 CFR §158.490, Wildlife and Aquatic Organisms Data Requirements, Guidelines Reference No.71-3 "Wild mammal toxicity"

¹⁵ McCann, J.A., W. Teeters, D.J. Urban and N. Cook. 1981. A short-term dietary toxicity test on small mammals. Pages 132-142 in D.W. Lamb and E.E. Kenaga (eds): Avian and Mammalian Wildlife Toxicology: Second Conference, ASTM STP 757, American Society for Testing Materials.

assess secondary risk. Reproduction data are used to assess chronic risk, not secondary risk. The available secondary-hazards data are presented in the comparative risk assessment. Additional data on potential for secondary exposure would help refine the assessment, and we would have incorporated any relevant information if registrants or other stakeholders had made any available. [see also EFED Response to Comment 1]

Comment 20: The Agency should consider factors such as diet and food preferences, proximity of habitat to use areas, home range, etc. in assessing risks. [18]

EFED Response to Comment 20: The Agency has received no such data from the rodenticide registrants or other stakeholders [see also EFED Response to Comment 1]. As noted in the comparative risk assessment, there are many factors that influence which nontarget animals might be exposed to rodenticide baits. They include the species found in and around treatment areas, species' food habits and foraging behavior, home range, propensity to feed in and near human buildings, bait availability (e.g., quantity, how applied, where applied, when applied), and other such factors. However, there is no doubt that many birds and nontarget mammals are attracted to and will consume grain-based foods. Additionally, many nontarget predators and scavengers feed on rats, mice or other target species. They are not likely to avoid feeding on rats, mice, voles, ground squirrels, or other animals that have eaten bait.

Comment 21: EPA has not utilized the large set of subchronic/chronic mammalian toxicity studies that are available for most, if not all, of the rodenticides. [16, 17, 18]

EFED Response to Comment 21: EFED utilizes the rat two-generation reproduction test¹⁶ to assess chronic risks to mammals. This study is required by OPP's Health Effects Division (HED) to support pesticides with food uses or where use of the product is likely to result in human exposure over a significant portion of the human lifespan. This study is not currently available for any of the rodenticides. HED requires numerous other subchronic/chronic studies (e.g., dermal, inhalation, oncogenicity, neurotoxicity) to assess risks to humans, but these generally are not relevant to assessing risk to mammalian wildlife. For assessing chronic risk to birds, EFED uses avian reproduction studies with the northern bobwhite and mallard¹⁷. The avian reproduction studies have previously been required by the Agency on a case-by-case basis, but the updated guideline requirements soon to be published will require these studies for all pesticides having outdoor uses. EFED can better assess the potential for adverse reproductive effects when these data become available. [see also EFED Response to Comment 22]

¹⁶ 40 CFR §158.340, Toxicology Data Requirements, Guidelines Reference No. 83-4 "Reproduction, 2-generation"

¹⁷ 40 CFR §158.490, Wildlife and Aquatic Organisms Data Requirements, Guidelines Reference No. 71-4 "Avian reproduction"

Comment 22: The RRTF disagrees that sublethal doses can have adverse effects. Bell Laboratories, Inc. states that EPA's present infatuation with the concept of 'sub-lethal effects' of anticoagulants is an attempt to find a problem where none exists. [10, 15]

EFED Response to Comment 22: EFED disagrees with these comments. Despite the lack of reproductive data for birds and mammals [see EFED Response to Comment 21], evidence exists that sublethal doses can have adverse effects. For example, poisoning symptoms (e.g., bleeding, delayed blood-coagulation times) have been reported in birds and mammals that survived exposure in some of the secondary-hazard studies discussed in the comparative risk assessment (see secondary-hazards tables for birds and mammals). The Warfarin RED¹⁸ notes that warfarin is a teratogen, and product labels are required to warn "Exposure to warfarin during pregnancy should be avoided. Warfarin may cause harm to the fetus, including possible birth defects." The Rodenticide Cluster RED¹⁹ reports developmental toxicity (e.g., vaginal bleeding, hypotonicity) in rats and rabbits exposed to bromadiolone at about two orders of magnitude less than the LD50 dose. In brodifacoum studies, internal hemorrhage and significantly prolonged prothrombin time of rabbits was reported for those dosed, during gestation, at about two orders of magnitude less than the LD50 dose. A recently published article reported that brodifacoum was detected in two dog pups that died a few hours after birth (Munday and Thompson 2003)²⁰. Of 13 pups in a single litter, eight were born dead or died within 48 hours of birth. Three puppies that died shortly after birth were necropsied. Two exhibited hemorrhage in the thoracic and peritoneal cavities, intestinal serosa, and meninges, and brodifacoum was detected in the liver of both puppies. The mother did not have clinical signs of coagulopathy before or subsequent to whelping, and the authors suggest that fetuses may be more susceptible to brodifacoum than are adult animals. EFED believes that reproductive studies are needed to further clarify possible adverse reproductive effects of the nine rodenticides and to assess the possible significance of sublethal doses in primary exposure.

The Avian Effects Dialogue Group (see footnote 2) also discussed the issue of sublethal effects of pesticides on birds. The Group notes that ". . . effects that are sublethal under the controlled environmental conditions of a laboratory might result in decreased survival or reproduction in the field." The Group also discussed several of the factors that may result in sublethal effects becoming lethal under field conditions or which may lead to a reduction in reproductive success. Such factors include physiological parameters, environmental conditions, synergisms with other chemicals, formulation type, and route of exposure.

¹⁸ Warfarin and its Sodium Salt. Reregistration Eligibility Document. 1991. SRRD/OPP/EPA. <http://www.epa.gov/pesticides/reregistration/status.htm>

¹⁹ Reregistration Eligibility Decision (RED): Rodenticide Cluster. 1998. EPA738-R-98-007. 307 pp. <http://www.epa.gov/pesticides/reregistration/status.htm>

²⁰ Munday, J. S. and L. J. Thompson. 2003. Brodifacoum Toxicosis in two neonatal puppies. Vet. Pathol. 40: 216-219

Comment 23: It is inappropriate to compare different modes of action. [11]

EFED Response to Comment 23: EFED compares the potential nontarget risks of the nine rodenticides. Six of the rodenticides are anticoagulants and three are not. However, all nine rodenticides are registered for control of commensal rats and mice in and around buildings. Therefore, it is appropriate to compare all nine, because they are alternatives for one another for control of commensal rats and mice in and around buildings.

Comment 24: Using rat toxicity data is not appropriate for 1-kg mammals, such as canine or feline, because rodenticides are more toxic to rodents than to other mammals. [11, 13]

EFED Response to Comment 24: There is no scientific basis for that statement. As can be seen from the toxicity tables in the comparative risk assessment, rodenticides are not necessarily more toxic to rats and mice or other rodents than to other mammals. Brodifacoum, for example, is very highly toxic to the rabbit (LD50 = 0.29 mg/kg), possum (LD50 = 0.17 mg/kg), dog (LD50 = 0.25-1.0 mg/kg), and pig (LD50 <2.0 mg/kg), and diphacinone is very highly toxic to the mongoose (LD50 = 0.2 mg/kg) and coyote (LD50 = 0.6 mg/kg). We have followed EFED policy in using rat or mouse toxicity data to extrapolate to a 1-kg mammal and, based on the available toxicity data, believe it is appropriate in the comparative risk assessment.

Comment 25: Information from field studies is irrelevant to use of rodenticides for commensal uses. [11]

EFED Response to Comment 25: Field studies are useful in demonstrating that exposure to rodenticide baits or consumption of target or nontarget animals poisoned from eating bait can have adverse effects to nontarget birds and mammals. More emphasis could be placed on information from commensal studies if registrants were to conduct such studies for each of the nine rodenticides and using focal species that feed on rats and/or mice. One commensal study was undertaken with potential exposure of barn owls to brodifacoum-poisoned rats and mice on farms in New Jersey²¹. That study provided a wealth of information on barn owl biology, but found that the owls fed predominantly on voles, not rats and mice. Other avian and mammalian predators and scavengers, as well as avian and mammalian primary consumers, need to be addressed in commensal settings.

Comment 26: Syngenta questions why EFED cited residues in a possum "when the issue is with birds". [11]

EFED Response to Comment 26: The Agency's issue of residue levels and risks to nontarget animals is not limited to birds but also includes nontarget mammals.

²¹ Hegdal, P.L. and R. W. Blaskiewicz. 1984. Evaluation of the potential hazard to barn owls of talon (brodifacoum bait) used to control rats and house mice. Environ. Toxicol. Chem. 3:167-179

Comment 27: EPA has not used residue data to quantify secondary exposure. [18, 21, 23]

EFED Response to Comment 27: Residue data alone do not quantify exposure. However, the presence of residue in animals that have eaten bait does confirm exposure and potential risk. [see also EFED Response to Comment 1]

Comment 28: The greatest risk to nontarget wildlife is from over-the-counter rodenticides available for unregulated homeowner use. [1]

EFED Response to Comment 28: This is an issue that will be addressed during the mitigation phase of reregistration.

Comment 29: The 2000 draft of the comparative risk assessment contains important statements about birds and mammals that are omitted from the version released to the public. [5]

EFED Response to Comment 29: The initial version of the Agency's comparative risk assessment contained information related to possible risk mitigation. OPP management decided that those issues would best be addressed during the mitigation phase of reregistration and not in the risk assessment.

Comment 30: The true impacts of brodifacoum on birds of prey are understated. [6]

EFED Response to Comment 30: As stated in the comparative risk assessment, EFED believes that brodifacoum poses a potentially high risk to birds of prey exposed to primary consumers of brodifacoum bait. The incident data confirm that birds of prey, especially owls (e.g., great horned owl), hawks (e.g., red-tailed hawk), and eagles (e.g., golden eagle), are being exposed to brodifacoum, and the toxicity data demonstrate that brodifacoum is very highly toxic to birds. Thus, preliminary information on both exposure and hazard indicate potential risk to birds of prey, as do the available incident data.

Comment 31: The RRTF disputes long-term bioaccumulation, because binding sites in the liver are limited. [10]

EFED Response to Comment 31: The RRTF has not provided any documentation to support this assertion. Moreover, as we note in the *"Incident Data: Birds and Nontarget Mammals"* section of the comparative risk assessment, retention and accumulation of anticoagulants is not limited to the liver but occurs in other organs and tissues as well. Concentrations in the liver are often, but not always, higher than in other tissues. However, because the liver comprises only

about 4 to 7% of the weight of a rat or mouse (Newton et al. 1990²², Howald et al. 1999²³), most residue actually may accumulate in other parts of the carcass. For example, Newton et al. (1990) reported a much higher mean residue concentration in liver (2.13 ± 0.33 ppm) than in the remainder of the carcass (0.36 ± 0.05 ppm) of 10 mice fed brodifacoum bait. However, the mean total amount of residue in the carcass (without the liver) was 11.85 ± 1.54 ppm versus only 3.51 ± 0.66 ppm in the liver. The section of the comparative risk assessment entitled "*Comparative Toxicokinetics: Absorption, Metabolism and Excretion of Anticoagulants*" also discusses some of the residue levels detected in various organs and tissues of exposed animals.

Comment 32: Regarding diphacinone, the RRTF and HACCO, Inc. note that residue data in ground squirrels (EPA MRID nos 435346-01 and -02) were not included in the risk assessment, and the "wrong" rat LD50 is used. Also, they believe that EFED should accept a secondary-hazards test with the rat (Bullard et al. 1976²⁴) to fulfill a data requirement (70-A-SS) for a secondary-poisoning test with a mammalian predator or scavenger. [10, 14]

EFED Response to Comment 32: Based on the EPA MRID numbers provided by the registrant, EFED has obtained copies of the efficacy field tests in which residues were determined in ground squirrels. We have included those data in the refined risk assessment. Regarding the rat LD50, the existence of a "core" study does not mean that the results from other scientifically sound studies, albeit ones which deviated in minor ways from Agency guidelines, should be ignored. In a preliminary risk assessment, the Agency typically uses the toxicity values for the most sensitive organisms tested in scientifically sound studies in the assessment of risk. A refined assessment will attempt to address the magnitude and likelihood of the risk based on a distribution of available data, if sufficient data exist to make such an analysis.

The Rodenticide Cluster RED issued in July, 1998, required secondary toxicity studies with a mammalian predator and an avian predator to support reregistration of 0.005% ai and 0.01% ai diphacinone baits. More than five years have passed without diphacinone registrants providing the required data. The Bullard et al. (1976) study does not fulfill this data requirement for several reasons. Because the rat is a target species for all diphacinone products with commensal uses, it isn't considered to be of ecological or regulatory relevance for fulfilling a data requirement for a nontarget species. Moreover, the rats were fed only liver tissue from cattle sublethally dosed with diphenadione. Cattle are not a target species, they were only sublethally dosed, and only liver tissue was fed to the rats. At this time, a more appropriate question is why

²² Newton, I., I. Wyllie, and P. Freestone. 1990. Rodenticides in British barn owls. *Environmental Pollution* 68:101-117

²³ Howald, G.R., P. Mineau, J.E. Elliott, and K.M. Cheng. 1999. Brodifacoum poisoning of avian scavengers during rat control on a seabird colony. *Ecotoxicol.* 8:431-447

²⁴ Bullard, R.W., R.D. Thompson, and G. Holgvin. 1976: Diphenadione (diphacinone) residue in tissue of cattle. *J. Agric. Food Chem.* 24:261-263.

haven't diphacinone registrants addressed the outstanding data requirements rather than attempting to cite inadequate and inappropriate data.

Comment 33: Syngenta asks why the Agency assumes that incidents with avian and mammalian predators and scavengers are the result of secondary exposure. "The incident data is principally based upon carcass autopsies and thus cannot determine the route of exposure. It is unknown." [11]

EFED Response to Comment 33: For predator and scavengers, EFED simply states that poisoning was likely due to secondary exposure based on the species involved and their food habits. We acknowledge that tertiary exposure likely occurs as well. However, it seems highly unlikely that species such as the great horned owl, red-tailed hawk, golden eagle, or weasels would consume bait, and registrants have provided no information that primary exposure is important for these species. Nevertheless, we realize that some omnivores may eat bait as well as poisoned animals, and the actual routes of exposure may be unknown for some species. For example, we do know that dogs will consume rodenticide baits²⁵ [see also EFED Response to Comment 15], and it is feasible that wild canids (e.g., coyote, kit fox, red fox) may do so in addition to capturing and feeding on dead and dying rodents and nontarget birds and mammals that have eaten bait.

Comment 34. Syngenta claims that dog LD50 values are incomplete for brodifacoum, and that the Agency has been given other publications with more robust LD50 values than the 0.25 to 1 mg/kg value cited in the comparative assessment. They state that the definitive dog LD50 of 3.56 mg/kg was established in New Zealand (M.E.R. Godfrey, 1981, New Zealand J. Expt. Agriculture 9:147-149). [11]

EFED Response to Comment 34: EFED has utilized the toxicity data submitted by registrants to support the registration of brodifacoum. Those data are submitted to OPP's Health Effects Division (HED) and are provided in HED's "Tox Oneliners" database. For brodifacoum, the database contains only one acute-oral toxicity study with the dog, and EFED has cited that value in the comparative risk assessment. The database does contain results of a dog study from New Zealand in 1981 (EPA MRID No. 251781), but that was an antidote study in which the dosed dogs also were treated with vitamin K. To use an LD50 derived from an antidote study would be misleading and inappropriate.

Comment 35: Zinc phosphide liberates phosphine, not phosgene as stated in two instances in the risk assessment. [15]

EFED Response to Comment 35: This has been corrected in the refined risk assessment.

²⁵ e. g., Marsh, R.E. 1985. Are anticoagulant rodenticides a problem for household pets? Pest Control 53(8):20-22,24 and 53(9):26-28,31

Comment 36: Data in Diaz and Whitacre (1976)²⁶ indicate that elimination of diphacinone in the rat is rapid and similar to chlorophacinone. These data were not included in Table 37 or in EPA's analysis, which relied only on elimination data for blood and liver. [10]

EFED Response to Comment 36: These data are discussed in the risk assessment. The tabulated data are half-lives and retention times (days). Those values are not obtainable from Diaz and Whitacre (1976); as stated in the risk assessment, nearly a third of the dose administered was not recovered in the study, which limits its usefulness.

Comment 37: The risk assessment states that difethialone is expected to pose similar risks to brodifacoum due to their very similar chemical structures. It does not, however, make this conclusion for diphacinone and chlorophacinone, which also differ by only one atom in their structures. Rather, in some areas, it reaches relatively different conclusions about these two compounds. How can these dissimilar conclusions be justified? [15]

EFED response to Comment 37: This comment is somewhat misleading. The risk assessment actually says the conclusions of comparable risks for brodifacoum and difethialone are assumed based not only on very similar chemical structures but also on nearly identical acute-toxicity profiles and physical/chemical properties (see "*Attachment A: Chemical Structures and Selected Physical/Chemical Properties of the Rodenticides*" and the toxicity tables in the comparative risk assessment). In contrast, although chlorophacinone and diphacinone have similar chemical structures, they differ to a greater extent in their toxicity and physical/chemical structures. Additionally, some secondary-hazards data are available for both chlorophacinone and diphacinone, whereas secondary-hazards data have not been submitted for difethialone.

A more relevant question is why hasn't LiphaTech, Inc. submitted secondary-hazards data for difethialone. EFED is aware that a paper involving difethialone secondary-hazards information for birds and mammals was presented at a symposium²⁷, although the performing laboratory (National Wildlife Research Center) declined to provide any additional details on the study when they were contacted. Subsequently, at a meeting with OPP in September of 2001, LiphaTech, Inc. stated that they had contracted the study and would submit it for review. They have not done so, even though submission of adverse-effects data is required under FIFRA 6a(2) reporting.

²⁶ Diaz, L.I. and D.M. Whitacre. 1976. Excretion and retention of ¹⁴C-diphacinone in rats. Unpubl. report, submitted by Velsicol Chemical Corporation. 8 pp

²⁷ Goldade, D.A., P.J. Savarie, J.C. Hurley, S.A. Gaddis, and J.J. Johnson. 2001. Design of a laboratory secondary hazard study. Pages 146-156 in J. J. Johnston (ed.), *Pesticides and Wildlife*. American Chemical Society Symposium Series 771

Comment 38: APHIS and TZPC question why EFED hasn't used use information they provided to an EFED reviewer at a meeting in 1996. [16, 17]

EFED response to Comment 38: EFED welcomed any relevant use data for zinc phosphide and the other rodenticides. We are not aware of the information referred to, which apparently was use information from the early to mid-1990s, and there is no such information in EFED's zinc phosphide chemical file. However, we do question whether use data from more than 10 years ago would be relevant at this time. APHIS and the ZPC had ample opportunity to provide up-to-date usage data during the comment periods. [see also EFED Response to Comment 3]