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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: **September 21, 2020**

SUBJECT: **Zinc Phosphide:** Draft Human Health Risk Assessment for Registration Review of Zinc Phosphide.

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Petition No.: NA
Risk Assessment Type: Qualitative
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Regulatory Action: Registration Review
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As part of registration review, PRD of the Office of Pesticide Programs (OPP) has requested that HED evaluate the hazard and exposure data and conduct dietary, occupational, and residential exposure assessments, as needed, to estimate the risk to human health that will result from the currently registered uses of pesticides. This memorandum serves as HED's qualitative draft human health risk assessment from the registered uses of the non-anticoagulant rodenticide active ingredient, zinc phosphide.

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1.0 Introduction

Zinc phosphide (Zn_3P_2) is a non-anticoagulant rodenticide used to control numerous pest species including mice, ground squirrels, prairie dogs, voles, moles, rats, muskrats, nutria, and gophers. It is a solid that releases highly toxic phosphine gas when in contact with aqueous solutions and soils with high moisture content. Zinc phosphide toxicity is directly related to phosphine gas production, which is liberated more rapidly when solution pH deviates from neutrality. This feature makes zinc phosphide a particularly effective oral toxicant. Once zinc phosphide is ingested, contact with the acidic environment in the gut accelerates phosphine generation, which is absorbed into the blood stream and distributed systemically. Although a mammalian mode of action (MOA) is not established for zinc phosphide or phosphine, given its propensity for phosphine release, the zinc phosphide MOA is likely consistent with the phosphine MOA. Zinc phosphide is indiscriminate and a hazard to non-target species.

In 2008, the agency issued a risk mitigation decision (RMD) for ten rodenticides, in which zinc phosphide was included, with the intent to minimize non-target exposure so that rodenticide products could remain available without causing adverse effects to human health and the environment. The ten rodenticides included in the RMD could be divided into three categories: first-generation anticoagulants, second-generation anticoagulants, and non-anticoagulants. The RMD set restrictions on rodenticides intended to minimize exposure to children and non-target wildlife, including domestic animals[1].

While the scoping document (Wray A. *et al.*, D431578, 04/20/2016) identified certain data requirements and quantitative analyses anticipated during registration review, the agency's human health risk management goals for registration review of rodenticides reflect those articulated in the RMD and include minimizing non-target (e.g., human) exposures for currently registered products of anticoagulant and non-anticoagulant rodenticides to the extent possible through mitigation. To support the registration review human health risk management goals for zinc phosphide, and to retain a risk assessment strategy consistent with that for other rodenticides, HED is providing a qualitative analysis of risks in the draft human health risk assessment.

2.0 Use Pattern Summary

Zinc phosphide is formulated as either a bait/granular/solid [1-2% active ingredient (a.i.)], dust (10-63% a.i., tracking powder and as pre-mix for bait), or pellet/tablet (2% a.i.), and may be applied by aircraft, ground equipment, hand and/or handheld equipment, and bait stations. All occupational labels require handlers to wear at least baseline attire (long-sleeved shirt, long pants, and shoes plus socks) with gloves. Some labels have additional requirements, including particulate filtering facepieces, respirators, protective eyewear, coveralls, and/or chemical-resistant apron.

Current registrations permit use on indoor and outdoor residential and agricultural areas including areas in and around homes, on lawns, around bulbs, in and around outside buildings/barns, rights-of-way/fencerows/hedgerows, indoor and outdoor commercial or

[1] Available at www.regulations.gov in document ID EPA-HQ-OPP-2006-0955-0820.

institutional premises and equipment (including food handling establishments), golf courses, reforestation areas, alfalfa, barley, berries (dormant), oats, sugar maple, wheat, cucurbits (reduced tillage and no-till corn), macadamia nut orchards, orchards/grooves (post-harvest and dormant), timothy (hay). These registrations include both food and non-food uses. Tolerances are established for alfalfa, barley, dry bean, grapes, grass, sugar beets, sugarcane, timothy, potato, and wheat. A tolerance for regional registration is established for globe artichoke and sugar beets. All zinc phosphide registrations for tracking powder products and field-use products are classified as restricted use pesticides (RUP), with the exception of those limited to manual underground baiting. Residential and occupational exposures are anticipated based on the use pattern for currently registered zinc phosphide products. Although zinc phosphide is considered a food-use chemical based on its use pattern and application on fields and in underground borrows, dietary exposure is not anticipated (See Section 5.0).

The agency required RUP classification for rodenticide field and tracking powder products to address risks associated with those products prior to the implementation of the RMD [Zinc Phosphide Reregistration Eligibility Decision (RED), EPA 738-R-98-006, July 1998]; therefore, the mitigation measures described in the RMD did not apply to those uses. The details of the RMD can be found in docket number EPA-HQ-OPP-2006-0955-0764 at www.regulations.gov and the decisions pertaining to zinc phosphide are summarized below.

Consumer-use products:

- Products sold in quantities ≤ 1 pound.
- Loose, treated whole-grain/pellets/meal are prohibited for indoor and above-ground outdoor uses.
- Bait products must include at least one bait station and may include bait refills.
- When applied outdoors above-ground and in areas accessible to children, non-target wildlife or domestic animals, baits must be contained in bait stations.
- Products for use outdoors and above-ground must be placed within 50 feet of a building.

Commercial/Professional-use products:

- Must be sold in quantities of ≥ 4 pounds.
- May not be offered for sale in consumer stores (hardware, grocery, etc.).
- Must be placed within 100 feet of a structure (fence and perimeter baiting beyond 100’ of a man-made structure are prohibited) when used outdoors and above ground, see 50-foot Document Clarification Letter to Bell (03.20.12) in docket number EPA-HQ-OPP-2006-0955-0820 found at www.regulations.gov.
- For uses of non-anticoagulants, product labels require bait stations if children, wildlife, or domestic animals may be exposed.

A summary of the use directions is provided in table A.1. of Appendix A.

3.0 Tolerances

Tolerances are established (40 CFR §180.284) for "residues of phosphine resulting from the use of the rodenticide zinc phosphide."

The tolerance expression for phosphine should be updated to comply with HED's Interim Guidance on Tolerance Expressions (S. Knizner, 5/27/09). The current tolerance expression is as follows: Tolerances are established for residues of the phosphine resulting from the use of the rodenticide zinc phosphide in or on the raw agricultural commodities as follows:

The tolerance expression should be revised to read: Tolerances are established for residues of the insecticide phosphine, including its metabolites and degradates, resulting from the application of zinc phosphide. Compliance with the tolerance levels specified below, is to be determined by measuring only phosphine, in or on the commodity.

The uses on alfalfa, barley, dry bean, sugar beet, timothy, potato, and wheat to kill rodents are supported by field trial data that support tolerances with regional registration. Therefore, the tolerances for alfalfa, barley, dry beans, and sugar beets should be deleted from 40 CFR 180.284(a) and moved to 40 CFR 180.284(c), which is for tolerances with regional registrations. HED has no objection to maintaining US tolerances for grapes, grass, potato, sugarcane, timothy, and wheat in 40 CFR 180.284(a) as there were no residues above the limit of quantification (LOQ) in these commodities. The residue data for alfalfa, barley, dry beans, and sugar beets support the stated use region of WA, OR, and ID. Residue data for alfalfa also supports registered uses in CA. The regional restrictions will remain on alfalfa, barley, dry beans, and sugar beets unless registrants provide additional residue data to support a nationwide tolerance.

There are no international harmonization issues associated with this action since there are no Codex, Canadian, or Mexican maximum residue limits (MRLs) for residues of phosphine from use of zinc phosphide on any crop. A summary of the established tolerances is presented in Appendix C.

Table 3.0. Tolerance Summary for Phosphine Resulting from Use of Zinc Phosphide (40 CFR §180.284).

Commodity/Correct Commodity Definition	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
40 CFR 180.284(a)			
Alfalfa, forage	0.2	Remove	*Move to* 40 CFR 180.284(c)
Alfalfa, hay	0.2	Remove	*Move to* 40 CFR 180.284(c)
Barley, grain	0.05	Remove	*Move to* 40 CFR 180.284(c)
Barley, hay	0.2	Remove	*Move to* 40 CFR 180.284(c)
Barley, straw	0.2	Remove	*Move to* 40 CFR 180.284(c)
Bean, dry, seed	0.05	Remove	*Move to* 40 CFR 180.284(c)
Beet, sugar, leaves	--	**0.2**	*Move to* 40 CFR 180.284(c) Commodity definition correction
Beet, sugar, tops	0.2	Remove	
Beet, sugar, roots	0.05	Remove	*Move to* 40 CFR 180.284(c)
Grape	0.01	0.01	
Grass, forage		**0.1**	Commodity definition correction

Table 3.0. Tolerance Summary for Phosphine Resulting from Use of Zinc Phosphide (40 CFR §180.284).			
Commodity/Correct Commodity Definition	**Established Tolerance (ppm)**	**Recommended Tolerance (ppm)**	**Comments**
Grass, rangeland, forage	0.1	Remove	
Grass, hay		**0.1**	Commodity definition correction
Grass, rangeland, hay	0.1	Remove	
Potato	0.05	Remove	*Move to* 40 CFR 180.284(c)
Sugarcane, cane	0.01	0.01	
Timothy, hay	0.5	Remove	*Move to* 40 CFR 180.284(c)
Timothy, forage	0.5	Remove	*Move to* 40 CFR 180.284(c)
Wheat, grain	0.05	Remove	*Move to* 40 CFR 180.284(c)
Wheat, hay	0.05	Remove	*Move to* 40 CFR 180.284(c)
Wheat, forage	0.05	Remove	*Move to* 40 CFR 180.284(c)
Wheat, straw	0.05	Remove	*Move to* 40 CFR 180.284(c)
40 CFR 180.284(c)			
Alfalfa, forage		**0.2**	
Alfalfa, hay		**0.2**	
Artichoke, globe	0.01	**0.01**	
Barley, grain		**0.05**	
Barley, hay		**0.2**	
Barley, straw		**0.2**	
Bean, dry, seed		**0.05**	
Beet, sugar, leaves	0.02	**0.2**	
Beet, sugar, roots	0.04	**0.05**	
Potato		**0.05**	
Timothy, hay		**0.5**	
Timothy, forage		**0.5**	
Wheat, grain		**0.05**	
Wheat, hay		**0.05**	
Wheat, forage		**0.05**	
Wheat, straw		0.05	

4.0 Hazard Characterization Summary

The zinc phosphide toxicity database contains a limited number of guideline studies (Appendix B) that were used to evaluate zinc phosphide hazard to mammals. The non-rodent developmental, two-generation reproduction, metabolism, and chronic and carcinogenicity studies were waived in the Reregistration Eligibility Decision (RED) based on the use patterns, residue data, and personal protective equipment (PPE) mitigation. The agency reaffirmed this decision as part of a document that covered all rodenticide data requirements, and recommended waiving the non-rodent subchronic and immunotoxicity studies, and utilizing inhalation data from the phosphine toxicity database in lieu of recommending a subchronic inhalation study. However, at that time, the agency also recommended to retain the subchronic dermal study requirement for registration review due to the large uncertainty surrounding the dermal

assessment (TXR 0050666 U. Habiba 06/08/2016). The HASPOC decision and the dermal data requirement is discussed in more detail in Section 6.

As part of registration review for zinc phosphide, a broad survey of the literature was conducted to identify studies that report toxicity following exposure to zinc phosphide and/or phosphine via exposure routes relevant to human health pesticide risk assessment not accounted for in the agency's zinc phosphide toxicology database. No studies were identified in either the zinc phosphide or phosphine/metal phosphide literature searches that contained potentially relevant information (either quantitative or qualitative) for the zinc phosphide human health registration review risk assessment. Refer to Appendix B.3 for more detailed information on the search strategy and results of the literature review.

Zinc phosphide is a potent oral pesticide that is meant to kill target mammalian species. Accordingly, it is highly toxic via the oral route of exposure both acutely and following repeat dosing. Ingestion of zinc phosphide caused severe acute toxicity (Category I; LD_{50} = 21 mg/kg) and lethality at low repeat doses (1-5 mg/kg/day) in rats exposed for 1-3 months. There was an apparent progression of toxicity in the rat with the lethal dose level decreasing with increasing exposure duration, at least within the first three months of exposure. In surviving animals and at sublethal doses treatment-related effects were observed in the kidneys (hydronephrosis and pyelonephritis), liver (increased liver weight), and heart (increased heart weight), which is consistent with the phosphine toxicity profile. No adverse neurotoxic symptoms were observed following acute exposure up to 10 mg/kg; however, tremors were noted in male rats after $\geq$8 weeks of oral exposure to 2 mg/kg/day and 13 weeks of oral exposure to 0.5 mg/kg/day, and the severity of the tremors increased with dose.

Zinc phosphide is less acutely toxic when the route of exposure is through the skin (Category III; LD_{50} > 2000 mg/kg). Clinical signs (listlessness and anorexia) and body weight loss were noted at acute dermal doses $\geq$1000 mg/kg, gross lesions in liver and kidneys at doses $\geq$2000 mg/kg, and mortality at 5000 mg/kg. It is not an acute skin irritant. No subchronic dermal or dermal penetration studies are available to confirm if systemic toxicity and skin irritation occur after repeated exposures. An end-use zinc phosphide product (2% a.i.) was not identified as a skin sensitizer, but there are no studies available to characterize the skin sensitizing properties of formulations with a higher percentage of a.i. or the technical product.

Inhalation toxicity from zinc phosphide could originate from inhalation of particulate zinc phosphide and/or direct contact with evolved phosphine gas. The effects of inhaling phosphine gas are covered in the aluminum/magnesium phosphide RED (Aluminum/Magnesium Phosphide RED, EPA 738-R-98-017, December 1998). Consistent with the zinc phosphide database, mortality is a common endpoint in repeat inhalation studies with phosphine, and is observed at air concentrations as low as 7.5 ppm. Phosphine is also classified as Toxicity Category I for acute inhalation toxicity. Other effects resulting from inhalation of phosphine include portal of entry respiratory toxicity as well as systemic neurotoxicity and kidney effects. The open literature also suggests the cardiovascular system is a primary target of phosphine (Scuito *et al.* 2016[2]).

[2] Sciuto AM, Wong BJ, Martens ME, et al. (2016). Phosphine toxicity: a story of disrupted mitochondrial metabolism. Ann N Y Acad Sci 1374:41–51.

The effects of inhaling particulate zinc phosphide, however, are not well defined in the toxicity database. Phosphine gas will be liberated from inhaled particulates as they encounter moisture in the respiratory system, which could mimic direct phosphine exposure; however, it may not be a major contributor to toxicity under basal conditions given that the pH of the respiratory tract is slightly acidic to neutral (pH 5.5-7.9; Fischer and Widdicombe 2006[3]). Alternatively, particulates could be absorbed in the respiratory tract or cleared into the gastrointestinal system where they would be hydrolyzed and release phosphine gas. Mild and moderate acute toxicity was noted following inhalation exposure to tracking powder (10% a.i.) and bait (2% a.i.) end-use products, respectively; however, no acute or sub-chronic inhalation studies are available for the technical product to assess route specific exposure to particulates. Acute inhalation was designated Category I for the technical product in lieu of the registrant submitting a study. Additionally, the technical product caused mild and transient mucous membrane irritation following acute ocular exposure.

From the limited available data, there was no evidence that developing fetuses were more susceptible to zinc phosphide exposure compared to adults. No developmental effects were observed in fetuses up to dose levels (4 mg/kg/day) that resulted in maternal mortality. Likewise, no developmental effects were noted in fetuses from pregnant mice exposed up to 4 mg/kg/day during gestation. Furthermore, there was no evidence of prenatal sensitivity in the phosphine toxicity database.

There were no *in vivo* studies available to evaluate the carcinogenic potential of zinc phosphide from chronic exposure; however, no evidence of carcinogenicity was observed in the chronic inhalation phosphine study in rats. Zinc phosphide was negative for mutagenic activity in the bacterial reverse mutation assay and, though it did induce mutagenicity in mouse lymphocytes *in vitro*, there is no evidence of *in vivo* genotoxicity in the rat bone marrow micronucleus assay. Consequently, there is low concern for mutagenicity.

Similar to other rodenticides, occupational and residential risks will only be discussed qualitatively in the risk assessment; therefore, incidental oral, dermal, and inhalation points of departure (POD) are not required. Moreover, dietary PODs were not selected because dietary exposure is not anticipated to result from use of currently registered zinc phosphide products.

A summary of the studies in the toxicity database and the results of the open literature search are presented in Appendix B.

5.0 Exposure Considerations

Dietary

In the July 1998 RED (Zinc Phosphide RED, EPA 738-R-98-006, July 1998), the agency concluded that acute or chronic dietary exposure associated with the use of zinc phosphide is unlikely. In subsequent years, residue data from field trials conducted to support the last registration submission [alfalfa, barley, bean (dry), beet (sugar), potato, timothy and wheat] upheld the previous conclusion. Phosphine residues were below the LOQs (<0.05 or <0.1 ppm)

[3] Fischer H and JH Widdicombe. 2006. Mechanisms of acid and base secretion by the airway epithelium. J Membr Biol. 211(3): 139-150.

in most of the crops; with the exception of several livestock feed stuffs. These residue data provide considerable evidence that finite residues of phosphine from the use of zinc phosphide are not present on human food items. Because any low-level residues of zinc phosphide ingested by livestock would be immediately converted to phosphine and metabolized to naturally occurring phosphorus compounds, residues of zinc phosphide in livestock feeds are not expected to result in residues of phosphine in livestock commodities (Morton T., D457812, 06/16/2020).

Based on zinc phosphide's conversion to phosphine gas, the characteristics of phosphine gas are also relevant. As noted in a separate phosphine review (Morton T., D457813, 06/16/2020), exposures to phosphine were not expected based on the physical/chemical properties of phosphine, its use pattern, and non-detectable residues of phosphine in food commodities. Under normal environmental conditions, phosphine (PH_3) exists as a gas. The solubility of phosphine in water at normal atmospheric pressure is approximately 340 ppm. Because of its high vapor pressure (2.93×10^4 mm Hg at 25 ˚C) and Henry's Law Constant (0.1 atm m^3/mol), phosphine is expected to mainly remain in the atmosphere. The available residue data for phosphine gas as a fumigant show that with adequate aeration or further processing after treatment, residues of phosphine dissipate to nondetectable levels on fumigated commodities, even at a maximum label rate of 2,500 ppm phosphine on fresh fruits and vegetables. In addition, a depuration study demonstrated that sorption of phosphine in treated commodities and shipping material is low and depuration is rapid. Given that no residues in or on any commodity were detected after aeration following a holding period of just 24 hours and that any phosphine gas below the limit of detection (LOD) would likely dissipate as foods are cooked or prepared, the agency concluded the registered uses of phosphine as a quarantine fumigant of imported/exported fresh fruits and vegetables should be considered nonfood uses, i.e., uses that are not likely to yield residues in or on food.

A Drinking Water Assessment (DWA) has not been conducted for any registered uses. The Environmental Fate and Effects Division (EFED) concluded that a DWA will not be performed for the registration review of zinc phosphide because exposure through drinking water is expected to be minimal, due to the insolubility, formulations (bait/tracking powders), and the expectation that little will move off the field.

Residential/Occupational/Non-Occupational
The RMD for rodenticides placed limits on the allowable rodenticide registrations in order to minimize exposure to children, non-target wildlife, and domestic animals.

Zinc phosphide end-use product formulations with limited potential for dermal and inhalation exposures include ready-to-use (RTU) bait stations applied in and around homes.

Zinc phosphide end-use products with potential dermal and inhalation exposures include "loose" formulations not in RTU bait stations including granules, tracking powders and grain meals, pellets/tablets, and impregnated bait of various types (i.e., barley, oats, wheat, artichoke, apples, carrots, meats, etc.). It is registered for use in underground burrows, as tracking powder indoors or in structural voids around buildings, in bait stations in and around homes, in golf courses and parks, in agricultural fields and orchards, and non-crop areas including rights-of-way and pasture lands.

HED anticipates the uses of these formulations could generate particulates and therefore there is potential for inhalation and/or dermal exposure as they are applied, distributed, used to fill/refill bait stations, or otherwise contacted.

HED previously recommended mitigation measures for residential uses to minimize accidental ingestion and reduce residential handler exposure, which were partially implemented in the 2008 RMD[4] outlined above. Based on the remaining current allowances, there is a potential for residential handler exposures from the application of pellets/bait to underground burrows in home lawns for control of gophers. The liberation of phosphine gas from the pellets/bait during application would be expected to be very limited due to the lack of conditions necessary for liberation mentioned above (i.e., aqueous solutions or high moisture content soil). The tracking powder, granule bait, and bait station uses in and around homes are restricted-use products, and therefore, residential handler exposure is not anticipated.

Residential post-application exposures from outdoor underground burrow applications is not expected considering zinc phosphide does not react fast enough, even when wetted, to produce lethal concentrations (to burrowing rodents) of phosphine gas inside the confined space of a burrow. Therefore, it is assumed to not produce sufficient concentrations of phosphine gas in the unconfined terrestrial areas in which it is applied (Mroz R. and Wente S., D431577, 6/22/2016). In indoor use environments for applications of tracking powder, the conditions (i.e., aqueous solutions or high moisture content soils with non-neutral pHs) required to liberate phosphine gas from the zinc phosphide products would not be present,. Phosphine is slowly produced through hydrolysis of zinc phosphide in the ambient terrestrial environment and occurs only slowly under circumneutral pHs. (Mroz R. and Wente S., D431577, 6/22/2016). Additionally, dermal and incidental oral post-application exposures to the tracking powder and above ground bait uses in and around homes are not expected due to the mitigation measures requiring that the above ground bait uses require tamper-resistant bait stations as well as restricting applications of both bait stations and tracking powders in locations accessible to children and/or pets.

For golf course and park uses, there are directed spot non-broadcast uses (i.e., bait placed at burrow openings) as well as broadcast uses permitted. There may be potential for residential post-application dermal and inhalation exposures but will be limited for the directed spot non-broadcast uses. However, the broadcast uses of zinc phosphide in golf courses and parks may lead to dermal, inhalation, and incidental oral (children only) exposures, particularly to children which would be contrary to the agency's human health risk management goals for zinc phosphide articulated in the RMD.

HED anticipates these and other loose formulation uses could generate particulates and therefore there is potential for occupational inhalation and/or dermal exposure as they are applied (e.g. mixers/loaders, application by hand, handheld, ground/aerial equipment), distributed, used to fill/refill bait stations, or otherwise contacted. Direct exposure to phosphine gas is not anticipated for occupational handlers based on the liberation of phosphine gas from the products during

[4] Available at www.regulations.gov. Document number EPA-HQ-OPP-2006-0955-0820. The 2008 Risk Mitigation Decision required all residential consumer use products be in securable bait form, in a tamper resistant bait station, within 50 ft of a building, and ≤1 lb of bait.

application would be expected to be very limited due to the lack of conditions necessary for liberation mentioned above (i.e., aqueous solutions or high moisture content soil).

Occupational post-application dermal exposures are not anticipated because no significant contact with foliar or other surface residues are expected for workers in areas previously treated with zinc phosphide. Occupational post-application inhalation exposures due to the generation of phosphine gas are anticipated to be limited due to the timing of the zinc phosphide application in agricultural settings (i.e., dormant orchards/crops, do not apply to actively growing crops), as well as the field conditions required to liberate phosphine gas from zinc phosphide products occurring on a limited basis. Post-application, workers are not expected to be present as often during these times. Occupational workers are not expected to be present after applications in non-agricultural settings, except for workers performing golf course maintenance. As noted above phosphine is slowly produced through hydrolysis of zinc phosphide in the ambient terrestrial environment and occurs only slowly under circumneutral pHs. Additionally, zinc phosphide does not react fast enough, even when wetted, to produce lethal concentrations (to burrowing rodents) of phosphine gas inside the confined space of a burrow. Therefore, it is assumed to not produce sufficient concentrations of phosphine gas in the unconfined terrestrial areas in which it is applied (Mroz R. and Wente S., D431577, 6/22/2016). Some zinc phosphide labels require applications on warm, clear days, not to be applied to bare soil, and not applied to snow covered ground, which would further limit the conditions for phosphine gas release.

Non-occupational/bystander exposure resulting from off-site transport (i.e., spray drift) is unlikely due to how zinc phosphide is formulated and used, except for the granular broadcast applications of zinc phosphide on agricultural fields, rangeland, and commercial orchards. However, the approach outlined in the revised (2012) Standard Operating Procedures for Residential Risk Assessment (SOPs) – Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift, indicates that drift is not a concern when solid materials are being applied (e.g., by aerial equipment).

Therefore, only the potential for volatilization may be evaluated for zinc phosphide during the Registration Review process. Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-0037). The agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During registration review, the agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for zinc phosphide.

The only bystander inhalation exposure pathway of concern for zinc phosphide is the direct result of the liberation of phosphine gas from the solid formulation of zinc phosphide when in contact with aqueous solutions and soils with high moisture content. While volatilization is an

exposure pathway for zinc phosphide through its release of phosphine gas, the contribution of phosphine from the use of zinc phosphide is minimal in comparison to the direct use of phosphine.[5]

6.0 Data Requirements

Based on the conclusions from a Hazard and Science Policy Council (HASPOC) meeting (U. Habiba, TXR 0050666, 06/08/2016), the agency recommended that a subchronic dermal toxicity study be required for zinc phosphide. The agency further recommended the registrant consider conducting a dermal penetration study to refine the dermal absorption factor as an alternative to conducting the dermal toxicity study. The agency recommended waiving the remaining outstanding required studies as outlined in Section 4 above.

In response to the data-call-in, a technical registrant, HACCO, Inc., submitted a request to waive the subchronic dermal study requirement. The HACCO request indicated that the data currently available in the zinc phosphide toxicity database were sufficient for evaluating dermal risk. Rather than conduct a dermal toxicity or penetration study, the registrant proposed using the acute oral and acute dermal toxicity studies to refine the subchronic dermal absorption factor. HED has reviewed the submission and denied the waiver request (Wray A., TXR 0057931, 09/04/2019). Although HED does consider endpoints from dermal and oral studies as an option to estimate dermal penetration when dermal absorption data are not available, in this case, mortality was used as the endpoint to compare across studies and HED does not consider effects above the maximum tolerated dose to be appropriate for this extrapolation method.

Although the dermal toxicity data remain outstanding, the zinc phosphide toxicity profile clearly demonstrates that acute and repeat-dose exposure to zinc phosphide results in severe toxicity at low dose levels. Given the hazard profile and known toxicity of the zinc phosphide, submission of additional toxicity data will not significantly further HED's understanding of the hazard from zinc phosphide, nor will additional data modify the conclusion that human exposure to zinc phosphide should be limited to the extent possible in order to reduce potential risk. Existing data and understanding of the hazard of zinc phosphide supports the human health risk management goals. Therefore, HED recommends waiving the required subchronic dermal toxicity study at this time.

7.0 Cumulative Exposure/Risk Characterization

In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing

[5] B. Van Deusen, 09/21/2020, D453164. Phosphide (Al and Mg) and Phosphine. Human Health Non-Occupational Bystander Assessment to Support Preliminary Interim Decision.

common mechanism groups (CMGs)[6] and conducting cumulative risk assessments (CRA)[7]. The agency has utilized this framework for the fumigant phosphine, the fumigant metal phosphides (i.e., aluminum phosphide and magnesium phosphide) as well as the rodenticide zinc phosphide, which all share phosphine as the primary toxic degradate and toxic moiety. Since the metal phosphides are considered different forms of phosphine, it was determined that phosphine and the metal phosphides do not form a candidate CMG and no further cumulative evaluation is necessary (Wray A., D458104, 06/18/2020). Furthermore, although phosphine is a common toxic degradate for these chemicals, a quantitative aggregate phosphine assessment is not necessary because dietary exposures are not anticipated and potential residential exposure was evaluated qualitatively (Wray A., D458104, 06/18/2020).

8.0 Considerations of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (https://www.archives.gov/files/federal-register/executive-orders/pdf/12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Spray drift can also potentially result in post-application exposure and it was considered in this analysis. Further considerations are also currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to other types of possible bystander exposures and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

9.0 Incident and Epidemiological Data Review

HED completed a Tier I updated analysis of exposure incidents for the anticoagulant and non-anticoagulant rodenticides including zinc phosphide (Recore S. and Evans E., D456699, 03/04/2020). The purpose of the review and database search is to identify potential patterns in the frequency and severity of the health effects attributed to commensal rodenticide exposure. For this evaluation, HED evaluated its Incident Data System (IDS) and aggregate data reported

[6] *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)

[7] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

in the American Association of Poison Control Centers (AAPCC) Annual Report for rodenticide incident trends over time, as a result of the 2008 RMD. Additionally, HED evaluated NIOSH Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides, California Pesticide Illness Surveillance Program (PISP), and IDS for occupational incidents. Rodenticides were previously reviewed in 2015 (Recore S. and Evans E., D426573, 11/24/2015). At that time, the 2008 RMD had only recently been fully implemented so insufficient information was available to determine if the RMD impacted the frequency or severity of incidents for the rodenticides.

The IDS contained a total of 24 incidents reported between January 2015 and July 2019 that were attributed to a product containing zinc phosphide. Nine incidents were reported in the Main-IDS, eight of which involved the single a.i. zinc phosphide (only). These eight incidents were either of moderate (seven incidents) or major severity (one incident). A total of 15 incidents were reported in the aggregate-IDS, and were all of minor severity.

Trends over time were evaluated in the IDS and AAPCC for the non-anticoagulants as a group. The number of non-anticoagulant incidents reported to IDS (2009 to 2018) increased 81%, and the number of incidents reported to AAPCC (2004 to 2017) increased by 76%. HED does not have access to more detailed data to examine the reason for this trend, but the observed increase may be the result of non-anticoagulants having replaced the second-generation anticoagulants for residential consumer use.

Although the number of incidents involving non-anticoagulant rodenticides increased over time, the total frequency of rodenticide incidents reported to both IDS and AAPCC appears to be decreasing over time. In IDS, the total number of rodenticide incidents slightly decreased from 198 incidents in 2009 to 146 incidents reported in 2018. Likewise, the total number of rodenticide incidents reported to AAPCC has been declining steadily since 2004 with 19,432 rodenticide incidents reported in 2004 and 8,494 incidents reported in 2017. AAPCC data were also reviewed for reduction in reported rodenticide incidents in children under the age of six years old. A comparison of child rodenticide exposures from 2011 to 2017 identified a 46% decline in child rodenticide incident reports. Overall, the IDS and AAPCC data for all rodenticides suggest that the 2008 RMD may have contributed to an overall decrease in exposure incidents involving rodenticide products.

Occupational incidents were separately evaluated for the rodenticides. Twenty-one occupational exposure incidents were reported to the NIOSH SENSOR-Pesticides database from 2011-2015, nine occupational exposure incidents reported to California PISP from 2012-2016, and two occupational incidents were reported in the IDS (2015-2019) for all rodenticide products. Two major severity cases, one in the Main-IDS and one in SENSOR-Pesticides, involved zinc phosphide. In both the SENSOR-Pesticides and PISP datasets, most occupational case reports involved symptomatic exposures to a zinc phosphide product (62% and 67%, respectively); primarily during the manual application of the product by the case. Several occupational incidents reported to SENSOR-Pesticides describe veterinary workers exposed secondarily when treating dogs that ingested zinc phosphide products. Nausea and vomiting as well as neurological, respiratory, cardiovascular, and ocular symptoms were reported in zinc phosphide incidents. Overall, there was a low frequency of occupational incidents reported in SENSOR-

Pesticides, California PISP, and Main IDS; however, zinc phosphide was involved in many of the incidents reported.

10.0 Conclusions

Zinc phosphide (Zn_3P_2) is a non-anticoagulant rodenticide used to control numerous pest species including mice, ground squirrels, prairie dogs, voles, moles, rats, muskrats, nutria, and gophers. Current registrations permit use on indoor and outdoor residential and agricultural areas including areas in and around homes, on lawns, in and around outside buildings/barns, rights-of-way/fencerows/hedgerows, ornamentals, indoor and outdoor commercial or institutional premises and equipment (including food handling establishments), golf courses, reforestation areas, alfalfa, artichokes, barley, berries (dormant), oats, sugar maple, wheat, cucurbits, reduced tillage and no-till corn, macadamia nut orchards, orchards/groves (post-harvest and dormant), timothy (hay). These registrations encompass both food and non-food uses.

Zinc phosphide is highly toxic following oral exposure and presumed to be highly toxic via inhalation. Acute dermal exposure to zinc phosphide is less toxic compared to the other routes of exposure; however, little information is available to evaluate dermal absorption and toxicity resulting from repeated dermal exposure. There is no evidence of prenatal sensitivity in the toxicity database. There is low concern for mutagenicity.

The agency does not anticipate dietary exposure to phosphine from use of zinc phosphide based on the residue data and the physical/chemical properties of zinc phosphide and phosphine. Zinc phosphide end-use products with limited potential exposures include ready-to-use (RTU) bait stations, or other packaging which prevents exposure. All zinc phosphide end-use products are RUPs except for the residential pellet/bait for underground gopher uses. Zinc phosphide products are also formulated into numerous baits, some of which are considered “loose” formulations. These formulations include granules, tracking powders and grain meals, as well as impregnated bait of various types (i.e., barley, oats, wheat, artichoke, apples, carrots, meats, etc.) and pellets/tablets.

There is limited potential for residential handler dermal and inhalation exposures to adults from the registered underground gopher treatments. Residential post-application exposures from outdoor underground applications is not expected. In indoor use environments for applications of tracking powder, the conditions (i.e., aqueous solutions or high moisture content soils with non-neutral pHs) required to liberate phosphine gas from the zinc phosphide products would not be present,. Additionally, dermal and incidental oral post-application exposures to the tracking powder and above ground bait uses in and around homes are not expected due to the mitigation measures requiring tamper-resistant bait stations as well as restricting applications in locations accessible to children and/or pets. However, residential post-application dermal, inhalation, and incidental oral (children only) exposures are expected from the broadcast applications of zinc phosphide to golf courses and parks, which is contrary to the agency’s risk management goals for zinc phosphide.

Occupational handler dermal and inhalation exposures are anticipated from any contact with loose formulations. Occupational post-application dermal exposures are not anticipated because

no significant contact with foliar or other surface residues are expected for workers in areas previously treated with zinc phosphide. Occupational post-application inhalation exposures due to the generation of phosphine gas are anticipated to be limited due to the timing of the zinc phosphide application in agricultural settings (i.e., dormant orchards/crops, do not apply to actively growing crops), as well as the field conditions required to liberate phosphine gas from zinc phosphide products occurring on a limited basis. Post-application, workers are not expected to be present as often during these times. Occupational workers are not expected to be present after applications in non-agricultural settings, except for workers in golf courses. Some zinc phosphide labels require applications on warm, clear days, not to be applied to bare soil, and not applied to snow covered ground which would further limit the conditions for phosphine gas release.

Based on the available hazard and toxicity profile for the zinc phosphide, HED concludes that any potential exposure may result in adverse effects and potential risks of concern. Based on the toxicity profile of zinc phosphide, HED's understanding of the hazard of zinc phosphide, and the risk management approach for the registration review of rodenticides to minimize non-target (e.g., human) exposures, HED recommends to waive the existing human health data requirements, and to not require any additional toxicological data for zinc phosphide at this time. HED concludes that additional data will not inform or impact the overall risk management strategy to limit potential non-target exposures.

The incident data suggest that the 2008 RMD may have contributed to an overall decrease in residential exposure incidents involving rodenticide products; however, incidents involving non-anticoagulants have increased over time. Moreover, the frequency of reported occupational incidents for rodenticide products was low, but many of the incidents involved zinc phosphide.

Based upon the available hazard and toxicity profile, HED concludes that zinc phosphide is extremely toxic by oral exposure and likely to be highly toxic via inhalation and, to a lesser extent, dermal exposure. Labeled uses of these products should be modified, as needed, to ensure that occupational dermal and inhalation exposures are limited to the extent possible. HED notes that all zinc phosphide occupational product labels indicate the need for gloves among the PPE for occupational handlers and that additional PPE including but not limited to particulate filtering facepieces, respirators, protective eyewear, and coveralls may also be required. Products intended for homeowner use do not require PPE on the registered labels. Likewise, any non-occupational exposures should also be limited to the extent possible. The agency's human health risk management goals for registration review of rodenticides reflect those articulated in the RMD and include minimizing non-target (e.g., human) exposures for currently registered products of anticoagulant and non-anticoagulant rodenticides to the extent possible through mitigation. Therefore, a quantitative risk assessment was not conducted and is not necessary.

11.0 References

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Appendix A. Use Pattern Summary Table

Table A.1 Summary of Directions for Registered Commercial Uses of Zinc Phosphide.

Representative Label, Application Timing, Type, and Equipment	Max Single Application Rate	Max Seasonal or Yearly Application Rate	PPE	EPA Registration Number (EPA Reg. No.) and Use Directions and Limitations
Indoor Uses				
Tracking Powder (12455-16 and 61282-101, House Mice) RUP Spoon, hand-powered duster,	(12455-16 and 61282-101) 10% ai. Evenly Sprinkle 3 to 6 grams in approximately 3 by 24 inch patches.	NS	All handlers, including loaders and applicators must wear: Coveralls, long sleeved-shirt and long pants; chemical-resistant shoes plus socks; waterproof gloves; when mixing/loading or cleaning equipment, wear a chemical-resistant apron.	For use inside homes, industrial or ag buildings, or outside of buildings into structural voids. Apply only in locations inaccessible to children, pets, or domestic animals. When using this product in homes, only treat in concealed, inaccessible places such as spaces between floors and walls. Using a hand-powered duster, dust into wall voids and spaces between floors. Maintain powder in treated areas for 7 days or until fresh signs of mouse activity cease to appear.
Rodent Bait AG (12455-17, Norway Rats, Roof Rats, House Mice) RUP	(56228-6) 2.1% ai. For rats - 2 teaspoons of bait per placement. For outdoor use, place bait in active rodent burrows or tamper-resistant bait stations. For mice – apply 1 teaspoon of bait per placement at 8 to 12 foot intervals. For outdoor use, place bait in tamper-resistant bait stations.	NS	Baseline attire* plus gloves, persons loading pellets or baits into aircraft or mechanical ground equipment or loading/ applying with hand-pushed or handheld equipment must wear NIOSH-approved particulate filtering facepiece respirator and protective eyewear.	Apply bait in locations out of reach of children, pets, domestic animals, and non-target wildlife, or in tamper-resistant bait stations. Bait stations must be secured or immobilized and be resistant to destruction by dogs, children, or others. Bait stations are mandatory for outdoor, above-ground use. Do not broadcast bait. May be used in and within 100 feet of man-made structures (homes or other residences, food processing facilities, industrial/commercial or ag buildings, transport vehicles, docks, or trash receptacles). RTI – Do not treat the same area at less than 30 day intervals. EPA Reg. Nos. (12455-131 No PPE but states intended for commercial use, also 61282-56 similar directions)
Fruit and Nut Tree Orchards (Dormant)				

Table A.1 Summary of Directions for Registered Commercial Uses of Zinc Phosphide.				
Representative Label, Application Timing, Type, and Equipment	**Max Single Application Rate**	**Max Seasonal or Yearly Application Rate**	**PPE**	**EPA Registration Number (EPA Reg. No.) and Use Directions and Limitations**
Rodent Bait AG (12455-17) Zinc Phosphide in Oat Pellets (71096-14)	Hand Baiting: Apply 1-2 teaspoon amount (4-8 grams) per placement, 2-3 lb/A (0.04-0.06 lb ai/A) (3-5 lb/A or 0.06 – 0.1 lb ai/A for EPA Reg. No. 71096-14) Ground Broadcast: cyclone seeder or hand at rate of 6-10 lb/A (0.12-0.2 lb ai/A). Aerial: 6-10 lb/A (0.12-0.2 lb ai/A)	Macadamia nuts: 4 treatments per year 20 lb/A (0.42 lb ai/A, EPA Reg. No. 56228-6)	Baseline attire plus gloves, persons loading pellets or baits into aircraft or mechanical ground equipment or loading/ applying with hand-pushed or handheld equipment must wear NIOSH-approved particulate filtering facepiece respirator and protective eyewear.	Apply only after fall harvest, before spring growth, and when no rain or snow is expected for 3 consecutive days. RTI for post-harvest or dormant season applications is 30 days. Do not graze animals in treated areas. Avoid applying to bare ground. Macadamia nut orchards and adjacent noncrop areas – active orchards may be treated up to 30 days prior to a harvesting round. EPA Reg. Nos. (4-152, use in apple, pear, quince, apricot, cherry, nectarine, peach, plum, and nut tree orchards and citrus groves; 814-9
Nonbearing Nursery Stock, Christmas Tree Farm, Poplar/Cottonwood, Ornamentals, Nonbearing fruit tree plantations				
Zinc Phosphide Concentrate (56228-6, 2.1%)	Ground Broadcast by cyclone seeder or by hand at rate of 6-10 lb/A (0.13-0.21 lb ai/A) Hand baiting: 4 grams per location at rate of 2-3 lbs/A (0.04-0.06 lb ai/A) Aerial to christmas tree farms, hardwood seedling plantations, windbreaks – 6-10 lb/A (0.13-0.21 lbs ai/A)	NS	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	Do not aerially apply bait to vineyards or to any actively growing crops. Avoid applying to bare ground. Rodent Bait AG (12455-17)
Non-residential lawns, ornamentals, golf courses, airports, and parks				
Rodent Bait AG (12455-17) Zinc Phosphide Concentrate (56228-6, 2.1%)	4 grams per mound per year. 1 lb of bait will treat 1 to 8 acres depending on number of pocket gopher	NS	Baseline attire plus gloves, persons loading pellets or baits into aircraft or mechanical ground equipment or loading/	Airport (Hand baiting - teaspoon – 4 grams at mouth of burrow holes; Broadcast ground cyclone seeder or mechanical spreader mounted on vehicle, 6-10 lbs/A (0.12-0.2 lbs ai/A), 1 app per year) (EPA Reg. No. 12455-102)

Table A.1 Summary of Directions for Registered Commercial Uses of Zinc Phosphide.				
Representative Label, Application Timing, Type, and Equipment	**Max Single Application Rate**	**Max Seasonal or Yearly Application Rate**	**PPE**	**EPA Registration Number (EPA Reg. No.) and Use Directions and Limitations**
	burrow systems present. Ground Broadcast by cyclone seeder or hand at 6-10 lbs/A (0.13-0.21 lbs ai/A – EPA Reg. No. 56228-6, 2.1% ai		applying with hand-pushed or handheld equipment must wear NIOSH-approved particulate filtering facepiece respirator and protective eyewear.	
Alfalfa or Timothy				
Zinc Phosphide Concentrate (56228-6, 2.1%)	Broadcast air or ground: 10 lbs/A (0.21 lb ai/A) Hand baiting: 2-3 lbs/A (0.04-0.06 lb ai/A)	2 apps per year 20 lbs/A (0.42 lb ai/A)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	All applications must occur shortly after cutting hay or prior to next growth reaching 2 inches in length. RTI – 25 days Do not apply to actively growing timothy or timothy/alfalfa /clover mixtures. Rodent Bait AG (12455-17)
Artichokes (CA only)				
Zinc Phosphide Concentrate (56228-6, 2.1%)	Hand baiting: 40 lbs/A (0.22 lb ai/A, 0.54% ai)	1 app per year 40 lbs/A (0.22 lb ai/A)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	RTI – 1 year Do not broadcast on growing crop.
Grape Vineyards				
Rodent Bait AG (12455-17)	Broadcast between rows by cyclone seeder or by hand at rate of 6-10 lbs/A (0.12-0.2 lb ai/A)	NS	Baseline attire plus gloves, persons loading pellets or baits into aircraft or mechanical ground equipment or loading/ applying with hand-pushed or handheld equipment must wear NIOSH-approved particulate filtering facepiece respirator and protective eyewear.	Do not apply by air. EPA Reg. No. (814-9)

Table A.1 Summary of Directions for Registered Commercial Uses of Zinc Phosphide.				
Representative Label, Application Timing, Type, and Equipment	**Max Single Application Rate**	**Max Seasonal or Yearly Application Rate**	**PPE**	**EPA Registration Number (EPA Reg. No.) and Use Directions and Limitations**
Rangeland, pastures, and adjacent noncrop areas				
Zinc Phosphide Concentrate (56228-6, 2.1%)	Hand Baiting: 1 tablespoon (12 grams) of bait at 2 locations per mound at rate of 6 lbs/A (0.13 lbs ai/A). Ground Broadcast bait via cyclone seeder, hand, or ground driven dispensing devices at 6 lbs/A (0.13 lb ai/A) Aerial rangeland grass – 3-6 lbs/A (0.06-0.13 lb ai/A)	1 application per year.	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	Do not aerially apply bait to pasture grass. EPA Reg. No. 13808-6, 56228-14, Rodent Bait AG (12455-17)
Noncrop Rights-of-Way				
Rodent Bait AG (12455-17)	Broadcast bait using hand or ground driven dispensing devices at 6 lbs/A (0.12 lb ai/A) Broadcast bait using cyclone seeder or hand at 6-10 lbs/A (0.13-0.21 lb ai/A – EPA Reg. No. 56228-6, 2.1% ai) Aerial 10 lbs/A (0.2 lbs ai/A – EPA Reg. No. 71096-14)	Treat only once during treatment period.	Baseline attire plus gloves, persons loading pellets or baits into aircraft or mechanical ground equipment or loading/ applying with hand-pushed or handheld equipment must wear NIOSH-approved particulate filtering facepiece respirator and protective eyewear.	EPA Reg. No. 56228-14,
Dormant Strawberries, Bushberries, and Caneberries				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using cyclone seeder or hand at 6-10 lbs/A (0.13-0.21 lb ai/A)	2 apps 20 lbs/A (0.4 lbs ai/A)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	Apply in dormant season. PHI – 70 days. Do not apply by air. RTI – 21 days. EPA Reg. No. 12455-17

Table A.1 Summary of Directions for Registered Commercial Uses of Zinc Phosphide.				
Representative Label, Application Timing, Type, and Equipment	**Max Single Application Rate**	**Max Seasonal or Yearly Application Rate**	**PPE**	**EPA Registration Number (EPA Reg. No.) and Use Directions and Limitations**
Cucurbits, reduced tillage and no-till corn				
Rodent Bait AG (12455-17) Pre-planting or at-planting.	In-furrow application equipment only at 4-6 lbs/A (0.08-0.12 lb ai/A)	Treat only once during treatment period.	Baseline attire plus gloves, persons loading pellets or baits into aircraft or mechanical ground equipment or loading/ applying with hand-pushed or handheld equipment must wear NIOSH-approved particulate filtering facepiece respirator and protective eyewear.	In-furrow application only. Cucurbits (chayote, chinese waxgourd, citron melon, cucumber, gherkin, edible gourd, muskmelon, pumpkin, squash, and watermelon). Do not broadcast bait.
Barley				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using air or ground-driven dispensing devices at 6 lbs/A (0.13 lb ai/A)	2 apps for voles 12 lbs/A (0.25 lb ai/A/year)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	PHI – 50 days RTI – 25 days Rodent Bait AG (12455-17)
Beans (Dry)				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using hand or ground driven dispensing devices at 6 lbs/A (0.13 lb ai/A)	No more than 1 app per growing season.	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	Do not apply by air. PHI – 30 days Rodent Bait AG (12455-17)
Sugar Beets				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using air or ground-driven dispensing devices at 10 lbs/A (0.21 lb ai/A)	2 apps, 20 lbs/A (0.42 lb ai/A/year)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	PHI – 30 days Apply at planting Rodent Bait AG (12455-17)

Table A.1 Summary of Directions for Registered Commercial Uses of Zinc Phosphide.				
Representative Label, Application Timing, Type, and Equipment	**Max Single Application Rate**	**Max Seasonal or Yearly Application Rate**	**PPE**	**EPA Registration Number (EPA Reg. No.) and Use Directions and Limitations**
Potatoes				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using air or ground-driven dispensing devices at 10 lbs/A (0.21 lb ai/A)	2 apps, 10 lbs/A (0.21 lb ai/A/year)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	PHI – 30 days Rodent Bait AG (12455-17)
Wheat				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using air or ground-driven dispensing devices at 6 lbs/A (0.13 lb ai/A)	2 apps for voles 12 lbs/A (0.25 lb ai/A/year)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	PHI – 50 days RTI – 25 days Rodent Bait AG (12455-17)
Sugarcane				
Zinc Phosphide Concentrate (56228-6, 2.1% ai)	Broadcast bait using air, ground-driven dispensing devices, or by hand at 5 lbs/A (0.11 lb ai/A)	For 12 month crop - 2 apps, 10 lbs/A (0.2 lb ai/A/year)	Baseline attire, gloves, NIOSH-approved particulate filtering facepiece respirator, and protective eyewear.	36-month cycle crop – PHI – 30 days, 4 apps per crop or 20 lbs/A (0.4 lb ai/A/crop) 24-month cycle crop – PHI – 90 days, 4 apps per crop or 20 lbs/A (0.4 lb ai/A/crop) 12-month cycle crop – PHI – 90 days RTI – all cycles – 30 days Rodent Bait AG (12455-17)
Residential Lawns – Residential Handler Uses				
Gopha-Rid (Pelleted bait, 2% ai, 12455-30) Intended for Residential Use	1 teaspoon of bait per burrow or tunnel	NS	No PPE listed for applications. Gloves listed for collection and disposal of dead, exposed animals.	Used to control pocket gophers in manual, below-ground applications in lawns. Bait must be applied directly into the burrow or tunnel systems. Do not apply to gardens. EPA Reg. Nos. 12455-18, 4-285, 149-16, 90780-4, 36029-12, 61282-50, 61282-51, 61282-56

*Baseline attire defined as long-sleeved shirt, long pants, shoes plus socks.
NS = not stated. PHI = pre-harvest interval. RTI = re-treatment interval.

Appendix B. Toxicology Profile and Executive Summaries

B.1 Toxicology Data Requirements

The toxicity data requirements (40 CFR 158.500) for zinc phosphide food and non-food uses are in Table B.1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Table B.1 Toxicology Data Requirements

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	Oral Subchronic (rodent)	yes	yes
870.3150	Oral Subchronic (nonrodent)	yes	yes[1]
870.3200	28-Day Dermal	no	-
870.3250	90-Day Dermal	yes	yes[2]
870.3465	90-Day Inhalation	yes	yes[1]
870.3700	Developmental Toxicity (rodent)	yes	yes
870.3700	Developmental Toxicity (nonrodent)	yes	yes[1]
870.3800	Reproduction	yes	yes[1]
870.4100	Chronic Toxicity (rodent)	yes	yes[1]
870.4100	Chronic Toxicity (nonrodent)	no	-
870.4200	Oncogenicity (rat)	yes	yes[1]
870.4200	Oncogenicity (mouse)	yes	yes[1]
870.4300	Chronic/Oncogenicity (rat)	yes	yes[1]
870.5100	Mutagenicity—Bacterial reverse mutation assay	yes	yes
870.5300	Mutagenicity—gene mutation test-mammalian	yes	yes
870.53xx	Mutagenicity—chromosome aberration test	yes	yes
870.53xx	Mutagenicity—other	yes	yes
870.6100	Acute Delayed Neurotoxicity (hen)	no	no
870.6100	90-Day Neurotoxicity (hen)	no	no
870.6200	Acute Neurotoxicity Screening Battery (rat)	yes	yes
870.6200	90-Day Neurotoxicity Screening Battery (rat)	yes	yes
870.6300	Developmental Neurotoxicity	no	-
870.7485	General Metabolism	CR	yes[1]
870.7600	Dermal Penetration	CR	yes[2]
870.7800	Immunotoxicity	yes	yes[1]

[1] Based on agency recommendation for a waiver (TXR 0050666, U. Habiba, 06/08/2016)

[2] Dermal toxicity and/or dermal penetration data were previously required based on the agency decision (TXR 0050666, U. Habiba, 06/08/2016). However, the agency re-evaluated the available hazard and toxicity profile for zinc phosphide and concluded additional dermal data are not anticipated to further the agency's understanding of the hazard posed by zinc phosphide nor alter the agency conclusion that exposure should be limited to the extent possible to minimize risk. Consequently, dermal toxicity and/or dermal penetration data are not necessary nor required at this time.

B.2 Toxicity Profiles

Table B.2.1 Acute Toxicity Profile – Zinc Phosphide				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute Oral (rat) TXR 5010729 – Minimum	00085366 (1981) 94% a.i.	LD_{50} = 21.21 (13 – 35) mg/kg (M & F)	I
870.1200	Acute Dermal (rabbit) TXR 0003939 - Minimum	00006030 00022578 (1977) 94% a.i.	2000 mg < LD_{50} < 5000 mg/kg (M & F)	III
870.1300	Acute Inhalation (rat)	N/A	N/A	I[1]
870.2400	Primary Eye Irritation (rabbit) TXR 0003939 - Minimum	00029247 00020988 (1977) 94% a.i.	Slight conjunctival redness, chemosis and discharge decreasing in severity in 72 hours	III
870.2500	Primary Skin Irritation (rabbit) TXR 0003939 - Guideline	00006029 00020989 (1977) 94% a.i.	Non-irritant	IV
870.2600	Dermal Sensitization (guinea pig)	None available	N/A	N/A

[1] In lieu of performing study, zinc phosphide was designated as Toxicity Category I

The SCN endpoints were updated for the zinc phosphide registration review. All other endpoints were retained from the previous assessment (D256974, B. Wooge 09/30/2003).

Table B.2.2 Subchronic, Chronic and Other Toxicity Profile – Zinc Phosphide		
Guideline No./ Study Type/Animal Species and Strain	**MRID No. or Study Authors (year)/ Classification /Doses**	**Results**
870.3100 22-Day oral toxicity (rat) Range-finding study for 90-day study below Crl: CD BR VAF/Plus rats	43436601 (1994) **Supplementary** TXR 0011464 97.3% a.i. 0, 0.1, 0.5, 2, 3.5*, and 5 mg/kg/day in propylene glycol via gavage for 22 days *Started on week 3 after adverse effects were observed in the 5 mg/kg/day dose group	NOAEL = 2 mg/kg/day LOAEL = 5 mg/kg/day based on mortality (3/3 males and 1/3 females died at 5 mg/kg/day between days 7 and 11), increases in absolute liver weight and liver/brain weight ratio in surviving females *similar adverse effects observed in the 3.5 mg/kg/day dose group, without mortality

Table B.2.2 Subchronic, Chronic and Other Toxicity Profile – Zinc Phosphide		
Guideline No./ Study Type/Animal Species and Strain	**MRID No. or Study Authors (year)/ Classification /Doses**	**Results**
870.3100 90-Day oral toxicity (rat) Crl: CD BR VAF/Plus rats	43436601 (1994) **Acceptable/Guideline** TXR 0011464 97.3% a.i. 0, 0.1, 1, and 3 mg/kg/day in propylene glycol via gavage for 91 days	NOAEL = 0.1 mg/kg/day LOAEL = 1 mg/kg/day based on increased mortality and kidney hydronephrosis in males
870.3700a Prenatal developmental in rats Crl: CD BR VAF/Plus rats	43083501 (1994) **Acceptable/Guideline** TXR 0011120 97.3% a.i. 0, 1, 2, and 4 mg/kg/day in propylene glycol via gavage on GD 6 thru 15, inclusive	Maternal NOAEL = 2 mg/kg/day Maternal LOAEL = 4 mg/kg/day based on mortality (on days 10-16) Developmental NOAEL = 4 mg/kg/day Developmental LOAEL was not established
870.3700a Prenatal developmental in mice Swiss Webster mice	00112919 (1982) **Supplementary** TXR 0003041 80% a.i. 0.004, 0.04, 0.4, and 4 mg/kg/day in propylene glycol via gavage on gestation days 5-17, inclusive	Maternal NOAEL = 4 mg/kg/day Maternal LOAEL was not established Developmental NOAEL = 4 mg/kg/day Developmental LOAEL was not established
870.5100 Gene Mutation (Ames Assay) *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538	42987301 (1994) **Acceptable** TXR 0010808 97.1% a.i. suspended in DMSO 0, 333, 667, 1000, 1667, and 5000 µg/plate	**Negative** for gene mutation, with and without S9 mammalian metabolic activation

Table B.2.2 Subchronic, Chronic and Other Toxicity Profile – Zinc Phosphide		
Guideline No./ Study Type/Animal Species and Strain	**MRID No. or Study Authors (year)/ Classification /Doses**	**Results**
870.5300 Mouse Lymphoma Assay L5178Y cells	42987302 (1994) **Acceptable** TXR 0010808 97.2% a.i. 0, 8, 9, 10, 20, 30, 40, 50, 60, 70, and 80 µg/mL	**Positive** for gene mutation. Increased mutants at the thymidine kinase locus (TK) were induced from 10 – 80 µg/mL with and without S9 present
870.5385 Micronucleus Cytogenetic Assay ICR mice	42987303 (1994) **Acceptable** TXR 0010808 97.1% a.i. suspended in corn oil 0, 38, 75, and 150 mg/kg via IP injection	**Negative** for mutagenicity. No evidence of increase aberrations.
870.6200 Acute Neurotoxicity (rat) Crl: CD BR VAF/Plus rats	43284301 (1994) **Acceptable/Guideline** TXR 0011660 94.7% a.i. 0, 1, 5, and 10 mg/kg suspended in propylene glycol via gavage	NOAEL = 10 mg/kg LOAEL = not established
870.6200 Subchronic Neurotoxicity (rat) Crl: CD BR VAF/Plus rats	43903801/43903802 (1995) **Acceptable/Guideline** TXR 0058049 97.1% a.i. 0, 0.1, 0.5, and 2 mg/kg/day suspended in propylene glycol via gavage for 13 weeks.	NOAEL = 0.1 mg/kg/day LOAEL = 0.5 mg/kg/day based on tremors.

B.3. Literature Study Summary

As part of registration review for zinc phosphide, a broad survey of the literature was conducted to identify studies that report toxicity following exposure to zinc phosphide via exposure routes relevant to human health pesticide risk assessment that may not be accounted for in the agency's zinc phosphide toxicology database. The search strategy employed terms restricted to the name of the chemical plus any common synonyms, and common mammalian models to capture as broad a list of publications as possible for the chemical of interest. The search strategy returned 125 studies from the open literature.

In addition, a comprehensive general literature search was conducted for phosphine, aluminum phosphide, and magnesium phosphide as part of registration review for the fumigant uses of these chemicals. This search returned 1179 publications from the open literature. Given that zinc phosphide toxicity is attributed to phosphine gas release, publications identified in the phosphine/metal phosphide screen could also be relevant to the zinc phosphide hazard characterization.

Zinc Phosphide
Date and Time of Search: 01/30/2020; 02:30 pm

Search Details:

((*Zinc Phosphide*)) AND (rat OR mouse OR dog OR rabbit OR monkey OR mammal)

Studies Identified in PubMed*: **125**
SWIFT-Review** Tags:
90 for Animal
80 for Human (**35** were tagged as human but not as animal)
0 for NO TAG

Phosphine and Metal Phosphides
Date and Time of Search: 03/04/2019; 11:44 am

Search Details:

((*aluminium phosphide OR magnesium phosphide OR phosphine*)) AND (rat OR mouse OR dog OR rabbit OR monkey OR mammal)

Studies Identified in PubMed*: **1179**
SWIFT-Review** Tags:
585 for Animal
899 for Human (**591** were tagged as human but not as animal)
3 for NO TAG

All studies identified in the PubMed search were screened when the citation list was ≤100. Screening of larger citations lists (>100 citations) was conducted after prioritization in SWIFT-Review and focused on studies identified with the "Animal" and/or "Human" tag.

Conclusion of Literature Search: Following title/abstract and/or full text screening, no studies were identified in either the zinc phosphide or phosphine/metal phosphide literature searches as containing potentially relevant information (either quantitative or qualitative) for the zinc phosphide human health registration review risk assessment.

*PubMed is a freely available search engine that provides access to life science and biomedical references predominantly using the MEDLINE database.
**SWIFT-Review is a freely available software tool created by Sciome LLC that assists with literature prioritization. SWIFT-Review was used to prioritize citations lists that were larger than 100. Studies identified in the PubMed search were tagged and grouped based on the model of interest in the study (e.g. human, animal, *in vitro*, etc.).

Appendix C. US/International Tolerances and Maximum Residue Limits

Zinc Phosphide (088601)

Table C.1. Summary of US and International Tolerances and Maximum Residue Limits.

Residue Definition:

U.S. - 40 CFR 180.284:
Plant: Phosphine
Livestock:

Canada - None

Codex - None

Other[1] -

Commodity	*Tolerance (ppm)/Maximum Residue Limit (mg/kg)*			
	U.S.	Canada	Codex	Other
Alfalfa, forage	0.2			
Alfalfa, hay	0.2			
Artichoke, globe	0.01			
Barley, grain	0.05			
Barley, hay	0.2			
Barley, straw	0.2			
Bean, dry, seed	0.05			
Beet, sugar, leaves	0.2			
Beet, sugar, roots	0.05			
Grape	0.01			
Grass, forage	0.1			
Grass, hay	0.1			
Potato	0.05			
Sugarcane, cane	0.01			
Timothy, hay	0.5			
Timothy, forage	0.5			
Wheat, grain	0.05			
Wheat, hay	0.05			
Wheat, forage	0.05			
Wheat, straw	0.05			

Completed: T. Morton; 5/6/20 using Global MRL

Appendix D. Physical/Chemical Properties

Table D.1. Physicochemical Properties of Technical Grade Zinc Phosphide.		
Parameter	**Value**	**Reference**
Molecular Weight	258.09 g/mol	Zinc Phosphide RED, EPA 738-R-98-006, July 1998
Melting point/range	420°C	
Density (20°C)	4.51	
Water solubility	Insoluble in water	
Solvent solubility	Soluble in benzene and carbon disulfide. Insoluble in ethanol.	
Vapor pressure	Negligible in the dry state (solid)	
Dissociation constant	N/A	MRID No. 42986202
Octanol/water partition coefficient	N/A	MRID No. 42986202
UV/visible absorption spectrum	Not available	Hrdy D., D231421, 11/26/1996
Description	Technical zinc phosphide is a gray to black powder with a phosphine odor. It is stable in dry conditions, but reacts slowly with water (including atmospheric moisture) to form phosphine gas.	

Table D.2. Physicochemical Properties of Phosphine.		
Parameter	**Value**	**Reference**
Molecular Weight	33.9 g/mol	King M. *et al.*, D410399, 09/11/2013
Melting point/range	-132.8°C	
Density (20°C)	1.379 g/L	
Water solubility	31.2 mg/100 mL	
Henry's Constant	0.1 atm m^3/mol	Lowit M. *et al.*, D410398, 09/12/2013
Vapor pressure (25°C)	2.93×10^4 mm Hg	